

Dexamethasone as Adjunct in Peripheral Nerve Blocks to Extend Analgesia

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### Abstract

The purpose of this scholarly project is to educate and assess the comprehension of Student Registered Nurse Anesthetists (SRNA) on the benefits of the administration of dexamethasone as an adjuvant while performing peripheral nerve blocks. Opioid administration continues to have adverse effects. With a growing opioid epidemic and exponential health care costs, it is essential for anesthesia providers to be cognitive of other alternatives to pain management modalities. A literature review on dexamethasone was conducted and shown to prolong the action of peripheral nerve blocks, decrease narcotic usage, and in turn will provide quicker recovery times for orthopedic surgeries. After a completion of the literature review, a formal presentation was conducted with a PowerPoint to 21 SRNAs. Pre-tests were administered prior to the presentation to evaluate baseline knowledge of dexamethasone usage with peripheral nerve blocks. A post-test was then administered to assess for an increase in knowledge from the lecture. A statistical analysis was conducted of the pre-and post-test results and a paired T test. A statistically significant P value of  $< 0.001$  was obtained in this study. Students' average scores improved significantly from pre-to post- testing.

Keywords: Dexamethasone, Peripheral Nerve Blocks, Orthopedic, Pain management

## Dexamethasone as Adjunct in Peripheral Nerve Blocks to Extend Analgesia

### **Introduction/Problem Statement**

Historically, opioids have been utilized as a standard of care for analgesic relief for acute and chronic pain. Orthopedic procedures often require more intensive pain management. Despite the utilization of opioids, adverse effects may include sedation, respiratory depression, constipation, nausea, and vomiting. Today, the United States faces an opioid epidemic as rates of addiction, tolerance, and abuse continues to multiply. Prescribers have been guilty of over prescribing, and national medication shortages in the clinical setting have caused concern and need for other pain management alternatives (Dasgupta, 2018).

Anesthesia providers are faced with the challenge of an opioid shortage when treating acute perioperative pain. Multimodal medication regimens are being utilized. Research for the best and safest practices continue to be explored. Therefore, anesthesia providers need to be aware of alternatives to opioids. An alternative may include the use of peripheral nerve blocks (PNB).

PNB have been utilized since 1884. William Halstead performed the first peripheral nerve block on the brachial plexus (Bailard, 2014). Since that time, the use of PNBs have become more popular and a preferred method of pain management especially in orthopedic patients (Bailard, 2014).

The purpose of this scholarly project is to explore and educate senior Student Registered Nurse Anesthetists (SRNA) on dexamethasone as an adjunct in peripheral nerve blocks in orthopedic patients. The scholarly project focuses on answering the following questions:

Does recent scientific literature support the addition of dexamethasone as an adjunct to PNB for patients undergoing orthopedic surgery?

PICOT: In Adventist University Student Registered Nurse Anesthetists (P), does a half hour (T) presentation on dexamethasone as an adjunct to PNB increase analgesia in orthopedic patients (I), result in an increase knowledge base (O)?

### **Literature Review and Synthesis**

Utilizing several search engines that included Google Scholar, Cinahl, Access anesthesiology, and Cochran collection, data was gathered into this literature review. Search terms utilized included orthopedic procedures with peripheral nerve blocks, dexamethasone, perioperative pain, acute and chronic pain. All journals were peer reviewed, and anesthesia texts were included for background pain pathophysiology.

With the increase of life expectancy, weight, and the number of comorbidities, post-operative pain management in orthopedic surgeries is anticipated to continue to be a problem for providers (Lim, 2017). Pain management is particularly a concern within the first 24 hours because it affects functional recovery, rates of morbidity, and the risk of chronic pain (Natarajan, 2017). With adverse effects from medications such as opioids and NSAIDS, a demand to explore other alternatives to prolong analgesia effects is needed (Natarajan, 2017). Peripheral nerve blocks have been utilized due to its proven efficacy, however, adjuncts to the blocks continue to be researched as well (Bailard, 2014). Upon a thorough review of literature, dexamethasone intravenous and perineural administration proves to be beneficial in providing prolonged pain relief in orthopedic patients receiving peripheral nerve blocks (Naim, 2016; Natarajan, 2017).

After surgery, there is a concern that patients' acute post-operative pain may become chronic due to the peripheral and central nervous system changes that occur with the initial pain transmissions. These are inflammatory or neuropathic in nature (Richebe, 2018). Pain sensitization occurs when nerve fibers under inflammation magnifies and continues to send pain

signals (Wainger, 2014). This sensitization of afferent nociceptors, also referred to as hyperalgesia, occurs generally after an injury or surgery where inflammatory mediators are produced. There are two kinds of sensitization: peripheral and central (Wainger, 2014). The central sensitization or immune response after nerve injury may be thwarted beginning with pre-emptive pain management to reduce perioperative pain that can potentially convert to chronic pain (Wainger, 2014).

Chronic pain etiology is complicated. C-Fibers appear to be important factors in both inflammatory and neuropathic pain transmission with primary hyperalgesia that leads to central sensitization (Wainger, 2014). Central sensitization comes from changes in the spinal cord and brain due to the repeated stimulation of C-Fibers with decreased thresholds. Repeated identical stimulation sending information centrally can potentially lead to increased firing of those neurons which leads to chronic pain (Wainger, 2014). Although it is relatively uncommon, many patients with Chronic Regional Pain Syndrome (CRPS) developed it after surgery, and many of those surgeries were orthopedic in nature (Reuben, 2004). According to Reuben (2004) many of the symptomatology of post-surgical inflammation mimics CRPS, and differentiation is unclear when diagnosing this syndrome. Preoperative pain that is often found in orthopedic surgical candidates predisposes them to a higher risk of chronic pain. Preoperative pain that is more severe may alter the nociceptive pathways which can increase the patient's risk of developing CRPS (Wainger, 2014). Controlling pain in the acute phase potentially reduces the risks of developing any chronic pain syndromes.

Although historically opiates have been widely used in pain management, they have a history of physical side effects that are undesirable. Recently, there has been an association with prescription opiate drug abuse and mismanagement by providers overprescribing (Dasgupta,

2018). This has led to an opiate crisis and movement to reduce the amount of opiate use. The growing opioid crisis in the United States is mandating less consumption. There is also a more recent shortage of opiate medication supplies nationally and currently in local health care facilities. Due to opiates undesired effects, a move for the use of multimodal pain modalities is sought.

