12-2011

# Interoperative Pain Management: Attenuating Postoperative Pain in Paramedic Patients

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# INTRAOPERATIVE PAIN MANAGEMENT: ATTENUATING POSTOPERATIVE PAIN IN PEDIATRIC PATIENTS

by

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Bachelor of Science in Nursing, University of North Dakota, 2002

An Independent Study

Submitted to the Graduate Faculty

of the

University of North Dakota

in partial fulfillment of the requirements

for the degree of

Master of Science

Grand Forks, North Dakota

December

2011

PERMISSION

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| Title | Intraoperative Pain Management: Attenuating Postoperative Pain in Pediatric Patients |
| Department | Nursing |
| Degree | Master of Science |

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## Abstract

Intraoperative Pain Management: Attenuating Postoperative Pain in Pediatric Patients

More than 5 million children undergo surgery in the United States each year, and it is estimated that up to 75% (3.75 million) of them experience significant postoperative pain (Fortier, MacLaren, Martink, Perret-Karimi, & Kain, 2009). While we have come a long way in our knowledge of pain in children, it is often found that pain is inadequately assessed and treated. Aside from the cost associated with increased utilization of medical visits, psychological implications (anxiety, avoidance, sleep disturbances), and increased parental distress related to pediatric pain, there are many physiologic changes associated with pain that may delay or prevent wound healing. Increasing awareness of pharmacologic trends in pediatric analgesia may assist anesthesia staff in providing adequate intraoperative analgesia and decreasing postoperative pain.

Many components that contribute to postoperative pediatric pain have been studied. Due to the extensive amount of research available on this topic, for the purposes of this independent project, research will be limited to those children ages 2-12 years old undergoing tonsillectomy and adenoidectomy (T&A). T&A is one of the most common pediatric surgical procedures and is well known to be associated with significant postoperative pain (Fortier et al., 2009).

The purpose of this independent project is to identify pharmacologic agents that are presently being employed intraoperatively to provide analgesia to the pediatric population. A comprehensive review of the literature was performed using PubMed and CINAHL databases. Current research findings on the topic of interest and related topics were reviewed. Melzack and Wall's gate control theory of pain was used as a theoretical framework.

Intraoperative Pain Management: Attenuating Postoperative Pain in Pediatric Patients

Pain is defined by the International Association for the Study of Pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (IASP, 1994). Certified Registered Nurse Anesthetists (CRNAs) and other anesthesia providers are responsible for providing anesthesia, amnesia, and analgesia to patients who are undergoing surgical procedures. Analgesia is defined as the absence of pain in response to stimulation which would normally be painful (IASP, 1994). The physiological indicators of blood pressure, heart rate, and respiratory rate are among the most commonly used to assess pain in patients who are anesthetized. Inability to communicate verbally does not negate the possibility that an individual is experiencing pain and is in need of appropriate pain-relieving treatment (IASP, 1994).

Good pain management is associated with improved outcomes from surgery, quicker clinical recovery, shorter hospital stays, fewer readmissions, improved quality of life, and improved patient and parent satisfaction (Trudeau, Lamb, Gowans, & Lauder, 2009). In light of the present advances in technology and the progress that has been made in the science of pharmacology, a specific formula for providing children the most effective analgesia has eluded healthcare providers due to variability in children's perception and response to pain. Research conducted on the pediatric population is also subject to many ethical considerations which results in comparably few randomized controlled trials that direct pain management in children. Anesthesia providers must strive to provide adequate analgesia to the pediatric population. The clinical question of interest remains: what pharmacologic agents utilized intraoperatively provide the most effective analgesia in the immediate postoperative period?

## Purpose

The purpose of this independent project is to provide a current review of literature on intraoperative analgesic agents used to treat pain in the pediatric (2-12 years) population undergoing T&A. In order to adequately provide effective treatment based on research, clinicians need to be kept informed on the latest results in pediatric and pharmacologic studies. This information will be presented at the North Dakota Association of Nurse Anesthetists bi-annual meeting in Bismarck, North Dakota. With current evidence for practice presented, providers may incorporate the results of this review into their individual practices to provide more effective intraoperative analgesic management.

The basis of this project is to alert current practitioners to the significance of this problem, provide a review of the pain pathway, review the historical perspective of pain in pediatric patients, and to provide a review of literature on the current pharmacologic treatments of intraoperative pain.

## Significance

Up to 75% of children undergoing surgery experience postoperative pain with up to 50% experiencing severe pain (defined as a pain score greater than or equal to 8) after surgery (Fortier et al., 2010; Bean-Lijewski, Kruitbosch, Hutchinson & Browne, 2007). According to the National Health Statistics Reports (Hing & Burt, 2007), ambulatory (outpatient) surgery has been increasing in the United States and T&A is among the most common procedures performed on an outpatient basis for children under 15 years of age. This particular surgery is associated with increased risk of pain after surgery, adverse respiratory events, bleeding, and postoperative nausea and vomiting (Gulhas et al., 2003). It is important for anesthesia providers to adequately

treat intraoperative pain in order to smooth the transition from the operating suite to the PACU. Readiness for discharge home from the PACU is confirmed by patients scoring ≥ 9 on the standardized postanesthesia discharge scoring system (PADS) (Marschall & Chung, 1999). The criterion in which the system is based includes vital signs, activity level, nausea and vomiting, pain, and bleeding. This scoring system highlights the importance of choosing the appropriate pharmacologic agents to be administered intraoperatively. Pain at an unacceptable level to the patient or that which cannot be controlled with oral medication may delay discharge from the PACU and thus increase the cost of patient care.

Painful stimuli produce a "fight-or-flight" release of stress hormones which may exacerbate injury, prevent wound healing, lead to infection, and prolong hospitalization. Failure to control pain after T&A leads to decreased oral intake of liquids, dehydration, and greater risk of hemorrhage from healing surgical wounds (Mohommad, Shahrbano, & Ulhaq, 2008). Adequate treatment of perioperative pain in children can reduce the morbidity and mortality associated with surgery caused by activation of the stress response.

Kain et al. (2006) performed a cohort study on children undergoing tonsillectomy and adenoidectomy. Parental assessment of their child's pain was scored, the children's self report of pain was rated, and analgesic consumption was recorded throughout the postoperative recovery period (defined as the time the patient entered the post-anesthesia recovery until 14 days following the procedure.) Though it is difficult to determine whether conclusions are the result of association or cause-and-effect, increased anxiety before surgery was associated with increased postoperative pain, analgesic consumption, sleeping problems and decreased postoperative eating. Lonnqvist & Morton (2006) suggest careful pre-operative preparation of children and their families in order to minimize fear and anxiety.

## Theoretical Framework

The gate control theory of pain, proposed by Melzack and Wall in 1965, was chosen as the theoretical framework and used to analyze the relationship between pharmacologic intervention and perception of pain. Certified Registered Nurse Anesthetists (CRNAs) are responsible for both altering the way in which patients perceive pain and providing effective analgesia to optimize conditions for recovery from a surgical procedure that was indeed painful. In order to utilize Melzack and Wall's theory and provide analgesia, a basic understanding of the pain pathway is needed.

Pain signal processing involves transduction, transmission, modulation, & perception. Transduction is the process by which afferent nerve endings in the peripheral tissues participate in translating noxious stimuli into nociceptive impulses (painedu.org). Various stimuli may facilitate the transduction of pain. These include mechanical stimulation from a sharp object, potassium released from the inside of damaged cells, prostaglandins, histamines and bradykinin from immune cells that invade an area during inflammation, and substance P released from nearby nerve fibers. These stimuli cause the propagation of action potentials in the nociceptor neurons leading to the transduction of pain.

Transmission is the process by which impulses are sent to the dorsal horn of the spinal cord, and then along the sensory tracts to the brain (painedu.org). Primary afferent neurons are located in the dorsal root ganglia, which lie in the vertebral foramina at each spinal cord level (Morgan, Mikhail, & Murray, 2006). Each neuron has a single axon that bifurcates, sending one end to the peripheral tissues it innervates and the other into the dorsal horn of the spinal cord (Morgan, Mikhail, & Murray, 2006). In the dorsal horn, the primary afferent neuron synapses with a second-order neuron whose axons cross the midline and ascend in the contralateral

spinothalamic tract to reach the thalamus, reticular formation, nucleus raphe magnus, and periaqueductal gray (Morgan, Mikhail, & Murray, 2006). Second-order neurons synapse in thalamic nuclei with third-order neurons, which in turn send projections through the internal capsule and corona radiata to the postcentral gyrus of the cerebral cortex where sensations of pain, temperature, touch and pressure are interpreted and responses to the sensations are initiated (Nagelhout & Plaus, 2010).

