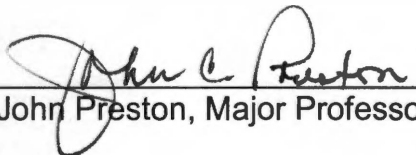
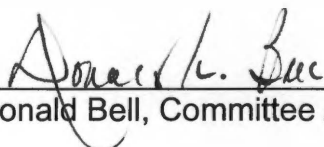


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I am submitting herewith a thesis written by Tonya Lynn DeWitt Campbell entitled "A Comparison of the Differential Effects of Atracurium and/or Lidocaine on Succinylcholine-induced Postoperative Myalgia." I have examined the final paper copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science in Nursing, with a major in Nursing.

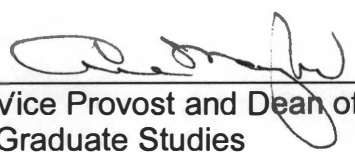

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**A Comparison of the Differential Effects of Atracurium and/or Lidocaine on
Succinylcholine-induced Postoperative Myalgia**

**A Thesis
Presented for the
Master of Science
in Nursing Degree
The University of Tennessee, Knoxville**

**Tonya Lynn DeWitt Campbell
December 2003**

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Thesis
2003
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Dedication

This thesis is dedicated to my best friend, my husband. Words cannot express the gratitude I feel, as I know you have made many monumental sacrifices for me during the writing of this paper. Thank you for your time, patience, and unrelenting understanding during the past year. I could not have succeeded without you! Thank goodness, we are finished!

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My fellow classmates also contributed by assisting with data collection. I felt that after I obtained informed consent from a patient, I had it licked. However, it goes without saying, that if it were not for those who helped me collect data, there would have not been a study. Your efforts and willingness to participate were not overlooked, "Thank you".

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application for IRB approval before the published timeline, an important aspect that kept this thesis on track.

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Abstract

It is well documented that the administration of succinylcholine (SCh), also known as suxamethonium, with general anesthesia causes muscle fasciculations, which may cause severe postoperative myalgia. However, such an association has not been well documented. Many authors have postulated that such pain is secondary to damage produced in the muscle during fasciculation. As a result, it is acceptable standard anesthetic practice to aim to prevent fasciculations when administering SCh during the administration of general anesthesia.

Today, studies utilizing subtherapeutic doses of nondepolarizing neuromuscular blockade have shown the greatest promise in reducing postoperative myalgia secondary to the use of SCh. This study has examined and compared the efficacy of pretreatment with lidocaine, atracurium, and the combination of the two in relation to the incidence and severity of postoperative myalgia. As statistical significance was not expected with such a small pilot population, this study was designed to determine the feasibility of conducting a larger study. Additionally, trends within this population were further examined to determine clinical significance.

This study was a prospective, double-blinded randomized clinical study utilizing 15 subjects who met inclusion criteria, and gave informed consent to participate in the study. Each patient was randomly assigned to one of three experimental groups that included lidocaine, atracurium, or a combination of the two medications. Each group followed the same study protocol.

Participants were followed every 24 hours for three days. Data collected was based on a postoperative myalgia survey of 14 questions to ascertain myalgia from routine postoperative discomfort. The answers were then graded on a Likert scale (postoperative myalgia evaluation scale). In this way data collection not only included those having myalgia, but also took into account the intensity of postoperative myalgia. Data analysis compared the groups, looking for a statistical significant difference to determine whether one pretreatment medication was better than another in preventing postoperative myalgia.

As expected, statistical significance was not found among the three pretreatment groups in relation to amount or intensity of postoperative myalgia. In other words, one pretreatment group did not show improved efficacy over another pretreatment group. However, several trends were identified, suggesting that each pretreatment medication may have advantages and disadvantages that may signify clinical significance, although not statistically significant.

In conclusion, this study proved to be feasible, and identified many new factors such as physical health status, cigarette smoking, medication therapy prior to surgical intervention, surgical type, and surgical position that may contribute to the phenomena of postoperative myalgia. Therefore, further research in this area is warranted.

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Chapter I

Introduction

Griffith & Johnson documented the first case of using human neuromuscular blockade during general anesthesia in 1942. Unauthenticated Curare, by Squibb, was administered to 25 patients experimentally. The investigators found that it provided excellent muscle relaxation without detrimental effects to the patient. However, their study concluded the following:

Its scope of usefulness is limited because of its somewhat fleeting action, and because it is in no sense an anesthetic agent. It is a potentially dangerous poison, and should be used only by experienced anesthetists in well-equipped operating rooms; but we have been so much impressed by the dramatic effect produced in every one of our patients that we believe this investigation should be continued (p. 420).

Today, intraoperative administration of neuromuscular blocking agents is routinely utilized to facilitate endotracheal intubation associated with general anesthesia, as well as provide skeletal muscle relaxation for optimal surgical conditions (Stoelting & Miller, 2000). Multiple new pharmacological agents, which provide akinesia, have been developed and refined over the last fifty years. In each instance, the goals of scientists have been to develop agents that provide the maximum desirable muscular paralysis while minimizing the undesirable side effects of the agents. Additional uses of neuromuscular blocking agents during this same time period have expanded to patient care areas outside the operating room, enabling other providers to administer such

agents. Situations where neuromuscular blocking agents may be used in the care of patients outside of the surgical arena include assisting ventilation in critically ill patients within the Intensive Care Unit, decreasing the muscle activity during electroconvulsive therapy, and providing an emergent airway to a patient within the Emergency Department (Pino & Basta, 1998). Such agents have become a mainstay not only for the anesthesia providers' arsenal, but for other medical professionals as well.

The Neuromuscular Junction

As described in Table 1, there are currently eleven distinct neuromuscular blocking agents available within the United States. Skeletal muscle paralysis is produced by the action of these agents and their ability to "block" or interrupt nerve impulses at the neuromuscular junction. Based on the mechanism of nerve interruption, onset, and duration (see Table 1), each agent is classified as either a depolarizing or a nondepolarizing agent (Stoelting, 1987). Pertinent to understanding this author's work is the definition and description of how neuromuscular blocking medications act at the cellular level. Therefore, for clarity and unification, a brief review from this author's perspective will be presented in the following section. A description of the normal neuromuscular junction and the associated mechanisms of action for each class of neuromuscular blocking agents will be reviewed.

The neuromuscular junction, also referred to as a myoneural junction, is the area between a prejunctional motor nerve fiber and a postjunctional skeletal muscle (Resnick & Henze, 2000). Transmission of a nerve impulse depends

Table 1: Neuromuscular Blocking Agents

Agent	Classification	Onset	Duration	Action
Succinylcholine (SCh)	Depolarizing	30-60 sec	5-15 min	Ultrashort
Mivacurium	Nondepolarizing	2-3 min	20-30 min	Short
Atracurium	Nondepolarizing	2-3 min	30-60 min	Intermediate
<i>cis</i> -Atracurium	Nondepolarizing	2-3 min	30-60 min	Intermediate
Rocuronium	Nondepolarizing	1-1.5 min	30-60 min	Intermediate
Vecuronium	Nondepolarizing	3-4 min	30-60 min	Intermediate
Doxacurium	Nondepolarizing	12 min	60-90 min	Long
Metacurium	Nondepolarizing	1-2 min	60-90 min	Long
Pancuronium	Nondepolarizing	2-3 min	60-90 min	Long
Pipecuronium	Nondepolarizing	3-4 min	60-90 min	Long
<i>d</i> -tubocurarine (DTC)	Nondepolarizing	3-4 min	60 – 90 min	Long, but no longer available

Adapted from Morgan & Mikhail, 1996

largely on the influx of calcium at this junction. Such an influx of calcium ions causes a release of the neurotransmitter acetylcholine from the nerve terminal. Once acetylcholine binds to the postjunctional receptors on the skeletal muscle, changes in membrane potential create an action potential difference that leads to skeletal muscle contraction (Stoelting & Miller, 2000). Relaxation of the skeletal muscle is facilitated by the enzyme acetylcholinesterase. This enzyme hydrolyzes acetylcholine, thus, eliminating from the neuromuscular junction the principle neurotransmitter responsible for the propagation of action potentials in skeletal muscle, which subsequently leads to muscular relaxation (Stoelting & Miller, 2000).

Depolarizing Neuromuscular Blockade

Of the eleven neuromuscular blocking agents available within the United States, only succinylcholine (SCh) is classified as a depolarizing agent. Chemically, its structure can be described as two acetylcholine molecules bound together. Therefore, SCh mimics the action of acetylcholine at the neuromuscular junction by creating an action potential within the skeletal muscle after the opening of prejunctional sodium channels, and causing a myoneural depolarization (Stoelting & Miller, 2000). However, because hydrolysis of SCh within the synaptic cleft is much slower than acetylcholine, each muscle cell remains depolarized, and the numerous action potentials which occur result in muscle twitches or fasciculations that can be observed. Relaxation of the skeletal muscle occurs because SCh occupies the postjunctional receptor site,

and sodium channels cannot reopen until the end plate repolarizes (Morgan & Mikhail, 1996).

Because of its chemical structure and metabolism by plasma cholinesterase, SCh has the two most desirable effects of any skeletal muscle relaxant available today: (1) fast onset and (2) short duration. Such properties allow for quicker control of the airway following loss of consciousness after the induction of a general anesthetic, facilitation of endotracheal intubation, and faster recovery of spontaneous respiration following muscular paralysis. Therefore, the use of SCh allows for safer care to the unconscious anesthetized patient when rapid securing of the airway is necessary.

Nondepolarizing Neuromuscular Blockade

Currently, there are ten nondepolarizing neuromuscular blocking agents available for use in the United States. All of their mechanisms of action are similar and involve the competitive inhibition of acetylcholine at the postjunctional receptor on the skeletal muscle at the level of the neuromuscular junction. Excessive quantity of nondepolarizer molecules at this site effectively prevents ion permeability, cellular depolarization, and ultimately inhibits the generation and propagation of action potentials. This disruption of cellular electrical activity allows for flaccidness of the skeletal muscle to predominate (Morgan & Mikhail, 1996).

Nondepolarizing neuromuscular blocking agents are classified into three groups according to their duration of action. These groups include short acting agents, intermediate acting agents, and long acting agents. However, in spite of

the suggestion made by the name, even the individual drugs in the short acting group have a longer time until onset and longer duration than SCh (see Table 1). SCh remains the best medication currently available for enabling an anesthesia provider to rapidly secure the surgical patient's airway. The ability to safely, efficiently, and rapidly control the respiratory functions and airway is one of the most important actions of an anesthesia provider (Morgan & Mikhail, 1996).

Despite many desirable effects, SCh also displays many adverse actions, which range from nuisance to serious. These side effects are listed in Figure 1. Obviously, the severe reactions are more important (Stoelting, 1987). Many studies exist on these reactions and conditions and much is known about these complications and their treatments. There is, however, a paucity of information regarding surgical patients and post-SCh administration myalgia. This paper will concentrate on the iatrogenic causes and treatments for SCh-induced postoperative myalgia, as it relates to the "gate control theory of pain".

Succinylcholine-induced Postoperative Myalgia

Past studies have indicated that the incidence of SCh-induced postoperative myalgia ranges from 1.5% - 89%, with the most common incidence being 50% (Wong & Chung, 2000). Certainly this is a sizable variation, and the lack of consistent scientific data on this subject is another important factor that encourages this author's current study. The most postulated mechanism for myalgia following SCh administration is believed to be from what is termed *fasciculation* (Wong & Chung, 2000). This phenomenon occurs almost

Adverse Side Effects of Succinylcholine

Cardiac dysrhythmias

Sinus bradycardia

Junctional rhythm

Sinus arrest

Fasciculations

Hyperkalemia

Myalgia

Myoglobinemia

Increased Intraocular pressure

Increased Intra gastric pressure

Trismus

Allergic reactions

Trigger for Malignant Hyperthermia

Adapted from Stoelting & Miller, 2000

Figure 1: Adverse Side Effects of Succinylcholine

immediately after the administration of SCh, and is observed as uncoordinated, uncontrollable, vigorous twitching of single muscle groups innervated by single motor nerve fibers (Anderson, Anderson, & Glanze, 1998 pp. 616). It occurs over the entire body without synchronous activity, allowing for shearing forces and biochemical damage to occur to the muscle cells and tissues. Such damage is believed to be a major contributing factor leading to postoperative muscle soreness (myalgia) (Wong & Chung, 2000).

Although it was originally postulated that postoperative muscle pain was linked to the use of SCh and its depolarizing action that caused fasciculations, the exact pathogenesis is still unknown. Many studies have concluded that the mechanism for SCh-induced fasciculation is a prejunctional phenomenon. Similarly, respected researchers have confirmed the correlation between fasciculation and SCh administration (Kitamura S, Yoshiya I, Tashiro C, & Nefishi T, 1981). However, it does not appear that the same relationship occurs between SCh-induced fasciculation and postoperative myalgia (Sosis, Broad, Larijani & Marr, 1987). Studies attempting to correlate muscle damage secondary to fasciculation, with changes in serum creatine phosphokinase levels, lactic acid levels, and electrolyte changes, have all discredited this theory. No studies to date have confirmed a statistically significant relationship between muscle damage secondary to the use of SCh, and postoperative myalgia (Wong & Chung, 2000). Therefore, these findings suggest that such muscle pain must occur from some additional mechanism, other than exclusively from muscular fasciculation.

The results of some studies have yielded data that suggests postoperative myalgia may not be associated at all with fasciculation, nor is it associated with the use of SCh (Mingus, Herlich, & Eisenkraft, 1990). Recent studies have demonstrated that no significant difference in postoperative myalgia is found between those subjects who receive SCh and groups of subjects that receive a nondepolarizing agent (Mingus, Herlich, & Eisenkraft, 1990). Few studies have determined that myalgia may occur even in the circumstance when SCh administration is avoided and only nondepolarizing agents are utilized (Trepanier, Brousseau, & Lacerte, 1988). Regardless of the cause, for those individuals who experience pain, the occurrence of postoperative myalgia is viewed as unacceptable. A closer look at the complex process of how pain is sensed, transmitted, modulated, and perceived may contribute to a better understanding of how to treat patients who experience this type of discomfort.

Myalgia

Postoperative myalgia is usually self-limiting in duration, and occurs up to three days postoperatively, with 24 to 48 hours being the most prominent time frame (Mikat-Stevens, Sukhani, Pappas, Fluder, Kleinman, & Stevens, 2000). It is often compared to the feeling one obtains after aggressively working the muscles, as may result from a period of strenuous physical exercise. It may occur in the chest wall, the upper abdomen, shoulders, neck, and back (Stoelting, 1987). Although the extent of muscle pain is generally mild, some patients may experience debilitating effects requiring bed rest and analgesic therapy for several days postoperatively. Even though the origin of such pain

remains unknown, explanations for the wide variance in occurrence and severity can be explained by the gate control theory.

This theory was first proposed in 1965, and continues to be the basis for effective postoperative pain management (Melzack & Wall, 1965). Melzack and Wall suggested that pain is transmitted from a peripheral site, such as the skin (or a muscle), to a specialized group of cells within the dorsal horn of the spinal cord known as the substantia gelatinosa. This area acts as a *gate* and responds in one of two ways: opening to transmit signals (as in the noxious stimuli associated with myalgia) to higher centers, or closing and thereby inhibiting the transmission (as by the actions of analgesics).

Although such a theory may sound simple, there are a complex series of physiologic responses that occur between the area of tissue damage (fasciculation) and the perception of pain (postoperative myalgia). Such complexity is referred to as nociception. Four physiologic processes trigger nociception, or pain perception: transduction, transmission, modulation, and perception (Ferrante, 1998).

Transduction, the first response to occur, happens upon administration of SCh. For those who believe fasciculation has a correlation to postoperative myalgia, it is theorized that the muscle tissue becomes injured by the fasciculation, and potassium is released into the extracellular fluid as a result of this injury or damage. Potassium is one of many pain-producing substances that stimulate a specialized group of sensory receptors called nociceptors. Other substances include hydrogen, serotonin, histamine, prostaglandins, and

bradykinins. Collectively these are known as algescic agents and, upon stimulation of the nociceptors, they cause electrochemical events at sensory nerve endings (Sackett & Cannon, 2000).

At this point the second step of nociception, transmission, occurs. The *gate* is opened as the propagation of electrical events is sent to the higher centers of the peripheral nervous system (PNS) and central nervous system (CNS). Such stimulation allows for the fourth process: perception of pain (Ferrante, 1998). Substance P is released within the cerebral tissue upon stimulation. It is this substance that conveys pain information in the cognitive centers of the brain and thereby allows for this stimulation to be identified as pain perception and associated responses enacted. Although transmission to the CNS occurs primarily through small diameter A-delta and C-fibers, interconnections between other sensory pathways can occur. One such pathway includes A-beta and A-alpha fibers. Stimulation of these large-diameter, fast, myelinated fibers causes the *gate* to close and prevents or inhibits transmission to the higher neural centers (Sackett & Cannon, 2000). Modulation, the third process, prevents the release of Substance P and consequently the perception of pain (Sackett & Cannon, 2000). It is this author's belief that it is this interplay between fibers that may most plausibly provide the explanation for the occurrence of such a wide range (1.5% - 89%) and severity of reported postoperative myalgia.

Although studies up to this point in time have not determined the mechanism by which postoperative myalgia occurs, it has been determined that the following groups of individuals have a higher incidence of exhibiting such postoperative

muscle soreness: females greater than males, individuals between the ages of 8 and 50 (Mingus, Shamsi, Recant, Eisenkraft, 1996), those persons who are ambulatory immediately after surgery (Oxorn, Whatley, Knox, & Hooper, 1992) those patients undergoing minor procedures, and people who are less physically fit than would be optimal (Newman & Loudon, 1966). Additionally, without any firm explanation, it has been observed that pregnancy appears to decrease postoperative myalgia (Crawford, 1971). Lastly, there does not appear to be an association with different ethnic backgrounds (Houghton, Aun, Gin, Lau, & Oh, 1993).

Many techniques have been attempted to prevent postoperative myalgia, and it seems as though the science has come full circle in the last 50 years. The current "gold standard" for prevention of postoperative myalgia in patients who receive SCh is through use of pretreatment doses of nondepolarizing agents. Despite critical opinions that such agents may cause difficulty with intubation, weakness, diplopia, difficulty in breathing, and prolongation of neuromuscular blockade, such agents consistently cause a 30% reduction of postoperative myalgia (Pace, 1990). Until further studies can demonstrate an alternative that constantly and dependably reproduce the same or similar outcomes with regard to the reduction of postoperative myalgia in patients who receive SCh, nondepolarizing agents will continue to be the current standard of treatment.