Acute postoperative pain patients run the risk of becoming chronic pain patients if this pain is not aggressively managed appropriately in the initial perioperative period (Wainger, 2014). Orthopedic procedures are some of the most painful procedures for patients. Yet patients are expected to have early mobility for best outcomes and pain may deter patients from wanting to move, which has many risks associated with poor surgical outcomes. Due to the desire to have these patients mobilizing early for best outcomes, local anesthetics and peripheral nerve blocks can offer the ability for patients to mobilize without the sensation of pain. Pain may reduce the desire and participation needed from patients in the early mobility plan. In the study conducted by Ikeuchi (2014) there was also a significant difference with over 50% of patients who could do a straight leg raise compared to those who did not receive dexamethasone two days postoperatively. This shows these patients who received dexamethasone in their PNB comparatively had more mobility.

The overall goal of all pain management modalities is to extend the duration of pain control with the least amount of side effects. Opiates have historically been used on patients for pain control and management (Dasgupta, 2018). With current issues regarding an opiate crisis developed in recent years, local anesthetics (LA) have become a popular alternative. LA in PNB provide less side effects from opiate use, and help patients mobilize quicker, which will lead to less overall complications and a shorter hospital stay which equals better outcomes (Ikeuchi,

2014; Naim, 2016). PNBs can be utilized as anesthesia or in analgesia. They can be performed as a single shot of medication perineural or a catheter can be placed at the site to lengthen the time of analgesia. A single shot block has a short duration after injection lasting only several hours. Other alternatives to prolong pain management include continuous PNBs which have become the analgesic gold standard following lower limb surgeries (Naim, 2016). There are some drawbacks to peripheral catheter usage according to Albrecht (2015) including catheter migration, pump failure, and possible anesthetic leakage from the site.

The use of dexamethasone in femoral nerve blocks following knee arthroplasty have been shown to reduce the amount of opioid use within the first 24 hours (Naim, 2016; Natarajan, 2017). In a randomized controlled study, the control group duration of block with bupivacaine was significantly prolonged with a  $P < 0.0001$ . This is not only cost effective for decreasing prolonged hospital stays, it contributes to better recovery and overall patient satisfaction.

The Ikeuchi (2014) study shows, dexamethasone in combination with local anesthetics in local infiltration analgesia reduces inflammation in total knee arthroplasty, thus providing an earlier pain relief and faster recovery times. Furthermore, the study revealed reduction in C-reactive protein and interleukin 6 in drainage fluids.

LAs and PNBs offer a more favorable profile to assist in pain management than many other multimodal pain management modalities. To maximize the local anesthetic efficacy in the peripheral nerve block, several adjuncts have been utilized to extend analgesia (Bailard, 2014; Fahmy, 2017;). Of these adjuncts, dexamethasone has been shown to have promise in extending the duration of LAs in PNBs.

In the effort to maximize the effect of the local anesthetics in PNBs, adjuncts have been proposed as additives to local anesthetics promising to provide extended analgesia via extending



the local anesthetic nerve blockade. One of the traditionally used adjuncts is epinephrine. Epinephrine is joined by sodium bicarbonate, clonidine, tramadol, buprenorphine, and dexamethasone as preferred options (Bailard, 2014). Several other less favorable adjuncts, that are also employed by some include ketamine, dexmedetomidine, midazolam, magnesium (Bailard, 2014; Fahmy., 2015). Versed showed to be neurotoxic when mixed with local anesthetic perineural (Knight et al., 2015). Ketamine has also shown adverse effects that are better controlled via alternate routes of administration (Knight et. al, 2015).

Of these adjuncts, dexamethasone, a glucocorticoid, possesses systemic properties such as analgesic, anti-inflammatory, immunosuppressive, and antiemetic properties (Ikeuchi, 2014). It also has the potential for reducing sleep disturbances during the postoperative period (Kawanishi et al, 2014). In addition, it has been shown to prolong the effects of LAs in PNBs, including extending analgesia even when compared to other medications in PNB. Although the exact mechanism of action that causes dexamethasone to extend the sensory component in the PNB is not completely understood, the effects could be local, systemic, or both (Fredrickson, 2013; Kawanishi et al., 2014). Over all, numerous studies have shown perineural dexamethasone increased the duration of sensory blockade and analgesia in comparison to placebo (Albrecht, 2015; Choi, 2014; De Oliveira, 2014; Fahmy et al., 2015; Huynh, 2015). Adjuvants generally effective in prolonging sensory blockade also prolong motor blockade. In a study by Knight et al. (2015) that that used bupivacaine 0.25% and dexamethasone in brachial plexus blocks, there was no dose dependent relationship in increasing the duration of motor blockade.

It has been reported dexamethasone causes perineural vasoconstriction that slows absorption of the local anesthetics in the local area (Kawanishi et al., 2014). This, in turn, extends the local anesthetics effects. In comparison to intravenous dosing of dexamethasone,

perineural dosing has shown a longer action in extending analgesia and sensory blockade (Pehora, 2017). The increase in time was not considered statistically significant, in an evaluation of 217 participants in 3 different studies, although the extension of sensory blockade was approximately three hours longer than with IV dosing of dexamethasone (Pehora, 2017). In two studies (Choi, 2014; Pehora, 2017) that reported the effect of perineural dexamethasone on post-op nausea and vomiting, it was found that there was a reduction in the group that received dexamethasone perineurally.

There is information that dexamethasone intravenously is equally as effective as dexamethasone perineurally. According to Kawanishi et al. (2014), to reach this level of equality, the low dosage of perineural dexamethasone that significantly prolonged the duration of post-op sensory blockade will be 4 milligrams (mg). This is in comparison to IV dexamethasone that will extend analgesia but must be in higher doses of 10 mg to reach the same effect as a perineural dose of 4 mg in PNB. Kawanishi et al. (2014) also reported that in a previous study by De Oliveira et al (2014) that to receive an effective adjunct in a multimodal pain management strategy to reduce post-operative pain doses need to be  $> 0.1\text{mg/kg}$  to be effective. It is common for many CRNA's to dose patients cautiously with 4 mg of IV dexamethasone. It appears this dosage may not give the full effect dexamethasone offers in pain management. In contrast, according to Natarajan (2017), systemic or perineural dexamethasone were both equally effective in prolonging duration of sensory and motor blockade. In a randomized double blind trial, the study used a total of 90 patients undergoing upper limb surgeries receiving supraclavicular blocks. Additionally, those patients who received dexamethasone showed a persistent decrease in postoperative pain scores and required less opioid consumption within the first 48 hours.

