2017

The Association between Intraoperative Single-Dose Dexamethasone and Postoperative Pain in Patients Undergoing Laparoscopic Cholecystectomy

Sara Hatfield
sara.hatfield@yahoo.com

THE ASSOCIATION BETWEEN INTRAOPERATIVE SINGLE-DOSE DEXAMETHASONE AND POSTOPERATIVE PAIN IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY

A Research Project submitted to
The Graduate College of Business
Marshall University

Final defense submitted in partial fulfillment of the requirements for the
Doctorate of Management Practice in Nurse Anesthesia (DMPNA) degree
conferred by Marshall University (MU) in partnership with the
Charleston Area Medical Center (CAMC) based on a collaborative agreement between the
MU College of Business and the CAMC School of Nurse Anesthesia

By:

Sara Hatfield

Marshall University

November 16, 2017

SIGNATURE PAGE

Approved By

Dr. Alberto Coustasse-Hencke, Dr.PH, MD, MBA, MPH
Committee Chair, Graduate College of Business, Marshall University

_____ _____
Signature Date

Dr. Priscilla Walkup, DMP, APRN, CRNA
CAMC School of Nurse Anesthesia

_____ _____
Signature Date

Ms. Kristen Kerns, APRN, CRNA
CAMC Health System, Memorial Hospital

_____ _____
Signature Date

TABLE OF CONTENTS

Page

COVER PAGE. I

SIGNATURE PAGE. II

TABLE OF CONTENTS. III

EXECUTIVE SUMMARY. IV

LIST OF TABLES. V

INTRODUCTION

- Background and Statement of the Problem. 1
- Literature Review. 4
- Statement of the Problem and Research Purpose. 10

METHODOLOGY

- Research Hypothesis. 10
- Research Design. 10
- Sample Population with Description of Sample. 11
- Procedure and Protocol. 13
- Statistical Design and Analysis. 14
- Ethical Considerations. 15

RESULTS

- Presentation, Analysis and Interpretation of Data 15

DISCUSSION

- Discussion of Study Results 21
- Study Limitations 24

IMPLICATIONS AND RECOMMENDATIONS 25

CONCLUSION. 26

REFERENCES 27

APPENDICES

- Appendix A: Data Collection Tool 1. 32
- Appendix B: Data Collection Tool 2 32
- Appendix C: IRB Approval Certification. 33

EXECUTIVE SUMMARY

Abstract: The purpose of this study was to examine the association between a single dose of intraoperative dexamethasone in patients undergoing outpatient laparoscopic cholecystectomy surgery and postoperative pain scores and the amount of postoperative opioid administration.
Introduction: Pain is one of the most common complaints in the postoperative period and the days following a patient's procedure. While opioids are commonly used for treating intraoperative and postoperative pain, anesthesia providers can lessen their use by adopting multimodal analgesia techniques. This study attempts to fill the research gap related to the association of a single dose of intravenous dexamethasone intraoperatively with postoperative pain in patients undergoing laparoscopic cholecystectomy surgery. Dexamethasone is safe to use intraoperatively and when given as a single dose, has minimal side effects.
Methodology: The design chosen for this research study was a retrospective, quantitative, case-control design. Data collection was conducted by using patient EMR's from CAMC. Data were obtained from patients ages 18-64 years who underwent outpatient laparoscopic cholecystectomy surgery requiring general anesthesia from June 15, 2007, to June 15, 2017. There were a total of 200 patients selected from the 5,700 charts that met the inclusion and exclusion criteria. The sample consisted of a case group (N=100) of patients who received an intraoperative 4-8 mg single dose of dexamethasone. The control group (N=100) consisted of patients who did not receive dexamethasone intraoperatively. Variables of age, gender, ASA physical classification status, BMI, LOS, dexamethasone dose, VAS pain scores on admission and VAS pain scores on discharge from the PACU, and total intraoperative and postoperative opioid administration in morphine equivalents were collected. A p-value of $< .05$ was considered significant.
Results: Comparison between the two groups showed no difference in mean age, BMI, ASA physical status, gender, LOS, or VAS pain scores on discharge from the PACU ($p > .05$). There was no association between the administration of dexamethasone intraoperatively and VAS pain scores on admission to or discharge from the PACU or total PACU opioid consumption ($p > .05$). An association was found between VAS pain scores on admission to the PACU and age ($p = .004$). An association was also found between VAS pain scores on discharge from the PACU and gender ($p = .007$) and ASA physical status ($p = .041$). Additionally, an association was found between total PACU opioid consumption and age ($p = .010$), female gender ($p = .002$), and ASA physical status ($p = .026$).
Conclusion: The administration of a single 4-8 mg dose of dexamethasone intraoperatively was not associated with lower VAS pain scores upon admission or discharge from the PACU or total PACU opioid consumption in patients undergoing laparoscopic cholecystectomy in the outpatient setting.
Implications/Recommendations: This research study did not support the association between the use of dexamethasone and reduced postoperative pain. Studies have proven the efficacy of dexamethasone and the reduction of PONV. PONV has also been shown to contribute to the overall discomfort of the patient in the postoperative period. For this reason, the practitioner should still consider using dexamethasone as part of a multimodal approach to patient management. Further research in the form of a randomized, prospective study should be implemented that could control factors such as the surgeon performing the procedure and anesthetic technique.
Key Words: cholecystectomy, dexamethasone, laparoscopic, opioids, pain, postoperative

LIST OF TABLES

PAGE

TABLE 1: DEMOGRAPHIC AND CLINICAL CHARACTERISTICS OF THE USE OF DEXAMETHASONE IN PATIENTS WHO UNDERWENT LAPAROSCOPIC CHOLECYSTECTOMY SURGERY ……..... 16

TABLE 2: COMPARISON OF INTRAOPERATIVE AND PACU OPIOID ADMINISTRATION AND VAS PAIN SCORES ON PACU ADMISSION AND DISCHARGE …… 17

TABLE 3: LINEAR REGRESSION ANALYSIS BETWEEN VAS PAIN SCORES ON ADMISSION TO THE PACU AND DEXAMETHASONE USE IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY……. 18