Modulation is the process of dampening or amplifying the pain-related neural signals (painedu.org). This is the step anesthesia providers may alter with pharmacologic agents. Modulation may occur peripherally at the nociceptor, in the spinal cord, or in supraspinal structures (Morgan, Mikhail, & Murray, 2006). Rich arrays of opioid receptors (mu, kappa, and delta) are present in the dorsal horn (painedu.com). In addition to an ascending tract, the nociceptive system contains descending pathways that send neurons from the frontal cortex, hypothalamus and other areas of the brain to the midbrain and medulla, and also down to the spinal cord (painedu.com). The result of the descending inhibitory input is that incoming nociceptive signals from the periphery are dampened, or even blocked entirely, at the "gate" in the dorsal horn (painedu.com).

Perception is the conscious awareness of the experience of pain. Perception results from the interaction of transduction, transmission, modulation, psychological aspects and other characteristics of the individual. All four steps along the pain pathway are tied together by the Gate Control Theory (painedu.com).

Melzack and Wall's gate control theory of pain proposes that the dorsal horn of the spinal cord operates similar to a gate by modulating the flow of nerve impulses from the peripheral fibers to the central nervous system. The internuncial neurons involved in the gating mechanism

are activated by large-diameter, faster-propagating fibers that carry tactile information (Porth, 2005). The transmission of impulses from the small-diameter myelinated and unmyelinated pain fibers could be blocked if fired simultaneously with the large-diameter fibers (Porth, 2005). The "gate" is influenced by the integration of inputs from sensory neurons, the segmental spinal cord level, and multiple descending influences from the brain. These inputs determine whether the gate will be opened or closed, either increasing or decreasing the intensity of the ascending pain signal (painedu.com). Melzack and Wall (1965) believed that past experiences, culture, attention and activities of the nervous system taking place simultaneously with the injury all determined how the pain would be perceived. The gate, then, can be opened or closed by transduction, transmission and modulation, and psychological intervention. It may also be influenced by pharmacologic manipulation that is administered by anesthesia providers.

## Definitions

For the purpose of this study, the following definitions are provided:

Intraoperative – Relating to the period of time during a surgical procedure

Postoperative – Relating to the period of time following a surgical operation until discharge from the hospital or surgical center

Perioperative – The period of time extending from when a patient goes into the hospital for surgery until the patient is discharged home. Before, during and after a surgery

General Anesthesia – Using anesthetic drugs to induce a reversible state of consciousness in which an individual is unable to respond to painful stimuli

Pain – "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" as defined by the International Association for the Study of Pain. Pain is subjective and response to pain may be highly variable among persons and may be highly variable in the same person at different times.

Analgesia - The absence of pain in response to stimulation which would normally be painful (IASP, 1994).

Noxious Stimuli – Another name for pain

Nociceptors - Specialized receptors that transduce noxious stimuli. Noci is Latin for harm

Nociception - The process by which a painful stimulus is relayed from the site of stimulation to the central nervous system. Nociceptive pain is pain caused by activation or sensitization of peripheral nociceptors. All nociception produces pain, but not all pain results from nociception. Serves to detect, localize, and limit tissue damage. Postoperative pain falls into this category.

Acute pain - Pain that is caused by noxious stimulation due to injury, a disease process, or the abnormal function of muscle or viscera. It is nearly always nociceptive. Moderate to severe acute pain may adversely influence postoperative morbidity and mortality.

Ambulatory surgery – A surgery in which a patient undergoes a procedure and is discharged home on the same day. Outpatient surgery

Postanesthesia Care Unit (PACU) - The area in which patients first recover from anesthesia.

## Process

A comprehensive review of the literature was performed using CINAHL and PubMed databases. Search terms utilized included but were not limited to pediatric, anesthesia, analgesia, intraoperative, pain, tonsillectomy and adenoidectomy, opioids, acetaminophen, morphine, fentanyl, total intravenous anesthesia, nonsteroidal anti-inflammatory, and hydromorphone. MESH terms utilized included but were not limited to pediatric, analgesia, tonsillectomy and adenoidectomy, intraoperative and postoperative. The material discovered in the literature review had a time range between the years 1941 and 2011. The basis of the review of literature was to gain a broader perspective on the medications that are currently being used and studied in the treatment of intraoperative pediatric pain. Types of studies found with related material included prospective comparisons, meta-analysis, and randomized double blind studies.

The delivery of this information will be provided to CRNAs and other anesthesia providers in the clinical setting, as well as at the North Dakota Association of Nurse Anesthetists bi-annual meeting. Information will be provided in the form of a power point lecture with the opportunity for discussion and questions after the material is presented.

## Review of Literature

Historically, there have been myths about the ability of infants and children to recognize and/or remember pain. A study by McGraw (1941) conveyed a message to many clinicians that infants do not feel pain or have any memory of pain therefore they do not require analgesia. There were also reports that children up to the age of two years old did not have the neurological capability of experiencing or remembering pain (Pabis, Kowalczyk, & Kulik, 2011). This "evidence" combined with the fear of opioid effects in children provided the basis for lack of

analgesic treatment in children for more than 30 years. In the 1950s, Italy first began researching pain in children. Before the 1970's, pediatric pain literature was almost non-existent. A search on pediatric pain via the University of North Dakota's Harley E. French Library of the Health Sciences revealed only nine articles published on pediatric surgical pain before 1980. Throughout the 1980s, there were 58 articles and discussion of pain management in the newborn. The majority of information on pain in children started in the 1990s and continues today. In 2001, the Joint Commission for the Accreditation of Healthcare Organizations (JCAHO) disseminated standards for pediatric pain. More knowledge is being gained on pediatric pain; however, there are many ethical considerations when performing studies on children, especially when researching pharmacologic methods of treatment.

It is important to review the past to realize how far research has come in the area of pain management in children. Lowery, Hardman, Manning, Hall, & Anand (2007) describe the development of structures needed to experience pain using postconceptual age. Sensory fibers are abundant by 20 weeks; a functional spinal reflex is present by 19 weeks; connections to the thalamus are present by 20 weeks; and connections to subplate neurons are present by 17 weeks with intensive differentiation by 25 weeks (Lowery et al., 2007). According to Lowery et al. (2007), the ability for a fetus to experience pain occurs when mature thalamocortical projections are present at 29-30 weeks. Research conducted during the past few decades has provided valuable data to refute previously held misconceptions concerning the inability for children to experience pain. This has considerably changed the practice of health care providers.

Many factors play a role in the pediatric patient's perception of pain and there are just as many studies available on attenuating postoperative pain. Treatments are being employed at various times throughout a child's perioperative experience and may include nonpharmacologic

methods such as: music therapy, pet therapy, hypnosis, play therapy, modeling and rehearsal which are used to help decrease anxiety preoperatively and postoperatively. Reduced anxiety may also come from allowing parents to be present during induction of anesthesia or from pharmacological agents provided orally.

The primary focus of this literature review involves the use of pharmacologic techniques employed intraoperatively to decrease pediatric pain in the immediate postoperative period. The medications reviewed will be divided into either non-opioid medications or opioid medications.