Neurotoxicity of adjuvants is also a concern. Neurotoxicity with the use of dexamethasone may not be as concerning due to its history of safe use in the epidural space in the treatment of nerve root irritation (Kawanishi et al., 2014). Knight et al. (2014) found that dexamethasone to be beneficial in extending the peripheral nerve block duration and reducing pain without neurotoxicity. Dexamethasone also affects C-fibers (associated with chronic pain) and directly affects nerve cells. It does this by inhibiting transmission of impulses from C-fibers and inhibiting discharge of neuronal cells (Pehora, 2017). Thus, potentially upsetting the potential path to chronic pain in the orthopedic patient. There is also a concern with diabetic patients as dexamethasone is known to increase blood glucose levels. These are modest but transient, but the significance of these transient increases need further evaluation (Baillard, 2014).

In conclusion, dexamethasone has shown to improve duration of the analgesia provided by PNB, with a concurrent increase in duration of sensory and motor blockade as well. Dexamethasone does need further evaluation when comparing its use in upper versus lower PNB. There seems to be a difference, but lacking enough evidence to compare the two, leaves information that should be further explored. There is some contrasting information regarding the equality of IV versus perineural dexamethasone that needs further study. There needs to be more studies on other adjuvants as well to further understand their mechanisms of action. Exploration of adjuvants needs to focus more on efficacy and safety in the use of perineural analgesia. There is minimal information on adjuncts in PNB utilized on pediatric patients. There are several trials still underway specifically analyzing the effects of dexamethasone in PNB (Pehora, 2017). Perineural use of dexamethasone overall appears to be a safer and favorable adjuvant to PNB in orthopedic patients' pain management.

### **Contribution and Dissemination/Justification/Project Aims**

The target population included senior year Student Registered Nurse Anesthetists at Advent Health University. These students are highly skilled and have a beginning knowledge base about the current issues of perioperative pain, local anesthetics, peripheral nerve blocks, and many of the adjuvants that are normally utilized in the anesthesia realm via intravenous administration (IV). They are also knowledgeable about the current issues surrounding opiate use and opiate shortages.

The project served to expound upon the knowledge base possessed by these students. During a half hour presentation including a PowerPoint, students were educated on the addition of peripheral nerve block adjuvants to enhance analgesia within orthopedic patient populations. It was predicted that this new information would be received with a minimum of 50% increase in mean test scores after post-testing of presentation materials were tallied. This increased knowledge base would serve to assist in enhancing the students' clinical experiences and help them provide patient care grounded evidence-based practice. The enhancement and fine tuning of this new information would add to their base of knowledge of local anesthetics with the addition of the adjuvant dexamethasone. This will help guide them when making clinical choices to manage pain in their anesthetic plan.

### **Project Methods**

After obtaining Scientific Review Board (SRB) and Institutional Review Board (IRB) approval, a Quasi-experimental design was implemented to analyze data collected from a convenience sample of senior year Advent Health Student Registered Nurse Anesthetists (SRNA). A literature reviewed was thoroughly conducted and utilized in a PowerPoint presentation as an educational platform for the SRNA seniors.

The SRNA seniors were issued pre- and post-testing forms that did not include any identifiable information except for a lettering system that corresponded to the pre-and post- test belonging to the test taker, but did not identify the test taker themselves.

Pre-educational session questionnaires were produced and distributed prior to the presentation of information in a classroom setting at Advent Health University. Post session testing was also distributed to compare both questionnaires for results on knowledge base increase related to the subject of dexamethasone adjunct in peripheral nerve blocks. Tests were compiled anonymously. This was all done after attendees signed an agreement to both the participation in the educational event and to the collection of their testing scores.

All paper materials were stored in an unlabeled sealable folder to maintain anonymity. Forms were kept at a secure location in the home of Wendy Sayavongsone. Data was only accessible by direct contributors such as researchers, project chair or mentor, and the consulted statistician, who had access to anonymous data with no identifiable information attached to testing scores. After statistical information aggregation, and graduation of both researchers from the Nurse Anesthesia Program at AHU, testing forms will be disposed of appropriately according to SRC and IRB standards.

Inclusion criteria included SRNA seniors with baseline knowledge of local anesthetics, medication profiles of adjuvants used in other forms, and knowledge of the current opiate crisis. Exclusion criteria were any person who was not a senior year Advent Health SRNA with inclusion criteria met.

### **Timeline**

The initial Project Proposal was emailed to the Project Chair and Mentor by May 28, 2018. Changes were completed on a rolling basis, and the final draft was completed in July 2018.

SRC and IRB initial application submission was completed by July 2018. A literature review was initiated in May 2018. The project was implemented in the fall of 2018. Using a convenience sample of approximately 23 SRNA students, data collections was performed on the same day of educational presentation to analyze the retention of information presented. Utilizing an educational conference, surveys and test scoring were compiled for analysis. A PowerPoint presentation was created in the fall prior to implementation. The final PowerPoint was completed and submitted by December 2018. The final draft of the Scholarly Project Paper was completed by February 2019. Presentation posters are to be prepared by March 2019. Poster presentation dates are tentatively scheduled for April 2019.

### **Data Collection Plan**

The data collection took place in two parts. After attendees signed a consent form for the presentation and collection of testing data, pre-and post-testing forms were handed to attendees in alphabetically paired pre-and post- test packets. The initial pre-testing was retrieved from attendees before the presentation was initiated. Post testing was administered and collected immediately after the half hour educational presentation. Attendees were allowed sufficient time to answer questions presented on both pre- and post-testing for consistent results. Researchers collected pre-and post-tests immediately after attendees completed each of the tests. The surveys contained a minimum of ten questions, each in a multiple-choice answer worth 1 point each for a total of 10 possible points.

Each student was given a pre- and post-testing form labeled with the same letter designation to allow observation of each student's increase in knowledge retention. We expected an increase in knowledge of dexamethasone as an adjuvant in PNB after a 30-minute presentation.

### **Evaluation Plan**

Surveys were collected and statistically analyzed in the SPSS program for data variables. Roy Lukman, PhD was consulted for pre-and post-testing statistical analysis. Quantitative data was compiled to show evidence or lack of evidence, as it relates to an increase in knowledge by Senior SRNA's after an informational presentation is given for a half hour. An evaluation of success for the quantitative study was defined as an increase in post test scores.