TABLE 4: LINEAR REGRESSION ANALYSIS BETWEEN VAS PAIN SCORES ON DISCHARGE FROM THE PACU AND DEXAMETHASONE USE IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY……. 19

TABLE 5: LINEAR REGRESSION ANALYSIS BETWEEN PACU OPIOID CONSUMPTION AND DEXAMETHASONE USE IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY …… 19

TABLE 6: INDEPENDENT T-TEST COMPARING GENDER AND VAS PAIN SCORE ON ADMISSION, VAS PAIN SCORE ON DISCHARGE, TOTAL INTRAOPERATIVE OPIOIDS, AND TOTAL PACU OPIOIDS IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY……..... 20

TABLE 7: GENDER AND VAS PAIN SCORE ON ADMISSION, VAS PAIN SCORE ON DISCHARGE, TOTAL INTRAOPERATIVE OPIOIDS, AND TOTAL PACU OPIOIDS IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY ……...…. 21

INTRODUCTION

Background and Significance

The development of minimally invasive surgery techniques has profoundly impacted the field of surgery. By performing a procedure laparoscopically, smaller incisions are required, less pain is experienced, and patients experience shorter hospital stays (Srivastava & Niranjan, 2010). Cholecystectomy is one of the most common reasons for hospital admission, and laparoscopic surgery is currently the gold standard for treatment of symptomatic gallstones or acute cholecystitis (Sugrue, Sahebally, Ansaloni, & Zielinski, 2015). In the United States, approximately 750,000 laparoscopic cholecystectomies are performed each year (Stewart, 2014).

According to Barash et al. (2013), the pain experienced after a laparoscopic case is primarily visceral. That is, the pain originates from organ nociceptors. Bisgaard (2006) reviewed evidence related to analgesic treatment after laparoscopic cholecystectomy and recommended a multimodal analgesia technique consisting of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), cyclooxygenase-2-specific inhibitors, weak or strong opioids, and local anesthetics. Parenteral glucocorticoids should also be considered as they have been shown to reduce both postoperative pain with little evidence of complications (Bisgaard, 2006). Despite the many advances in pain management and the increased knowledge surrounding multimodal analgesia, managing pain in the postoperative period has remained a challenge for clinicians (White, 2008). Furthermore, disparities in pain management exist related to gender, race, and ethnicity (Cooney, 2016; LeResche, 2011; Mossey, 2011).

According to LeResche (2011), females tend to experience a higher rate of the pain than males. The cause of this difference is multifactorial and poorly understood. Mossey (2011) concluded that racial and ethnic minority groups receive less adequate pain treatment when

compared to non-Hispanic whites. Contributing factors have included underreporting of pain and varying cultural beliefs related to pain (Mossey, 2011). Obese patients, or those having a Body Mass Index (BMI) greater than 30, often present with multiple comorbidities making pain management challenging. The practitioner must appropriately balance the use of pharmacologic methods of managing pain with obesity-associated respiratory complications such as obstructive sleep apnea (Cooney, 2016).

The International Association for the Study of Pain and the American Pain Society has used terms such as "unpleasant" and "emotional experience" when defining pain. Pain can be associated with actual or potential damage (Nagelhout & Plaus, 2010). Uncontrolled acute pain can lead to the development of chronic pain and a reduction in quality of life (Kehlet, Jensen, & Woolf, 2006). According to Garimella and Cellini (2013), appropriate pain management leads to shorter hospital stays, reduced cost, and increased patient satisfaction. Also, according to the authors, the focus should be placed on relieving pain, minimizing side effects, and using a multimodal technique. Multimodal analgesia focuses on using a variety of medications from different drug classes combined with nonpharmacological pain interventions. Using drugs with varying mechanisms of action allows the provider to mediate pain at many different levels and offers a personalized, patient-centered approach to pain management (Manworren, 2015). While opioids are commonly used for treating intraoperative and postoperative pain, lessening their use by employing a multimodal analgesia technique may reduce unwanted side effects (Garimella & Cellini, 2013). According to the authors, the patient is less likely to experience common side effects such as respiratory depression, nausea and vomiting, pruritus, and urinary retention.

Dexamethasone, a glucocorticoid, reduces tissue damage and inflammation by reducing inflammatory mediators that amplify and maintain pain perception and by possibly inhibiting

phospholipase A2 (Flood, Rathmell, & Shafer, 2015). According to the authors, when used intraoperatively, and as a single dose, minimal side effects are experienced. Dexamethasone has been successfully used to reduce Post Operative Nausea and Vomiting (PONV), and some research shows it plays a role in reducing postoperative pain. With an elimination half-time of 3.5-5.0 hours and duration of action of 36-54 hours, dexamethasone remains in the patient's systemic circulation after the surgery is completed (Flood et al., 2015).

While its use in preventing PONV is well studied, dexamethasone's impact on postoperative pain remains controversial (Hermans, Pooter, Groote, Hert, & Linden, 2012). Additionally, some practitioners may be hesitant to use the drug based on concerns related to decreased wound healing and the potential rise in blood glucose levels after dexamethasone administration (Murphy et al., 2014). More research has been conducted involving a condition called Opioid-Induced Hyperalgesia (OIH). This condition has lead to a state of hyperalgesia in response to chronic opioid exposure. The nociceptor becomes sensitized, and a paradoxical response is experienced whereby the patient becomes more sensitive to painful stimuli (Stoicea et al., 2015).

OIH is among the many reasons clinicians have begun to shift towards an opioid-sparing anesthesia technique. Even though acute opioid exposure is unlikely to cause hyperalgesia, tolerance, or addiction, many patients presenting to the operating room have previously used, or are currently using, opioids. According to Wilkerson, Kim, Windsor, and Mareiniss (2015), there has been an opioid abuse epidemic in the United States. According to the authors, abuse ranges anywhere from heroin use to the abuse of prescribed opioids such as hydrocodone or oxycodone.