## Non-Opioid Medications

Nonsteroidal anti-inflammatory drugs (NSAIDs) inhibit platelet cyclooxygenase which is an enzyme that catalyzes the synthesis of prostaglandins from arachidonic acid (Stoelting & Hillier, 2006). Prostaglandins mediate a number of bodily processes including inflammation and pain. NSAIDS also prolong bleeding time by preventing the biosynthesis of thromboxane $A_2$, leading to reduced platelet aggregation (Stoelting & Hillier, 2006). NSAIDs are frequently used in children for treatment of fever (antipyretic), postoperative pain (analgesic) and inflammatory disorders (anti-inflammatory). They can be administered orally, intravascularly or intramuscularly. According to Rainsford (2009), the volume of distribution (Vd) and plasma clearance (CL) of NSAIDs are increased in children (up to 5 years old) compared to adults, though elimination half-life is similar in children and adults. These pharmacokinetic differences may be clinically significant and children may require relatively higher loading and/or maintenance doses. As children age, lower dosages may be required to achieve the same level of pain relief. According to Kokki (2003), NSAIDs are more effective in preventing pain than in the relief of established pain. NSAIDs are contraindicated in patients in whom sensitivity reactions are precipitated by aspirin (acetylsalicylic acid) or other NSAIDs. They should be used with

caution in children with liver dysfunction, impaired renal function, hypovolemia or hypotension, coagulation disorders, thrombocytopenia, or active bleeding from any cause (Kokki, 2003). NSAIDS are generally well tolerated and severe adverse effects in children are rare. The analgesic efficacy of ketorolac, ketoprofen, diclofenac and ibuprofen in the treatment of postoperative pain has been mainly studied following a single dose, in children of > or = 1 year of age undergoing minor surgeries (Litalien & Jacqz-Aigrain, 2001). A few studies indicate that ketorolac may increase bleeding more so than other NSAIDs, but evidence is conflicting (Kokki, 2003).

Ketorolac is a NSAID with potent analgesic effects and relatively low risk of adverse effects (Forrest, Heitlinger, & Revell, 1997). It is a particularly useful drug for postoperative pain management both as the sole analgesic and to supplement opioids. Ketorolac reversibly inhibits the metabolism of arachidonic acid, which is released when cells are damaged (Stoelting & Hillier, 2006). According to Bean-Lijewski & Hunt (1996), metabolism of arachidonic acid via the cyclooxygenase pathway results in the production of prostaglandins and thromboxanes, which are potent vasodilators and modulators of peripheral pain. The result is a decreased sensitization of tissue nociceptors that occurs with surgery. Ketorolac when combined with an opioid exhibits marked opioid-sparing effects, allowing a lower dosage of opioid to be used and improves the degree and quality of pain relief. Using the drugs together reduces the incidence of opioid-related adverse effects such as respiratory depression, cardiovascular depression, nausea/vomiting, urinary retention, sedation and ileus.

Of the studies reviewed, the recommended intravenous dosage of ketorolac in children is 0.5-0.75 mg/kg. The maximum duration of treatment for ketorolac is 48 (1 mg/kg)-72 (0.5 mg/kg) hours. Ketorolac is approved in pediatric patients >2 years. It may induce life-

threatening bronchospasm in patients with nasal polyposis, asthma, and aspirin sensitivity (Stoelting & Hillier, 2006).

Numerous clinical trials of postoperative pain treatment in children have shown that ketorolac is as effective as the major opioid analgesics and more effective than codeine (Forrest et al., 1997). While ketorolac has been proven to improve post-tonsillectomy pain in children, controversy exists regarding use of ketorolac and the risk of postoperative hemorrhage in children undergoing this procedure. Marret, Flahault, Samama, & Bonnet (2003) conducted a small meta-analysis of seven prospective, randomized, double-blind trials in adults and children. Results indicated that the risk of reoperation for hemostasis, which is associated with a high risk of morbidity related to pulmonary aspiration and difficult tracheal intubation, was nearly fourfold greater after NSAIDs, prompting recommendations to avoid NSAIDs following ENT surgery (Marret et al., 2003). A study designed by Splinter, Rhine, Roberts, Reid, & MacNeill (1996) was meant to test the effect of codeine and ketorolac on postoperative vomiting in tonsillectomy patients. The study was terminated due to ethical reasons after five of the 35 patients who received ketorolac required admission to the hospital due to bleeding.

Evidence of contradictory studies includes one performed by Agrawal, Gerson, Seligman, Dsida in 1999. Over a 2-year period investigators examined office records of 310 pediatric patients, 213 who received ketorolac administered as a single dose at the conclusion of the tonsillectomy procedure and 97 patients who did not receive ketorolac. Postoperative hemorrhage was not found to differ significantly between these 2 groups (2.3% vs. 3.1% respectively, P=0.71). Ketorolac was not found to increase the incidence of posttonsillectomy hemorrhage and was actually associated with a significant decrease in the length of hospital stay as well as a decreased likelihood of overnight hospital stay after surgery.

A more recent evaluation by the Cochrane Anesthesia Review Group included 13 pediatric trials involving 955 children undergoing tonsillectomy and receiving NSAIDs perioperatively compared to another analgesic or placebo. In the review, a subgroup analysis for ketorolac was performed. NSAIDs were not found to significantly alter perioperative bleeding (Peto odds ratio 1.46, 95% CI 0.49-4.40) and in seven trials involving 567 children the odds ratio for bleeding requiring reoperation was 0.91 (CI 0.22-3.71) when ketorolac was excluded (Cardwell, Siviter, & Smith, 2005).

Many uncontrollable elements influence whether patients will experience posttonsillectomy hemorrhage, such as the skill of the surgeon, operative technique used, and the patient's coagulation status which is not routinely performed. While NSAIDs have been proven to decrease postoperative pain, ketorolac use in tonsillectomy patients remains controversial due to the potential increase in postoperative bleeding.

Perioperative use of cyclooxygenase (COX)-2 selective NSAIDs may offer a safer alternative in the management of posttonsillectomy pain than nonselective NSAIDs currently available in pediatric formulations. According to Ivani, Tonetti, & Mossetti (2005), COX-2 inhibitors do not interfere with platelet function and are associated with fewer bleeding complications. The most recent studies on COX-2 selective NSAIDS suggest analgesic effects similar to conventional NSAIDS when used for acute pain postoperatively or preoperatively.

Acetaminophen in a widely used analgesic and antipyretic, however it lacks significant anti-inflammatory effects and the mode of action is not completely understood. Its site of analgesic action is within the CNS and it may also work to activate serotonin receptors inhibiting the cyclooxygenase pathway in prostaglandin synthesis (Stoelting & Hillier, 2006). In the past, acetaminophen had been given to children primarily by rectal suppository after induction of

anesthesia. Studies have determined that an initial rectal acetaminophen dose of approximately 40 mg/kg is needed in children to achieve target antipyretic serum concentrations. It is now available on the market as Ofirmev, a drug that may be administered intravenously (IV). IV infusion dosing for children 2-12 years old is 10-15 mg/kg every 4- 6 hours, not to exceed five doses (50-75 mg/kg) in 24 hours. When given IV it must be administered over 15 minutes and the maximum dose per day is 75 mg/kg. Ofirmev does not bind significantly to serum proteins. Maximum concentration occurs at the end of the 15 minute intravenous infusion of ofirmev, which is 70% higher than following oral administration of acetaminophen. Unlike salicylates, acetaminophen does not produce gastric irritation or alter aggregation characteristics of platelets. Bleeding time is not prolonged as it is with NSAIDs resulting in lower risk with use in patients undergoing tonsillectomy. The risk associated with acetaminophen use includes hepatic toxicity with daily dosages that exceed 75 mg/kg and it is contraindicated in patients with hypersensitivity to acetaminophen or in patients with severe hepatic impairment or active liver disease. Acetaminophen is a safe and effective analgesic, however often provides unsatisfactory analgesia when used alone (Romsing, Ostergaard, Drozdziewicz, Schultz, & Ravn, 2000).

Acetaminophen has been used for analgesia for years; however, Ofirmev (the intravenous form of acetaminophen) was just recently launched in the United States on the 18th of January, 2011. The effectiveness and analgesic duration of IV versus rectal acetaminophen can be found in a trial completed by Capici, et al, (2008). The randomized, controlled study involved 50 children undergoing adenoidectomy/tonsillectomy assigned to either receive 40 mg/kg rectal or 15 mg/kg IV acetaminophen. The time to first rescue analgesia request was longer in children receiving rectal acetaminophen (median 10 hrs) compared to those receiving IV acetaminophen (median 7 hrs), indicating rectal acetaminophen 40 mg/kg provides longer analgesia for

moderately painful procedures when compared to 15 mg/kg acetaminophen IV. Research on IV acetaminophen in children is limited due to its recent release; however Atef & Fawaz (2008) conducted a randomized, double blind, prospective, placebo-controlled study on 76 adult subjects. Subjects were either assigned to an acetaminophen group or the placebo group to determine the analgesic efficacy and safety of intravenous acetaminophen in adults undergoing bipolar diathermy tonsillectomy. Results indicated subjects in the acetaminophen group required significantly less rescue analgesics than those in the placebo group ($P < 0.001$). A disadvantage of using IV acetaminophen is the time frame of administration. Indications include giving the infusion over a period of 15 minutes before the start of surgery. General anesthesia in pediatric patients is typically induced using inhalation agents, which is immediately followed by obtaining IV access. Administering the medication prior to surgery would require IV access to be established preoperatively or may require waiting for 15 minutes before proceeding with the surgery. This puts the patient at risk of being under general anesthesia for a longer period of time. More information will continue to emerge on this new form of acetaminophen.