### **Limitations**

Pre- and post-testing were utilized in the evaluation process with approximately 23 senior SRNA cohort participants. Data was statistically analyzed for evidence of knowledge retention after a 30-minute PowerPoint presentation about dexamethasone as adjuvant in PNB in orthopedic patients. With a relatively small convenience sample size, it is uncertain if these results were representative of senior SRNA's in other master level nurse anesthesia programs. It is also not indicative of long term learning or retention of educational information due to the post-test being administered immediately after. It is unclear if its use in the clinical setting would be realized due to the variety of settings senior students may be employed in after graduation.

### **Findings**

After completion of the research conducted, statistical analysis of the results was achieved. Paired samples t-test were used to analyze the data. The pre-test mean value was 3.6500 points out of 10 possible points with a standard deviation of 1.56525. The post-test mean value was 8.3500 points out of 10 possible points with a standard deviation of 2.00722. A 95% confidence interval was obtained at a lower limit of -5.77477 and an upper limit of -3.62523. A paired sample test was also performed between pre-and post-test results, and a t-value of -9.153

was obtained and associated with a P-value of  $<.001$ . These findings showed statistical significance (Appendix D).

### **Conclusion**

Upon reviewing the statistical analysis, it can be concluded that the post-test mean is significantly higher than the pre-test mean. From the data findings, it can be implied that the 30-minute educational presentation improved the SRNA's knowledge of dexamethasone as an adjuvant in PNB. Limitations of the study, however, included a small sample size from one specific setting. A sample size of 23 SRNA students from one specific nurse anesthesia program is limited in its representation of other populations and programs. Also, the research conducted reflects only short-term memory retention since post-test evaluation was conducted immediately after the presentation. Considerations for future research include larger sample sizes from multiple nurse anesthesia programs. In addition, it may be beneficial to look at memory retention over a greater time lapse period.



## References

- Albrecht, E., Kern, C., & Kirkham, K. R. (2015). A systematic review and meta-analysis of perineural dexamethasone for peripheral nerve blocks. *Anaesthesia*, 70(1), 71-83. <https://doi.org/10.1111/anae.12823>
- Bailard, N. S., Ortiz, J., & Flores, R. A. (2014). Additives to local anesthetics for peripheral nerve blocks: Evidence, limitations, and recommendations. *American Journal of Health-System Pharmacy*, 71(5), 373-385. <https://doi.org/10.2146/ajhp130336>
- Choi, S., Rodseth, R., McCartney, C. J. L. (2014). Effects of dexamethasone as a local anaesthetic adjuvant for brachial plexus block: A systematic review and meta-analysis of randomized trials. *British Journal of Anaesthesia*. 112(3), 427-39. <https://doi.org/10.1093/bja/aet417>
- Dasgupta, N., Beletsky, L., & Ciccarone, D. (2018). Opioid Crisis: No Easy Fix to Its Social and Economic Determinants. *American Journal Of Public Health*, 108(2), 182-186. <https://doi.org/10.2105/AJPH.2017.304187>
- De Oliveira, G. S., Alves, L.J., Nader, A., Kendall, M. C., Dale, R. R., & McCarthy, R. J. (2014). Perineural dexamethasone to improve postoperative analgesia with peripheral nerve blocks: A meta-analysis of randomized controlled trials. *Pain Research and Treatment*, 9. <http://dx.doi.org/10.1155/2014/179029>
- Fahmy, N. G., Ahmed, D. M., & Sameer, G. M. (2015). A comparative study between the addition of MgSO<sub>4</sub> against dexamethasone to bupivacaine in the prolongation of ultrasound-guided interscalene nerve block for shoulder arthroscopy. *Ain Shams Journal of Anesthesiology*, 8(3), 402-406. <https://doi.org/10.1155/2014/179029>

- Huynh, M., Marret, E., Francis, B. (2015). Combination of dexamethasone and local anaesthetic solution in peripheral nerve blocks: A meta-analysis of randomised controlled trials. *European Journal of Anaesthesiology*, 32(11), 751-758.  
<https://doi.org/10.1097/EJA.0000000000000248>
- Ikeuchi, M., Kamimoto, Y., Izumi, M., Fukunaga, K., Aso, K., Sugimura, N., & Tani, T. (2014). Effects of dexamethasone on local infiltration analgesia in total knee arthroplasty: a randomized controlled trial. *Knee Surgery, Sports Traumatology, Arthroscopy*, 22(7), 1638-1643. <http://doi.org/10.1007/s00167-013-2367-5>
- Kawanishi, R., Yamamoto, K., Tobetto, Y., Nomura, K., Kato, M., Go, R., Takeda, Y. (2014). Perineural but not systemic low-dose dexamethasone prolongs the duration of interscalene block with ropivacaine: a prospective randomized trial. *Local and Regional Anesthesia*, 7, 5–9. <http://doi.org/10.2147/LRA.S59158>
- Knight, J. B., Schott, N. J., Kentor, M. L., & Williams, B. A. (2015). Neurotoxicity of common peripheral nerve block adjuvants. *Current Opinion in Anesthesiology*, 28(5), 598-604.  
<https://doi.org/10.1097/ACO.0000000000000222>
- Lim, D., Gold, M. (2017). Intravenous dexamethasone for prolonged duration of axillary nerve blockade. *AANA Journal*, 85(3), 189-194.
- Naim, H., Elshafaie, K., Soaida, S., Abdel-Haq, M., & Nawar, K. (2016). Systemic versus perineural dexamethasone as an adjuvant to bupivacaine in combined femoral and sciatic nerve blocks in lower-limb vascular surgeries: A prospective randomized study. *Ain-Shams Journal of Anaesthesiology*, 9(4), 569. <https://doi.org/10.4103/1687-7934.198258>.
- Natarajan, S., Karthikeyan, G., & Murguan, T. (2017). Comparison of analgesic properties of perineural and systemic dexamethasone in patients undergoing upper limb surgeries

under supraclavicular block. *International Archives of Integrated Medicine*, 4(11), 220-228.

Pehora, C. (2017). Dexamethasone as an adjuvant to peripheral nerve block. *Cochrane Database of Systematic Reviews*, (11), <https://doi.org/10.1002/14651858.CD011770.pub2>

Reuben, S. (2004). Preventing the development of complex regional pain syndrome after surgery. *Anesthesiology*, 101(5):1215-1224.