The need to identify safe, effective, non-opioid analgesics has become increasingly important. Using a multimodal technique, dexamethasone may be beneficial as an adjunct pain

medication. The present study investigated the association between single-dose intraoperative dexamethasone and postoperative pain in patients undergoing outpatient laparoscopic cholecystectomy surgery. Studies regarding this topic have shown positive results. The knowledge gained from the present study could be applied to anesthesia practice at Charleston Area Medical Center (CAMC) in West Virginia and other facilities where outpatient laparoscopic cholecystectomies are performed.

The researcher's study focused on procedures completed in the outpatient setting. According to Seleem, Gerges, Shreif, Ahmed, and Ragab (2011), laparoscopic cholecystectomy surgery is commonly performed as day surgery or ambulatory surgery. That is, patients are discharged on the same day the procedure is performed. The authors concluded that laparoscopic cholecystectomies could be implemented as day surgeries with minimal complications and led to higher patient satisfaction. Common reasons for unanticipated hospital admission after day surgery included pain, PONV, surgical complications such as bleeding or a conversion from laparoscopic to an open surgical technique, and a patient's request for admission (Lau & Brooks, 2001).

Literature Review

Several randomized, controlled clinical trials have been completed examining the relationship between dexamethasone and postoperative pain (Bisgaard, Klarskov, Kehlet, & Rosenberg, 2003; Hermans et al., 2012; Lim et al., 2011; Mohtadi et al., 2014; Moyano, Garcia, & Caicedo, 2016; Waldron, Jones, Gan, Allen, & Habib, 2013; Yamanaga et al., 2017). While many have resulted in evidence supporting its use, others have found no association between the two. Therefore, the evidence is somewhat inconclusive and controversial. A study conducted by Lim et al. (2011) consisting of 120 patients between the ages of 20-65 years undergoing

laparoscopic cholecystectomy showed a reduction in postoperative pain with the use of dexamethasone. The subjects were randomly allocated to either a control group (N), a group who received 8 mg of dexamethasone 1-2 hours before surgery (S1) or a group who received 8 mg of dexamethasone intraoperatively (S2). Group N received normal saline 1 hour before induction and post gallbladder resection, group S1 received 8mg of dexamethasone 1 hour before induction and normal saline post gallbladder resection, and group S2 received normal saline 1 hour before induction and 8mg of dexamethasone post gallbladder resection. The scholars concluded that the Visual Analogue Scores (VAS) during 48 hours after the procedure of groups S1 and S2 were significantly lower than that of group N. The authors examined the consumption of Ketorolac and Tramadol postoperatively in each group. Group N consumed 51.0 ± 33.1 mg of Ketorolac and 16.6 ± 55 mg of Tramadol. Group S1 consumed 30.0 ± 29.1 mg of Ketorolac and 6.5 ± 17.5 mg of Tramadol. Group S2 consumed 25.2 ± 29.1 mg of Ketorolac and 5.5 ± 19.5 mg of Tramadol. The investigators found that a single dose of 8 mg of intravenous dexamethasone given 1 hour before induction or after the start of the procedure as part of a multimodal analgesia regimen reduced postoperative pain (Lim et al., 2011).

Another double-blinded, prospective study conducted by Mohtadi et al. (2014) examining the impact of dexamethasone and postoperative pain in patients undergoing laparoscopic cholecystectomy found similar results. The study consisted of 122 patients, aged 18-60 years old assigned to either a case group (D) or a control group (C). The groups received a single-dose of intravenous dexamethasone (0.01 mg/kg, up to 8 mg) or a 2 mL injection of normal intravenous saline, respectively. Postoperative pain intensity was measured by VAS scores, and total meperidine consumption in milligrams was recorded for 24-hours postoperatively. The authors found a significant reduction of pain intensity in group D compared to group C after 2, 6, and 12

hours of surgery. At 2 hours, group C had VAS scores of 5.15 ± 2.80 and group D had VAS scores of 3.88 ± 1.03. At 6 hours, group C had VAS scores of 4.86 ± 2.78 and group D had VAS scores of 3.08 ± 1.79. At 12 hours, group C had VAS scores of 4.03 ± 1.94 and group D had VAS scores of 3.03 ± 1.74. However, no significant differences were noted between the two groups immediately after or 24 hours post surgery. The consumption of meperidine was significantly less in group D when compared to group C (44.26 ± 7.32 mg versus 60.24 ± 10.55 mg).

A randomized, double-blind clinical trial conducted by Bisgaard et al. (2003) also examined preoperative dexamethasone and surgical outcome after laparoscopic cholecystectomy. Eighty patients were randomized to receive either 8 mg of dexamethasone or a placebo 90 minutes before the procedure. The primary endpoints for this study were fatigue and pain. The researchers measured C-Reactive Protein (CRP), pulmonary function, pain scores, and nausea and vomiting episodes preoperatively and during the first 24 postoperative hours. The results showed a significant reduction in postoperative CRP levels ($p = .01$), incisional pain during the first 24 postoperative hours ($p < 0.05$), fatigue ($p = 0.01$) and total requirement of opioids in the dexamethasone group ($p < 0.05$). The investigators also observed a significant reduction in pain scores during the first postoperative week ($p < 0.05$). The added total VAS scores in the first postoperative week were a median of 53 for the dexamethasone group and 157 for the placebo group. Patients in the treatment group resumed recreational activities faster (1 day versus 2 days) than the control group ($p < 0.05$).

Yamanaga et al. (2017) examined the effect of dexamethasone on PONV and pain in patients undergoing general anesthesia for laparoscopic donor nephrectomy. This retrospective cohort study compared donors who received a lower dose (4-6 mg) or a higher dose (8-14 mg) of

dexamethasone with a control group who did not receive dexamethasone. The results showed a 28% reduction in postoperative pain and a 29% reduction in opioid consumption among the higher dexamethasone (8-14 mg) group. However, the results were not significant for the lower dexamethasone (4-6 mg) group. Total postoperative opioid consumption was 35.2 ± 29.8 mg for the control group, 27.8 ± 19.6 mg for the low dose group, and 25.1 ± 28.0 mg for the high dose group. Postoperative complications (2.7% for the control group, 4.3% for the low dose group, and 0% for the high dose group) and hospital length of stay (2.68 ± 0.62 for the control group, 2.63 ± 0.59 for the low dose group, and 2.66 ± 0.62 for the high dose group) did not differ significantly between the groups. The researchers concluded that a single perioperative dexamethasone dose of 8-14 mg decreased antiemetic and narcotic requirements in the first 24 hours after surgery. Additionally, there was no increase in surgical complications related to the administration of dexamethasone.