Dexamethasone is a synthetic corticosteroid with an anti-inflammatory effect of 0.75 mg equivalent to that of 20 mg of cortisol (Stoelting & Hillier, 2006). Dexamethasone has combined antiemetic and anti-inflammatory effects that may decrease postoperative tissue injury, edema and pain after electrocautery tonsillectomy (Elhakim, Ali, Rashed, Riad, & Refat, 2003). Dexamethasone is being widely used in the pediatric population for tonsillectomy. It has been shown to attenuate the morbidity that children experience in the first 2 days after surgery (Giannoni et al., 2002). Common dosing of Dexamethasone is 0.5 mg/kg IV. The benefit to using dexamethasone is that a single dose is considered safe. Risks involve long-term administration of corticosteroids that may be associated with adverse events, such as increased risk of infection,

delayed wound healing, glucose intolerance, adrenal suppression, and vascular necrosis of the hip or other joints (Stoelting & Hillier, 2006).

Past studies conducted on dexamethasone's analgesic potential in children have produced conflicting results; however, the most recent studies concur that dexamethasone contributes to analgesia when used in children undergoing tonsillectomy. Elhakim et al. (2003) produced a randomized, double-blind, placebo-controlled study using 120 participants to determine if a single dose of dexamethasone affected the severity of postoperative vomiting and pain in children undergoing electrocautery tonsillectomy under standardized general anesthesia. Results of the study revealed that the time to first oral intake was shorter and the time to first dose of analgesic was longer in the dexamethasone group ($P < 0.01$). Pain scores 30 min after extubation were lower ($P < 0.05$) in the dexamethasone group and at 12 and 24 hours postoperative swallowing was significantly less painful in the dexamethasone group than in the control group ($P < 0.01$). In a similar but smaller prospective, double-blinded, placebo-controlled study conducted by Kaan, Odabasi, Gezer, and Daldal (2006), 62 children (4-12 years of age) were randomly assigned to receive a single dose of 0.5 mg/kg iv dexamethasone preoperatively. Patients who received preoperative dexamethasone had a significantly less pain score during the first 6 hr postoperatively ($P < 0.05$), adequate oral intake time was shorter ($P<0.05$) and discharge time was earlier ($P<0.05$) than those treated with placebo. In those studies, preoperative dexamethasone was found to significantly reduce early post-tonsillectomy pain at rest and during swallowing, resulted in improved quality of oral intake during the first 24 hours, and facilitated meeting discharge criteria.

Dexamethasone has also proven effective when used to supplement other analgesics. Mohamed, Ibraheem, & Abdelraheem (2009) performed a double-blind randomized control trial

on 150 children participants to determine the postoperative analgesic efficacy of the pre-surgical intravenous administration of dexamethasone in conjunction with glossopharyngeal nerve block (GNB) in children undergoing tonsillectomy. The study compared pre-operative dexamethasone IV injection with GNB to using either method alone. Absolute analgesia time was significantly longer in the group having both methods than either of the other two groups (P=0.000). Time to first request for analgesia was also significantly longer in the group that received both compared to the other groups (P=0.000). Patients in the group with both were discharged earlier from the hospital (P=0.000). Contradicting this study is one performed by Giannoni, White, & Enneking (2002). A prospective, randomized, double–blinded study was performed on 50 children comparing the effects of ropivicaine/clonidine injection with either dexamethasone (1 mg/kg up to 16 mg) or placebo saline (0.25 mL/kg up to 4 mL). Results indicated similar reported pain and narcotic use in the postanesthesia care unit and at home on all postoperative days measured. Overall, there was no decrease in pain and there was a trend to a longer recovery to normal activity in the group that received dexamethasone. Due to the small sample size of this study statistical effect may have been blunted.

Ketamine is a phencyclidine derivative that produces "dissociative anesthesia," characterized by evidence on EEG of dissociation between the thalamocortical and the limbic system, which is responsible for interpretation of painful signals (Stoelting & Hillier, 2006). The state of unconsciousness produced is different from other anesthetics and the patient appears nonreactive to his/her environment. Ketamine binds noncompetitively to N-methyl-D-aspartate (NMDA) receptors located in the spinal cord dorsal horn (Stoelting & Hillier, 2006). Spinal cord sensitization is responsible for pain associated with touching or moving an injured body part, a process triggered by C fiber nociceptive input and activation of NMDA receptors (Stoelting &

Hillier, 2006). Ketamine is hypothesized to provide preventative analgesia by preventing or reversing central sensitization and consequently reducing postoperative pain (Honarmand, Safavi, & Jamshidi, 2008). The induction dose of ketamine is 1-2 mg/kg IV or 4-8 mg/kg IM. A subanesthetic dose of 0.2-0.5 mg/kg injected IM is proven to produce intense analgesia when injected through the tonsillar capsule.

Ketamine is water-soluble and has a rapid onset of action, relatively short duration of action, high lipid solubility, and is poorly bound to plasma proteins. Peak plasma concentrations of ketamine occur within 1 minute after IV administration and within 5 minutes after IM injection (Stoelting & Hillier, 2006). Benefits of using ketamine as an anesthetic include maintenance of blood pressure and preservation of laryngeal reflexes. It may be used for children presenting with neuromuscular disease associated with malignant hyperthermia triggered by volatile agents or neuromuscular blocking drugs. Ketamine is rarely associated with allergic reactions and does not evoke the release of histamine. Risks of using ketamine include psychodysphoric symptoms including visual, auditory, proprioceptive and confusional illusions, which may progress to delirium. Emergence delirium may limit the clinical usefulness of ketamine in children (Stoelting & Hillier, 2006).

Ketamine may be used intravascularly for analgesia; however, some of the most recent studies published have been on the use of ketamine for peritonsillar infiltration. Honarmand et al. (2008) conducted a randomized, double-blinded, placebo-controlled study to determine the effect of preincisional peritonsillar infiltration of two doses of ketamine and placebo of normal saline on postoperative pain relief in children undergoing adenotonsillectomy. Children's Hospital Eastern Ontario Pain Scale (CHEOPS) scores were significantly higher in the placebo group compared to the other two groups ($P < 0.001$). Results indicated that peritonsillar infiltration

with 0.5 or 1 mg/kg dose of ketamine given approximately 3 min before surgery provides efficient pain relief for the first 24 hours after surgery without side-effects in children undergoing adenotonsillectomy. Time to extubation was significantly longer in the ketamine groups than the saline group. Although the study seemed to be well thought out, further research on the difference between a ketamine injection and that of a local anesthetic (opposed to saline) would be intriguing. Erhan, Goksu, Alpay, & Bestas (2007) conducted a similar study to determine the effectiveness of ketamine 0.5 mg/kg by peritonsillar infiltration. Results indicated the CHEOPS value, the time to first anesthetic, and the total amount of analgesic were all in favor of ketamine use ($p<0.05$).

An interesting randomized, controlled and double-blinded study on IV use of ketamine was conducted by Inanoglu, Ozbakis, Turhanoglu, Okuyucu, & Akoglu (2009) to determine the analgesic effects of IV ketamine with peritonsillar infiltration of bupivacaine on children undergoing tonsillectomy. The study involved three groups. Group I received intravenous and peritonsillar saline, Group II received intravenous saline and peritonsillar bupivacaine, and group III received intravenous 0.5 mg/kg ketamine and peritonsillar 0.25% bupivacaine 3-5 ml per tonsil. CHEOPS scores were used to evaluate pain and it was recorded at 6 different time intervals. Analgesic requirements were significantly ($P<0.05$) less and time to first analgesia were significantly ($P<0.05$) longer in the ketamine group.