Many studies have implicated the use of lidocaine for reliable prevention of postoperative myalgia in association with SCh use. Of the current available studies, all but one have suggested that lidocaine is of equal efficacy, and is

safer than the traditional treatment of nondepolarizing agents. Additionally, multiple authors' studies agree that combination therapy with lidocaine and a nondepolarizing neuromuscular blocking agent has shown to more significantly improve outcomes of measured pain in subjects receiving SCh perioperatively. Therefore, the focus of this study will be to compare the differential effects of atracurium and/or lidocaine on SCh-induced postoperative myalgia as it relates to the gate control theory of pain. The null hypothesis is as follows:

Null Hypothesis

There will be no difference in postoperative myalgia in subjects receiving SCh who also receive one of three pretreatments: atracurium, lidocaine, or the combination of atracurium and lidocaine.

Chapter II

Review of the Literature

The Development of Succinylcholine

In 1906, Hunt & Taveau were the first to synthesize SCh. They were looking for agents that would maintain hemodynamics during general anesthesia in anesthetized animals (Hunt & Taveau, 1906). Since they were using SCh in conjunction with *d*-tubocurarine (DTC), the muscle relaxant properties of SCh were not recognized. In fact, this association was not made until 1949 (Churchill-Davidson, 1984). Within a year of this discovery, SCh was being utilized in small doses as a muscle relaxant during general anesthesia in humans (Foldes, McNall, & Borrego-Hinojosa, 1952). Today, this drug continues to be widely utilized by anesthesia professionals in the implementation of muscular paralysis for subjects undergoing surgical intervention.

Side Effects of Succinylcholine

By the end of 1952 adverse side effects of SCh were first being noted. Although not the focus of the original study on SCh, the initial side effect identified was that of prolonged respiratory depression. This was attributed to the administration of “unnecessarily high doses of succinylcholine” (Foldes, McNall, & Borrego-Hinojosa, 1952, p. 600). However, further study resulted in an association of SCh termination with plasma cholinesterase, the mechanism by which SCh is metabolized, and the cause for occasional extended action of SCh was identified. As a result of their research, prolonged respiratory depression in subjects who were administered SCh was correlated to those subjects who had

low levels of plasma cholinesterase (Foldes, McNall, & Borrego-Hinojosa, 1952). Others confirmed such findings the very same year (Evans, Gray, Lehmann, & Silk, 1952).

Reports of a possible relationship between fasciculation and postoperative myalgia started infiltrating the literature in 1952 (Brodsky & Ehrenwerth, 1980). In one study comparing inpatient subjects to outpatient subjects, Churchill-Davidson found that SCh caused marked postoperative myalgia despite the fact that the surgical procedure may have been minor (Churchill-Davidson, 1954). Interestingly enough, the author compared groups that were equal in terms of group size and age, and found that outpatient subjects had a significantly higher rate (66%) of muscle pain than was observed in the inpatient subjects population (13.9%). This is a similar finding when compared to the majority of today's studies (Wong & Chung, 2000).

Treatments for the Prevention of Postoperative Myalgia

The previously noted study by Churchill-Davidson was the first to attempt to find a treatment for the prevention of postoperative myalgia. The first use of gallamine, a nondepolarizing neuromuscular blocking agent, was used in conjunction with SCh in an effort to abolish fasciculation and prevent postoperative myalgia. Churchill-Davidson found that pretreatment with small doses of gallamine, prior to the administration of SCh, totally abolished fasciculation within both groups. Additionally, although not completely resolved, the incidence of postoperative myalgia for outpatient subjects decreased from 66% to 40%. Complete abolishment of both fasciculation and postoperative

myalgia for the inpatient subject group was achieved. These initial findings appeared to offer support that fasciculation and postoperative myalgia were directly related (Churchill-Davidson, 1954).

Further studies by Foster, in 1960, determined the incidence of myalgia to be increased among ambulatory outpatient subjects. Additionally, he identified many facts about myalgia in relation to SCh administration, which still hold true today. These included the following: Postoperative myalgia occurs less frequently in subjects over the age of 60, there is a low incidence of pain in children, and muscle pains varied in accordance to the type of surgery (Foster, 1960). Furthermore, he confirmed that gallamine lowered the incidence and severity of postoperative myalgia. Despite this encouraging finding, he concluded that the use of nondepolarizing agents, as a pretreatment prior to SCh, should not be recommended. Such agents were found to cause marked respiratory depression or airway difficulties at the termination of the procedure (Foster, 1960). Others, throughout the literature of that time, agreed with Foster's supposition. In 1977, Baraka declared the competitive and antagonistic affects of SCh were thought to delay the onset and decrease the degree of neuromuscular blockade. Therefore, for purposes of preventing SCh-induced postoperative myalgia, choosing a nondepolarizing agent for intubation and completely avoiding the administration of SCh would be a better choice within the context of the anesthetic plan (Baraka, 1977).

Because of such effects associated with the use of nondepolarizing agents as a pretreatment for the prevention of postoperative myalgia in subjects who have

received SCh, other methods have been investigated in the last 50 years that have followed Churchill-Davidson's seminal work in this area. Within the literature, there are at least 13 other treatments that have been studied in an attempt to prevent or lessen postoperative myalgia. These include self-taming, stretching exercises, magnesium sulfate, propofol, vitamin C, dantrolene, lidocaine, calcium gluconate, benzodiazepines, chlorpromazine, aspirin/nonsteroidal anti-inflammatory drugs, phenytoin, altering induction agents, and dosage/timing of SCh administration (Wong & Chung, 2000). Some have shown to be successful, while others have failed. The following section will further describe the rationale for, and success or failure of, each of these treatments as they appear in the current literature.

Self-taming

In much the same way a small dose of a nondepolarizing agent is given as a pretreatment for the prevention of myalgia associated with SCh administration, giving small doses of SCh prior to the full dose has been attempted for the same reason. This idea is known as "self-taming" (Baraka, 1977). It is thought that the *taming effect* desensitizes the neuromuscular junction. Therefore, excitation between the nerve terminals and the muscular membrane cannot occur allowing for decreased fasciculation. Additionally, unlike the effects caused by pretreatment with a nondepolarizing agent, onset and duration of the block can be preserved (Baraka, 1977).

In 1979, Brodsky and Brock-Utne found a 25% incidence of fasciculation when using a self-taming technique as described by Baraka. This is very similar

to Baraka's results of a 20% incidence. However, unlike Baraka, Brodsky and Brock-Utne found no relationship between this decrease in fasciculation and postoperative myalgia. Therefore, they concluded there was no advantage to utilizing a "self-taming" technique for the purpose of preventing postoperative muscular soreness in conjunction with SCh administration.

Like Churchill-Davidson and Foster's studies, Brodsky and Brock-Utne (1979) found an increased incidence of postoperative myalgia in subjects who ambulate (outpatient subjects). However, they emphasized the following: "muscle aches may occur postoperatively even when succinylcholine has not been used, and it is impossible to differentiate SCh-induced myalgia from muscle soreness due to other causes" (p. 267). This provides further supportive evidence for what we believe today, which is that fasciculation and postoperative myalgia may not be directly associated. Therefore, prohibiting fasciculation may not be the mechanism by which to improve patient outcomes in relationship to postoperative muscular pain.

Although true, the above statement by Brodsky and Brock-Utne takes into account only part of the phenomenon. There are numerous studies throughout the literature comparing the incidence of postoperative myalgia with the use of depolarizing agents and nondepolarizing agents, and these studies fail to support Brodsky and Brock-Utne's statement. Trepanier, Brousseau, and Lacerte (1988) compared SCh with atracurium in relation to postoperative muscle pain. The incidence of postoperative myalgia among the group that received SCh was 76%, and the group who received atracurium was 23%. Therefore, these

authors concluded the use of atracurium significantly reduced postoperative myalgia in comparison to SCh.

However, when pretreatment doses of a nondepolarizing agent are utilized prior to the administration of SCh, and these subjects are compared to the members of a group who receives only a nondepolarizing agent, there is evidence to support Brodsky and Brock-Utne's statement. Deehan, Henderson, and Stewart (2000) compared subjects who received SCh after being pretreated with gallamine to subjects who received only mivacurium. Although their findings found a 26% incidence of postoperative myalgia in the pretreated SCh group, and only a 9.5% finding in the mivacurium group, they were not statistically significantly different. These findings provide additional evidence that postoperative myalgia may result from causes other than SCh exclusively.

The study findings of Mikat-Stevens, Sukhani, Pappas, Fluder, Klienman and Stevens (2000) corresponded to the findings of the research study conducted by Deehan and associates. These investigators compared a group of subjects who received SCh following pretreatment with DTC to a group of subjects who only received mivacurium. Again, they found that the pretreated SCh group had an increased incidence of myalgia at 21%. These findings, however, were not significantly different from the 18% incidence noted in the mivacurium group. Thus, like Deehan and associates, these authors concluded that pretreating subjects with nondepolarizing neuromuscular blocking agents, prior the administration of SCh, does not cause a decrease in postoperative myalgia.

Stretching Exercises

It is known that athletes who stretch prior to exercise have decreased muscle damage and pain afterwards (Harris, 1984). MaGee & Robinson (1987) theorized that perhaps the same would be true for subjects undergoing anesthesia requiring the use of SCh for endotracheal intubation. They postulated that the stretch receptors on the muscle fibers could undergo desensitization in much the same way *self-taming* occurs. Their study concluded with a significant finding of only 15% of the experimental stretching group having postoperative myalgia, while 55% of the control group reported pain. Thus, signifying that stretching prior to the administration of SCh decreased postoperative myalgia. Although not the focus of this study, it is interesting to note that MaGee & Robinson (1987) also found a correlation between fasciculation and the degree of pain: The greater the measured fasciculation, the greater degree of reported postoperative pain. Interestingly, in many of today's studies, this correlation does not appear to occur.

Magnesium Sulfate

A classic example where absence of fasciculation does not coincide with an absence of postoperative pain involves the administration of magnesium. Specifically, pretreatment of magnesium sulfate does not diminish complaint of postoperative discomfort following the administration of SCh. Theoretically, magnesium sulfate has neuromuscular blocking properties and should abolish fasciculation. If the absence of fasciculation equates to the absence of discomfort, subjects adequately treated with magnesium sulfate should not

fasciculate, and so should have their pain prevented. A study performed by Chestnutt and Dundee (1985) found that magnesium significantly decreased fasciculation, nearly abolishing it. However, only slight decreases were identified in relation to postoperative myalgia in their study subjects. 64% of the treated group had postoperative pain, as opposed to 80% of the untreated group, not a significant difference in regards to their study.

Stacey, Barclay, Asai, & Vaughan (1995) confirmed Chestnutt and Dundee's finding. They discovered a significant decrease in fasciculation with the use of magnesium sulfate, but no difference in postoperative myalgia. Oddly, in similar fashion to the findings of Chestnutt and Dundee, serum potassium levels were found to be normal. Therefore, despite the abolishment of fasciculation and normal potassium levels, subjects pretreated with magnesium sulfate continue to have postoperative muscle soreness. Therefore, it was concluded that magnesium sulfate shows no promise in being a pretreatment for the prevention of postoperative myalgia in subjects who receive SCh.

Propofol

In terms of fasciculation, two recent studies have shown agreement with the above noted findings. First, Mingus, Shamsi, Recant, and Eisenkraft's (1996) study consisted of the following three groups: those who received thiamylal/SCh in group one, propofol/ SCh in group two, and propofol/saline in group three. All groups were demographically comparable, and none demonstrated significance in incidence or severity of postoperative myalgia despite significant differences in measured fasciculation between groups' one, two, and three. Although group

three did not receive SCh, 30% of the subjects in this group reported postoperative pain. In contrast, 50% of the subjects within group two, who received SCh, complained of postoperative myalgia. These results were not considered significant, therefore, allowing Mingus and associates to conclude that postoperative myalgia was not associated with fasciculation.

Manataki, Arnaoutoglou, Tefa, Glatzounis, and Papadopoulos (1999), performed a study comparing two groups of subjects. Both groups received propofol and SCh for induction, but differed in their maintenance of anesthesia. Group one was maintained with isoflurane, while group two received continuous propofol. No significant correlation was found between fasciculation, postoperative myalgia, or elevations in CPK between the group who had been maintained using propofol, as compared to the group who was maintained with isoflurane. Therefore, the authors concluded that fasciculation does not have a correlation with muscle damage. Additionally, they contended that postoperative myalgia and muscle damage are not caused by the same mechanism.

Vitamin C

Vitamin C is known to decrease muscle pain and soreness after unaccustomed exercise. It provides protection to the endothelial lining of capillaries, therefore preventing damage to muscle fibers (Syed, 1966). Gupte and Savant (1971) showed a decreased significance in the incidence of postoperative myalgia with the administration of vitamin C perioperatively. Currently, however, there are no studies that compare this intervention with other

treatments (Wong & Chung, 2000). Therefore, this remains an area for future study that may provide an alternative treatment for postoperative myalgia.

Dantrolene

Collier (1978) theorized that the more calcium released from the sarcoplasmic reticulum within the muscle during depolarization, the greater the speed and strength of resulting fasciculations. Ultimately, stronger fasciculations lead to greater muscle damage and results in increased postoperative myalgia.

Confirmation of this became reality in Collier's first study. In this investigation, he found an inverse relationship between calcium and potassium in those subjects who developed pain and concluded that postoperative myalgia was a result of muscle fiber damage, secondary to fasciculation, that was caused by the enhanced release of calcium.

Since dantrolene interferes with intercellular calcium transfer, Collier (1979) felt it was an appropriate medication to decrease fasciculation and postoperative myalgia. In his second study, 98 subjects were given dantrolene orally two hours prior to surgery. Not only did he find a significant difference in the strength of muscle fasciculation and potassium levels, he also found that myalgia decreased from 56% to 4% between the pretreated group and those who were not pretreated. Additionally, unlike the use of nondepolarizing agents as a pretreatment, he did not identify any alteration in the action of SCh in conjunction with dantrolene administration. Therefore, he concluded dantrolene to be an efficient treatment for the prevention of postoperative myalgia in subjects who received SCh.

Another study with dantrolene performed by Gysai, Delisle, and Bevan (1982) failed to show a reduction in postoperative myalgia. However, this study utilized small doses of intravenous dantrolene instead of the oral form. This was not the first instance identified in the literature where an intravenous form of a medication under investigation failed to have the same outcome, in reference to postoperative myalgia, as the oral form. The authors recommended further study of this subject matter in order to assess whether there was an association between route of administration and postoperative discomfort following intravenous SCh administration.

Following Collier's lead, and postulating that postoperative myalgia is a result of muscle damage, Laurence (1985) performed a study attempting to show a correlation between dantrolene pretreatment and muscle damage. Rises in myoglobin were measured to predict the amount of muscle damage. He hypothesized that pretreated subjects would show decreased myoglobin levels, thereby, indicating significantly less muscle damage had occurred. As postulated, significant differences in the amount of myoglobin were found among pretreated subjects versus those subjects who were not pretreated. Following analysis of the data collected in his study, this author concluded that his results agreed with Collier. His final conclusion was that oral dantrolene could potentially be beneficial in the prevention of postoperative myalgia.

Lidocaine

JE Usubiaga, Wikinski, JA Usubiaga, and Molina (1967) were the first to show that pretreatment with intravenous lidocaine prevented postoperative myalgia, as

well as a decrease in muscle soreness. They found minimal side effects associated with lidocaine when it was given at doses of 1.5 mg/kg. In 1973, Haldia, Chatterji, and Kackar replicated such findings by using 3–4 mg/kg of lidocaine, showing decreased postoperative myalgia. Today, 1.5 mg/kg is the most often used dose, as these past studies have shown equal efficacy between this dose and higher doses. Additionally, such a dose is well below the toxicity level of lidocaine.

In much the same way Collier found an inverse relationship among potassium and calcium in relation to the use of dantrolene, Chatterji, Thind, and Daga (1983) found a similar relationship with the use of lidocaine. Unlike their predecessors, who believed that lidocaine prevented soreness by producing a sedative effect, these authors concluded that lidocaine stabilized the cell membrane and consequently restricted ionic movement. The effect of lidocaine in subjects who received SCh was the suppression of muscle damage and the prevention of postoperative myalgia.

Calcium Gluconate

Shrivastava, Chatterji, Suman, and Daga (1983) further investigated the relationship between SCh administration and cellular damage. Specifically, they examined the previously observed inverse relationship of increased serum potassium and decreased serum calcium in relation to SCh-induced postoperative myalgia. These individuals theorized that the administration of calcium gluconate prior to the administration of SCh would prevent postoperative myalgia. Although they could not identify the mechanism by which this occurred,

they nonetheless observed that calcium gluconate significantly reduced the incidence of muscle pains from 45% to 5%. Additionally, the severity of pain was likewise reduced. A principle conclusion of these authors was that since similar studies were limited, further research on calcium gluconate and its association with postoperative myalgia was indicated before the use of this intervention could be established as a beneficial treatment.

Benzodiazepines

As well as myoglobin changes, studies have found that the administration of SCh can also cause electrolyte and other biochemical changes at the cellular level. As the above studies have eluded, these alterations are hypothesized to be a result of depolarization and muscle damage from fasciculation. In agreement with the gate control theory, some studies have attributed increases in serum potassium and creatine phosphokinase (CPK) as causative factors for postoperative myalgia (Fahmy, Malek, & Lappas, 1979). Fahmy and associates found that pretreatment with diazepam prior to SCh administration prevented fasciculations, hyperkalemia, and subsequent rises in CPK. Thus, they concluded this intervention led to a significant decrease in postoperative myalgia. In their work, only 12.5% of subjects receiving benzodiazepines experienced postoperative myalgia as compared to 65% of subjects in the untreated group.

Eisenberg, Balsley, and Katz (1979) had similar results of decreased muscle pain in subjects who received SCh as a component of their anesthetic plan, but who were pretreated with diazepam. In their study, only 13% of the treatment group displayed postoperative discomfort. This is contrasted to 33% of the

control group's subjects. Although, serum potassium levels remained normal in their study subjects, unlike Fahmy and associates, they found that CPK was elevated within the pretreatment group. Reasoning for this finding remains a mystery, and unlike the previous study, decreases in postoperative myalgia occurred despite a rise in CPK.

Prior to these two studies, Verma, Chatterji, and Mathur (1978) had also concluded that pretreating with diazepam decreased the incidence, severity, and duration of SCh-induced myalgia. Their results were similar to both of the above studies. They found in subjects receiving intraoperative SCh, only 16% of the subjects detailed postoperative myalgia with muscular pain after pretreatment, as opposed to 60% experiencing pain without pretreatment. Although serum potassium and CPK levels were not measured in this study, the outcome remained the same. These authors suggested that pretreatment with diazepam should be considered for decreasing postoperative myalgia in subjects receiving SCh.