Karaman et al. (2013) studied the effects of dexamethasone and pheniramine hydrogen maleate, either alone or combined, on stress response in patients undergoing elective laparoscopic cholecystectomy. Eighty subjects were randomly assigned to one of four groups. A control group, a dexamethasone (Dekort) group (8 mg/2 mL), a pheniramine hydrogen maleate (Avil) group (45.5 mg/2 mL), and a combined (Dekort + Avil) group with each having 20 patients. Authors reported that CRP levels and VAS scores were significantly lower in the dexamethasone group and combined group. Both the Dekort group and the Dekort + Avil group described a VAS score of 1 versus a VAS score of 2.5 for the control and a VAS score of 2 for the Avil group. Both dexamethasone and pheniramine were found to significantly reduce PONV ($P < .001$ for dexamethasone and $P = .005$ for pheniramine). The scholars concluded that

dexamethasone significantly decreased postoperative pain and systemic-acute phase response more so than pheniramine hydrogen maleate.

Oliveria, Almeida, Benzon, and McCarthy (2011) conducted a meta-analysis examining perioperative single dose systemic dexamethasone for postoperative pain. The effects of dexamethasone were evaluated by pooling studies into three groups based on dexamethasone dosage. The groups consisted of < 0.1 mg/kg (low group), 0.11-0.2 mg/kg (intermediate group), and a ≥ 0.21 mg/kg (high group). The analysis consisted of 24 randomized clinical trials with a combined 2,751 subjects. Results supported dexamethasone over the placebo for pain at rest and with movement. The intermediate and high groups showed a reduction in opioid consumption. The authors also found that preoperative administration of dexamethasone appeared to be more effective than intraoperative administration. Additionally, it was found that dexamethasone at doses greater than 0.1 mg/kg was an effective adjunct in a multimodal technique to reduce pain postoperatively.

Another meta-analysis conducted by Waldron et al. (2013) utilized multiple databases to search for randomized, controlled studies comparing pain outcomes in adult patients undergoing general anesthesia who were given dexamethasone versus a placebo or an antiemetic. Forty-five studies involving 5,796 patients were included. Dexamethasone administration doses ranged from 1.25-20 mg. Investigators showed that patients who received dexamethasone had lower pain scores at 2 hours [Mean Difference (MD) -0.49], lower pain scores at 24 hours (MD -0.48) and received less opioids at 2 hours (MD -0.87 mg morphine equivalents) and 24 hours (MD -2.33 mg morphine equivalents) post surgery. Additionally, dexamethasone-treated patients required fewer rescue analgesics, had a longer time to rescue analgesic (MD 12.06 minutes), and shorter stays in the Post-Anesthesia Care Unit (PACU), (MD -5.32 minutes). The authors also

investigated whether dexamethasone increased the risk of adverse effects postoperatively. The analysis found no increase in infection or delayed wound healing, but did identify increased blood glucose levels at 24 hours post surgery. The scholars concluded that a single-dose of intravenous dexamethasone had small but significant benefits regarding postoperative analgesia.

In contrast, a randomized controlled trial conducted by Moyano et al. (2016) examining the analgesia effect of dexamethasone after arthroscopic knee surgery found that intravenous dexamethasone had no clinical impact on postoperative pain during the first 48 hours after the procedure. Seventy-eight patients were randomized to receive either 10 mg of dexamethasone (DM group) or 0.9% normal saline (NS group). The authors concluded that pain reduction was achieved through the administration of morphine and it was not a result of dexamethasone administration. One limitation of this study is its applicability to procedures other than arthroscopic knee surgery.

Concern among clinicians exists regarding the effect of dexamethasone on the reversal of rocuronium using sugammadex. A prospective, single-blinded trial by Rezonja et al. (2016) featured 65 patients undergoing elective urological or abdominal surgery randomized to either a granisetron (control) or dexamethasone group (case). Neuro-Muscular Block (NMB) was assessed using Train-Of-Four (TOF) stimulation. The researchers concluded that the administration of dexamethasone did not delay the reversal of NMB when using sugammadex (mean of 121 ± 61 seconds for the control versus 125 ± 57 seconds for the dexamethasone group). Time to NMB reversal was more dependent on the ratio of train-of-four before sugammadex administration. However, a significant drop in plasma dexamethasone concentration was noted after the administration of sugammadex (810 ± 283 μg/l post administration versus 604 ± 208 μg/l pre-administration). The scholars concluded that

dexamethasone did not delay NMB reversal by sugammadex in patients who underwent general anesthesia.

Statement of Problem and Research Purpose

The purpose of this study was to examine the association between the intraoperative administration of dexamethasone in patients undergoing laparoscopic cholecystectomy surgery in the outpatient setting and postoperative outcomes including pain and opioid consumption. The study's purpose was to determine if an association existed between a single dose of dexamethasone intraoperatively and VAS pain scores upon admission and discharge from the PACU and total opioid consumption in the PACU.

METHODOLOGY

Research Hypothesis

The hypotheses were:

1) Patients undergoing laparoscopic cholecystectomy surgery who received a 4-8 mg single dose of dexamethasone intraoperatively will have lower pain scores upon admission to and discharge from the PACU than patients who did not receive a single dose of dexamethasone intraoperatively.
2) Patients undergoing laparoscopic cholecystectomy surgery who received a 4-8 mg single dose of dexamethasone intraoperatively will consume less total opioids while in the PACU than patients who did not receive a single dose of dexamethasone intraoperatively.