Eishammaa et al. (2011) conducted a double blinded, randomized trial of 60 children between the ages 2 and 7 to determine if ketamine, as an adjunct to fentanyl, improved postoperative pain control in children undergoing tonsillectomy. Children were divided into four groups including, fentanyl 1 mcg/kg group, fentanyl 2 mcg/kg group, ketamine 0.5 mg/kg group, and fentanyl 1 mcg/kg plus ketamine 0.5 mg/kg group. Results of this study indicated that the

administration of ketamine 0.5 mg/kg with 1 mcg/kg fentanyl may improve postoperative pain control without delaying home discharge; however, this data may be skewed by the small number of subjects in each individual group.

In the studies discussed it would appear ketamine may serve as a useful adjunct to treatment of post-tonsillectomy pain. Many researchers have not reproduced similar results. Batra et al. (2007) conducted a randomized, double-blind, placebo-controlled prospective study of 40 children and found that use of small-dose ketamine, in conjunction with remifentanil, did not have a significant morphine-sparing effect in the perioperative period and did not significantly decrease postoperative pain in children after tonsillectomy. Another randomized double-blind study that did not find a significant decrease in postoperative morphine consumption post-tonsillectomy was conducted by Abu-Shahwan in 2008. This study included 84 subjects and compared two groups, one that received morphine and another that received morphine and 0.25 mg/kg ketamine at induction. A lack of significant results in these studies may be due to the small number of subjects. Those studies that found ketamine contributing to decreased opioid use were often using the higher 0.5 mg/kg ketamine dose in their research.

Dexmedetomidine is a highly selective, specific, and potent alpha$_2$-adrenergic agonist with anxiolytic, sedative, and analgesic properties (Stoelting & Hillier, 2006). The primary analgesic effect is mediated via action of the alpha$_2$ receptors on the dorsal horn of the spinal cord and also by inhibition of substance P (Tobias, 2007). Pretreatment with dexmedetomidine attenuates hemodynamic responses to tracheal intubation, decreases plasma catecholamine concentrations during anesthesia, decreases perioperative requirements for inhaled anesthetics and opioids, and increases likelihood of hypotension (Stoelting & Hillier, 2006). It has analgesic and sedative properties with minimal impact on respiratory function and decreases analgesic

requirements after surgery. High doses (loading dose of 1 mcg/kg IV followed by 0.25-0.5 mcg/kg/hour IV) produces total IV anesthesia without associated depression of ventilation (Tobias, 2007). The elimination half-time is 2-3 hours, it is highly protein bound (>90%), undergoes extensive hepatic metabolism and is excreted by the kidneys (Stoelting & Hillier, 2006). It has an inhibiting effect on cytochrome P450 enzyme system which manifests as increased plasma concentrations of opioids (Tobias, 2007).

Advantages of using dexmedetomidine are the mild analgesic properties, the ability to cause sedation without respiratory depression, and the fact that it does not have an effect on coagulation (Olutoye et al., 2010). Disadvantages include the sympatholytic effects and vagomimetic actions that result in decreased arterial blood pressure and heart rate which may be of concern in anesthetized children with a rate dependent cardiac output (Stoelting & Hillier, 2006). It also has a tendency to increase the range of temperatures likely to trigger thermoregulatory defenses, which may promote perioperative hypothermia.

Dexmedetomidine has been gaining popularity for use as an anesthetic in adults and studies are now being conducted to determine its relevance in pediatric anesthesia. Olutoye et al. (2010) conducted a prospective, randomized, double-blind study on 109 pediatric patients. The patients were put into one of four groups and received either a single IV dose of dexmedetomidine (0.75 mcg/kg), dexmedetomidine (1 mcg/kg), morphine (50 mcg/kg) or morphine (100 mcg/kg). Median time to first postoperative rescue analgesic was significantly longer in the dexmedetomidine 1 mcg/kg and morphine 100 mcg/kg compared to the other two groups ($P < 0.01$). Those participants who received dexmedetomidine compared to those who received morphine had significantly slower postoperative heart rate. The number of children who required >1 dose of rescue analgesic was significantly higher in the dexmedetomidine 0.75

mcg/kg group compared with dexmedetomidine 1.0 mcg/kg and morphine 100 mcg/kg groups (P=0.03 and P=0.013). Another study conducted by Patel, et al. (2010) used a prospective, randomized, blinded, controlled approach to research 137 children. They were assigned to either a dexmedetomidine infusion group (2 mcg/kg over 10 minutes, followed by 0.7 mcg/kg/h until 5 minutes before the end of surgery) or IV fentanyl group (1 mcg/kg) to determine its effect on perioperative opioid use. The amount of participants who needed rescue fentanyl for pain was significantly lower in the dexmedetomidine group compared to fentanyl (P = 0.001). Mean heart rate and mean systolic blood pressure were significantly lower in group dexmedetomidine during the first 60 minutes (P = 0.019). In this study, those who received the dexmedetomidine bolus and infusion had decreased intraoperative opiate and anesthetic requirements and decreased opiate requirements in the PACU compared to the IV fentanyl group.

A separate double-blind, randomized trial was conducted by Pestieau et al. (2011) to determine whether high doses of dexmedetomidine had an impact on opioid requirements and the opioid-free interval after tonsillectomy. 109 patients were assigned to one of four treatment groups. Group one was given fentanyl 1 mcg/kg, group two was given fentanyl 2 mcg/kg (current standard of practice groups), group 3 was given dexmedetomidine 2 mcg/kg and group 4 was given dexmedetomidine 4 mcg/kg. Results showed that dexmedetomidine prolongs the opioid-free interval after tonsillectomy and appears to decrease overall morphine requirements as well as the risk of morphine-rescue administration. The dexmedetomidine groups did have a prolonged time to emergence from anesthesia and an increased length of stay in the PACU. Dexmedetomidine appears to have opioid-sparing effects and was recommended by the authors to be considered as an adjunct for analgesia during and after tonsillectomies.

Use of dexmedetomidine in young, healthy patients may be restricted by its association

with episodes of bradycardia and sinus arrest. Cardiac output in pediatric patients is heart rate dependent, requiring maintenance of a regular rate and rhythm. Hypertension has also been observed following an initial bolus dose of dexmedetomidine. As with any pharmacologic agent, caution must be used when administering to a patient.

Local anesthetics have proven to be effective as an adjunct in the relief of postoperative pain. Many studies have shown bupivacaine to be more effective than levobupivicaine and ropivacaine when injected by the surgeon into the peritonsillar area at the completion of surgery. A randomized clinical trial comparing rectal acetaminophen with peritonsillar infiltration of bupivacaine for postoperative analgesia after adenotonsillectomy in children was conducted by Dahi-Taleghani, Mousavifard, Tahmoureszade, & Dabbagh (2011). The trial included 110 participants who were randomly separated into two groups, one receiving 30 mg/kg rectal acetaminophen and one receiving 1 mg/kg bupivacaine injection after intubation and prior to tonsillectomy. Results indicated that there was no difference between the two groups regarding throat pain at rest, after swallowing, after taking fluid and after soft food intake. The minimal amount of risk associated with rectal acetaminophen administration made it superior to bupivacaine injection in their opinion.

## Opioid Medications

Opioids provide analgesia by binding to specific receptors located primarily in the brain and spinal cord. They inhibit the release of substance P blocking pain pathways ascending to the brain where pain is perceived (Stoelting & Hillier, 2006). They also activate descending pathways to inhibit the transmission of nociceptive information (Golembiewski, Torrecer, & Katke, 2005). Opioids are frequently used for postoperative treatment of moderate to severe pain. Adverse effects of opioids include: respiratory depression, sedation, nausea and vomiting,

pruritus, constipation and voiding difficulties. Depression of ventilation occurs primarily through an agonist effect at $mu_2$ receptors leading to a direct depressant effect on brainstem ventilation centers (Stoelting & Hillier, 2006). Opioid action on kappa receptors leads to sedation which may prolong post-operative recovery. Nausea and vomiting associated with opioids is due to direct stimulation of the chemoreceptor trigger zone in the floor of the fourth ventricle (Stoelting & Hillier, 2006). The proportional increase in side effects with opioid use may lead to administration of smaller doses of the medication and decreased analgesia for patients.