Chestnut, Lowry, Dundee, Panditt, and Mirakhur (1985), however, failed to confirm the above detailed findings. In a comparison trial of diazepam, midazolam, and DTC, these authors concluded that postoperative myalgia was not prevented by any of the benzodiazepine pretreatments. Interestingly enough, the DTC group had less reported myalgia than the other groups. Additionally, unlike the previous three studies, electrolyte and biochemical changes in these authors' study subjects were found to be inconsistent among all groups.

The unpredictable and inconsistent findings of the above detailed studies cause this author to conclude that biochemical and electrolyte changes after the administration of SCh may not have an association with postoperative myalgia. Additional support for this notion is provided by the study of McLoughlin, Elliot, McCarthy, & Mirakhur (1992). Although their pretreatment was not diazepam, but rather a variety of other medications, they reported that there was no correlation between myalgia and rises of CPK. Therefore, they concluded that biochemical changes and postoperative myalgia were separate and distinct entities.

Chlorpromazine

McLoughlin, Elliot, McCarthy, and Mirakhur (1992) provided some evidence that chlorpromazine was effective in preventing postoperative myalgia. It is thought that chlorpromazine inhibits phospholipase A2, a major enzyme, which is ultimately responsible for the release of fatty acids. It has been postulated that such release causes muscle damage, in turn causing postoperative myalgia. Therefore, inhibition of this enzyme should prevent such damage and its resultant myalgia. This concept was confirmed by their study. They found rises in CPK, serum potassium, and serum calcium insignificant when chlorpromazine was used as a pretreatment, indicating the preservation of muscle function. Additionally, only 15% of the chlorpromazine treated subjects reported having postoperative pain. Although McLoughlin and associates reported that the use of chlorpromazine should be further studied, Wong and Chung (2000) discourage its use, noting the side-effect profile of chlorpromazine would outweigh the benefits for its use in the prevention of postoperative myalgia.

Aspirin/Nonsteroidal Anti-Inflammatory Drugs

As some of the above studies indicated, fasciculation results in muscular damage and the release of CPK, myoglobin, and electrolyte disturbances. Work performed by Kahraman, Ercan, Aypar, and Erdem (1993) found elevations of enkephalins, prostaglandins, leukotrienes, and histamines in subjects that fasciculated. Such chemicals are major causes of nociception and start the cascade of events that fit into the framework of the gate control theory of pain (Sackett & Cannon, 1999). Prostaglandins not only sensitize pain receptors, but also potentiate the actions of histamine and bradykinins. Thus, the substances allow for increased pain modulation and perception by the patient.

Kahraman and associates hypothesized that by inhibiting prostaglandins perhaps postoperative myalgia could be decreased. Their study involved 34 healthy subjects undergoing elective ophthalmic surgery. Preoperatively each subject within the treatment group received oral diclofenac, a nonsteroidal anti-inflammatory (NSAID), prior to the administration of SCh. They reported a 30% reduction of postoperative myalgia in this experimental group, as compared to the untreated group. Although these authors found no correlation between myalgia and the severity of fasciculation, they concluded preoperative administration of diclofenac nonetheless reduced postoperative myalgia.

Previous work performed by McLoughlin, Nesbitt, and Howe (1988) found similar results with the preoperative administration of oral aspirin. They identified a 36% reduction in postoperative myalgia among those subjects who were treated preoperatively with aspirin. These results, like those of other

investigators discussed in the following section, were once again attributed to the inhibition of prostaglandin synthesis. As previously noted, interrupting the cascading events of the gate control theory, resulting in decreased pain modulation and ultimately diminished pain perception.

More recent studies using ketorolac (a NSAID), by Leeson-Payne, Nicoll, and Hobbs (1994), did not support the findings of the previous two studies. They enrolled 60 healthy subjects within their study and administered intravenous ketorolac preoperatively. As mentioned, they concluded that ketorolac did not significantly prevent postoperative myalgia in subjects receiving SCh perioperatively. Their results were unexpected findings, since ketorolac is 350 times more potent in the inhibition of prostaglandins than aspirin. It is of importance to note that just as intravenous dantrolene did not have the same result as the oral form, here too a similar observation has been made with the use of NSAIDS. Again, this topic has been identified as an area for needed future study. Specifically, the question needing investigation is whether the oral form of ketorolac would show a difference from the intravenous form, with respect to postoperative myalgia in subjects receiving SCh in the perioperative period.

Phenytoin

Hartmen, Fiamengo, and Riker (1986) demonstrated that phenytoin prevents fasciculation by a prejunctional mechanism. However, this study was performed in vitro, and despite such findings, these results have not been replicated in humans. In fact, Hatta, Saxena, and Kaul (1992) not only found that there was no relation in the incidence of fasciculation, but there also was no

relationship/correlation among fasciculation, serum potassium levels, and postoperative myalgia when phenytoin was used as a pretreatment. Although phenytoin did not significantly prevent fasciculation or changes in serum potassium, they concluded that it significantly reduced postoperative myalgia by as much as 18.3%. They postulated that such a finding was caused by the stabilization of motor nerve terminals. As with calcium gluconate, there are relatively few studies using phenytoin as a pretreatment for postoperative myalgia. Therefore, much more research is indicated before we make changes in our current methods or practices with regards to phenytoin usage for the reduction of SCh related postoperative myalgia.

Nondepolarizing Agents

Since Churchill-Davidson's finding in 1954, that pretreatment of subjects with gallamine significantly reduced postoperative myalgia, numerous studies have been performed to assess the effectiveness of varying nondepolarizing agents on this phenomenon. Although the exact mechanism is not fully understood, the use of nondepolarizing neuromuscular blocking agents is currently the most widely accepted practice for treatment and prevention of postoperative myalgia in individuals who are to have SCh as part of their anesthetic plan (Deehan, Henderson, & Stewart, 2000). For purposes of this author's review, 10 studies will be examined in order to provide increased insight to this enigmatic pretreatment for the prevention of postoperative myalgia in conjunction with SCh usage.

Because they were the first nondepolarizing agents available, gallamine and DTC are the two most studied medications within the literature, which have been used for the pretreatment of fasciculation and prevention of postoperative myalgia. However, DTC is no longer commercially available due to agricultural and manufacturing constraints. Although the literature is suggestive that DTC prevented fasciculation better than any current modern nondepolarizing agents, this drug will not be a focus of this study since it is no longer commercially available (Pinchak, Smith, Shepard, & Patterson, 1994). Sadly, it is anticipated that this drug will never commercially resurface in the world of anesthesia again.

After Churchill-Davidson's original work, no less than six additional researchers performed studies utilizing gallamine in the pretreatment of postoperative myalgia in conjunction with SCh administration. Glauber (1966) found that pretreatment significantly reduced postoperative myalgia in female subjects, from 47.2% without pretreatment, to 16% with pretreatment. The same phenomena did not occur among the male subjects in his study. Male subjects reported a 48.4% incidence of experiencing pain without pretreatment, and 36.4% with pretreatment. Glauber made an interesting find through his work, however, that remains important for modern day research in this subject area. The pretreatment of DTC in his study was given as a single dose of 5 mg. It was not based on body weight. Therefore, it could be concluded that pretreatment in males did not reveal any statistical significance because the dose was not large enough to counteract the effects of SCh in the heavier and more fully muscled male subjects. This author believes that pretreatments should be based on

mg/kg basis for any degree of scientific significance to be ascertained from study results.

Brotsky, Brock-Utne, and Samuels (1979) were the first to investigate the use of pancuronium as a pretreatment for SCh-induced postoperative myalgia. They used two groups that were identical with respect to age, weight, anesthetic technique, and length of operation. Group one was pretreated with pancuronium, while group two did not have any pretreatment. Ninety-five percent of subjects within group two had fasciculation, while only 20% of group one exhibited movement. Statistically, pancuronium made a difference in fasciculation. However, in terms of postoperative myalgia, neither group had impressive findings. Although those pretreated with pancuronium did have less myalgia (20%), the measured difference was not significantly different from those who did not receive pretreatment (35%). Therefore, Brotsky and associates (1979) concluded that there was no correlation between fasciculation and postoperative myalgia. Additionally, they stated that pancuronium "does not decrease the incidence or severity of postoperative myalgia..." (p. 261).

O'Sullivan, Williams, and Calvey (1988) performed a comparison study of pretreatment doses of gallamine, pancuronium, and taming doses of SCh. Their findings were in agreement with many previous studies, in that gallamine inhibited fasciculation better than pancuronium. Additionally, they concluded that there was not an association between fasciculation and postoperative myalgia. However, in regards to postoperative myalgia, they found just the opposite from the previous study. Pancuronium had a greater effect on postoperative myalgia,

and significantly reduced postoperative pain better than gallamine. Ultimately, they reasoned that gallamine acts at the prejunctional site to decrease the rate of firing, and therefore decreases fasciculation. Pancuronium, on the other hand, was postulated to work at the postsynaptic site and decreases postoperative myalgia. Therefore, providing reasoning for what others have hypothesized throughout the literature, that fasciculation and postoperative myalgia are caused by different mechanisms.

Although varying results have been documented throughout the literature, atracurium is currently one of the most studied and most effective nondepolarizing agents for the prevention of postoperative myalgia (Pace, 1990). Perhaps this is because it is metabolized by Hoffman elimination in addition to being eliminated through ester hydrolysis, and therefore can be safely used for even the sickest of subjects who may have hepatic and renal dysfunction. This safety index is one reason why atracurium was chosen as the focus of this study. The following section reviews several studies found within the body of literature comparing atracurium to other nondepolarizing agents and their effectiveness in reducing postoperative myalgia.

Sosis, Broad, Larijani, and Marr (1987) compared atracurium, normal saline, and DTC and measured for both fasciculation and postoperative myalgia in subjects receiving SCh. They found that DTC prevented fasciculations better than atracurium, but the reverse was true for postoperative myalgia. Although the only significant finding was that both DTC and atracurium significantly decreased postoperative myalgia when compared to saline, neither was

significantly superior to the other. However, numerically, there is a 26% difference between the two groups. Eighty-five percent of subjects pretreated with atracurium were free from postoperative pain, while only 59% of subjects treated with DTC reported the absence of postoperative myalgias.

Hochhalter (1996) found just the opposite of Sosis and associates. This studies results indicated that atracurium, when compared to normal saline, decreased fasciculation, but had little effect on postoperative myalgia in subjects who received SCh. Additionally, Hochhalter concluded that there was no relation between fasciculation and postoperative myalgia, as several subjects were recorded as having very defining fasciculations, but no muscle soreness. Although atracurium was effective in preventing fasciculation (73%), the incidence of postoperative myalgia was not prevented, with 12% of the pretreatment group having pain. Although this does not sound like much of a difference when compared to other studies, this is a large dissimilarity considering there was only a rate of 33% overall reporting pain during the first 24 hours.

Martin, Carrier, Pirlet, Claprood, and Tetraults' (1998) study compared the following agents: normal saline (control), DTC, vecuronium, atracurium, rocuronium, and mivacurium. They observed the usual finding of 50% postoperative myalgia within the normal saline group. However, myalgia was not significantly diminished by any of the pretreatments. In terms of postoperative myalgia, they concluded that there was not any advantage to pretreatment. In fact, they noted that pretreatment could even be potentially dangerous, in that the

mivacurium group not only resulted in the need for a larger dose of SCh, but also resulted in a prolonged paralytic block.

Tsui, Reid, Gupta, Kearney, Mayson and Finucane (1998) compared atracurium, rocuronium and normal saline. Unlike previous studies, they found evidence that rocuronium significantly reduced both fasciculation and postoperative myalgia in subjects who received SCh as a component of their general anesthetic. Although atracurium was found to reduce postoperative myalgia, it was not until postoperative day number two that this finding became significant. Therefore, it was concluded that rocuronium was a better choice for the pretreatment of both fasciculation and postoperative myalgia than atracurium.

Previous work performed by Demers-Pelltier, Drolet, Girard, and Donati (1997) found similar results to Tsiu and associates. Their work compared rocuronium, DTC, and normal saline in subjects who also received SCh. They concluded that rocuronium and DTC were equivalent in preventing fasciculations. However, like Tsui and associates, they found that rocuronium significantly decreased postoperative myalgia over DTC. Like many previous studies, this investigation demonstrated that pretreatment with a nondepolarizing agent delayed the onset of SCh and shortened the duration of the block. In this case, rocuronium had much more of an enhanced affect than did DTC. In order to prevent such a problem, higher doses of SCh would be needed. As previously mentioned, this discovery opened inquiry to an additional confounding variable, one that had not been anticipated prior to its identification. Did the increased dose of SCh affect the degree or amount of postoperative myalgia?

Because of varying results among studies comparing differing agents, it has been suggested and demonstrated that combination therapy appears to be the most useful method in preventing postoperative myalgia (Wong & Chung, 2000). Until the exact mechanism of myalgia is determined, attacking investigation of this subject at differing angles may be the best approach. Melnick, Chalasani, Uy, Phitayakorn, Mallett, and Rudy (1987) found that DTC in combination with lidocaine provided subjects who received SCh with less postoperative myalgia than either medication used separately. The incidence of pain in the combination group was only 8.3%. This was 30% less than the incidence reported in any of the other groups. Their results, therefore, lead many authorities in this area of investigation to the conclusion that combination therapy improves patient outcomes in terms of postoperative SCh-induced myalgia.

Raman and San (1997) also found combination therapy to be effective in reducing myalgias. Their study established that subjects pretreated with both atracurium and lidocaine had a significantly lower incidence of postoperative myalgia following SCh administration than those pretreated with each medication separately. The control group had a 75% incidence, atracurium had a 35% incidence, lidocaine had a 30% incidence, and the combination group only had a 5% incidence of postoperative myalgia. These findings support utilizing two lines of attack, as lidocaine works as a cell membrane stabilizer. Although different studies have demonstrated differing results, atracurium is thought by most to be active at prejunctional sites (Wong & Chung, 2000).

Although many facts about SCh have been known since 1960, only 10 years after the first routine use during general anesthesia, the definitive cause of postoperative myalgia remains unidentified. Foster quoted the following passage from a 1960 journal article (p. 25):

Every time suxamethonium [succinylcholine] is used consideration must be given to the indications for its use and the incidence of muscle pains afterwards, and we must all hope that the chemists will produce a new relaxant with the advantages of suxamethonium [succinylcholine] but without its capacity for producing these pains.

How ironic, that nearly half a century later, we continue searching for the same answers to questions that first were documented in 1960.

Chapter III

Materials and Methods

The overall purpose of this pilot study was to discover the feasibility and practicality of subsequently implementing a full-scale study aimed at identifying the best medication or combinations of medications that reduce postoperative myalgia following the administration of SCh when it is utilized as part of a general anesthetic. This pilot study examined and compared the efficacy of pretreatment with atracurium, lidocaine, or the combination of these two medications in relation to the reported incidence of postoperative myalgia in subjects who received SCh. The Postoperative Myalgia Survey (PMS) was utilized to collect data regarding muscle pain in subjects who had received SCh as a component of general anesthesia at 24, 48, and 72 hours postoperatively. This instrument is a 14-question survey that not only allows subjects to describe their pain both quantitatively and qualitatively, but also allowed the researcher to distinguish whether the pain being experienced by the subject was truly myalgia, rather than some other type of related surgical discomfort. The researcher applied data gathered from the utilization of the PMS to a second instrument, known as the Postoperative Myalgia Evaluation Scale (PMES).

The PMES is a modification of the Visual Analog Pain Scale (VAPS) and was used to rate and record the overall severity of the myalgia on a 0 - 3 Likert scale, based on the occurrence and severity of myalgia as it was described by the subject. Because the focus of this study did not consider it adequate to only report myalgia experienced by the subject, which was collected by the PMS, the

PMES was employed to specify the incidence and severity of the reported myalgia as it related to each of the three study groups.

Throughout the remainder of this chapter, this author will explore and present operational definitions, the research design, subject sample and setting, inclusion and exclusion criteria, informed consent, study protocol, instrumentation, data analysis, assumptions, study limitations, specific risks and protection measures, and potential benefits as they relate to the pilot study.

Operational Definitions

As it is essential for all readers of this manuscript to assure consistent understanding of some pivotal terminology, the following section lists the operational definitions that should be used throughout the remainder of this paper.

1. American Society of Anesthesiologists (ASA) - The American Society of Anesthesiologists is an educational, research and scientific association of physician anesthesiologists who have organized to raise and maintain the standards of the medical practice of anesthesiology and improve the care of the patient.
2. ASA Physical Status Classification (PSC) I and/or ASA PSC II – Describes the physical status of a patient at the time of surgery. Appendix A holds specific definitions.
3. Endotracheal Anesthesia – General anesthesia that is delivered to the lungs through the trachea via an endotracheal tube.

4. Endotracheal tube – A large tube that is inserted through the nose or mouth into the trachea, by which oxygen, anesthetic gases, and/or volatile anesthetics are delivered.
5. Laparoscopic Surgery – Intra-abdominal surgery performed through small incisions with the use of laparoscopic instruments. These are surgical instruments that include a camera that transmits the image inside the body cavity by allowing the surgeon to guide the surgical instruments and perform the procedure.
6. Neuromuscular junction – The area between the ends of myelinated nerve fibers and it's corresponding skeletal muscle.
7. Outpatient – A non-hospitalized patient who receives same day medical treatment, is discharged less than 24 hours following admission, and then returns home for convalescence.
8. Postoperative myalgia – muscle soreness that occurs after surgery. It is best described as the feeling one gets after a period of aggressive, physical exercise.

Research Design, Sample, and Setting

After approval was obtained from the Investigational Review Board (IRB) committees at the University of Tennessee Medical Center-Knoxville and the University of Tennessee in Knoxville, this prospective, randomized, double-blind study was carried out as a pilot study on 15 subjects who met the requirements of the ASA PSC I and/or ASA PSC II (Appendix A). The convenience sample was selected from all adult outpatients who were listed on the daily surgical

schedule for laparoscopic surgery at a Level I Adult and Pediatric Trauma Center in the Southeast United States. The entire investigation took place on 2-North in the main operating room surgical suites.

Inclusion and Exclusion Criteria

All subjects met the following inclusion criteria in order to be enrolled in the study. These criteria included the following:

1. Subjects between 18 – 50 years of age, as postoperative myalgia is shown to be most prominent in this age group.
2. Subjects requiring elective, outpatient laparoscopic surgery under general endotracheal anesthesia, as this helped to eliminate surgical incisional pain.
3. Subjects with a body mass index (BMI) between 18 – 30, as subjects less than 18 may have experienced weakness from a pretreatment dose of nondepolarizing agent (atracurium).
4. ASA PSC of I or II, as sickly subjects (ASA PCS's > II) have increased reasons to experience postoperative myalgia.
5. Ambulatory (outpatient) subjects only, as these subjects would have been expected to exhibit the most postoperative myalgia.