Research Design

This study used a retrospective, quantitative, case-control format. This design was appropriate because data was available from patients who have undergone laparoscopic cholecystectomies. The case-control design allowed for easy identification of patient

demographics such as age and gender and clinical characteristics that could compare patients who received a single dose of intraoperative dexamethasone with those who did not. A retrospective, case-controlled study design was employed to analyze the data to gain substantial research findings while adhering to limited financial and time constraints when compared with alternative study designs (Schulz & Grimes, 2002).

CAMC is a not-for-profit, 956-bed academic medical center system and regional referral center comprised of CAMC Memorial Hospital, CAMC General Hospital, and CAMC Women and Children's Hospital located in Charleston, West Virginia. Also, Teays Valley Hospital is located in Hurricane, West Virginia (CAMC, 2017a). CAMC General is one of only two Level I Trauma Centers in the state of West Virginia (CAMC, 2017b).

A review of electronic medical records (EMR) at CAMC was conducted using patients requiring a laparoscopic cholecystectomy in the outpatient setting who underwent general anesthesia between June 15, 2007, and June 15, 2017 (McKesson Corporation, 2017). Two groups were developed for comparison. The case group consisted of subjects who underwent laparoscopic cholecystectomy surgery and received a single dose of dexamethasone intraoperatively. The control group consisted of subjects who experienced laparoscopic cholecystectomy surgery and did not receive dexamethasone intraoperatively.

Sample Population and Description of Sample

The sample population for this study consisted of 200 patients who underwent a laparoscopic cholecystectomy in the outpatient setting between June 15, 2007, and June 15, 2017. The search yielded 5,700 randomized records that matched the inclusion and exclusion criteria. Patient records were filtered to show outpatient records and were randomized by selecting every 5^{th} record until the predetermined sample size of 200 was met. The sample

consisted of a case group of 100 subjects, 18 to 64 years old who received a 4-8 mg single dose of dexamethasone intraoperatively. Each group consisted of 50 males and 50 females, as the researcher manipulated this variable. Of the 100 case subjects, 90 received 8 mg of dexamethasone, and 10 received 4 mg of dexamethasone. The control group consisted of 100 subjects, 18-64 years old who did not receive dexamethasone intraoperatively. The subjects were identified by using the International Classification of Diseases, 9th revision, and 10th revision, Clinical Modification codes: 51.23 (ICD-9-CM/laparoscopic cholecystectomy) and 0FT44ZZ (ICD-10-CM/resection of gallbladder, percutaneous endoscopic approach).

Inclusion Criteria:

1. Patients 18 to 64 years of age.
2. American Society of Anesthesiologists (ASA) physical status classification I-III.
3. Patients who underwent outpatient laparoscopic cholecystectomy under general anesthesia and did or did not receive a 4-8 mg single-dose of dexamethasone intraoperatively.

Exclusion Criteria:

1. Patients less than 18 years of age or older than 64 years of age.
2. Patients with an ASA physical status greater than III.
3. Laparoscopic cholecystectomy converted to open cholecystectomy.
4. Patients whose home medications included opioids or analgesics for treatment of chronic pain.
5. Patient whose home medications included glucocorticoids.
6. Patients who received dexamethasone in the preoperative period or PACU on the day of surgery.

7. Patients with a documented history of drug or alcohol abuse.

Procedures and Protocol

A retrospective chart review was conducted using the EMR databases at CAMC for patients who underwent outpatient laparoscopic cholecystectomy surgery requiring general anesthesia between June 15, 2007, and June 15, 2017. The patients who met the inclusion criteria were selected for this study. Patient demographics and clinical variables collected from the records included age, gender, ASA physical classification status, height, weight, BMI, Length Of Surgery (LOS), dexamethasone dosage or not, intraoperative opioid administration, postoperative opioid consumption, and pain scores upon admission and discharge from the PACU.

Age was measured in years at the time of arrival to the hospital. Gender was classified as male or female. ASA physical classification status is a subjective measurement based on overall health that is assigned to the patient by the anesthesia provider conducting the preoperative anesthesia assessment. There are six ASA physical status classifications: (I) normal, healthy patient, (II) patient with mild systemic disease, (III) patient with severe systemic disease, (IV) patient with severe systemic disease that is a threat to life, (V) patient is not expected to live without surgery, and (VI) patient is brain-dead and is donating organs (ASA, 2017). BMI was collected from the preoperative anesthesia evaluation or calculated using the patient's height in meters and weight in kilograms following CDC guidelines (Centers for Disease Control and Prevention, 2017). LOS was recorded in minutes. Total intraoperative and PACU opioid consumption data was collected and converted to morphine equivalents in milligrams using an opioid conversion calculator, allowing for comparison among different opioids (ClinCal, 2017). Dexamethasone administration was measured in milligrams. Pain assessments, a subjective

measurement, were recorded using a numeric rating scale of 0-10. A score of "0" indicated no pain and a score of "10" indicated the worst pain imaginable (Breivik et al., 2008).

The final anesthesia record was used to identify the primary independent variable, the use or not of dexamethasone and other independent variables. Patient records were also reviewed to determine the dependent variables: total amount of opioid consumption and pain scores in the PACU upon admission and discharge. The researcher examined the anesthesia records, preoperative evaluation records, medication administration records, and PACU records for specific data. The data was organized using Microsoft Excel. Each selected patient was assigned a study number. This number allowed patient identifiers to remain private and confidential (Appendix A). Patient demographic data such as age, gender, height, weight, BMI, length of surgery, ASA physical status, dexamethasone administration, total opioid consumption intraoperatively, and pain scores and opioid consumption in the PACU was organized using an Excel spreadsheet (Appendix B).

Statistical Design and Analysis

The purpose of this research was to examine the association between single-dose intraoperative dexamethasone and postoperative pain in patients undergoing laparoscopic cholecystectomy surgery. The dependent variables included the consumption of opioids in the PACU, pain scores on admission to the PACU, and pain scores at discharge from the PACU. The independent variables were the administration of IV dexamethasone and dosage, age, gender, BMI, LOS and ASA physical status classification. Chi-squared test was used to determine if there was a statistically significant difference related to gender and ASA classification between the two groups. Independent t-tests were used to compare the mean difference of age, BMI, LOS, VAS pain scores on admission and discharge from the PACU, and total intraoperative and total

opioid consumption in the PACU between the two groups. A p-value of < .05 was statistically significant for this research study. Statistical analysis used SPSS software (SPSS IBM Company, 2017).