Wainger, B. J., & Brenner, G. J. (2014). Mechanisms of chronic pain. In D. E. Longnecker, M. F. Newman, W. M. Zapol, S. C. Mackey, & W. S. Sandberg (Eds.). *Anesthesiology* (3rd ed., pp. 1439-1453). New York, NY, McGraw-Hill Global Education Holdings.

## Appendix A

**ADU NAP CAPSTONE PROJECT – INFORMED CONSENT**

We are MSNA students in the Nurse Anesthesia Program (NAP) at Adventist University of Health Sciences (ADU). We are doing a Capstone Project called *Dexamethasone as Adjunct in Peripheral Nerve Blocks to Extend Analgesia*. This project is being supervised by a project chair within the Nurse Anesthesia Program. We would like to invite you to participate in this project. The main purpose of this form is to provide information about the project so you can make a decision about whether you want to participate.

**WHAT IS THE PROJECT ABOUT?**

The purpose of this project is to educate and assess the comprehension of Student Registered Nurse Anesthetists (SRNA) on the benefits of the administration of dexamethasone as an adjuvant while performing peripheral nerve blocks.

**WHAT DOES PARTICIPATION IN THIS PROJECT INVOLVE?**

If you decide to participate in this project, you will be asked to complete an anonymous pre-assessment, attend a classroom presentation, and then complete an anonymous post-assessment. The assessment will address an increase in knowledge from the lecture. A statistical analysis will be conducted of pre-and post-test results and a p-value will be obtained. Your participation by attendance at the presentation and completion of the survey is anticipated to take approximately half an hour.

**WHY ARE YOU BEING ASKED TO PARTICIPATE?**

You have been invited to participate as part of a convenience sample of students currently enrolled in the ADU NAP. Participation in this project is voluntary. If you choose not to participate or to withdraw from the project, you may do so at any time. If you choose not to participate your refusal to participate in this research study will involve no penalty or loss of benefits to you. If you choose to participate, you can change your mind later and withdraw your consent and discontinue participation from this study at any time. If you choose to withdraw, inform the PI of your wishes.

**WHAT ARE THE RISKS INVOLVED IN THIS PROJECT?**

Although no project is completely risk-free, we don't anticipate that you will be harmed or distressed by participating in this project.

**ARE THERE ANY BENEFITS TO PARTICIPATION?**

We don't expect any direct benefits to you from participation in this project. The possible indirect benefit of participation in the project is the opportunity to gain additional knowledge about dexamethasone as an adjuvant while performing peripheral nerve blocks.

**HOW WILL THE INVESTIGATORS PROTECT PARTICIPANTS' CONFIDENTIALITY?**

The results of the project will be published, but your name or identity will not be revealed. To maintain confidentiality of assessments, the investigators will conduct this project in such a way to ensure that information is submitted without participants' identification. Participants will be issued pre-testing and post-testing forms that will not include any identifiable information. A lettering system will correspond to the pre-and post- test belonging to the test taker, but it will not identify the test taker themselves. All paper materials will be stored in an unlabeled sealable folder to maintain anonymity. The paper test results will then be input and stored on the researchers' password protected personal computer. After statistical information aggregation, and graduation of both researchers from the Nurse Anesthesia Program at ADU, testing, forms will be disposed of appropriately via crosscut shredding. Data will only be accessible by direct contributors such as researchers, project chair or mentor, and the consulted statistician. After the scholarly project is complete the data and test results will be deleted from the personal computer listed above. Thus, the investigators will not have access to any participants' identities.

**WILL IT COST ANYTHING OR WILL I GET PAID TO PARTICIPATE IN THE PROJECT?**

Your participation will cost approximately half of an hour of your time, but will require no monetary cost on your part. You will not be paid to participate.

**VOLUNTARY CONSENT**

You do not have to participate in this research study and choosing not to participate in this study will not involve any penalty or loss of benefit to you. The decision to participate or not participate in this research study is completely up to you. If you choose to participate, you can change your mind later and withdraw your consent and discontinue participation from this study at any time. If you chose to withdraw from the study informed the PI of your wishes. By signing this form, you are saying that you have read this form, you understand the risks and benefits of this project, and you know what you are being asked to do. The investigators will be happy to answer any questions you have about the project. If you have any questions or concerns about the project process or the investigators, please contact the Nurse Anesthesia Program at (407) 303-9331.

Date \_\_\_\_\_

\_\_\_\_\_  
Participant Signature/ Participant Name (PRINTED LEGIBLY)

\_\_\_\_\_  
Participant Name (PRINTED LEGIBLY)

## Appendix B

## Dexamethasone as Adjunct in Peripheral Nerve Blocks to Extend Analgesia

1. Chronic pain etiology can be from changes in the spinal cord and brain due to repeated stimulation of which fibers?
  - A. A-fibers
  - B. B-fibers
  - C. C-fibers
  - D. D-fibers
2. Opioids are associated with which of the following factors except?
  - A. Respiratory depression
  - B. Nausea
  - C. Peristalsis
  - D. Addiction
3. Dexamethasone is categorized as what type of drug class?
  - A. Aminosteroid
  - B. Glucocorticoid
  - C. Mineralocorticoid
  - D. Neurosteroid
4. The effects of dexamethasone as an antiemetic works by which of the following?
  - A. Inhibition of phospholipase A2
  - B. Inhibition of serotonin
  - C. Inhibition of COX 1 and 2
  - D. Inhibition of GABA
5. The effects of dexamethasone as an adjunct to analgesia works by which of the following?
  - A. Decreases nociceptive C-fiber activity and inhibits potassium channels
  - B. Decrease in A-delta fiber activity and inhibits calcium channels
  - C. Decrease in C-fiber activity and inhibits sodium channels
  - D. Decrease in B-fiber activity and inhibits calcium channels
6. All the following are true about the use of dexamethasone except?
  - A. Anti-inflammatory
  - B. Immunosuppressant
  - C. Analgesic
  - D. All the above are true

7. Which of the following enzyme metabolizes dexamethasone?

- A. CYP3A4
- B. Cytochrome P450
- C. methyltransferase
- D. glycine-N-acyltransferase

8. Dexamethasone side effects can include the following except?

- A. Insomnia
- B. Decreased appetite
- C. Perineal Itching
- D. Gluconeogenesis

9. Local anesthetic adjuncts act by which of the following mechanisms except?

- A. Local vasoconstriction
- B. Direct effects on peripheral nerves
- C. Release of cytokine mediators
- D. Systemically by anti-inflammatory effects