Subjects were assessed to determine if any exclusion criteria applied to them. If so, they were not enrolled in the study. Exclusion criteria included the following:

1. Subjects not meeting inclusion criteria as described above.

2. Subjects' known to be pregnant, as it has been shown that pregnancy decreases the incidence of postoperative myalgia.
3. Subjects with co-existing disease states, as they would have fallen into an ASA PSC level of greater than II.
4. Subjects who were non-ambulatory, bedridden, or wheelchair bound, as SCh may have been contraindicated.
5. Subjects who experience shivering upon emergence, as this alone could have caused postoperative myalgia.
6. Subjects who did not have access to a telephone, as follow up calls would have not been possible.
7. Subjects younger than 18, as informed consent would have been a parental decision.
8. Subjects older than 50, as SCh-induced myalgias are reported less commonly in this group.
9. Subjects allergic to any of the study medications, or medications employed in the standard study plan (Appendix B).
10. Subjects with any conditions that would be contraindicated by the administration of any drug within the standard plan (e.g. Malignant Hyperthermia, neuromuscular disorders, or myofascial pain syndromes).
11. Any subject who was unable to give full voluntary and informed consent.
12. Any subject who received narcotic reversals, such as narcan.

Informed Consent

Informed consent (Appendix C) was obtained upon completion of the preoperative interview and determination that the subject met inclusion criteria. The use of this consent had been approved by the IRB's of both the University of Tennessee Medical Center-Knoxville, and the University of Tennessee, Knoxville prior to the initiation of the study (Appendix D). The study was explained in terms understandable to the subject, and the subject was given sufficient time to consider participation prior to providing consent. Subjects were ensured that they would not be treated differently, regardless of their decision concerning participation. Those who agreed to participate in the study were informed that, if at anytime they would better be served by being withdrawn from the study, the researcher would do so immediately and continue to provide any and all intervention that was required to safely care for them.

Study Protocol

Preoperatively, all subjects were premedicated with midazolam 0.025 mg/kg and an appropriate antibiotic as requested by the surgeon. Subjects were assigned by pharmacy to one of the following three double-blinded study groups by use of computer generated randomization.

1. Group A was pretreated with atracurium 0.05 mg/kg intravenously (IV) prior to the administration of 1.5 mg/kg IV of SCh.
2. Group B received 1.5 mg/kg of lidocaine prior to the administration of 1.5 mg/kg of SCh.

3. Group C received both pretreatment medications at the above indicated doses prior to the administration of 1.5 mg/kg IV of SCh.

It was decided by the researcher to avoid a control group since many studies indicate that a 50% incidence of postoperative myalgia can be expected from the administration of SCh. In addition, although the literature was not clear on the effectiveness of pretreatment when SCh is utilized, depriving subjects of a medication that might be of benefit by reducing postoperative discomfort was not ethically acceptable to this author.

The following study protocol was utilized on all groups:

1. After the researcher obtained informed consent, the subject was transported to the operating room and positioned on the operating table appropriately for the surgical procedure.
2. Standard ASA monitoring was utilized (Appendix E).
3. Pre-oxygenation was obtained with 100% oxygen for 2 minutes or 5 vital capacity breaths.
4. The pretreatment drug was given along with fentanyl 1.5 mcg/kg. (This dose of fentanyl was given to blunt stimulation from laryngoscopy and has not been demonstrated to affect myalgias in previous investigations).
5. Five minutes after the administration of the pretreatment drug an appropriate induction dose of propofol (2-2.5 mg/kg IV) was given for induction.
6. After complete muscle relaxation was verified, (0/4 twitches following ulnar nerve stimulation via cutaneous electrodes), tracheal intubation was

performed and endotracheal tube placement was verified by standard methods.

7. Anesthesia was maintained with oxygen, and air or nitrous oxide, and by titrating sevoflurane 0.6%-5% to hemodynamic stability and a surgical level of anesthesia. The Bispectral Index (BIS) monitor was utilized as an adjunctive monitor to help assess the subject's level of anesthetic depth.
8. If the subject's blood pressure and heart rate fluctuated (Appendix F) (increased or decreased) greater than 20% of base line, then vasodilators, vasopressors, inotropes, or chronotropes were administered as appropriate for the situation. If the subject failed to respond, they were eliminated from this study and further appropriate treatment was instituted.
9. The following drugs were administered as their need arose: narcotics, (fentanyl 2-10 mcg/kg), nondepolarizing muscle relaxants, antiemetics, steroids, antibiotics, vasoactive drugs, and muscle relaxant reversals. These medications were not part of the study protocol, but are routinely employed in the anesthetized patient. (See Appendix B for this study's formulary doses and adverse effects of drugs).
10. After completion of the surgery, anesthesia was discontinued. The subject was given 100% oxygen to breathe. They were extubated when extubation criteria were met (Appendix G). Following extubation, the subject was taken to the post-anesthesia recovery room. If the subject's nurse observed any postoperative shivering, it was documented on the

PMES in Appendix H. (Such subjects were withdrawn from the study, as shivering has been shown to cause myalgias).

11. All subjects were contacted 24, 48, and 72 hours postoperatively by telephone and asked the questions listed on the PMS (Appendix I). The researcher then rated and recorded the level of myalgias using the PMES (Appendix H).

As described, pre-treatment medications in all three groups were administered to subjects using a double-blind format. The surgical pharmacy randomly assigned subjects to one of the three study groups by computerized, random selection. Syringes of study medications were labeled with numbers (from 1-15) by the pharmacy staff for each patient enrolled in the study. The pharmacy was the only provider who knew which patient received which study medication prior to completion of the study. The pharmacy staff was instructed to disclose this information if and only when the following occurred:

1. All data had been collected.
2. The study was complete or it was closed.
3. Lastly, in the case that it became necessary to know what medications had been given, as in the case of an allergic reaction.

Every pretreatment medication came in a syringe that contained the same volume amount, regardless of the exact medication. This was done so the researcher in no way could identify which pretreatment medication was given. Dosages of all medications were calculated based on per kg of body weight by the pharmacy prior to anesthetic administration. At the end of the study, the

drugs were identified to conclude whether there was a difference between the pretreatment groups with respect to comparison of one another. The same researcher was used to gather all postoperative information regarding myalgia. This data was analyzed after the completion of data collection.

All subjects were assigned a number once enrolled in the study. Subjects were sequentially numbered 1-15. A Demographic Data Sheet (See Appendix J), served as the master enrollment list, and was maintained on all subjects who agreed to participate in the study. This data sheet contained the following information:

1. Name
2. Phone Number
3. Subject number (1-15)
4. ASA Class
5. Weight in Kg
6. Height in inches
7. Gender
8. Smoking history
9. Preoperative narcotic and NASID use (dose and duration)
10. Postoperative narcotic and NASID use (dose & duration)

For reasons related to postoperative data collection, it was necessary to maintain the subject's name and telephone number. However, subjects were not to be identified by any method other than on the Demographic Data Sheet, unless it became necessary for the safety of the subject as in the case of an

allergic reaction or unstable hemodynamics. As mentioned previously, such subjects would have been removed from the study. In these instances, the double-blinded protocol medication would have been revealed so as to provide the most appropriate and prompt intervention possible.

Instrumentation

The PMS (Appendix I) is a tool that was utilized by the researcher to confirm the patient was experiencing postoperative myalgia, as opposed to some other type of postoperative surgical discomfort. The PMS is a 14-question survey that determines the type, location, and amount of pain being experienced. Additionally, it inquired about the subject's activity level, as well as any treatments they attempted to help alleviate the muscular soreness. This survey has only been utilized in one previous study, which was discovered in the body of associated literature: The works of Mikat-Stevens, Sukhani, Pappas, Fluder, Kleinman, and Stevens (2000). Therefore, the PMS has no proven validity or reliability. Its use in this study is being justified by the following reasoning. Many past studies on the subject of SCh use and postoperative myalgia have failed to carefully distinguish between myalgia and surgical discomfort. The PMS aids the investigator in establishing this distinction, which was considered by this author to be of fundamental significance to the purpose of this investigation. Utilizing two tools within this study helped to assure, with greater confidence, that proper assessment of the type of postoperative pain was distinguished allowing for the overall study results to be truly reflective of postoperative myalgia as it related to perioperative SCh administration.

The PMES (Appendix H) is a four-point ordinal scale that measures the severity of postoperative myalgia from zero to three, where [0] indicates absence of pain other than characteristic surgical gas, [1] indicates mild muscle stiffness or pains, when specifically asked about, in the nape of the neck, or in shoulders and lower chest on deep breathing, [2] indicates moderate muscle stiffness and pains spontaneously complained of by the patient [3] indicates severe, incapacitating, generalized muscle stiffness or pain. Although the PMES, or very similar scale, has been used in several previous studies of comparable nature and scope as this one, this scale had no proven reliability or validity. However, numerous respected scientists have accepted this instrument as a valid and reliable measure of postoperative myalgia in subjects following the administration of SCh with general anesthesia. These same authors have utilized this instrument for the purpose it was used in this author's investigation. Such studies have had similar scope and intent as the current one (Mingus, Herlich, & Eisenkraft, 1990; McLoughlin, Elliot, McCarthy, Mirakhur, 1992; Raman & San, 1997). All such authors have been published in a variety of respected and refereed scientific medical journals including: *Anaesthesia* and the *Canadian Journal of Anaesthesia*. Consequently, since there were no alternative tools that existed which had a proven higher index of validity or reliability, this author chose to utilize these two tools in the current study in hopes of obtaining a more accurate picture of the phenomena of postoperative myalgia in relation to SCh administration. The goal of using these two tools was to accurately measure the occurrence and severity of postoperative myalgia

following SCh administration subsequent to the pretreatment of atracurium, lidocaine, or the combination of the two. Since it was important to maintain consistency and provide reliable measurements of postoperative myalgia, the same researcher administered the survey and rated the severity of soreness to study subjects for up to 72 hours postoperatively (See protocol #11).

Data Analysis

Comparison of the mean scores of the three study groups would traditionally have been performed by analysis of variance (ANOVA) utilizing parametric testing. However, this statistical application would have required a specific distribution of the mean and variance. Testing of the PMES lies within a gray area, and such, a distribution could not be assumed. Therefore, a nonparametric ANOVA with post-hoc analysis was employed. Specifically, the Kruskal-Wallis, a test for two or more independent samples, and the Bonferroni test utilizing a significance level of $p \leq 0.05$ was employed.

The Kruskal-Wallis test calculates results based on the sums of the ranks of the combined groups in the PMES. For example, the scores for each variable (0, 1, 2, 3) was ranked, and the mean ranks for the variables were compared. If a significant difference was found ($p \leq 0.05$) a post-hoc analysis utilizing the Bonferroni method was planned to be employed to identify where the difference occurred. Because this method is more sensitive in small comparisons, it was utilized in this pilot study of 15 subjects. Such methods were utilized not only to determine which pretreatment medication(s) were significantly effective in

reducing postoperative myalgia, but also to determine which postoperative day subjects experienced the most/least myalgia.

Assumptions

The basic assumptions made regarding this study were as follows:

1. The PMS and PMES were predictive and accurate instruments for measuring postoperative myalgia.
2. The population sample was representative of a random sample.
3. The researcher was consistent at determining if the pain was myalgia verses surgical discomfort.
4. The researcher consistently rated the postoperative myalgia as described by the patient in the PMES.

Study Limitations

1. The review of the literature may not have been wholly reflective of reality.
2. There may have been unanticipated individual varying responses to the prescribed anesthetic plan.
3. There may have been sources of error concerning myalgia during data collection. However, this study attempted to take this into account by:
(A) utilizing two tools that had been used significantly within the anesthesia literature, and (B) having the same researcher gather/rate the levels of myalgia.
4. In regards to conclusions, to using the pretreatment medications of atracurium, lidocaine, or a combination of medications may not be able to

be generalizable to larger populations because of this pilot study's small sample size.

5. Because the average incidence of SCh-induced postoperative myalgia is only 50% according to the literature, the benefits of a control group may have been useful for comparison.
6. Neither the PMS nor PMES being utilized to measure postoperative myalgia has undergone extensive psychometric testing for validity or reliability.
7. This study made no attempt to control for the amount or type of medications that were prescribed and utilized by the subject preoperatively. Data on subject use of medications preoperatively, however, was collected.

Specific Risks and Protection Measures for Human Subjects

All medications utilized for this study have side effects that could have caused adverse reactions (Appendix B). Although rare, some possible side effects that could have occurred included nausea, vomiting, sedation, prolonged muscle weakness, high potassium, increased body temperature, and seizures. Such reactions may have occurred in subjects receiving these drugs in the course of anesthesia regardless of whether or not the patient was participating in the study. Therefore, although there were associated risks to subjects in relation to their participation in this study, the potential for additional physical, psychological, social, legal, or other risks were estimated to be no greater than those compared to surgical subjects who did not enroll in this study and who

had received the same anesthetic medications and interventions commonly utilized in acceptable anesthetic practice. No drug or procedure in this study was proposed to be used in any manner that was outside of the normal anesthetic standard of care or acceptable patient care practice. Consequently, no additional amount of risk for injury was predicted for any subjects who agreed to participate in the study.

Anonymity and confidentiality of data collected was indefinitely maintained. During the data collection phase, and at all times following this period, all data was under the direct supervision and control of the researcher, or an authorized assistant. Each subject was assigned a number (not the medical record or social security number), and other than the Demographic Data Sheet/Master Subject List (for purposes of follow up call and data collection), no linkage between the subject and subject number was made. Storage of this information will be maintained in a locked area within the anesthesia department at the University of Tennessee Medical Center-Knoxville for a period of five years following the study. At the conclusion of this time period, the records will be destroyed by means of shredding.

Although such patient data safeguards, as above, are included in the design of this study, patient data may be released through publication of research findings in such a fashion that subjects may be able to identify themselves with their data. This remote possibility is no greater for this study than any other research project. Lastly, upon postoperative follow-up at 24, 48, and 72 hours,

the PMS (Appendix I) was utilized to assure that no physical, psychological, or social damage occurred as a result of this study.

Study Benefits

In conclusion, there are currently no proven therapeutic alternatives to the treatment of postoperative myalgia. Many studies have undertaken the task to examine this concept. However, to date, study results have been inconclusive in yielding definitive results. Therefore, potential benefits of this study, which established the justification for conducting this investigation, included the following:

1. A more comfortable recovery.
2. Decreases in the loss of productivity through earlier return to preoperative level of functioning, with respect to the individual subject's baseline in activities of daily living related to decreased myalgia postoperatively.
3. Fewer returns to the emergency room related to postoperative discomfort and concern over the source of discomfort.
4. The potential for a decreased need of postoperative pain medication.
5. The potential for decreases in health care expenditures related to poor resource utilization.

Chapter IV

Results

This chapter presents the results of this author's pilot study, which was designed to compare the efficacy of atracurium, lidocaine, and the combination of the two therapies on the outcome of postoperative myalgia following the administration of SCh during general anesthesia. The purpose of this investigation was not to document statistical significance in relation to premedication efficacy for such a small pilot population, but rather to determine the overall feasibility of conducting a larger study. Additionally, a secondary purpose of this pilot study was to look for trends within this population that might contribute to outcome and indicate clinical importance with need for further and future investigation.

As this study has shown, besides the use of SCh, other influential factors can contribute to postoperative myalgia including ASA PSC, history of cigarette smoking, surgical position, the use of pre-surgical pain medications and surgical type. Therefore, the purpose of this chapter is two-fold: First to provide the outcome of differing pretreatment groups on postoperative myalgia, and second to offer descriptive statistics about the population, the above influential factors, and their interactions with the pretreatment groups. Through the use of these results, this author contends that further support and investigation is indeed justified and that the conduction of a larger study on SCh use and myalgia is warranted.

Descriptive Statistics

The study population was comprised of 15 subjects undergoing elective laparoscopic surgery requiring general anesthesia with the use of SCh. Of the 15 enrolled in the study, two were excluded. One subject was excluded due to a change in intraoperative procedure, and the other subject was excluded because of the unforeseen use of a laryngeal-tracheal anesthetic (LTA) that contained lidocaine. Use of this intervention could have potentially influenced the observed results and therefore altered the outcome of the study. Of the remaining 13 subjects, gender distribution included 12 (92%) females and one male (8%) who ranged in age from 21 to 46, with a mean age of 33. All subjects were healthy with eight (62%) having an ASA PSC of I, and 5 (38%) being an ASA PSC of II. Two subjects (15%) were smokers, and eight (62%) were taking nonsteroidal or narcotic medications for pain prior to surgical intervention.

The 13 subjects were placed in one of three computer randomized pretreatment groups: (1) atracurium 0.05 mg/kg, (2) lidocaine 1.5 mg/kg, (3) or a combination of atracurium 0.05 mg/kg and lidocaine 1.5 mg/kg. Because past studies have indicated that there is a 50% incidence in SCh postoperative myalgia without any pretreatment, this author felt it unethical to include such a group for control (Wong & Chung, 2000). Therefore, since the main purpose of the study was to determine the feasibility of instituting the scientific investigation, and also whether these small pilot groups would follow the recurring trends that are found within today's research literature, lack of a control group was not of issue to this author or other investigators performing this study.

Pretreatment Group Efficacy

After one of the researchers obtained subject consent, a hospital pharmacist was responsible for keeping track of the subjects computerized randomized classification, as well as compounding and preparing the correct study drug regimen for administration. As a result, the subjects were well distributed in the three pretreatment groups with five subjects (38%) in the atracurium group, four (31%) in the lidocaine group, and four (31%) in the combination atracurium and lidocaine group. In terms of pain intensity, the results from the subjects in each pretreatment group were then compared to one another each day (for a total of three days). This author utilized the Kruskal-Wallis test, a nonparametric version of the one-way analysis of variance for independent samples, which was calculated based on rank sums of the pretreatment groups for comparison between the pretreatment groups. It is important to note that intensity and the number of participants experiencing pain over the course of three days is different. Table 2 and Figure 2 describes and illustrates the percent of each group experiencing pain, while the rest of this section predominantly refers to intensity of pain.

A comparison of the mean scores of intensity of pain for the first postoperative day is presented in Table 3 and illustrated in Figure 3. No significant difference was found between any of the pretreatment groups. In other words, statistically speaking, none of the pretreatment medications exhibited any increased ability to prevent postoperative myalgia when compared to the others. However, as

Table 2.