Ethical Considerations

The CAMC and West Virginia University-Charleston Division Institutional Review Board approved this study on July 20, 2017 (Appendix C).

RESULTS

Presentation, Analysis, and Interpretation of Data

The study sample consisted of 200 patients between 18-64 years old within the CAMC medical system who underwent outpatient laparoscopic cholecystectomy surgery. The patients were divided into two groups based on whether dexamethasone was administered intraoperatively. The case group (n=100) included patients who received intraoperative dexamethasone, and the control group (n=100) consisted of patients who did not receive dexamethasone. A comparison between the two groups means difference using independent t-tests showed no statistical difference in age, BMI, ASA physical status, gender, or LOS, (Table 1). The mean age for the case group was 43.6 ± 13.9 years versus a mean of 44.6 ± 12.6 years for the control group, and the mean difference was not statistically significant ($p > .05$). The mean BMI for the case and control groups was 33.6 ± 8 kg/m^2 and 31.8 ± 6.9 kg/m^2, respectively, and the mean difference was not statistically significant ($p > .05$). Each study group consisted of 50 males and 50 females. The majority of all subjects (N=187) were classified as an ASA physical status classification of II or III. The mean LOS for the case group was 53.5 ± 21.6 minutes and 51.9 ± 21.8 minutes for the control group ($p > .05$). A p-value of < .05 was considered significant.

Table 1: Demographic and Clinical Characteristics of the use of Dexamethasone in Patients Who Underwent Laparoscopic Cholecystectomy Surgery.

Variable	Total Sample	Study Groups		Statistical Value
	Total N=100 Mean (SD)	Did not receive dexamethasone N=100 (50%) Mean (SD)	Received dexamethasone N=100 (50%) Mean (SD)	p-Value
Age (years)	44.1 (13.2)	44.6 (12.6)	43.6 (13.9)	(NS)
BMI (kg/m2)	32.7 (7.5)	31.8 (6.9)	33.6 (8)	(NS)
Gender (F/M)	F = 100 M = 100	F = 50 M = 50	F = 50 M = 50	(NS)
ASA I N (%) ASA II N (%) ASA III N (%)	13 (6.5%) 105 (52.5%) 82 (41%)	7 (7%) 47 (47%) 46 (46%)	6 (6%) 58 (58%) 36 (36%)	(NS)
LOS (minutes)	52.7 (21.7)	51.9 (21.8)	53.5 (21.6)	(NS)
Dexamethasone Dose (mg) 0 4 8	Frequency 100 10 90	Frequency 100 0 0	Frequency 0 10 90	(NS)

NS=Not Significant (p > .05), SD=Standard Deviation, BMI=Body Mass Index, ASA=American Society of Anesthesiologists physical status classification, LOS=Length of surgery, M=male, F=female, Dose=milligrams.

A comparison of the two groups showed a statistically significant difference in mean difference of VAS pain scores on admission to the PACU, total intraoperative opioid administration, and overall PACU opioid administration. Upon admission to the PACU, patients

who received dexamethasone presented a mean pain score of 2.7 ± 3.5 versus 3.9 ± 3.6 for those who did not receive dexamethasone ($p < .05$). There was no statistically significant mean difference in VAS pain scores upon discharge from the PACU between the two groups ($p > .05$), (Table 2). Upon discharge from the PACU, patients who received dexamethasone presented a mean pain score of 2.4 ± 1.8 versus 2.8 ± 1.2 for those who did not receive dexamethasone ($p > .05$). Those who received dexamethasone received a mean of 24.9 ± 10.3 morphine equivalents intraoperatively and the group who did not receive a mean of 28.6 ± 11.6 morphine equivalents. This finding was statistically significant ($p < .05$). Total PACU opioid consumption was statistically significant with a mean difference of 5.6 ± 5.7 morphine equivalents for patients who received dexamethasone intraoperatively and 8 ± 7.2 morphine equivalents for patients who did not receive dexamethasone ($p < .05$), (Table 2).

Table 2: Comparison of Intraoperative and PACU Opioid Administration and VAS Pain Scores on PACU Admission and Discharge.

Variable	Total Sample	Study Groups		Statistical Value
	Total Sample N=100 Mean (SD)	Did not receive dexamethasone N=100 (50%) Mean (SD)	Received dexamethasone N=100 (50%) Mean (SD)	p-Value
VAS – PACU admission (0-10)	3.3 (3.6)	3.9 (3.6)	2.7 (3.5)	.018*
VAS – PACU discharge (0-10)	2.6 (2)	2.8 (2.2)	2.4 (1.8)	(NS)
Intraoperative opioid administration (morphine equivalents)	26.8 (11.1)	28.6 (11.6)	24.9 (10.3)	.018*
PACU opioid administration (morphine equivalents)	6.9 (6.6)	8 (7.2)	5.6 (5.7)	.013*

*Indicated significant value ($p < .05$), NS= Not Significant ($p > .05$), SD=Standard Deviation, VAS = Verbal Analogue Scale pain score, PACU = post-anesthesia care unit.

A linear regression analysis was conducted to evaluate the association of VAS pain scores on admission to the PACU with age, gender, BMI, ASA, dexamethasone administration or not, and dexamethasone dosage. The researcher found a statistically significant association between VAS pain scores on admission to the PACU and age ($p = .004$), (Table 3).