Morphine is the prototype opioid and the agent to which all other opioids are compared. It has low lipid solubility and peak effect occurs 15-20 minutes after IV injection (Stoelting & Hillier, 2006). Morphine undergoes an extensive first-pass effect and is metabolized hepatically to morphine-3-gluronide (M-3-G) and morphine-6-glurcorunide (M-6-G) (Golembiewski et al, 2005). M-6-G provides greater analgesia than morphine and M-3-G provides no analgesia. Both byproducts are renally excreted (Golembiewski, 2005). The pediatric dose is 0.05-0.2 mg/kg/dose up to 15 mg and it provides several hours of analgesia. Disadvantages of using morphine include histamine release, pruritis, and hypotension. It must be used with caution in patients with hepatic impairment because it is metabolized by the liver. The active metabolites could accumulate and cause excessive sedation and respiratory depression. Caution should be used when administering to patients with renal impairment as well. According to Brown, Laferriere, Lakheeram, & Moss (2006), postsurgical administration of opiates in patients with obstructive sleep apnea (OSA) has recently been linked to an increased risk for respiratory complications. Previous recurrent hypoxemia in OSA has also been associated with increased analgesic sensitivity to subsequent morphine administration (Brown et al., 2006). Tonsillectomy and adenoidectomy is often performed on children with enlarged (hypertrophic) tonsils that

cause obstruction (often manifested by snoring) when the children are lying supine. The significance of these findings is due to the relationship between OSA and patients undergoing surgery for T&A.

Fentanyl is a phenylpiperidine-derivative synthetic opioid agonist. It is 75-125 times more potent than morphine due to greater lipid solubility (Stoelting & Hillier, 2006). It is more rapid in onset and shorter in duration of action than morphine and hydromorphone. Fentanyl has a larger volume of distribution and longer elimination half-time than morphine (Golembiewski et al., 2005). A common dose in pediatric patients is 1-2 mcg/kg IV. Fentanyl does not produce histamine release as morphine does. Risks of using fentanyl include persistent or recurrent depression of ventilation, bradycardia, hypotension, decreased cardiac output and chest rigidity with high doses. The analgesic effects of fentanyl last for up to one hour. Available literature suggests that differences in metabolism require modification in dosing and that 2-6 year old children have a more rapid metabolism, meaning that such children may require more frequent dosing. Fentanyl is used as the primary intraoperative analgesic in the majority of the literature reviewed. Recent studies have been directed at finding an alternative to fentanyl as an analgesic due to the respiratory depressant effects it possesses.

Remifentanil is a selective mu opioid agonist, structurally unique due to its ester linkage which renders it susceptible to hydrolysis by nonspecific plasma and tissue esterases to inactive metabolites. This form of metabolism imparts brevity of action, precise and rapidly titratable effect due to its rapid onset and offset, noncumulative effects, and rapid recovery after discontinuation of its administration. It has an analgesic potency similar to fentanyl and effect-site (blood/brain) equilibration time much faster than that of fentanyl (1.1 min vs. 6.8). It has a small volume of distribution, is rapidly cleared and renally excreted. Beneficial effects of

remifentanil include rapid onset of drug effect, precise titration to the desired effect, ability to maintain a sufficient plasma opioid concentration to suppress the stress response, and rapid recovery from the drug's effects. With remifentanil there is a predictability of drug effect due to esterase metabolism. Lack of accumulation during extended periods of infusion prevents prolonged clearance not seen with sufentanil or fentanyl. There is no histamine release with remifentanil. The common recommended dose is 1 mcg/kg IV over 60-90 seconds. The combination of remifentanil and propofol is synergistic resulting in severe depression of ventilation. A longer-acting opioid must be administered for post-operative analgesia when remifentanil is used. Associated side effects include nausea and vomiting, depression of ventilation and mild decreases in systemic blood pressure and heart rate.

Davis et al. (2000) conducted a double-blinded study to determine the effectiveness of remifentanil versus fentanyl in pediatric tonsillectomy patients. The two groups were randomly selected to receive either remifentanil bolus with continuous infusion 0.25 microg/kg/min or a fentanyl bolus of 2 mcg/kg followed by a placebo continuous infusion. Remifentanil provided faster extubation times, although those patients had higher pain-discomfort scores. The researchers concluded that remifentanil was as effective intraoperatively as fentanyl, however better intraoperative prophylactic analgesic regimens for postoperative pain control were necessary to optimize remifentanil's use as an analgesic for children. More research is being conducted on remifentanil in association with painful procedures in neonates such as endotracheal intubation and mechanical ventilation and central line placement.

Sufentanil is a thienyl analogue of fentanyl. The analgesic potency is 5-10 times that of fentanyl with greater affinity to opioid receptors. It is highly lipid soluble, has extensive protein binding, and has a smaller volume of distribution than fentanyl. Elimination half-time is between

that of fentanyl and alfentanil. A common dose is 0.1-0.4 mcg/kg. Sufentanil use is beneficial over fentanyl due to production of longer periods of analgesia and less depression of ventilation. It should be used with caution in patients with chronic renal failure and chest wall rigidity may occur with high doses. The only study found on the use of sufentanil in tonsillectomy was conducted by Bayrak, Gunday, Memis, & Turan (2007). Results indicated that an intranasal sufentanil dose of 2 micrograms/kg provided anxiety and cooperation scores similar to that of oral midazolam when used perioperatively.

Hydromorphone is a hydrophilic opioid and a semi-synthetic derivative of morphine. It is 5-10 times more potent, has a longer serum half-life (3 vs 2 hr), and volume of distribution (4.5 vs 3 L/kg) than morphine. It produces more sedation and evokes less euphoria than morphine. Hydromorphone has a lipid solubility range that falls between morphine and fentanyl. Breakdown products include hydromorphone-6-glucuronide and hydromorphone-3-gluronide which have no analgesic properties and are renally excreted. H-3-G may have potential to cause neuroexcitatory effects when high levels occur in a patient with renal failure with chronic dosing. The recommended pediatric dose is 1 mcg/kg. Journal articles recently published describe medication errors related to hydromorphone overdose. Many patients are experiencing acute respiratory depression, sedation, severe hypotension and in multiple cases cardiopulmonary arrest and death. While the drug when used appropriately seems to be effective, errors occur due to misunderstanding about the drugs equi-analgesic dosing when compared with morphine. McDonnell (2011) looked at opioid medication errors in pediatric practice and found that medication errors involving hydromorphone and codeine resulted in the most significant harm reported. Pharmacological advantages that hydromorphone offers over morphine include a longer half-life and lack of metabolites. Unfortunately, literature on hydromorphone use in

pediatric patients is rare and studies conducted to support hydromorphone for clinical use is nonexistent.

## Discussion

Each painful experience a patient has accumulated through their lifetime plays a role in how the patient will respond to the existing painful experience. Family background, emotional status, expectations, and physiological variables all affect a patient's perception of and experience with pain. A large component present in children is the emotional part of the pain experience. They are affected by factors such as the presence or absence of caregivers and fears related to unfamiliar surroundings, people and procedures. Each person will respond differently to the same painful procedure, so how do we know that someone is, in fact, having pain.

Pain can be assessed in a variety of ways, including self-report, behavioral observation or physiologic measures. Verbal self-report of pain is considered the gold standard for assessment. In patients undergoing general anesthesia verbal self-report is not an option. Pain is assessed by CRNAs throughout the intraoperative period through physiologic measures. Blood pressure, heart rate, and respiratory rate are among the most commonly used physiologic means to monitor pain. Inability to communicate does not imply that pain does not exist, but children who can't verbalize are an example of the importance of an accurate and sensitive assessment of pain.

Pain scales have been developed to help assess and guide the administration of analgesics; however, they lack precision and reliability to exclusively direct analgesic dosing. While assessment tools have become a standard measure in which to monitor a child's pain, choosing the appropriate assessment tool for the patient's age, developmental stage and context of the pain experience is difficult and creates variability among providers. Refining or modifying

pain scales may be needed to make pain assessment more reliable and consistent.