10. Peripheral nerve blocks adjuncts aside from dexamethasone are typically all except?

- A. Clonidine
- B. Magnesium
- C. Tramadol
- D. Glycopyrrolate

## Appendix C

## Dexamethasone as Adjunct in Peripheral Nerve Blocks to Extend Analgesia

Presented by:

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## Objectives

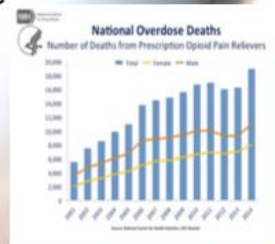
- Identify the risk factors of opioid use and the growing epidemic crisis
- Describe the advantages of regional anesthetics
- Discuss the pharmacokinetics of dexamethasone and its effect on the body
- Educate on the benefits of dexamethasone as an adjunct in peripheral nerve blocks in orthopedic patients

## Background of Problem

- Opioids historically have been the standard of care for analgesic relief to treat acute and chronic pain
- **Undesired adverse effects of opioids may include sedation, respiratory depression, constipation, nausea, and vomiting** (Lim, 2017)
- There is a growing association with prescription opiate drug abuse, addiction, and mismanagement by providers overprescribing
- There is also shortages of opiate medication supplies nationally and locally

## The Opioid Epidemic

- In the late 1990s, healthcare providers began to prescribe opioids at greater rates with pharmaceutical companies supporting and reassuring providers that patients would not be addicted
- At that time, minimal research on the effects of addiction and abuse. Studies began to show a positive correlation between rates of opioid death and prescribing
- In 2017, the U.S Department of Health and Human Services (HHS) declared a state of emergency with a five step plan to combat the opioid epidemic.
- National opiate crisis and movement calls for healthcare providers to reduce the amount of opiate use as well



## Pain management

- According to the Joint Commission pain management is a standard of care.
- Failure to maintain adequate pain management may negatively affect reimbursement rates to healthcare facilities from the Centers for Medicare and Medicaid Services.
- Poor pain management is also associated with:
  - Higher risks of extended hospital stays and readmission
  - Increased risks of hospital related complications and costs

## Regional Anesthesia

- 1884-William Halstead perform the first peripheral nerve block on the brachial plexus with cocaine (Baillard, 2014)
- Technological advancements such as the nerve stimulator and use of ultrasound guidance has allowed better assurance of correct placement of Peripheral nerve blocks (PNBs)
- Peripheral nerve blocks (PNBs) have become more popular and are a preferred method of pain management for surgical anesthetics particularly for orthopedic patients



## Advantages of PNBs and adjuncts

- Intra-operative
  - Less bleeding
  - Decreased stress response
  - Improved hemodynamic stability
  - Avoidance of general anesthesia
- Post-operative
  - Faster recovery
  - Improved pain scores and patient satisfaction
  - Decreased opioid requirements

## Project Questions

Does recent scientific literature support the addition of dexamethasone as an adjunct to PNB for patients undergoing orthopedic surgery?

PICOT: In Adventist University Student Registered Nurse Anesthetists (P), does a half hour (T) presentation on dexamethasone as an adjunct to PNB increase analgesia in orthopedic patients (I), result in an increase knowledge base (O)?

## Case Study

A 70-year old male with a history of diabetes, hypertension, and osteoarthritis reports of having chronic knee pain. He is scheduled to have right arthroplasty. He currently takes the following medications:

- Gabapentin
- Metoprolol
- Metformin
- Oxycodone-acetaminophen

Due to risk factors and the promotion of faster healing time, the orthopedic surgeon requests a single shot saphenous block in the pre-operative area and a spinal with MAC sedation

## Chronic pain

- Sensitization of afferent nociceptors, also referred to as hyperalgesia, occurs generally after an injury or trauma to tissues including surgery where inflammatory mediators are produced
- Pain sensitization occurs when nerve fibers under inflammation due to trauma magnifies and continues to send those pain signals
- Two kinds of sensitization: Peripheral and Central
- Central sensitization or immune response after nerve injury may be thwarted beginning with pre-emptive pain management to reduce perioperative pain that can potentially convert to chronic pain
- **C-Fibers appear to be important factors in both inflammatory and neuropathic pain transmission with primary hyperalgesia that leads to central sensitization.**

## Complex Regional Pain Syndrome

- Complex regional pain syndrome (CRPS), previously known as reflex sympathetic dystrophy is a syndrome of pain and sudomotor or vasomotor instability and develops most often after trauma to tissues including orthopedic surgeries (Ruben, 2004)
- It is chronic pain that lasts greater than 6 months and commonly affects one limb (arm, leg, hand, or foot)

## Complex Regional Pain Syndrome

- CRPS are divided into two types:
- CRPS I requires
  - (1) continuing pain, allodynia, or hyperalgesia disproportionate to the injury;
  - (2) edema evidence at some time, changes in skin blood flow, or abnormal sudomotor activity in the region of pain; and
  - (3) no other conditions that would otherwise account for the degree of pain and dysfunction.
- CRPS II is a pain syndrome that starts after a nerve injury and is not necessarily limited to the distribution of the injured nerve. Diagnostic criteria is the same as CRPS I
- Those who develop CRPS are recommended to have regional anesthesia preferred over general if possible.

## Local Anesthetics

According to Lim (2017):

- Local anesthetics block the conduction of electrical impulses to nerve fibers
- They bind to voltage gated sodium channels (Na<sup>+</sup>) and prevent the initiation of an action potential
- The nonionized local anesthetic molecules are lipid soluble and gain access across the cell membrane by diffusion.
- The chemical equilibrium results in ionized local anesthetic molecules that bind to the sodium channel and block nerve conduction, particularly on C-fibers.