Table 3: Linear Regression Analysis Between VAS Pain Scores on Admission to the PACU and Dexamethasone Use in Patients Undergoing Laparoscopic Cholecystectomy

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	6.105	1.537		3.971	.0001
	Age	-.063	.022	-.231	-2.892	.004*
	Gender: F=1, M=0	.467	.524	.065	.891	.374
	BMI	-.048	.036	-.100	-1.343	.181
	ASA	.790	.512	.131	1.542	.125
	DEX: Y=1, N=0	-2.413	2.304	-.336	-1.047	.296
	Dose	.171	.297	.186	.577	.565

Dependent Variable: VAS pain scores on PACU admission. *Indicates Statistical Significance at $p < .05$, Gender (M=male, F=female), BMI=Body Mass Index, ASA=American Society of Anesthesiologists physical status classification, DEX (Y=yes, N=no), Dose=milligrams.

A linear regression analysis was conducted to evaluate the association between VAS pain scores on discharge from the PACU with age, gender, BMI, ASA, dexamethasone administration or not, and dexamethasone dosage. The results indicated a statistically significant association between VAS pain scores on discharge from the PACU and gender ($p = .007$) and ASA physical status ($p = .041$), (Table 4).

Table 4: Linear Regression Analysis Between VAS Pain Scores on Discharge from the PACU and Dexamethasone Use in Patients Undergoing Laparoscopic Cholecystectomy

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	1.128	.881		1.281	.202
	Age	-.003	.012	-.019	-.236	.814
	Gender: F=1, M=0	.825	.300	.203	2.751	.007*
	BMI	-.003	.020	-.010	-.137	.891
	ASA	.603	.294	.177	2.052	.041*
	DEX: Y=1, N=0	-.834	1.320	-.205	-.632	.528
	Dose	.067	.170	.128	.395	.693

Dependent Variable: VAS pain scores on PACU discharge. *Indicates Statistical Significance at $p < .05$, Gender (M=male, F=female), BMI=Body Mass Index, ASA=American Society of Anesthesiologists physical status classification, DEX (Y=yes, N=no), Dose=milligrams.

A linear regression analysis was conducted to evaluate the association between total opioid consumption in the PACU and age, gender, BMI, ASA physical status, dexamethasone administration or not, and dexamethasone dosage. The results indicated a statistically significant association between total opioid consumption in the PACU and age ($p = .010$), gender ($p = .002$), and ASA physical status ($p = .026$), (Table 5).

Table 5: Linear Regression Analysis Between PACU Opioid Consumption and Dexamethasone Use in Patients Undergoing Laparoscopic Cholecystectomy

Model		Unstandardized Coefficients		Standardized Coefficients	t	Sig.
		B	Std. Error	Beta		
1	(Constant)	6.605	2.746		2.405	.017
	Age	-.101	.039	-.204	-2.608	.010*
	Gender: F=1, M=0	2.905	.936	.222	3.105	.002*
	BMI	-.012	.064	-.014	-.195	.846
	ASA	2.052	.915	.187	2.241	.026*
	DEX: Y=1, N=0	-5.284	4.116	-.403	-1.284	.201
	Dose	.407	.530	.242	.768	.444

Dependent Variable: Total PACU Opioid Consumption in Morphine Equivalents. *Indicates Statistical Significance at $p < .05$, Gender (M=male, F=female), BMI=Body Mass Index,

ASA=American Society of Anesthesiologists physical status classification, DEX (Y=yes, N=no), Dose=milligrams.

An independent t-test analysis compared gender to VAS pain score on admission, VAS pain score on discharge from the PACU, total intraoperative opioid administration, and total opioid consumption in the PACU. The analysis showed a statistically significant association between gender and VAS pain score on discharge from the PACU ($p = .026$) and total PACU opioid consumption ($p = .003$), (Table 6).

Table 6: Independent T-Test Comparing Gender and VAS Pain Score on Admission, VAS Pain Score on Discharge, Total Intraoperative Opioids, and Total PACU Opioids in Patients Undergoing Laparoscopic Cholecystectomy

		t-test for Equality of Means		
		df	Sig. (2-tailed)	Mean Difference
VAS Score: Admission	Equal variances assumed	198	.277	-.5550
	Equal variances not assumed	197.550	.277	-.5550
VAS Score: Discharge	Equal variances assumed	198	.026*	-.640
	Equal variances not assumed	184.920	.026*	-.640
Total Intraoperative Opioids	Equal variances assumed	198	.801	-.39670
	Equal variances not assumed	193.458	.801	-.39670
Total PACU Opioids	Equal variances assumed	198	.003*	-2.76400
	Equal variances not assumed	183.043	.003*	-2.76400

*Indicates statistical significance at $p < .05$. VAS=Verbal Analogue Scale, PACU=post-anesthesia care unit.

Further analysis was conducted to assess whether the statistical significance applied to males or females. Using ANOVA, group difference means indicated that females had a mean VAS pain score on discharge from the PACU of 2.89 and males had a mean VAS pain score of 2.25. Females consumed a mean of 8.28 morphine equivalents in the PACU and males consumed

a mean of 5.52 morphine equivalents. These findings were statistically significant ($p < .05$), (Table 7).

Table 7: Gender and VAS Pain Score on Admission, VAS Pain Score on Discharge, Total Intraoperative Opioids, and Total PACU opioids in Patients Undergoing Laparoscopic Cholecystectomy

	Gender: F = 1, M = 0	N	Mean	Std. Deviation
VAS Score: Admission	0	100	3.015	3.5108
	1	100	3.570	3.6825
VAS Score: Discharge*	0	100	2.25	1.731
	1	100	2.89	2.274
Total Intraoperative Opioids	0	100	26.5745	10.24703
	1	100	26.9712	11.95831
Total PACU Opioids*	0	100	5.5185	5.43688
	1	100	8.2825	7.29542

*Indicates statistical significance at $p < .05$. Gender (M=male, F=female), VAS=Verbal Analogue Scale, PACU=post-anesthesia care unit.

DISCUSSION

Discussion of Study Results

The purpose of the present study was to determine the association between a single dose of intraoperative dexamethasone and postoperative pain. The hypotheses predicted patients undergoing laparoscopic cholecystectomy surgery who received a single 4-8 mg dose of dexamethasone intraoperatively would have lower VAS pain scores upon admission and discharge from the PACU. Additionally, these patients would have consumed less total opioids in the PACU. The researcher wanted to make the case and control groups as similar as possible and therefore, purposefully chose 50 males and 50 females for each group.