Once the appropriate pain scale has been chosen, the patient has been assessed as having significant pain, and the decision to proceed with administration of an analgesic has been made, healthcare providers continue to experience barriers to treating pain. The primary concern in providers administering opioid analgesics is the fear of causing respiratory depression in the child. Other barriers that have been researched include fear of addiction and an overall lack of knowledge on pediatric pain treatment.

Inadequate treatment of pain leads to adverse physiological effects which may delay healing and contribute to increased healthcare costs. Increased respiratory rate and decreased volume can lead to retained secretions and atelectasis. Heart rate, cardiac output, and systemic vascular resistance may be increased with pain and lead to increased blood pressure and myocardial O2 consumption. Pain increases the release of stress hormone and also increases the metabolic rate. It depresses the immune system predisposing patients to infection.

Effective control of postoperative pain involves several preventative strategies that include preoperative analgesia, appropriate use of intraoperative analgesic techniques, and identification of children at risk for significant postoperative pain. There are several complimentary and integrative medicine approaches that may be used in addition to pharmacologic methods of analgesia. Acupuncture and acupressure, therapeutic touch, yoga, massage, heat and cold therapy, naturopathy, and physical therapy/occupational therapy have all been studied in relation to attenuating postoperative pain. Cognitive and behavioral approaches including: patient/family education, psychotherapy, relaxation and imagery, therapeutic play, music therapy, and animal therapy have been researched as well.

Pharmacologic agents chosen to treat pain vary from practitioner to practitioner. As more

research is conducted on the pharmacokinetic and pharmacodynamic properties of these agents, more knowledge is being revealed on mechanism and sites of action of these analgesic drugs. Although these analgesic drugs continue to be investigated, ethical considerations in the study of pediatric populations often hinders researchers from performing randomized controlled trials that direct pain management in children.

Multimodal analgesia is the concept of using different classes of analgesics for pain alteration at various receptor sites to provide the maximum analgesic effect with reduced analgesic-related side effects (Joshi, 2005). Many clinicians are utilizing the multimodal approach to pain management in an attempt to reduce the unwanted side effects of giving large doses of a particular drug. For instance, acetaminophen and NSAIDs when given in conjunction with opioids may reduce the amount of opioid required. This may lead to decreased risk of side effects in opioids such as respiratory depression and nausea/vomiting. It is also important to note the synergistic effects of analgesics, anxiolytics, antiemetics, and antihistamines require ongoing assessment of sedation and analgesia.

Treating pain early and effectively is safer, more efficacious and results in improved patient comfort. It may also result in less total analgesic administered.

## Outcome

This information was presented to CRNAs and current nurse anesthesia students at the Fall 2011 meeting of the North Dakota Association of Nurse Anesthetists in Bismarck, ND. Included in the power point presentation were an introduction, statement of problem, purpose of the study, significance of the study, areas of inquiry, overview of methods, and references.

## Implications for Nursing

Dosing analgesics for the management of postoperative pain in children continues to challenge anesthesia providers and the nurses recovering them. Finding the specific combination of medications that provides the most effective relief of postoperative pain in children may be an idealistic goal. It is critical that anesthesia providers and recovery nurses realize that children, like adults, do not all respond to pain the same way.

There is a continued need for research in the area of intraoperative pain management, especially in the pediatric population. Of those analgesics that have been studied, many have conflicting results which contributes to confusion. It was disappointing to learn that there was limited or no information on children regarding some analgesics commonly used in adults. Providers need to stay current on the most recent studies and their findings on pediatric pain management and challenge themselves to provide a multimodal analgesic that result in effective postoperative pain control. Anesthetic practice may need to be altered as new information and techniques for intraoperative pain management emerge. Hospital policies need to incorporate standards for the assessment and treatment of postoperative pediatric pain in the postanesthesia care unit. It is important that patients and their parents are satisfied with their perioperative experience.

## Conclusion

Postoperative pediatric pain remains a significant morbidity associated with surgery in children. Many analgesic medications with a variety of dosages and means of administration were identified in the literature. Although the research does not seem to highlight one intraoperative analgesic technique proven to be the most effective, many combinations of

medications may be used to provide analgesia. There is a continued need for research on postoperative pediatric pain and on analgesic agents that have not yet been studied in children. Pain management should be one of the primary goals of healthcare providers managing pediatric patients undergoing surgical procedures.

**References**

Abu-Shahwan, I. (2008). Ketamine does not reduce postoperative morphine consumption after tonsillectomy in children. *Clinical Journal of Pain, 24*(5), 395-398.

Agrawal, A., Gerson, C., Seligman, I. & Dsida, R. (1999). Postoperative hemorrhage after tonsillectomy: Use of ketorolac tromethamine. *Otolaryngology-Head and Neck Surgery, 120*(3), 335-339.

Atef, A. & Fawaz, A. (2008). Intravenous paracetamol is highly effective in pain treatment after tonsillectomy in adults. *European Archives of Otorhinolaryngology, 265*(3), 351-355.

Batra, Y., Shamsah, M., Al-Khasti, M., Rawdhan, H., Al-Qattan, A., & Belani, K. (2007). Intraoperative small-dose ketamine does not reduce pain or analgesic consumption during perioperative opioid analgesia in children after tonsillectomy. *International Journal of Clinical Pharmacology and Therapeutics, 45*(3), 155-160.

Bayrak, F., Gunday, I., Memis, D., & Turan, A. (2007). A comparison of oral midazolam, oral tramadol, and intranasal sufentanil premedication in pediatric patients. *Journal of Opioid Management, 3*(2), 74-78.

Bean-Lijewski, J. & Hunt, R. (1996). Effect of ketorolac on bleeding time and postoperative pain in children: A double-blind, placebo-controlled comparison with meperidine. *Journal of Clinical Anesthesia, 8*, 25-30.

Bean-Lijewski, J., Kruitbosch, S., Hutchinson, L., & Browne, B. (2007). Post-tonsillectomy pain in children: Can we do better? *Otolaryngology-Head and Neck Surgery, 137*, 545-551.

Brown, K., Laferriere, A., Lakheeram, I., & Moss, I. (2006). Recurrent hypoxemia in children is associated with increased analgesic sensitivity to opiates. *Anesthesiology, 105*(4), 665-669.

Capicia, F., Ingelmo, P., Davidson, A., Sacchi, C., Milan, B., Sperti, L., Lorini, L, & Fumagalli, R. (2008). Randomized controlled trial of duration of analgesia following intravenous or rectal acetaminophen after adenotonsillectomy in children. *British Journal of Anaesthesia, 100*(2), 251-255.

Cardwell, M., Siviter, G., & Smith, A. (2005). Non-steroidal anti-inflammatory drugs and periopertative bleeding in paediatric tonsillectomy. *The Cochrane Library, 18*(2), 1-44.

Dahi-Taleghani, M., Mousavifard, S., Tahmoureszade, S., & Dabbagh, A. (2011). Rectal acetaminophen versus peritonsillar infiltration of bupivacaine for postoperative analgesia after adenotonsillectomy in children. *European Archives of Otorhinolaryngology, 268*(4), 581-584.

Davis, P., Finkel, J., Orr, R., Fazi, L., Mulroy, J., Woelfel, S., Hannallah, R., Lynn, A., Kurth, C., Moro, M., Henson, L., Goodman, D., & Decker, M. (200). A randomized, double-blinded study of remifentanil versus fentanyl for tonsillectomy and adenoidectomy surgery in pediatric ambulatory surgical patients. *Anesthesia and Analgesia, 90*(4), 863-871.

Eishammaa, N., Chidambaran, V., Housny, W., Thomas, J., Zhang, X., & Michael, R. (2011). Ketamine as an adjunct to fentanyl improves postoperative analgesia and hastens discharge in children following tonsillectomy-a prospective, double-blinded, randomized study. *Paediatric Anaesthesia, 21*(10), 1009-1014.

Elhakim, M., Ali, N., Rashed, I., Riad, M., & Refat, M. (2003). Dexamethasone reduces postoperative vomiting and pain after pediatric tonsillectomy. *Canadian Journal of Anesthesia, 50*(4), 392-397.

Erhan, O., Goksu, H., Alpay, C., & Bestas, A. (2007). Ketamine in post-tonsillectomy pain. *International Journal of Pediatric Otorhinolaryngology, 71(*5), 735-739.