## Adjuncts to LA

Patients rank post-operative pain as one of the highest concerns after surgery, causing a necessity for prolonged postoperative analgesia (Choi, 2014)

Strategies to prolong analgesia beyond the pharmacological duration of the LA needed and include:

- Placement of indwelling perineural catheters to allow prolonged infusion or the co-administration of adjuvants
- **Adjuncts aside from dexamethasone include epinephrine,  $\alpha_2$  agonists (i.e. clonidine and dexmedetomidine), midazolam, magnesium, and tramadol**

## Dexamethasone

- Created in 1957 as a high potency synthetic **glucocorticoid** with little mineralocorticoid effects
- **Anti-inflammatory, analgesic, immunosuppressive, and anti-emetic effects**
- Anesthesia providers commonly use dexamethasone to reduce **post-operative nausea and vomiting (PONV)** which is by drug's **inhibition of phospholipase A2**
- Metabolized by the liver, by **CYP3A4** enzymes
- Side effects may include **insomnia, hyperglycemia, appetite stimulant, and perineal itching via intravenous use**

## Dexamethasone: Pharmacokinetics

- Although not completely understood, dexamethasone mechanism of action may stem from (Albrecht, 2015 & Fahmy, 2015):
  - **Decreased nociceptive C-fiber activity via a direct effect on glucocorticoid receptors**
  - **Inhibition of potassium channels**
- Other theories suggest a local **vasoconstrictive effect**, resulting in reduced local anesthetic absorption, or a **systemic anti-inflammatory effect** following vascular uptake of the drug and **direct effects on the peripheral nerves themselves**
- Dexamethasone lacks neurotoxicity & has been used safely in the epidural space in the treatment of nerve root irritations

## Literature Review

A thorough literature review was conducted. All journals were peer reviewed, and anesthesia texts were included for background pain pathophysiology.

Findings included the following:

- Use of dexamethasone in femoral nerve blocks following knee arthroplasty have been shown to reduce the amount of opioid use within the first 24 hours (Naim, 2016; Natarajan, 2017)
- Dexamethasone intravenous and/or perineural administration proves to be beneficial in providing prolonged pain relief in orthopedic patients receiving peripheral nerve blocks (Naim, 2016; Natarajan, 2017)
- LA in PNB provide less side effects from opiate use, and help patients mobilize quicker, which will lead to less overall complications and a shorter hospital stay which equals better outcomes (Ikeuchi, 2014; Naim, 2016)

## Effects of dexamethasone on local infiltration analgesia in total knee arthroplasty: a randomized controlled trial

In a study conducted by Ikeuchi (2014), forty patients undergoing total knee arthroplasty were randomized to either the steroid or control group.

- 20 ml of 0.75 % ropivacaine, 400 mg of isepamicin and 6.6 mg of dexamethasone were injected into the peri-articular tissues in the steroid group, while the drugs without dexamethasone were injected in the control group. Injection sites for local infiltration analgesia include synovium, joint capsule, periosteum and fasciae.
- **Results:** Reduction in post-operative pain was associated with a decrease in serum C-reactive protein and interleukin 6 in drainage fluid. The number of patients who were able to perform straight leg raise within postoperative pain day 2 was 15/20 in the steroid group, which was significantly higher than the control group 5/20
- **Conclusion:** Adding steroid to local anaesthetics in local reduced inflammation and contributed to quicker recovery



### Systemic versus perineural dexamethasone as an adjunct to bupivacaine in combined femoral and sciatic nerve blocks in lower-limb vascular surgeries: a prospective randomized study

In a study conducted by Naim (2016), 63 patients aged 18-70 years old receiving a combined femoral and sciatic nerve block were compared into three groups:

- Group P received perineural dexamethasone plus bupivacaine 0.5%
- Group I received intravenous dexamethasone plus perineural bupivacaine 0.5%,
- Group B received perineural bupivacaine 0.5% alone

**Results:** Sensory and motor block onset showed nonsignificant difference between the three groups. Sensory block duration was significantly longer in group P than in groups I and B. Motor block duration was significantly prolonged in groups P and I when compared with group B. Motor block duration was longer in group P than in group I; however, the difference was statistically non-significant (p-value 0.34). The duration of analgesia was significantly longer in group P than in the other groups, and significantly longer in group I compared with group B.

**Conclusion:** Use of equal doses of perineural or intravenous dexamethasone as an adjunct in single injection combined femoral and sciatic nerve blocks is associated with extended duration of sensory and motor blocks, extension of postoperative analgesia duration, and reduced postoperative analgesic requirements.

### Comparison of analgesic properties of perineural and systemic dexamethasone in patients undergoing upper limb surgeries under supraclavicular block

In a study conducted by Natarajan (2017), 90 patients aged 18-60 years old were compared on receiving a supraclavicular brachial plexus block with a single perioperative dose of intravenous Dexamethasone and perineural Dexamethasone

Patients received the following:

- Group A- local anesthetics and perineural dexamethasone (15 cc of 2% Lignocaine with adrenaline and 15 cc of 0.5% Bupivacaine along with 8 mg of Dexamethasone added in solution form)
- Group B- local anesthetics & intravenous dexamethasone (15 cc of 2% Lignocaine with adrenaline and 15 cc of 0.5% Bupivacaine and systemic Dexamethasone 8mg by intravenous route one hour before surgery)
- Group C- local anesthetics only (15 cc of 2% Lignocaine with adrenaline and 15 cc of 0.5% Bupivacaine)

**Results:** The Sensory and Motor block onset time between the intervention groups group A VS group B and group A VS group C were found to be statistically significant ( $p < 0.05$ ) and the association between group B VS group C was found to be not statistically significant ( $p > 0.05$ ) as per unpaired t-test.

**Conclusion:** Systemic Dexamethasone is equally effective as perineural Dexamethasone in providing the significant duration of sensory, motor blockade and quality of analgesia. Dexamethasone consistently decreases the postoperative pain scores and decrease the early & number of doses of opioid consumption (48 hours).

### Perineural but not systemic low-dose dexamethasone prolongs the duration of interscalene block with ropivacaine: a prospective randomized trial

In a study conducted by Kawanishi (2014), 39 patients prospective-randomized-placebo controlled trial presenting for arthroscopic shoulder surgery received the following:

- Group C: Ropivacaine 0.75%
- Group Dperi: Ropivacaine 0.75% plus perineural dexamethasone 4 mg
- Group Div: Ropivacaine 0.75% plus intravenous dexamethasone 4 mg

Primary outcome: duration of analgesia

Defined: time between block and first request for analgesic

**Results:**

- Median times of sensory block in groups C, Dperi, and Div were 11.2 hours, 18.0 hours, and 14.0 hours (IQR 12.7–15.1 hours), respectively.
- Significant differences were observed between groups Dperi and C ( $P=0.001$ ). Kaplan–Meier analysis for the first analgesic request showed significant differences between groups Dperi and C ( $P=0.005$ ) and between groups Dperi and Div ( $P=0.008$ ), but not between groups C and Div.