Postoperative Myalgia: Percent of each Pretreatment Group per Day

	Day 1	Day 2	Day 3
Atracurium	60%	40%	20%
Lidocaine	50%	50%	50%
Combination	50%	50%	50%

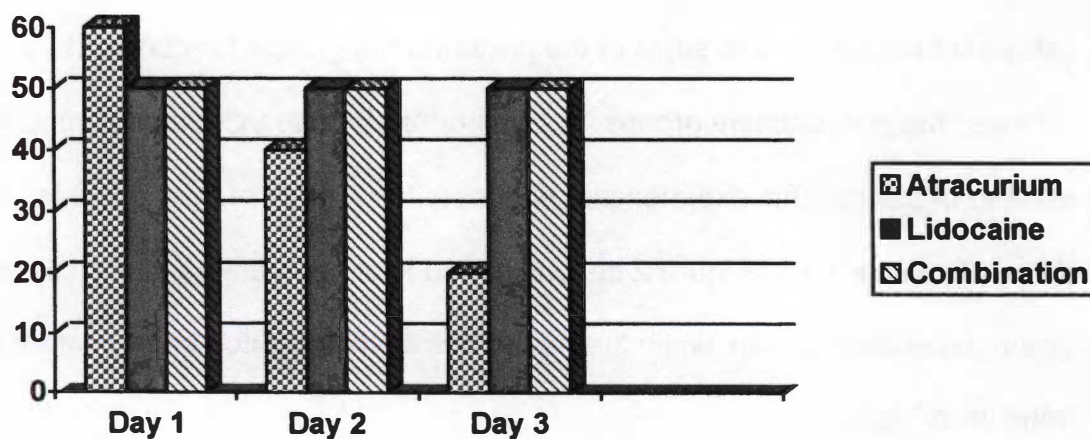


Figure 2.

Postoperative Myalgia: Percent of each Pretreatment Group per Day

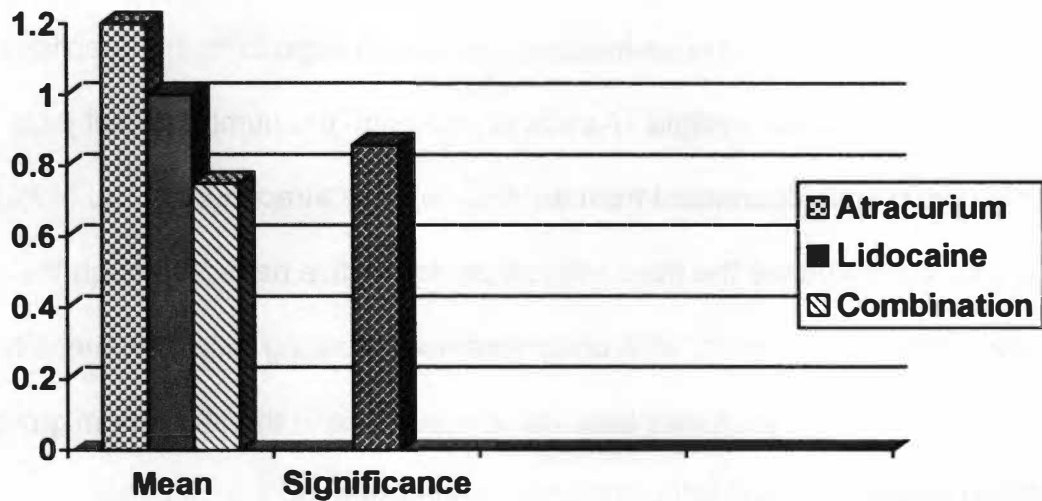
Table 3.

Pain Comparison of Pretreatment Groups on Postoperative Day One

	Mean	Standard Deviation	Significance (Kruskal-Wallis)	Age Range	Mean Age
Atracurium	1.20	1.30	NS – 0.858	32 - 46	41
Lidocaine	1.00	1.15	NS – 0.858	22 - 30	27
Combination	.75	0.96	NS – 0.858	21 - 41	31

* = Significant difference at the $\alpha = 0.05$ level

NS = Not Significant



* = Significant difference at the $\alpha = 0.05$ level

Figure 3.

Pain Comparison of Pretreatment Groups on Postoperative Day One

mentioned above, the atracurium group was found to have the most postoperative myalgia on day 1, with 60% of subjects having pain, followed by 50% within both the lidocaine and combination groups. Although the same percentage of subjects complained of pain in the latter two groups, the combination group was found to have reported less intense pain scores regarding postoperative myalgia on day one, in comparison to the subjects in the atracurium and lidocaine group. This was a finding that is well supported within the literature (Raman & San, 1987).

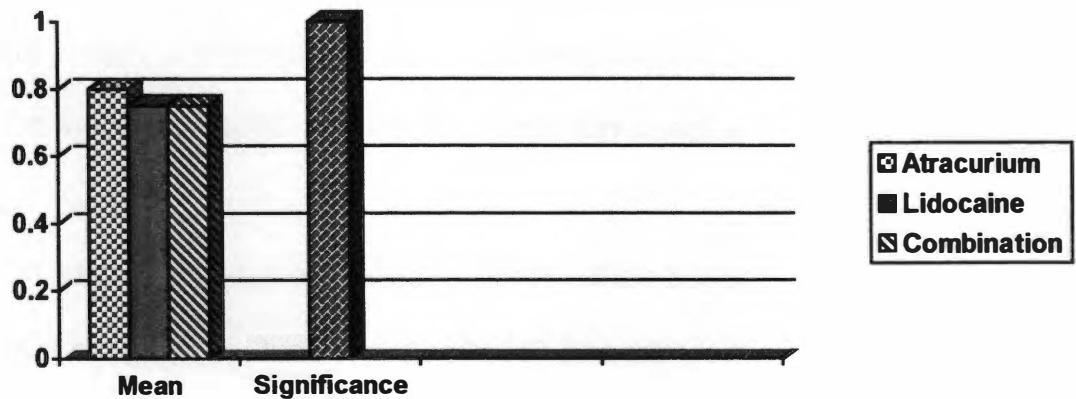
Table 4 and Figure 4 describes and illustrates the comparison of the mean scores for intensity of postoperative pain in the three pretreatment groups on postoperative day two. Like the first postoperative day, no significant difference was found among any of the pretreatment groups in regards to the intensity of reported postoperative myalgia. As above, although the number of subjects complaining of pain decreased from the first day, the atracurium group (40%) continued to experience the most intense postoperative pain. Although the lidocaine group remained at 50% of subjects experiencing pain, the intensity reported by these subjects was less than the subjects in the atracurium group. Lastly, in the combination lidocaine/atracurium group, 50% of subjects complaining of pain did not exhibit any decrease in the intensity of postoperative pain from day one. This was unlike the subjects in the atracurium and lidocaine groups. This was a surprising finding since this had not been reported in the literature (Melnick, Chalasani, Uy, Phitayakorn, Mallett, & Rudy, 1987).

Table 4.

Pain Comparison of Pretreatment Groups on Postoperative Day Two

	Mean	Standard Deviation	Significance (Kruskal-Wallis)	Age Range	Mean Age
Atracurium	0.80	1.10	NS – 1.000	32 – 46	41
Lidocaine	0.75	0.96	NS – 1.000	22 – 30	27
Combination	0.75	0.96	NS – 1.000	21 – 41	31

* = Significant difference at the $\alpha = 0.05$ level
 NS = Not Significant



* = Significant difference at the $\alpha = 0.05$ level

Figure 4.

Pain Comparison of Pretreatment Groups on Postoperative Day Two

As described in Table 5 and illustrated in Figure 5, there was no significant differences in terms of intensity of postoperative myalgia demonstrated between the three pretreatment groups on postoperative day three. Although the atracurium group had started out with the most pain (60%) on day one, it had gradually decreased each consecutive day and actually ended up reporting the least amount (20%) of pain by postoperative day three. One subject, however, continued to experience pain on postoperative day number three, and reported the intensity of their pain as moderate.

In terms of the amount of pain, 50% of the subjects in the lidocaine group, on day three reported the same amount of pain as the atracurium group in terms of intensity. Although this group started out reporting mid-range levels of pain intensity on day one (between atracurium and the combination group) and decreased slightly on day two, they did not improve by day three. Again, this was an interesting finding that is not congruent with the current literature of Melnick and associates.

Additionally, as mentioned earlier in this chapter, the subjects in the combination group of atracurium and lidocaine started out reporting the least amount of intense pain. However, the scores reported by the subjects in this group on postoperative day two was exactly the same as on postoperative day one. Although, subjects within the combination group continued to improve in terms of pain intensity, they surprisingly reported pain scores that fell between the scores reported by the subjects in the atracurium and lidocaine groups on day three. This too, was a finding that differed from current literature.

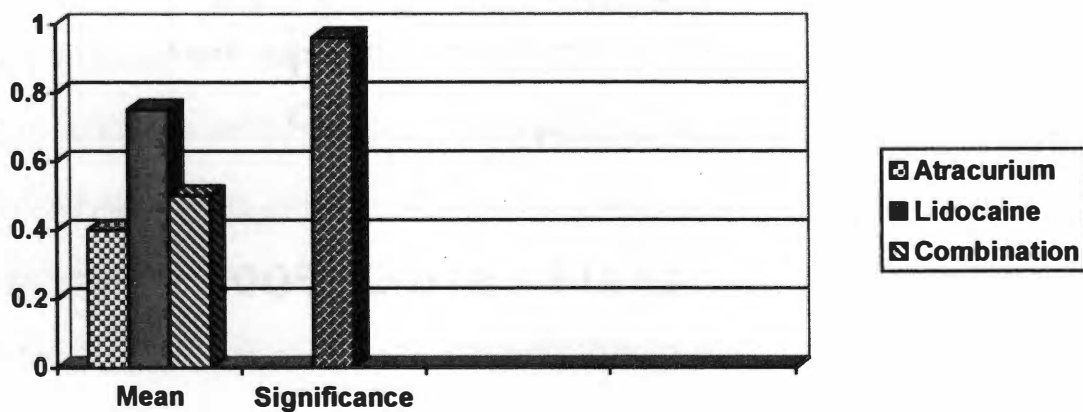
Table 5.

Pain Comparison of Pretreatment Groups on Postoperative Day Three

	Mean	Standard Deviation	Significance (Kruskal-Wallis)	Age Range
Atracurium	0.40	0.89	NS – 0.725	32 - 46
Lidocaine	0.75	0.96	NS – 0.725	22 - 30
Combination	0.50	0.58	NS – 0.725	21 - 41

* = Significant difference at the $\alpha = 0.05$ level

NS = Not Significant



* = Significant difference at the $\alpha = 0.05$ level

Figure 5.

Pain Comparison of Pretreatment Groups on Postoperative Day Three

Additionally, on day three the combination lidocaine/atracurium group continued to exhibit 50% of its subjects complaining of postoperative myalgia.

ASA Physical Status Classification and Postoperative Myalgia

As is evident from examining the results listed in Table 6 and illustrated in Figure 6, ASA PSC did not have a statistical significance on postoperative myalgia. This is not unexpected due to small sample size. However, some potentially interesting clinical aspects arise from comparing ASA PSC to postoperative myalgia. Within this pilot study, 62% of subjects were classified as ASA PSC I, while 38% were ASA PSC II. Of the eight subjects classified as ASA PSC I, three (37.5%) were in the atracurium group, four (50%) were in the lidocaine group, and one (12.5%) was in the combination group. Within the ASA PSC I group, three individuals (37.5%) complained of pain. The lidocaine group exhibited the most pain during day one (50%), followed by the atracurium group (33%). The combination lidocaine/atracurium group in this class (ASA PSC I) remained pain free on day one. Additionally, as an experienced anesthesia practitioner might anticipate for this collection of subjects, the lidocaine group reported the highest pain scores, with two individuals declaring their pain as moderate on the first postoperative day.

On day two and three, only two subjects (25%) exhibited pain within this ASA PSC I sub classification. On both days, these were subjects from the lidocaine group and they rated their pain scores as mild and moderate.

The ASA PSC II group contained five (38%) subjects. Four (80%) of these subjects complained of pain on the first postoperative day. This was a much

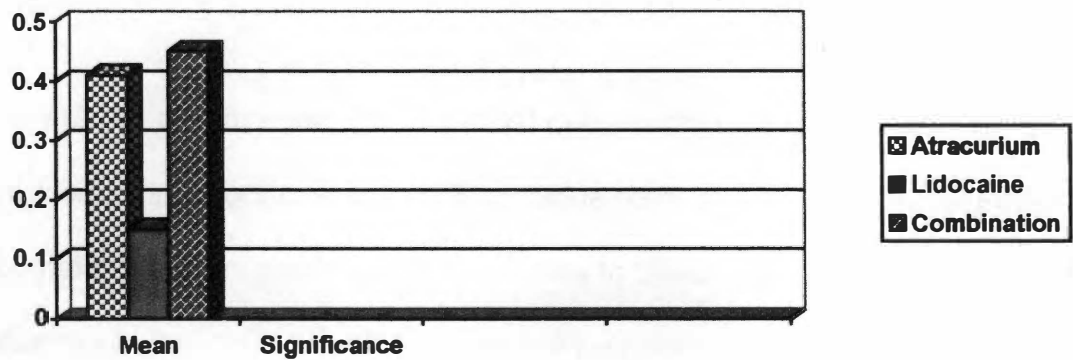
Table 6.

ASA Physical Status Classification and Postoperative Myalgia

	Day 1 Pain	Significance (Kruskal-Wallis)	Day 2 Pain	Significance (Kruskal-Wallis)	Day 3 Pain	Significance (Kruskal-Wallis)
ASA	0.41	NS	0.15	NS	0.45	NS

* = Significant difference at the $\alpha = 0.05$ level

NS = Not Significant



* = Significant difference at the $\alpha = 0.05$ level

Figure 6.

ASA Physical Status Classification and Postoperative Myalgia

higher incidence when compared to the ASA PSC I group, where only 37.5% reported pain. Additionally, the ASA PSC II group did not have any subjects in the lidocaine group. Therefore, comparisons between the pretreatment groups and ASA PCS I and II was limited since the ASA PSC II group did not contain any subjects in one of the pretreatment groups. This finding is interesting when one considers the fact that the lidocaine group reported the highest pain scores on all three days in the ASA PSC I group. Therefore, this leads this author to postulate that perhaps subjects classified as an ASA PSC II may have a higher incidence of postoperative myalgia when SCh is used in conjunction with a general anesthetic.

When further examining this group (ASA PSC II), two subjects (40%) were in the atracurium group, while three subjects (60%) were in the combination group. All subjects (100%) complained of pain in the atracurium group with rated pain scores of moderate and severe on postoperative day one, while two subjects (67%) in the combination group complained of pain with ratings of mild to moderate. Following progression to postoperative day two, the amount and intensity of pain for the combination lidocaine/atracurium group remained the same on day two as reported on day one. The amount and intensity of pain scores for the atracurium group improved, as all subjects rated their pain as moderate. By day three, both groups had improved in amount and intensity of pain. The atracurium group had only one subject (50%) complaining of moderate pain and the two subjects (67%) within the combination atracurium/lidocaine group reported only mild pain ratings.

Smoking History and Postoperative Myalgia

Of the 13 subjects, only two (15%) were smokers. Both subjects had significant smoking histories of one to two packs of cigarettes consumed per day for five years. Interestingly enough, postoperative pain studies revealed that these individuals had higher pain scores that lasted (and did not improve) for the duration of the third postoperative day. Table 7 and Figure 7 displays and illustrates this data. In addition, further analysis revealed that each of these two subjects received the combination pretreatment.

Recalling the pattern of this group (which started out reporting the least amount of intense pain, but increased to an average amount of intense pain) suggests that smoking may be an influential factor responsible for increasing postoperative pain in subjects who receive SCh. However, as the following data will show, further analysis also revealed other factors that may have contributed to this outcome: Lithotomy position during anesthesia, subjects self-administering medications prior to surgical intervention, and the fact that both individuals had diagnostic laparoscopic procedures.

Nonsmokers (85%) were members of all three pretreatment groups. They were found to demonstrate the general population trends that have been previously noted within each pretreatment group. The atracurium group had the most number of subjects and 60% of these subjects reported the most intense, severe pain on the first postoperative day. The lidocaine group had a 50% incidence of moderate pain, and surprisingly, the combination group did not report any pain.

Table 7.

Smokers and Nonsmokers: Postoperative Pain

	Day 1 Mean pain score	Standard Deviation	Day 2 Mean pain score	Standard Deviation	Day 3 Mean pain score	Standard Deviation
Nonsmoker	0.91	1.14	0.64	0.92	0.45	0.82
Smoker	1.50	0.71	1.50	0.71	1.50	0.71

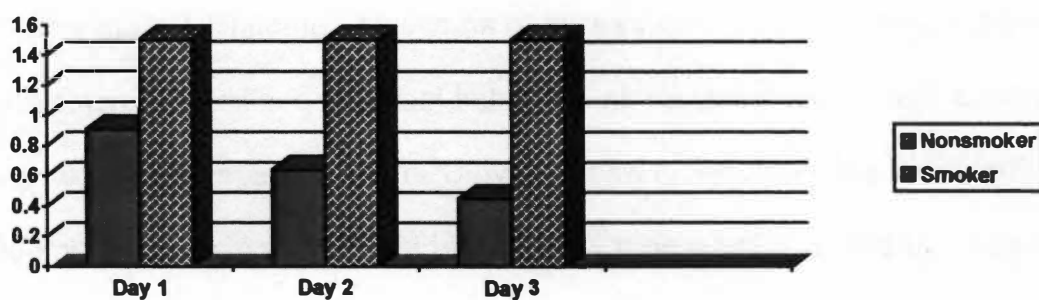


Figure 7.

Smokers and Nonsmokers: Postoperative Pain

For postoperative days two and three, reported levels of pain in the atracurium group declined in frequency as well as intensity. 40% of the subjects reported with moderate pain and 20% of the subjects reported with mild pain. The lidocaine group (50%) continued to repeat the same frequency and intensity with mild and moderate pain reported on both days. Again, ironically, the combination atracurium/lidocaine group reported being free from pain for both days.

Surgical Position

This study involved the enrollment of subjects who were having surgical procedures that required they be placed in either the supine or the lithotomy position. Although not statistically significant, as indicated by Table 8 and illustrated by Figure 8, when subject position is broken down and evaluated separately it does appear to have some clinical significance in reference to postoperative pain. Eight (61.5%) subjects were in lithotomy, while five subjects (38.5%) were in supine position.

As Table 9 and Figure 9 demonstrate, those subjects in lithotomy position did experience more postoperative myalgia for all three days as compared to those subjects who remained in supine position. These findings lead this author to question if lithotomy position may have been a contributing factor to postoperative myalgia in these subjects.

There were subjects enrolled in all three pretreatment groups who were placed in lithotomy or supine positions. However, when examining only subjects in the supine position, only one individual complained of pain for all three

Table 8.