Forrest, J., Heitlinger, E., & Revell, S. (1997). Ketorolac for postoperative pain management in children. *Drug Safety, 16*(5), 309-329.

Fortier, M., MacLaren, J., Martin, S., Perret-Karimi, D., & Kain, Z. (2009). Pediatric pain after ambulatory surgery: Where's the medication? *Pediatrics, 124*(4), 588-595.

Giannoni, C., White, S., & Enneking, F. (2002). Does dexamethasone with preemptive analgesia improve pediatric tonsillectomy pain? *Otolaryngology-Head and Neck Surgery, 126*(3), 307-315.

Golembiewski, J., Torrecer, S., & Katke, J. (2005). The use of opioids in the postoperative setting: Focus on morphine, hydromorphone, and fentanyl. *Journal of PeriAnesthesia Nursing, 20*(2), 141-143.

Gulhas, N., Durmus, M., Demirbilek, S., Togal, T., Ozturk, E., & Ersoy, O. (2003). The use of magnesium to prevent laryngospasm after tonsillectomy and adenoidectomy: A preliminary study. *Pediatric Anaesthesia, 13*(1), 43-47.

Hing, E. & Burt, C.W. (2007). Characteristics of office-based physicians and their practices: United States, 2003-04. Series 13, No. 164. Hyattsville, MD: National Center for Health Statistics.

Honarmand, A., Safavi, M., & Jamshidi, M. (2008). The preventative analgesic effect of preincisional peritonsillar infiltration of two low doses of ketamine for postoperative pain relief in children following adenotonsillectomy. A randomized, double-blind, placebo-controlled study. *Pediatric Anesthesia, 18*, 508-514.

Inanoglu, K., Ozbakis, B., Turhanoglu, S., Okuyucu, S., & Akoglu, E. (2009). Intravenous ketamine and local bupivacaine infiltration are effective as part of a multimodal regime for reducing post-tonsillectomy pain. *Medical Science Monitor, 15*(10), 539-543.

Ivani, G., Tonetti, F., & Mossetti, V. (2005). Update on postoperative analgesia in children. *Minerva Anestesiologica, 71*, 501-505.

Joshi, G. (2005). Multimodal analgesia techniques and postoperative rehabilitation. *Anesthesiology Clinics of North America, 23*(1), 185-202.

Kaan, M., Odabasi, O., Gezer, E., & Daldal, A. (2006). The effect of preoperative dexamethasone on early oral intake, vomiting and pain after tonsillectomy. *International Journal of Pediatric Otorhinolaryngology, 70*(1), 73-79.

Kain, Z., Mayes, L., Caldwell-Andrews, A., Karas, D., & McClain, B. (2006). Preoperative anxiety, postoperative pain, and behavioral recovery in young children undergoing surgery. *Pediatrics, 118*, 651-658.

Kokki, H. (2003). Nonsteroidal anti-inflammatory drugs for postoperative pain: A focus on children. *Paediatric Drugs, 5*(2), 103-123.

Litalien, C. & Jacqz-Aigrain, E. (2001). Risks and benefits of nonsteroidal anti-inflammatory drugs in children: A comparison with paracetamol. *Paediatric Drugs, 3*(11), 817-858.

Lonnqvist, P., & Morton, N. (2006). Paediatric day-case anaesthesia and pain control. *Current Opinion in Anaesthesiology, 19*, 617-621.

Lowery, C., Hardman, M., Manning, N., Hall, R., & Anand, K. (2007). Neurodevelopmental changes of fetal pain. *Seminars in Perinatology, 31*, 275-282.

Marret, E., Flahault, A., Samama, C., & Bonnet, F. (2003). Effects of postoperative, nonsteroidal, anti-inflammatory drugs on bleeding risk after tonsillectomy. *Anesthesiology, 98*, 1497-1502.

Marschall, S. & Chung, F. (1999). Discharge criteria and complications after ambulatory surgery. *Anesthesia & Analgesia, 88*, 508-517.

McDonnell, C. (2011). Opioid medication errors in pediatric practice: Four years' experience of voluntary safety reporting. *Pain Research and Management, 16*(2), 93-98.

McGraw, M.B. (1969). Neural maturation as exemplified in the changing reaction of the infant to pin prick: The neuromuscular maturation of the human infant. (Ed.: McGraw MB), Hafner, New York, 42-47.

Melzack, R. & Wall, P.D. (1965). Pain mechanism: A new theory. *Science, 150*(3699), 971 -979.

Mohamed, S., Ibraheem, A., & Abdelraheem, M. (2009). Preoperative intravenous dexamethasone combined with glossopharyngeal nerve block: Role in pediatric postoperative analgesia following tonsillectomy. *European Archives of Otorhinolaryngology, 266*(11), 1815-1819.

Mohommad, S., Shahrbano, S., & Ulhaq, T. (2008). Tramadol for pain relief in children undergoing adenotonsillectomy: A comparison with dextromethorphan. *The Laryngoscope, 118*, 1547-1549.

Morgan, G.E., Mikhail, M.S., & Murray, M.J. (2006). Clinical Anesthesiology (4th Ed.). New York: McGraw-Hill Companies, Inc.

Nagelhout, J.J. & Plaus, K.L. (2010). Nurse Anesthesia (4th Ed.). Missouri: Saunders Elsevier.

Olutoye, O., Glover, C., Diefenderfer, J., McGilberry, M., Wyatt, M., Larrier, D., Friedman, E., & Watcha, M. (2010). *Anesthesia and Analgesia, 111*(2), 490-495.

Pabis, E., Kowalczyk, M., & Kulik, T. (2011). Pain in children in historical perspective. *Anaesthesiology Intensive Therapy, 42*(1), 37-41.

Part III: Pain terms, a current list with definitions and notes on usage (p 209-214). Classification of chronic pain, 2nd ed., IASP Task Force on Taxonomy, edited by H.Merskey and N. Bogduk, IASP Press, Seattle, 1994. Retrieved from the International Association for the Study of Pain (IASP) website: http://www.iasp-pain.org

Patel,A., Davidson, M., Tran, M., Quraishi, H., Schoenberg, C., Sant, M., Lin, A., & Sun, X. (2010). Dexmedetomidine infusion for analgesia and prevention of emergence agitation in children with obstructive sleep apnea syndrome undergoing tonsillectomy and adenoidectomy. *Anesthesia and Analgesia, 111*(4), 1004-1010.

Pathophysiology of Pain. (2011). Retrieved from http://www.painedu.org/tools/pathophysiology_pain.asp

Pestieau, S., Zuezado, Z., Johnson, Y., Anderson, J., Cheng, Y., McCarter, R., Choi, S., & Finkel, J. (2011). *Canadian Journal of Anesthesia, 58*, 540-550.

Porth, C.M. (2005). Pathophysiology: Concepts of Altered Health States (7th Ed.). Pennsylvania: Lippincott Williams & Wilkins.

Rainsford, K.D. (2009). Ibuprofen: pharmacology, efficacy and safety. *Inflammopharmacology, 17*(6), 275-342.

Romsing, J., Ostergaard, D., Drozdziewicz, D., Schultz, P., & Ravn, G. (2000). Diclofenac or acetaminophen for analgesia in paediatric tonsillectomy outpatients. *Acta Anaesthesiologica Scandinavica, 44*(3), 291-295.

Splinter, W., Rhine, E., Roberts, D., Reid, C., & MacNeill, H. (1996). Preoperative ketorolac increases bleeding after tonsillectomy in children. *Canadian Journal of Anaesthesia, 43*(6), 560-563.

Stoelting, R.K. & Hillier, S.C. (2006). Pharmacology & Physiology in Anesthetic Practice (4th Ed.). Pennsylvania: Lippincott Williams & Wilkins.

The assessment and management of acute pain in infants, children, and adolescents. (2001). APS Bulletin, 11(5). Retrieved from The American Pain Society website: http://www.ampainsoc.org/library/bulletin/sep01/article1.htm

Tobias, J. (2007). Dexmedetomidine: Applications in pediatric critical care and pediatric anesthesiology. *Pediatric Critical Care Medicine, 8*(2), 115-131.

Trudeau, J., Lamb, E., Gowans, M., & Lauder, G. (2009). A prospective audit of postoperative pain control in pediatric patients. *AORN Journal, 90*(4), 531-542.