**Conclusion:** Perineural but not intravenous administration of 4 mg of dexamethasone significantly prolongs the duration of effective postoperative analgesia resulting from a single-shot ISB with ropivacaine 0.75%.

## Research Limitations

- Dexamethasone does need further evaluation when comparing its use in upper versus lower extremity peripheral nerve blocks.
- Studies on finding dosages are needed for both IV and perineural administration of dexamethasone
- Additional studies should be conducted that elucidate the mechanism by which dexamethasone causes analgesia

## Research Limitations

Other questions:

- Safety in pediatrics
- Safety in geriatrics
- Endocrine effects with patients with diabetes or adrenal suppression with perineural administration

## Conclusion

- Dexamethasone has overall shown to improve duration of the analgesia provided by adjunctive therapy with dexamethasone in PNB, with a concurrent increase in duration of sensory and motor blockade as well in comparison to placebo.  
(Albrecht, 2015; Choi, 2014; De Oliveira, 2014; Fahmy et al., 2015; Huynh, 2015).
- Perineural use of dexamethasone overall appears to be a safer and favorable adjunct to PNB in orthopedic patients' pain management.

## References

- Albrecht, E., Kem, C., & Kinkham, K. R. (2015). A systematic review and meta-analysis of perineural dexamethasone for peripheral nerve blocks. *Anaesthesia*, 70(1), 71-83. <https://doi.org/10.1111/anae.12823>
- Ballard, N. S., Ortiz, J., & Flores, R. A. (2014). Additives to local anesthetics for peripheral nerve blocks: Evidence, limitations, and recommendations. *American Journal of Health-System Pharmacy*, 71(5), 373-385. <https://doi.org/10.2146/ajhp130336>
- Choi, S., Rodeth, R., McCarthy, C. J. L. (2014). Effects of dexamethasone as a local anaesthetic adjunct for brachial plexus block: A systematic review and meta-analysis of randomized trials. *British Journal of Anaesthesia*, 112(3), 427-38. <https://doi.org/10.1093/bja/aet417>
- Dasgupta, N., Bekesky, L., & Ciccarone, D. (2018). Opioid Crisis: No Easy Fix to Its Social and Economic Determinants. *American Journal Of Public Health*, 108(2), 182-186. <https://doi.org/10.2195/AJPH.2017.304187>
- De Oliveira, G. S., Alves, L. J., Nader, A., Kendall, M. C., Dale, R. R., & McCarthy, R. J. (2014). Perineural dexamethasone to improve postoperative analgesia with peripheral nerve blocks: A meta-analysis of randomized controlled trials. *Pain Research and Treatment*, 9. <https://doi.org/10.1155/2014/179029>
- Fahmy, N. G., Ahmed, D. M., & Sameer, G. M. (2015). A comparative study between the addition of MgSO4 against dexamethasone to bupivacaine in the prolongation of ultrasound-guided interscalene nerve block for shoulder arthroscopy. *Ain Shams Journal of Anesthesiology*, 8(3), 402-406. <https://doi.org/10.1155/2014/739029>
- Huynh, M., Marnet, E., Francis, B. (2015). Combination of dexamethasone and local anesthetic solution in peripheral nerve blocks: A meta-analysis of randomized controlled trials. *European Journal of Anesthesiology*, 32(11), 751-758. <https://doi.org/10.1097/EJA.0000000000000248>
- Ikeuchi, M., Kamimoto, Y., Izumi, M., Fukunaga, K., Aso, K., Sugimura, N., & Tan, T. (2014). Effects of dexamethasone on local infiltration analgesia in total knee arthroplasty: a randomized controlled trial. *Knee Surgery, Sports Traumatology, Arthroscopy*, 22(7), 1638-1643. <http://doi.org/10.1007/s00167-013-2367-6>

## References

- Kawanishi, R., Yamamoto, K., Tobetto, Y., Nomura, K., Kato, M., Go, R., Takeda, Y. (2014). Perineural but not systemic low-dose dexamethasone prolongs the duration of interscalene block with ropivacaine: a prospective randomized trial. *Local and Regional Anesthesia*, 7, 5-9. <http://doi.org/10.2147/LRA.S59158>
- Knight, J. B., Schott, N. J., Kentor, M. L., & Williams, B. A. (2015). Neurotoxicity of common peripheral nerve block adjuvants. *Current Opinion in Anesthesiology*, 28(5), 695-504. <https://doi.org/10.1097/ACO.0000000000000222>
- Lim, D., Gadd, M. (2017). Intravenous dexamethasone for prolonged duration of axillary nerve blockade. *AANA Journal*, 85(3), 189-194.
- Naim, H., Elhatale, K., Soaid, S., Abdel-Haq, M., & Nawar, K. (2016). Systemic versus perineural dexamethasone as an adjunct to bupivacaine in combined femoral and sciatic nerve blocks in lower-limb vascular surgeries: A prospective randomized study. *Ain-Shams Journal of Anesthesiology*, 9(4), 569. <https://doi.org/10.4103/1687-7934.198258>
- Natarajan, S., Karthikyan, G., & Murguan, T. (2017). Comparison of analgesic properties of perineural and systemic dexamethasone in patients undergoing upper limb surgeries under supraclavicular block. *International Archives of Integrated Medicine*, 4(11), 220-228.
- Pehora, C. (2017). Dexamethasone as an adjunct to peripheral nerve block. *Cochrane Database of Systematic Reviews*, (11). <https://doi.org/10.1002/14651858.CD011779.gv05>
- Reuben, S. (2004). Preventing the development of complex regional pain syndrome after surgery. *Anesthesiology*, 101(5):1215-1224.
- Waller, B. J., & Brenner, G. J. (2014). Mechanisms of chronic pain. In D. E. Longnecker, M. F. Newman, W. M. Zapel, S. C. Mackey, & W. S. Sandberg (Eds.), *Anesthesiology* (3rd ed., pp. 1439-1453). New York, NY: McGraw-Hill Global Education Holdings.

## Appendix D

## Results

Paired Samples Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Pre-Test	3.6500	20	1.56525	.35000
	Post-Test	8.3500	20	2.00722	.44883

Paired Samples Test

		Paired Differences				t	df	Sig. (2-tailed)	
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower				Upper
Pair 1	Pre-Test - Post-Test	-4.70000	2.29645	.51350	-5.77477	-3.62523	-9.153	19	.000