Surgical Position and Postoperative Myalgia

	Day 1 Pain	Significance (Kruskal-Wallis)	Day 2 Pain	Significance (Kruskal-Wallis)	Day 3 Pain	Significance (Kruskal-Wallis)
Position	0.28	NS	0.19	NS	0.33	NS

* = Significant difference at the $\alpha = 0.05$ level

NS = Not Significant

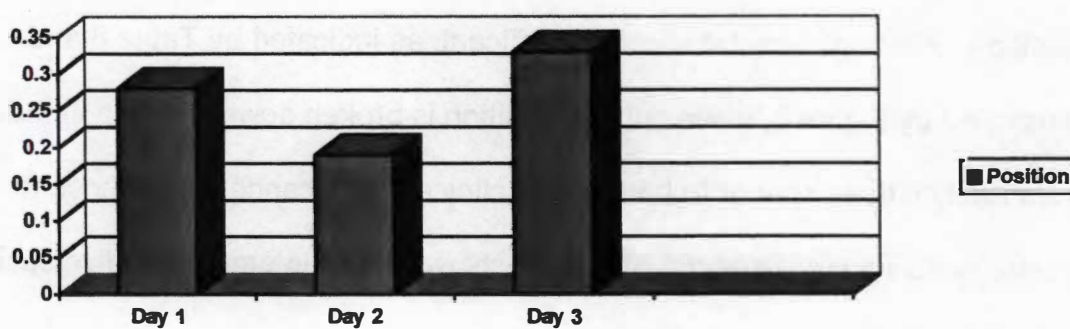


Figure 8.

Surgical Position and Postoperative Myalgia

Table 9.

Surgical Position and Postoperative Myalgia: Lithotomy and Supine

Position	Day 1 Mean	Standard Deviation	Day 2 Mean	Standard Deviation	Day 3 Mean	Standard Deviation
Lithotomy	1.38	1.06	1.13	0.99	0.63	0.74
Supine	0.40	0.89	0.20	0.45	0.40	0.89

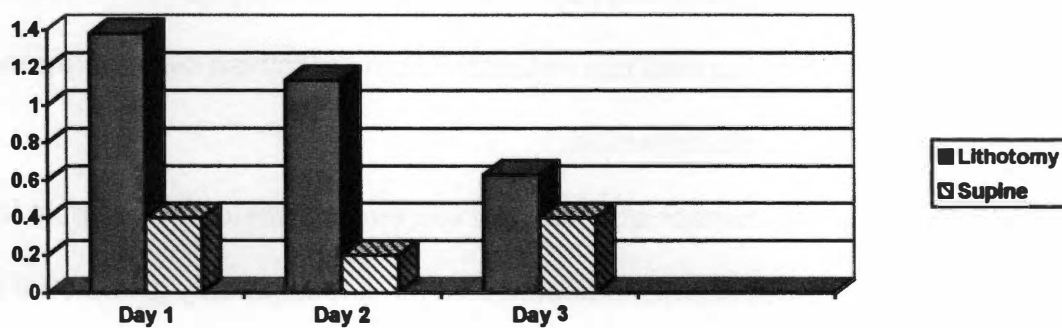


Figure 9.

Surgical Position and Postoperative Myalgia: Lithotomy and Supine

postoperative days. This subject was in the lidocaine only group and reported moderate pain on postoperative day one, mild pain on the second day postoperatively, and moderate pain by the third postoperative day.

Of subjects who were positioned in lithotomy, patterns of postoperative pain somewhat followed the general trends as detailed previously in this chapter for the pretreatment groups. The atracurium group started out with the most subjects (75%) complaining of pain and subjects who complained of the greatest intensity of pain. Over the three days of postoperative data collection, subjects complaining of pain gradually decreased to 50% and 25% by days two and three respectively. Subjects reported pain intensity did not diminish over the three days of postoperative data collection.

With respect to the number of subjects experiencing postoperative pain in the lithotomy position, study results indicated that the lidocaine only group (100%) and combination group (66%) reported similar discomfort for all three postoperative days. Both groups also reported the same pain intensity scores for the first two postoperative days, with lidocaine (1 subject) being moderate, and the combination group (3 subjects) being mild and moderate. By the third postoperative day, both groups also exhibited a decline in pain with lidocaine becoming mild, and the subjects in the combination group also reporting their pain as being only mild.

Pain Medication use Prior to Surgical Intervention and Postoperative Myalgia Again, as indicated by Table 10 and Figure 10, statistical significance between the use of medication and postoperative myalgia was not demonstrated

Table 10.

Premedication and Postoperative Myalgia

	Day 1 Pain	Significance (Kruskal-Wallis)	Day 2 Pain	Significance (Kruskal-Wallis)	Day 3 Pain	Significance (Kruskal-Wallis)
Medication	0.84	NS	0.61	NS	0.20	NS

* = Significant difference at the $\alpha = 0.05$ level

NS = Not Significant

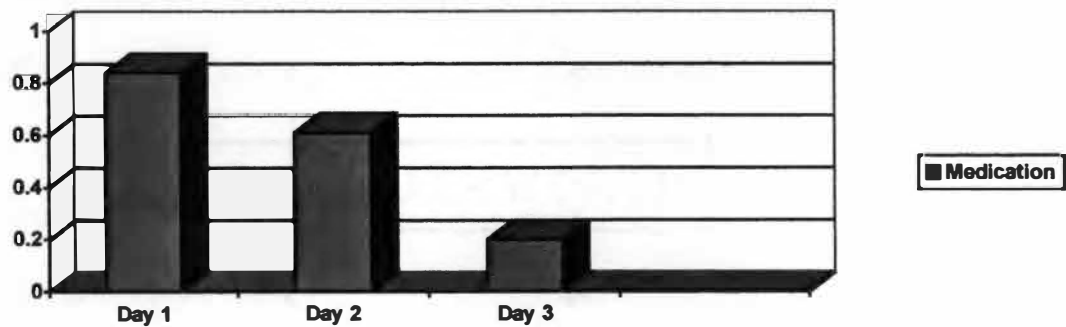


Figure 10.

Premedication and Postoperative Myalgia

due to small sample size. However, when analyzing this group independently, there does appear to be at least some clinical significance. Fifty-four percent (7 subjects) were taking some type of pain medication (either nonsteroidal or narcotics) prior to surgical intervention.

As Table 11 and Figure 11 will indicate, these individuals reported higher postoperative pain scores for all three days, than did those who were not taking any type of pain medication preoperatively. Additionally, subjects who did not report preoperative pain medication use required less postoperative pain medication as compared to subjects who reported taking pain medications preoperatively. Although the data was not collected, it would be interesting to find out how long such individuals had been taking pain medications prior to surgery in order to address: (1) Is there a greater incidence of postoperative myalgia in those who suffer from chronic pain as opposed to those with acute pain? And (2) how would this affect postoperative pain management?

Obviously, these are questions to explore for future study.

Type of Surgery and Postoperative Myalgia

The population for this pilot study involved only laparoscopic surgeries in an effort to distinguish postoperative myalgia from incisional pain. Therefore, this study involved the following various types of laparoscopic procedures:

Diagnostic laparoscopic procedures (62%), cholecystectomies (15%), tubal ligations (15%) and herniorrhaphies (8%). However, because of the limited population, not all surgical types were represented within each study group. As previously discussed in this chapter, statistical analysis of each surgical

Table 11.

Premedication Prior to Surgical Intervention and Postoperative Myalgia

	Day 1 Mean	Standard Deviation	Day 2 Mean	Standard Deviation	Day 3 Mean	Standard Deviation
Premed use	1.14	1.22	1.00	1.00	0.71	0.76
No Premed use	0.83	0.98	0.50	0.84	0.33	0.82

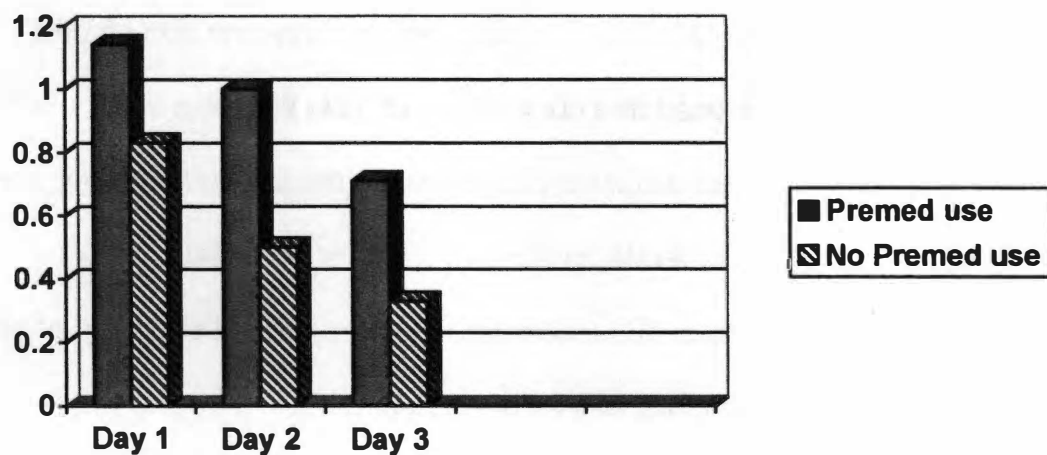


Figure 11.

Premedication Prior to Surgical Intervention and Postoperative Myalgia

procedure in groups containing adequate numbers of subjects could yield significant statistical results. Since this was a pilot study, determining statistical significance was not a goal. Therefore, this section will only provide descriptive data on those subjects that agreed to participate in the study. As the data Table 12 and Figure 12 illustrates, there was no statistical significance found between surgical type and postoperative myalgia.

Diagnostic Laparoscopic Procedures

Subjects undergoing diagnostic laparoscopic procedures were enrolled in the atracurium group (37.5%), lidocaine group (25%), and a combination atracurium/lidocaine group (37.5%). On postoperative day one six subjects (75%) having diagnostic procedures complained of pain, with pain scores ranging from mild to severe. All three subjects (100%) within the atracurium group had pain, reporting it as mild, moderate, or severe. On this same day, 50% (1 subject) of the lidocaine group had moderate pain, and 66% (2 subjects) of the combination group had both mild and moderate pain.

For postoperative day two, only five (63%) subjects complained of pain after a laparoscopic, diagnostic procedure. The lidocaine and combination groups did not differ in amount or rating of pain from day one. The only change came in the atracurium group. Here, only 2 subjects (66%) complained of pain, both reporting their pain as moderate. Therefore, it can be said that in this group, one patient felt better, and another felt worse on postoperative day two.

On the third postoperative day, only four (50%) subjects continued to complain of myalgia after their diagnostic laparoscopic procedure. These

Table 12.

Surgical Type and Postoperative Myalgia

	Day 1 Pain	Significance (Kruskal-Wallis)	Day 2 Pain	Significance (Kruskal-Wallis)	Day 3 Pain	Significance (Kruskal-Wallis)
Surgical Type	0.33	NS	0.21	NS	0.35	NS

* = Significant difference at the $\alpha = 0.05$ level

NS = Not Significant

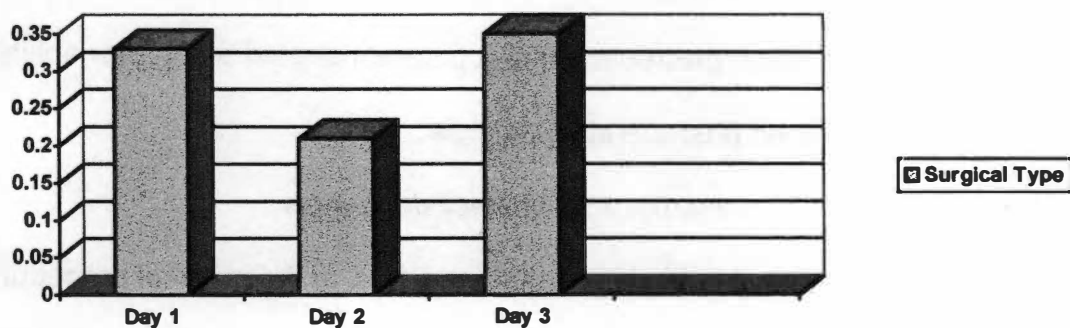


Figure 12.

Surgical Type and Postoperative Myalgia

comprised of 33% of the subjects in the atracurium group (1 subject), 50% of the subjects (1 subject) in the lidocaine group, and 66% of the subjects (2 subjects) in the combination group. As noted, in terms of percentages in the amount of pain, no change from day one was observed for the lidocaine group or the combination atracurium/lidocaine group except that pain was rated as mild in both groups. Although the greatest percentage of subjects complaining of pain (mild) were in the combination group, this observation could be deceiving, as the atracurium group had the worst description of pain (moderate) at the third postoperative day. Therefore, from a clinical practitioner's perspective, it is difficult to conclude which pretreatment group demonstrated a superior ability for preventing SCh-induced postoperative myalgia.

Laparoscopic Cholecystectomies

Laparoscopic Cholecystectomies comprised 15% of the surgical procedures performed on subjects enrolled in this study. This group was composed of only two subjects, with one subject representing the atracurium pretreatment group, and the other subject from the lidocaine pretreatment group. It is interesting to note that neither subject complained of pain on any of the three monitored postoperative days. Further analysis revealed that both subjects were female aged 40 and 41, nonsmokers, in supine position during anesthesia, and taking pain medications prior to surgical intervention. Additionally, they were from two different ASA PSC groups (I and II, respectively). It was ironic that these two subjects had increased risk factors for postoperative myalgia, such as (1) being female, (2) being middle-aged, and (3) taking pain medications prior to surgery,

yet neither exhibited any reported postoperative pain. These results suggest that other factors, besides the administration of SCh may play a role in the development of postoperative myalgia.

Laparoscopic Tubal Ligations

Laparoscopic Tubal Ligations comprised 15% of the surgical procedures performed on subjects who agreed to participate in this study. However, only the combination atracurium/lidocaine pretreatment group underwent this type of surgical intervention. Therefore, descriptive analysis of this surgical group presents inconsistent results at best. For example, on postoperative day one, one subject reported no pain and the other reported moderate pain. On postoperative day number two, one subject continued to report no pain, while the other reported an improvement from moderate to only mild pain. However, on the last postoperative day, the individual who reported mild pain on day two digressed to moderate pain. The other subject continued to remain pain free for all three days.

Further analysis revealed that both subjects were ASA PSC I females, aged 28 and 26 years, nonsmokers, positioned supine during anesthesia, and did not take any medications prior to surgical intervention. Since these two subjects were very similar, pretreated with the same pretreatment group, and had very differing responses to pain, this once again is suggestive that some other mechanism may contribute to postoperative myalgia in subjects who receive SCh.

Laparoscopic Herniorrhaphies

Laparoscopic hernia repairs consisted of only 8% (1 subject) of the surgical cases in this study. This subject was a 46 year-old male. He received atracurium as a pretreatment medication prior to the administration of SCh. Interestingly enough, he reported no pain for all three postoperative days. Further analysis revealed he was an ASA PSC I, nonsmoker, in supine position during anesthesia, and did not take any pain medications prior to surgical intervention. Thus, other than age, had very few risk factors associated with the development of postoperative myalgia.

As one can see from these results, many factors can play a role in the development of postoperative myalgia. This study confirmed several trends, which have been previously reported within the literature in regards to postoperative pain and myalgia. These include that the incidence of postoperative myalgia following SCh administration is: (1) Greatest in females, (2) increased in incidence in those patients closer to age 50, and (3) greater in subjects who are forced (by necessity of the nature of surgery) to assume varying positions (other than supine) during the anesthetized period. The results of this author's study has raised many new potential questions focusing on issues of: (1) Cigarette smoking, (2) preoperative pain medication utilization prior to surgical intervention, (3) ASA PSC on postoperative myalgia/pain, and (4) the effect of the type of surgical intervention in relation to postoperative myalgia. Obviously, the relationship of SCh with postoperative myalgia warrants further

study. Most likely many factors including those mentioned above, as well as others, may be contributing to this complex and poorly understood phenomenon.

Chapter V

Discussion

Current literature suggests that the average incidence of postoperative myalgia is approximately 50% for patients that receive SCh without any pretreatment regimen (Wong & Chung, 2000). Although the relationship between SCh and myalgia is not well established, this author believes the literature that supports the theory that pretreatment will provide a protective effect against the occurrence of postoperative myalgia when SCh is utilized (Pace, 1990; Raman & San, 1997). However, as mentioned earlier, determining an efficacious pretreatment regime was not the goal of this study. Rather, determining feasibility of conducting a larger study, and documenting trends within a small, experimental population that might signify clinical significance, warrant the need for research in this area. Indeed, as the rest of this chapter will describe, this study provided the basis for the formation of numerous new research questions, as well as debate the findings of old research questions, regarding the phenomena of postoperative myalgia attenuation following the use of SCh as a component of a general anesthetic.

Pretreatment Group Efficacy

Although the exact cause of SCh-induced postoperative myalgia is unknown, the current standard pretreatment utilizes the administration of a nondepolarizing agent three minutes prior to SCh administration (Wong & Chung, 2000). However, many have argued that the use of lidocaine is as effective as nondepolarizing agents. Additionally, lidocaine does not cause unwanted side

effects such as undesirable intubating conditions, the need to use higher amounts of SCh and delayed return of spontaneous respiration (Haldia, Chatterji, & Kackar, 1974). Furthermore, combination therapy utilizing lidocaine and a nondepolarizer have been shown to improve results in diminishing SCh-induced postoperative myalgia (Melnick, Chalasani, Uy, Phitayakorn, Mallett, & Rudy, 1987). These potential benefits formed the basis of support for this author's choices of study pretreatment medications.

As expected, due to the small sample size, analysis of data between postoperative myalgia and the efficacy of each pretreatment group did not reveal any of the pretreatments as superior for preventing postoperative myalgia. Recalling the study design, the three pretreatment groups were as follows: atracurium 0.05 mg/kg, lidocaine 1.5 mg/kg, or the combination group of both atracurium 0.05 mg/kg and lidocaine 1.5 mg/kg. Principal findings included the atracurium group having the most pain on postoperative day one, as 60% of the subjects within this group reported postoperative myalgia. Additionally, this group reported the most intense pain. The lidocaine and combination groups were comparable, as each reported a 50% incidence of postoperative myalgia on day one. Also, the combination group had the least intense pain. These findings are congruent with the literature (Raman & San, 1997). However, on day two, although the atracurium group exhibited the most intense pain, it was found to have a decreased amount of pain, as only 40% of subjects reported postoperative myalgia. Both the lidocaine and combination group exhibited the same amount of reported pain (50%), with the lidocaine group decreasing in

intensity and the discomfort of subjects in the combination group remaining the same as postoperative day one. By day three, this study found only 20% of subjects within the atracurium group to report myalgia. Additionally, this group reported the least intense pain of all three groups, followed by the combination group and then the lidocaine group. These findings are surprising, as it is inconsistent with the literature. Wong and Chung (2000), as well as Melnick, Chalasani, Uy, Phitayakorn, Mallett, and Rudy (1987), found that combination therapy was the best pretreatment therapy for postoperative myalgia.

One possible reason for such differing findings in this pilot study may have been related to the timing of lidocaine administration. One study by Laurence (1987), found that lidocaine 1.5 mg/kg was ineffective in reducing postoperative myalgia when it was given two to three minutes prior to SCh. This was the administration routine in this author's study. Melnick (1987), however, found that lidocaine 1.5 mg/kg was effective at preventing postoperative myalgia, as long as it was given 15 to 30 seconds prior to SCh. Therefore, in a larger study, this may be a factor in producing similar findings within the literature. More importantly, this variable could be a plausible explanation for decreased postoperative myalgia.

ASA Physical Status Classification and Cigarette Smoking

To date, there are not any studies indicating that either ASA PSC or cigarette smoking would have an effect on postoperative myalgia. However, despite pretreatment, this data analysis indicated that some clinical significance might exist between ASA PCS, cigarette smoking, and postoperative myalgia. In this

author's study, 80% of ASA PCS II subjects complained of pain, while only 37.5% of ASA PCS I subjects had discomfort. Interestingly enough, 50% of the ASA PCS II subjects (two subjects) were also smokers. Although the small number of subjects prevents any generalizations to other populations (N=2), an interesting correlation was identified, which might prove to be a focus for future investigation. Such information could lead one to believe that perhaps ASA PCS and/or cigarette smoking may contribute to the development of postoperative myalgia. Thus, further study is needed in this area.

Confounding Variables

After putting this research study into action, several surprising confounding variables were identified. These factors made data collection more difficult and time consuming than anticipated. The most significant variable was with issues within the pharmacy. Because only one pharmacist works within this institution's surgical suite, and each subjects' dose of medication was customized by their weight, an average of forty-five minutes advanced notice was required to compound the needed regimen. Therefore, often times, enrolled subjects were excluded because of insufficient time to allow the pharmacist to compound the pretreatment medications. Access to a research pharmacist would have significantly decreased this time period, and allowed for inclusion of many more subjects.

Additionally, because this author was responsible for the identifying plausible subjects, obtaining informed consent, notifying pharmacy, and providing the anesthetic care for the subject, there was limited ability to access eligible

subjects early enough for enrollment. In future studies, such variables could easily be avoided if one researcher were assigned to research duties, while another performed the anesthetic care.

Limitations

This pilot study attempted to control for outside variables that were identified in the literature as causative factors for postoperative myalgia. Such factors included age, dose of SCh, type of operation, positioning of the patient, and ambulation after surgery (Wong & Chung, 2000). Despite such attention to detail, this author has noted several additional limitations for this pilot study. The following will summarize such instances, and recommend that a larger study incorporate controls in these areas in an effort to strengthen future research.

As accepted by the nature of the project, one limitation of a pilot study is the sample size. This study's population consisted of a small convenience sample of 15 subjects. Therefore, generalizations could not be made to any other populations. Additionally, gender specific information would be difficult to attain since this group was comprised of only two male subjects and 13 female subjects. However, this study was successfully implemented and it did determine feasibility to gather the needed information in order to complete a larger study. Since this goal was the overall purpose, the pilot study should be viewed as wholly successful and beneficial.

Another limitation of this study is that it did not include a control group. Because past research has identified that postoperative myalgia occurs in 50% of the population receiving SCh without pretreatment, this author felt it unethical

to include such a group in the study design (Wong & Chung, 2000). However, past studies have also identified a 20.8% incidence of postoperative myalgia for subjects who did not receive any pretreatment muscle relaxant before the administration of SCh (Trepanier, Brousseau, & Lacerte, 1988). Therefore, a control group could have been useful in identifying whether pretreatment medications made a difference in postoperative pain; Or if the observed results were a phenomena due to some other factor.

Some studies have implicated intubation as a causative factor of postoperative neck myalgia (Trepanier, Brousseau, & Lacerte, 1988). Incorporating an assessment tool to evaluate the ease or difficulty of intubation, and then comparing this score to those subjects who complained of postoperative neck myalgia, could strengthen the overall outcome of a larger study. This analysis would allow for differentiation between SCh-induced postoperative myalgia and positioning-induced postoperative neck myalgia.

Strengths

It is ironic that one of the greatest observed strengths of this author's study was thought to be a weakness at the beginning of the investigation. The assessment of postoperative myalgia for three days was thought to have many factors that would inhibit data collection. However, this author observed that all of the participants actually enjoyed being called by the researcher, and were more than happy to provide any information that was requested. As a result, this aspect of the study proved to be an excellent public relations venture for this

surgical center. While completely unexpected, it demonstrates a value-added aspect to clinical research focusing on human subjects.

Additional strengths included assessment of not only the amount of pain (PMS), but also differentiating postoperative myalgia from surgical pain, as well as describing the intensity of postoperative muscle soreness (PMES). Past studies have focused on either PMS or PMES, but not both. Consequently, former studies have had difficulty in distinguishing myalgia from surgical pain. This author very quickly realized the importance of using both tools in this investigation. For example, the PMS was sensitive enough to help the investigator assure the subject was experiencing true myalgia, and not shoulder discomfort from surgical gas. Using two valid assessment tools strengthens the findings, and provides a more complete picture of postoperative myalgia in this pilot study. Therefore, suggesting that a larger project utilizing the same type of assessment tools and framework should be able to provide more complete answers to the mystery of postoperative myalgia.

Conclusion

Overall, this pilot study accomplished its purpose, thereby determining feasibility for a larger study. Although not statistically significant, the data obtained through the implementation of this pilot study identified areas that are clinically significant. Study results also identified other potential causative factors for postoperative myalgia, such as ASA PCS, cigarette smoking, surgical position, prior use of pain medications, and surgical type. Because so much remains controversial about the phenomena of postoperative myalgia, this

remains an area where intense research needs to be applied, so as to determine which interventions constitute the best practices to provide better care in the future.

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APPENDICES

Appendix A

ASA Physical Status Classification

<http://www.asahq.org/clinical/physicalstatus.htm>

ASA Physical Status Classification

- Class 1** **A normal healthy patient.**
- Class 2** **A patient with mild systemic disease and no functional limitations.**
- Class 3** **A patient with moderate to severe systemic disease that results in some functional limitations.**
- Class 4** **A patient with severe systemic disease that is a constant threat to life and functionally incapacitating.**
- Class 5** **A moribund patient who is not expected to survive 24 hours with or without surgery.**
- Class 6** **A brain-dead patient whose organs are being harvested.**
- Class E** **If the procedure is an emergency, an "E" follows the physical status**

Appendix B

Study Formulary

Study Formulary: Indications, contraindications, and adverse effects are from Micro Medex®. All dosages are commonly administered and accepted ranges for use in anesthesia. It is important to note that responses to adverse effects are not drug specific, and anesthesia providers will respond in a uniform way.

❖ Albuterol (Proventil) 1-2 puffs prn

- Indications
 - bronchospasm
 - exercised induced asthma
- Contraindications
 - hypersensitivity to albuterol
- Adverse effects
 - bronchospasms
 - arrhythmias
 - tremors/nervousness
 - palpitations
 - tachycardia
 - hypertension
 - hypokalemia
 - hyperglycemia

❖ Atracurium (Tracrium) 0.05 mg/kg (defasciculating dose)

- Indications
 - muscle relaxation
 - adjunct to anesthesia
- Contraindications
 - hypersensitivity to atracurium
- Adverse effects
 - flushing
 - hypotension
 - bradycardia
 - bronchospasm
 - tachycardia

❖ **Atropine Sulfate 0.4 – 1.0 mg**

- Indications
 - symptomatic bradycardia
 - bradyarrhythmias
- Contraindications
 - narrow angle glaucoma
 - myasthenia gravis
 - paralytic ileus
- Adverse effects
 - tachycardia
 - slight mydriasis
 - hot, flushed skin

❖ **Dobutamine hydrochloride (Dobutrex) 2.5 – 10 mcg/kg/min**

- Indications
 - increase cardiac contraction
- Contraindications
 - hypersensitivity to Dobutamine hydrochloride
 - hypersensitivity to sulfonamides
 - IHSS (idiopathic hypertrophic subaortic stenosis)
- Adverse effects
 - increased heart rate
 - hypertension
 - premature ventricular contractions

❖ **Decadron (Dexamethasone) 4-8mg**

- Indications
 - adrenal insufficiency
 - inflammatory disorders
 - nausea/vomiting
 - shock
- Contraindications
 - hypersensitivity to class
 - systemic fungal infection
- Adverse effects
 - adrenal insufficiency
 - steroid insufficiency
 - immunosuppression

❖ **Dolasetron (Anzemet) 12.5 mg**

- Indications
 - antiemetic
- Contraindications
 - hypersensitivity to dolasetron products
- Adverse effects
 - headache
 - dizziness
 - drowsiness
 - pain

❖ **Dopamine hydrochloride (Intropin) 2- 20 mcg/kg/min**

- Indications
 - correct hypotension
 - increase cardiac output
 - improve perfusion
- Contraindications
 - uncorrected tachyarrhythmias
 - pheochromocytoma
 - ventricular fibrillation
- Adverse effects
 - arrhythmias
 - hypotension

❖ **Ephedrine 5-10 mg prn**

- Indications
 - asthma
 - hypotension
- Contraindications
 - hypersensitivity to ephedrine/sympathomimetic amines
 - thyrotoxicosis
- Adverse effects
 - central nervous system stimulation
 - hypertension
 - palpitations
 - tremor

❖ **Epinephrine hydrochloride (Adrenalin Chloride) 0.01 – 0.03 mcg/kg/min**

- Indications
 - anaphylaxis
 - bronchospasm
 - restore cardiac rhythm
- Contraindications
 - narrow angle glaucoma
 - coronary insufficiency
 - organic brain damage
- Adverse effects
 - hypertension
 - tachycardia
 - ventricular fibrillation

❖ **Esmolol (Brevibloc) 0.25 mg/kg – 1.0 mg/kg**

- Indications
 - supraventricular tachycardia
 - hypertension
- Contraindications
 - hypersensitivity to esmolol/ beta-blockers
 - sinus bradycardia
 - 2nd, 3rd, degree AV block
 - cardiogenic shock
- Adverse effects
 - bronchospasm
 - severe hypotension
 - cardiac failure
 - nausea and vomiting
 - phlebitis

❖ **Fentanyl (Sublimaze) 0.7- 2 mcg/kg**

- Indications
 - pain
 - analgesic adjunct to anesthesia
 - anesthesia
 - acute or postoperative pain
- Contraindications
 - hypersensitivity to Fentanyl
- Adverse effects
 - respiratory depression
 - muscle rigidity
 - nausea and vomiting
 - sedation

❖ **Glycopyrrolate (Robinal) 0.007mg/kg**

- Indications
 - gastric and salivary secretion reduction
 - vagal-mediated bradycardia
 - peptic ulcer
 - neuromuscular blockade reversal
- Contraindications
 - glaucoma
 - obstructive uropathy
 - myasthenia gravis
 - severe ulcerative colitis
 - unstable cardiovascular status
- Adverse effects
 - dry mouth
 - blurred vision
 - tachycardia
 - urinary retention

❖ **Granisetron Hydrochloride (Kytril) 10-20mcg/kg**

- Indications
 - postoperative nausea and vomiting
- Contraindications
 - hypersensitivity to granisetron products
- Adverse effects
 - headache
 - constipation
 - asthenia
 - diarrhea
 - abdominal discomfort

❖ **Hydroxyl ethyl starch (Hextend) 6% 20 ml/kg**

- Indications
 - volume expander
 - hypotension
 - blood loss
- Contraindications
 - hypersensitivity
- Adverse reactions
 - hypertension

❖ **Ketrolac (Toradol) 30mg**

- Indications
 - short-term management of pain
- Contraindications
 - hypersensitivity to nonsteroidal anti-inflammatory drugs
 - gastrointestinal ulcers
- Adverse effects
 - edema
 - hypertension
 - pruritus
 - nausea
 - vomiting
 - G.I. bleeding
 - flushing

❖ **Labetalol (Trandate) 0.1 – 0.25 mg/kg**

- Indications
 - hypertension
 - hypertension emergency
- Contraindications
 - hypersensitivity to labetalol/ beta-blockers
 - congestive heart failure
 - hepatic failure
 - pheochromocytoma
 - 2nd, 3rd, degree AV block
 - severe bradycardia
- Adverse effects
 - ventricular arrhythmias
 - bronchospasm
 - SLE
 - hypotension
 - nausea and vomiting
 - urinary retention
 - rash
 - muscle spasms

❖ **Lidocaine (Xylocaine) 1.5 mg/kg**

- Indications
 - ventricular arrhythmias
 - anesthesia
- Contraindications
 - hypersensitivity to lidocaine/amide-type anesthetics
- Adverse effects
 - seizures
 - drowsiness
 - tremors
 - hypotension

❖ **Midazolam (Versed) 0.02-0.1 mg/kg**

- Indications
 - anesthesia induction
 - conscious sedation
- Contraindications
 - acute narrow angle glaucoma
 - hypersensitivity to benzodiazepines
- Adverse effects
 - amnesia
 - nausea and vomiting
 - respiratory depression

❖ **Morphine 0.05 - 0.2 mg/kg**

- Indications
 - for management of moderate to severe pain
 - preoperative sedation
 - anesthesia supplement
- Contraindications
 - hypersensitivity to opiates
 - paralytic ileus
 - acute/severe asthma
 - upper airway obstruction
- Adverse effects
 - hypotension
 - respiratory depression
 - nausea
 - sedation

❖ **Neostigmine (Prostigmine) 0.04 - 0.07mg/kg**

- Indications
 - myasthenia gravis
 - neuromuscular blockade reversal
 - post-op paralytic ileus
 - urinary retention
- Contraindications
 - hypersensitivity to neostigmine
 - intestinal or urinary obstruction
 - peritonitis
- Adverse effects
 - bradycardia
 - psychosis
 - agitation
 - abdominal distention
 - constipation

❖ **Nitroglycerin (Deponit) 0.1 – 7.0 mcg/kg/min**

- Indications
 - To control hypertension associated with surgery
- Contraindications
 - hypersensitivity to nitrites
 - head trauma
 - severe anemia
- Adverse effects
 - hypotension
 - tachycardia
 - flushing

❖ **Nitrous Oxide 10 – 70%**

- Indications
 - anesthetic adjunct
- Contraindications
 - pneumothorax
 - increased intracranial pressure
 - increased Intraocular pressure
- Adverse effects
 - nausea/vomiting
 - abdominal distention

❖ **Ondansetron Hydrochloride (Zofran) 4 mg**

- Indications
 - nausea and vomiting
- Contraindications
 - hypersensitivity to ondansetron
- Adverse effects
 - elevated liver function tests
 - headache
 - diarrhea

❖ **Phenylephrine (Neo-synephrine) 50-100 mcg prn**

- Indications
 - decongestant
 - hypotension
- Contraindications
 - hypersensitivity to phenylephrine
 - narrow angle glaucoma
 - hypertension
 - coronary artery disease
- Adverse effects
 - tachycardia
 - hypertension
 - myocardial infarction
 - subarachnoid hemorrhage

❖ **Promethazine (Phenergan) 6.25 - 25mg**

- Indications
 - nausea and vomiting
 - sedation
 - allergic reactions
- Contraindications
 - narrow-angle glaucoma
 - peptic ulcer disease
 - prostatic hypertrophy
 - bladder obstruction
 - MAOI therapy
 - hypersensitivity to phenothiazines
- Adverse effects
 - drowsiness
 - xerostomia
 - dizziness
 - extra pyramidal reactions

❖ **Propofol (Diprivan) 2-2.5 mg/kg**

- Indications
 - anesthesia
 - sedation
- Contraindications
 - hypersensitivity to eggs
- Adverse effects
 - seizures
 - hypotension
 - apnea
 - injection site pain
 - cardiac arrest

❖ **Sevoflurane (Ultane) 0.5 - 6%**

- Indications
 - anesthesia
- Contraindications
 - hypersensitivity to sevoflurane
 - patients with susceptibility to malignant hyperthermia
- Adverse effects
 - nausea and vomiting
 - excitatory movements
 - respiratory depression
 - decreased heart rate

❖ **Succinylcholine (Anectine) 1.5mg/kg**

- Indications
 - muscle relaxation
 - intubation
- Contraindications
 - malignant hyperthermia
 - acute phase of major trauma/major burns
 - hypersensitivity to succinylcholine
 - skeletal muscle myopathies
 - upper motor neuron injury
- Adverse effects
 - myoglobinemia
 - prolonged muscle relaxation
 - bradycardia
 - hyperkalemia
 - respiratory depression/apnea
 - hypersensitivity reactions
 - cardiac arrest

❖ **Vecuronium (Norcuron) 0.05- 0.1mg/kg**

- **Indications**
 - muscle relaxation
- **Contraindications**
 - hypersensitivity to pancuronium or vecuronium products
- **Adverse effects**
 - bronchospasm
 - bradycardia
 - hypotension/hypertension
 - tachycardia

Appendix C

Informed Consent

A Comparison of the Differential Effects of Atracurium and/or Lidocaine on Succinylcholine-induced Fasciculation and severity of Postoperative Myalgia

Investigators

Jack Chavez M.D., Fred Schrimpe, BSN, SRNA, Tonya Campbell, BSN, SRNA

Informed Consent

The study in which you are asked to participate has the goal of reducing muscle twitching and muscular soreness after surgery, which can occur with succinylcholine administration. This is a topic that is frequently studied. Many scientists feel that the muscle soreness some people experience after surgery is related to the muscle twitching occurring with succinylcholine administration. You are being asked to participate because you are in a group of patients who frequently have muscle soreness after surgery, namely, patients receiving succinylcholine for general tracheal anesthesia.

Succinylcholine is a muscle relaxant that allows your anesthesia provider to place a breathing tube in your windpipe to protect your airway after you are asleep. This tube allows you to breathe the anesthetic gases that will keep you asleep. This is done routinely for general anesthesia and will be required regardless of your participation in this study. You should be unaware of this tube placement and should not remember it. All subjects will be selected from the daily surgical schedule at the University of Tennessee Medical Center.

This study will examine two anesthetic medications that are routinely used to prevent muscular twitching and soreness. Neither drug has been proven superior in preventing muscle twitching or muscular soreness. We are asking permission to do two things during this study. First, to record any muscular twitching we may observe, and second, to ask you some simple questions after surgery about whether you are experiencing any muscular soreness. You will be contacted by phone 24, 48, and 72 hours after your surgery by one of the investigators. If your surgeon admits you to the hospital, you will be visited in your room by one of the investigators.

A Comparison of the Differential Effects of Atracurium and/or Lidocaine on Succinylcholine-induced Fasciculation and severity of Postoperative Myalgia

Investigators

Jack Chavez M.D., Fred Schrimpe, BSN, SRNA, Tonya Campbell, BSN, SRNA

The medications used will consist of a muscle relaxant (atracurium), or local anesthetic/numbing (lidocaine) medication. Some patients may receive both medications. These medications will be administered in a double blind method. This means that neither you nor the anesthesia provider will know which drug was given until the conclusion of the study. The doses of the medicines, however, will be carefully and safely prepared for you under the supervision of a licensed pharmacist. You will receive standard and acceptable doses of all medications, just as you would if you chose not participate in this study. They will look the same, and no one except the pharmacist will know what you received until all the patients have been studied.

You will be assigned a unique number that will be used to identify you and the information we gather. If something were to happen that required the knowledge of what drug you received we would use that number to obtain the necessary information. There may be around 100 patients involved in this study, and it will probably take several months to gather all the information we need.

Risks Associated with Participation

Since the medications you will receive today are routinely used for anesthetics, there is essentially no increased risk to you associated with your participation in this study. However all medications have side effects and could cause adverse reactions. Although rare, some possible side effects that could occur include nausea, vomiting, sedation, prolonged muscle weakness, high potassium, increased body temperature, and seizures.

If you experience the common side effects of pain, nausea, or vomiting after your surgery, standard medications for these conditions will be administered, just as they would be for anyone else. You are not expected to experience any increased discomfort as a result of your participation in this study.

All records are kept confidential. As stated earlier you will be assigned a number which will be used as your identifier, rather than using your name. These records will be kept in the Anesthesia Office under lock and key for a period of five years from the conclusion of the study. After five years, they will be destroyed.

FS 03/03 Patient Initials _____ Date _____

2 of 5

A Comparison of the Differential Effects of Atracurium and/or Lidocaine on Succinylcholine-induced Fasciculation and severity of Postoperative Myalgia

Investigators

Jack Chavez M.D., Fred Schrimpe, BSN, SRNA, Tonya Campbell, BSN, SRNA

The hope is to gain information from this study that may help patients in the future with their post-surgery recovery. The potential benefits to the subjects may include a more comfortable recovery time and possibly an earlier return to their pre-surgery level of function. All future patients who undergo surgery and receive succinylcholine could potentially benefit from this study. If this study demonstrates that one or the combination of pretreatment medications has superior ability to diminish or prevent muscle twitching and muscular soreness, then future patients may experience less discomfort after surgery.

Alternatives to participation

There is no superior drug or treatment to prevent succinylcholine induced muscle twitches or muscular soreness.

Confidentiality

Although study results may be published, your confidentiality will be maintained. Your name or information identifying you will not be released without written permission unless required by law. Under federal privacy regulations, you have the right to determine who has access to your personal health information (called "protected health information" or PHI). PHI collected in this study may include your medical history, the results of physical exams, lab tests, x-ray exams, and other diagnostic / treatment procedures, as well as basic demographic information. By signing this consent form, you are authorizing the researchers at the University of Tennessee Medical Center to have access to your PHI collected in this study and to receive your PHI from (Jack Chavez M.D.), and may the University of Tennessee Medical Center where you have received health care. In addition, your PHI may be shared with other persons involved in the conduct or oversight of this research, including the (FDA) Food and Drug Administration, the University of Tennessee Medical Center, and the University of Tennessee Graduate School of Medicine Institutional Review Board. Your PHI will not be used or disclosed to any other person or entity, except as required by law, or for authorized oversight of this research study by other regulatory agencies, or for other research for which the use and disclosure of your PHI has been approved

FS 3/03 Patient Initials _____ Date _____

3 of 5

A Comparison of the Differential Effects of Atracurium and/or Lidocaine on Succinylcholine-induced Fasciculation and severity of Postoperative Myalgia

Investigators

Jack Chavez M.D., Fred Schrimpe, BSN, SRNA, Tonya Campbell, BSN, SRNA

by the IRB. Your PHI will be used indefinitely. You may cancel this authorization in writing at any time by contacting the Principal Investigator listed on the first page of the consent form. If you cancel the authorization, continued use of your PHI is permitted if it was obtained before the cancellation and its use is necessary in completing the research. However, PHI collected after your cancellation may not be used in the study. If you refuse to provide this authorization, you will not be able to participate in the research study.

If you cancel the authorization, then you will be withdrawn from the study. Finally, the federal regulations allow you to obtain access to your PHI collected or used in this study. However, in order to complete the research, your access to this PHI may be temporarily suspended while the research is in progress. When the study is completed, your right of access to this information will be reinstated.

You understand that you are not waiving any legal rights or releasing the hospital or its agents from liability for negligence. You understand that in the event of physical injury resulting from research procedures, the University of Tennessee does not have funds budgeted for compensation either from lost wages or for medical treatment. Therefore, the University does not provide reimbursements for such injuries.

By signing this form, you indicate that: You have read the description of the above study and have freely volunteered to participate in it. You have had possible side effects and adverse reactions explained to you and have had alternative therapies explained. You have had an opportunity to ask questions of the investigator and have received acceptable answers. You understand you may withdraw from this study at any time and will still receive standard treatment for your condition.

Payment for Participation

There is no payment in any form to study participants.

FS 03/03 Patient Initials _____ Date _____

4 of 5

A Comparison of the Differential Effects of Atracurium and/or Lidocaine on Succinylcholine-induced Fasciculation and severity of Postoperative Myalgia

Investigators

Jack Chavez M.D., Fred Schrimpe, BSN, SRNA, Tonya Campbell, BSN, SRNA

Costs of Participation

There are no additional costs to you for participating in this study.

Contact/Questions

If you have any questions about the nature of this study, or feel that you have had an adverse reaction, please feel free to contact Jack Chavez, MD at (865-544-9220), Tonya Campbell (865-544-9220), or Fred Schrimpe (865-544-9220). If you have any questions about your rights as a research subject, please call the Institutional Review Board at (865-544-9781). Thank you for your consideration.
Consent of Subject

I have read or have had read to me the description of the research study as outlined above. The investigator or his/her representative has explained the study to me and has answered all of the questions I have at this time. I have been told of the potential risks, discomforts, side effects and adverse reactions as well as the possible benefits (if any) of the study.

I freely volunteer to participate in this study. I understand that I do not have to take part in this study and that my refusal to participate will involve no penalty or loss of rights too which I am entitled. I further understand that I am free to later withdraw my consent and discontinue participation in this study at any time. I understand that refusing to participate or later withdrawing from the study will not adversely affect my subsequent medical care.

Signature_____	Date_____
Investigator Signature_____	Date_____
Witness_____	Date_____

FS 03/03 Patient Initials _____ Date _____

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Appendix D

Investigational Review Board Approval Letters

THE UNIVERSITY OF TENNESSEE
GRADUATE SCHOOL OF MEDICINE



March 20, 2003

Jack Chavez, MD
Department of Anesthesiology
The University of Tennessee Medical Center
1924 Alcoa Highway
Knoxville, TN 37920

Office of Institutional Review Board
FWA 2301
1924 Alcoa Highway
Knoxville, TN 37920-6999
(865) 544-9781
FAX (865) 544-9275

RE: IRB #2233 "A Comparison of the Differential Effects of Atracurium and/or Lidocaine on Succinylcholine-induced Fasciculation and the Severity of Postoperative Myalgia"

Dear Dr. Chavez,

On March 18, 2003, the University of Tennessee Graduate School of Medicine in Knoxville Institutional Review Board reviewed your above referenced application. The Board voted full approval with no abstentions on this protocol including informed consent form. Your research application will be reviewed in one year.

The Institutional Review Board is in compliance with the requirements in Part 50, 56, Subchapter D. Part 312 of the 21 Code of Federal Regulations published January 27, 1981.

Any alterations in the protocol must be promptly reported to the Institutional Review Board. In addition, annual reapproval (**February 2004**) is required by the IRB, and it is your responsibility as the Principal Investigator to initiate the request for approval regardless of the time the study has been approved by the sponsoring agency.

You have individual responsibility for reporting to the Board in the event of adverse reactions.

Sincerely,

Joseph E. Fuhr, PhD
Chairman
Institutional Review Board
JEF: rl

3/25/03



May 16, 2003

IRB #: 6413 B

Institutional Review Board
Office of Research
404 Andy Holt Tower
Knoxville, Tennessee 37996-0146
865-974-3466
Fax: 865-974-2805

Title: A Comparison of the Differential Effects of Atracurium and/or Lidocaine on Succinylcholine-induced Fasciculation and Severity of Postoperative Myalgia

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John Preston, Advisor
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1200 Volunteer Blvd.
Campus

At the meeting of the Institutional Review Board (IRB) held May 15, 2003, the above protocol was reviewed and approved.

This approval for a period ending one year from the date of this letter. Please make timely submission of renewal or prompt notification of project termination (see item #3 below).

Responsibilities of the investigator during the conduct of this project include the following:

1. Prior approval from the Committee before instituting any changes in the project.
2. To retain signed consent forms from subjects for at least three years following completion of the project.
3. To submit a Form D to report changes in the project or to report termination at 12-month or less intervals.

The Committee wishes you every success in your research endeavor. This office will send you a renewal notice (Form R) on the anniversary of your approval date.

Sincerely,

Brenda Lawson
Compliances

Appendix E

Standard ASA Monitors

ANESTHESIA STANDARDS FOR BASIC INTRAOPERATIVE MONITORING

Note: Within these standards, "Anesthesia" is defined as all types of anesthesia care unless otherwise specified by the text.

STANDARDS FOR BASIC ANESTHETIC MONITORING

(Approved by House of Delegates on October 21, 1986 and last amended on October 21, 1998¹)

<http://www.asahq.org/publicationsAndServices/standards/02.html>

These standards apply to all anesthesia care although, in emergency circumstances, appropriate life support measures take precedence. These standards may be exceeded at any time based on the judgment of the responsible anesthesiologist. They are intended to encourage quality patient care, but observing them cannot guarantee any specific patient outcome. They are subject to revision from time to time, as warranted by the evolution of technology and practice. They apply to all general anesthetics, regional anesthetics and monitored anesthesia care. This set of standards addresses only the issue of basic anesthetic monitoring, which is one component of anesthesia care. In certain rare or unusual circumstances, 1) some of these methods of monitoring may be clinically impractical, and 2) appropriate use of the described monitoring methods may fail to detect untoward clinical developments. Brief interruptions of continual monitoring may be unavoidable. *Under extenuating circumstances, the responsible anesthesiologist may waive the requirements marked with an asterisk (*); it is recommended that when this is done, it should be so stated (including the reasons) in a note in the patient's medical record.* These standards are not intended for application to the care of the obstetrical patient in labor or in the conduct of pain management.

STANDARD I

Qualified anesthesia personnel shall be present in the room throughout the conduct of all general anesthetics, regional anesthetics and monitored anesthesia care.

OBJECTIVE

Because of the rapid changes in patient status during anesthesia, qualified anesthesia personnel shall be continuously present to monitor the patient and provide anesthesia care. In the event there is a direct known hazard, e.g., radiation, to the anesthesia personnel, which might require intermittent remote observation of the patient, some provision for monitoring the patient must be

made. In the event that an emergency requires the temporary absence of the person primarily responsible for the anesthetic, the best judgment of the anesthesiologist will be exercised in comparing the emergency with the anesthetized patient's condition and in the selection of the person left responsible for the anesthetic during the temporary absence.

STANDARD II

During all anesthetics, the patient's oxygenation, ventilation, circulation and temperature shall be continually evaluated.

OXYGENATION

OBJECTIVE

To ensure adequate oxygen concentration in the inspired gas and the blood during all anesthetics.

METHODS

Inspired gas: During every administration of general anesthesia using an anesthesia machine, the concentration of oxygen in the patient breathing system shall be measured by an oxygen analyzer with a low oxygen concentration limit alarm in use. *

Blood oxygenation: During all anesthetics, a quantitative method of assessing oxygenation such as pulse oximetry shall be employed. * Adequate illumination and exposure of the patient are necessary to assess color. *

VENTILATION

OBJECTIVE

To ensure adequate ventilation of the patient during all anesthetics.

METHODS

Every patient receiving general anesthesia shall have the adequacy of ventilation continually evaluated. Qualitative clinical signs such as chest excursion, observation of the reservoir breathing bag and auscultation of breath sounds are useful. Continual monitoring for the presence of expired carbon dioxide shall be performed unless invalidated by the nature of the patient, procedure or equipment. Quantitative monitoring of the volume of expired gas is strongly encouraged. *

When an endotracheal tube or laryngeal mask is inserted, its correct positioning must be verified by clinical assessment and by identification of carbon dioxide in the expired gas. Continual end-tidal carbon dioxide analysis, in use from the time of endotracheal tube/laryngeal mask placement, until extubation/removal or initiating transfer to a postoperative care location, shall be performed using a quantitative method such as capnography, capnometry or mass spectroscopy. *

When ventilation is controlled by a mechanical ventilator, there shall be in continuous use a device that is capable of detecting disconnection of components of the breathing system. The device must give an audible signal when its alarm threshold is exceeded.

During regional anesthesia and monitored anesthesia care, the adequacy of ventilation shall be evaluated, at least, by continual observation of qualitative clinical signs.

CIRCULATION

OBJECTIVE

To ensure the adequacy of the patient's circulatory function during all anesthetics.

METHODS

Every patient receiving anesthesia shall have the electrocardiogram continuously displayed from the beginning of anesthesia until preparing to leave the anesthetizing location. *

Every patient receiving anesthesia shall have arterial blood pressure and heart rate determined and evaluated at least every five minutes. *

Every patient receiving general anesthesia shall have, in addition to the above, circulatory function continually evaluated by at least one of the following: palpation of a pulse, auscultation of heart sounds, monitoring of a tracing of intra-arterial pressure, ultrasound peripheral pulse monitoring, or pulse plethysmography or oximetry.

BODY TEMPERATURE

OBJECTIVE

To aid in the maintenance of appropriate body temperature during all anesthetics.

METHODS

Every patient receiving anesthesia shall have temperature monitored when clinically significant changes in body temperature are intended, anticipated or suspected.

#Note that "continual" is defined as "repeated regularly and frequently in steady rapid succession" whereas "continuous" means "prolonged without any interruption at any time."

Appendix F

Acceptable Hemodynamic Monitoring Parameters

+/- 20% of baseline: Heart rate

+/- 20% of baseline: Blood Pressure

95% or above: Oxygen Saturation

35.6 C (96.0 F) – 37.8 C (100.0 F): Temperature

Appendix G

Extubation Criteria

Train of four is 4/4 without fade, and a positive sustained tetanus

Spontaneous respirations of >8, with a tidal volume of >250

Negative Inspiratory pressure (NIP) of –10

Eye opening to voice, or purposeful movement

Appendix H

Postoperative Myalgia Evaluation Scale (PMES)

0 = Absence of pain other than characteristic surgical gas pain

1 = Mild muscle stiffness or pains, when specifically asked about, in the nape of the neck, or in shoulders and lower chest on deep breathing

2 = Moderate muscle stiffness and pains spontaneously complained of by the patient

3 = Severe, incapacitating, generalized muscle stiffness or pain

Subject #	0	1	2	3
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
11				
12				
13				
14				
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23				
24				

Did the recovery room nurse report the patient shivering in the recovery room?

Appendix I

Postoperative Myalgia Survey (PMS)

Date of the telephone call _____ Postoperative Day: 1____ 2____ 3____
Subject's study number: _____ Date of surgery: _____ Type of surgery: _____

1. Do you have any soreness or stiffness in your body besides headache or surgical gas pains? Yes____ No____
2. Have you been up and about (ambulatory)? Yes____ No____
3. Is there pain and stiffness in the muscles? Yes____ No____
4. In which sites do you have muscle pain/stiffness?
Jaw____ Throat____ Neck____ Shoulder____ Arms____ Chest____ Abdomen____
Back____ Buttocks____ Thighs____ Calves____ Generalized____
5. When did you first notice the pain?
6. Rate the muscle stiffness/pain on a score 0-10 (0 being no pain, and 10 the worst pain ever) only on the sites reported to be painful by the patient.
Jaw____ Throat____ Neck____ Shoulders____ Arms____ Chest____ Abdomen____
Back____ Buttocks____ Thighs____ Calves____ Generalized____
7. What makes the muscle stiffness/pain worse? Movement____ Rest____
8. Describe the muscle pain/stiffness in your own words.
9. Do you think the muscle pain is restricting your normal activity? Yes____ No____
10. Is the muscle pain preventing you from getting out of bed? Yes____ No____
11. How would you rate this limitation of activity on a scale of 0-10? (0 being no limitation in activity, 10 being muscle pain limiting the patient to bed all the time except for essential activity)
12. Do you think the muscle pain is severe enough for you to take extra pain medication? Yes____ No____
13. Are you taking your prescribed pain medication to help your surgical pain or muscle pain? Yes____ No____
14. How many pain pills have you taken the last 24 hours?____

Appendix J

Demographic Data Sheet and Master Subject List

	Name	Phone #	Subject #	ASA	Wt. in kg	Ht. in inches	Gender	Smoking hx/# of yrs	Pre-op NSAID NARC	Pre-op NSAID NARC	Post-op NSAID NARC	Post-op NSAID NARC
									dose	duration	dose	duration
1												
2												
3												
4												
5												
6												
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Vita

Tonya Lynn DeWitt Campbell was born in Morgantown, West Virginia on June 27, 1969. She was raised in Springboro, Ohio and went to grade school at Clearcreek Elementary. Immediately following grade school, she moved and attended Bayonet Point junior high school in Bayonet Point, Florida. She graduated from Gulf High School in 1987. From there, she went to Maryville College, located in Maryville, Tennessee and received a Bachelor of Arts in Health Sciences in 1994. In 1995, she graduated with an Associates of Nursing from Roane State Community College, in Knoxville, Tennessee. She continued her education and received a Bachelor of Science in Nursing from the University of Tennessee, Knoxville in 2001.

After working as a critical care nurse for seven years, Tonya is currently pursuing her Master's in Nursing, with a concentration in Nurse Anesthesia, at the University of Tennessee in Knoxville, Tennessee. Future plans include a job in Corbin, Kentucky as a nurse anesthetist after graduation on December 14, 2003.

4. The fourth part of the document discusses the implications of the findings. It suggests that the results have significant implications for the field of study and may lead to further research in this area.

5. The fifth part of the document concludes the study. It summarizes the main findings and provides a final statement on the importance of the research.