The results of Chi-square and independent t-tests showed there were not statistically significant differences in mean age, BMI, gender, ASA physical status, or LOS between the case and control groups. T-tests comparing the two groups revealed a statistical significance between

dexamethasone administration and VAS pain scores upon admission to the PACU and total PACU opioid consumption. When dependent variables were included in a linear regression analysis, no statistically significant association was found between the administration of a single 4-8 mg dose of dexamethasone and VAS pain scores upon admission or discharge from the PACU or total PACU opioid consumption.

When factoring in age, gender, BMI, ASA physical status, dexamethasone administration or not, and dexamethasone dose, there was not a statistically significant association between dexamethasone administration and mean difference VAS pain score on admission to the PACU, VAS pain score on discharge from the PACU, or total opioid consumption in the PACU. These results are more applicable to the clinical setting; as patient characteristics must be taken into account when determining if an association exists between a pharmacological drug and a patient population. Analysis showed an association between age and VAS pain scores on admission to the PACU. There was also an association between gender and ASA physical status and VAS pain scores on discharge from the PACU. Additionally, there was an association between age, gender, and ASA physical status and total PACU opioid consumption.

Further analysis was conducted to examine the association between age categories and VAS pain score on admission to the PACU. Patients were assigned to either group 1 (18-35 years old), group 2 (36-50 years old), or group 3 (51-64 years old). An ANOVA showed a statistically significant difference in the mean VAS pain score on admission for group 3 compared to group 1 ($p = .046$). However, there was not a statistically significant difference in mean VAS pain score on PACU admission when comparing group 3 to group 2 ($p > .05$). Group 1 had a mean difference VAS pain score of 2.6 ± 2.9, group 2 had a mean difference VAS pain

score of 3.5 ± 3.7, and group 3 had a mean difference VAS pain score of 3.1 ± 3.5 (Data not shown). Additional analysis showed that compared to group 1, group 3 received statistically significantly less intraoperative opioids ($p = .024$), (24.4 ± 9.3 morphine equivalents versus 29.5 ± 11.9 equivalents), (Data not shown.) This is a possible explanation as to why group 3 had higher VAS pain scores upon admission to the PACU.

The results showed an association between female gender and higher VAS pain scores on discharge from the PACU. This is consistent with findings from a review by Lombana and Vidal (2012). The authors found that for various reasons including physiological, neural, hormonal, psychological, social, and cultural factors women tend to report pain more frequently and also have a lower threshold for pain when compared to men. Additionally, the authors concluded that women describe more postoperative effects such as PONV and headaches. Further analysis was conducted to examine the association between ASA physical status and VAS pain score on discharge from the PACU. Patients with an ASA 3 physical status had a mean pain score of 2.8 ± 1.9, which was statistically significantly higher than the means for patients with an ASA 2 physical status (2.6 ± 2.2) and patients with an ASA 1 physical status (1.5 ± 1.7), (Data not shown). A patient with an ASA physical status of 3 is classified as having severe systemic disease. The increase in comorbidity could be associated with increased postoperative pain. However, research needs to be conducted to see if an association exists between increasing ASA physical status and postoperative pain.

Linear regression analysis showed that females consumed significantly more opioids in the PACU. This is consistent with the findings from Lombana and Vidal (2012). Additionally, age and ASA status were found to have a statistically significant association with total opioid consumption in the PACU. Additional analysis was performed to determine the association.

Patients were once again assigned to group 1 (18-35 years old), group 2 (36-50 years old), or group 3 (51-64 years old) and an ANOVA was performed. The results showed no statistically significant difference in mean opioid consumption in the PACU between the three groups ($p > .05$), (Data not shown). However, when examining the association between ASA and total opioid consumption in the PACU, the researcher found that patients with an ASA 3 physical status consumed significantly more opioids compared to patients with an ASA 1 and ASA 2 physical status. Again, this association could be related to an increase in patient comorbidity and the fact that fewer opioids were given intraoperatively for group 3. A large-scale, randomized prospective study is needed to show whether increasing ASA physical status is related to increased pain and opioid consumption in the postoperative period.

The present study showed no association between the administration of a single dose of dexamethasone and VAS pain score upon admission and discharge from the PACU or total PACU opioid consumption. Therefore, the researcher's hypotheses were rejected. Several studies have shown a reduction in postoperative pain and PACU opioid administration when dexamethasone was given intraoperatively (Bisgaard et al., 2003; Lim et al., 2011; Mohtadi et al., 2014; Waldron et al., 2013). However, other studies have shown no association (Moyano et al., 2016). This could be explained by the study's small sample size, the inclusion of only one hospital network, and the retrospective study design.

Study Limitations

There were multiple limitations to this study. The study used a retrospective, case-control design, which limits the findings to an "association" only. A prospective study where the researcher can have more control and technique is consistent is needed to prove causation. There was not a standard anesthetic or surgical technique for each case. All patients involved in this

study were from hospitals within the CAMC network and may not represent the overall population. While current opioid use and drug or alcohol abuse were included in the exclusion criteria, patients may have failed to reveal this information to the provider. To assess pain, the VAS pain score was used. However, pain has been subjective and varies between individuals. An objective measurement of pain is not available.

The participants in the study were administered different doses of dexamethasone at different times. Additionally, only intraoperative and postoperative opioids were included in the study. Other medications that could not be transferred to morphine equivalents such as Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), local anesthetics, and intravenous acetaminophen could have impacted postoperative pain scores and opioid consumption. Finally, a lack of documentation by nurses, anesthesia providers, and the researcher could have affected the results.

IMPLICATIONS AND RECOMMENDATIONS

This study provides clinical evidence to practitioners and researchers about the use of dexamethasone in patients undergoing laparoscopic cholecystectomy in the outpatient setting. A review of the literature recommends the use of a multimodal analgesia technique for managing postoperative pain. This research study did not support the association between the use of dexamethasone and reduced postoperative pain. Studies have proven the efficacy of dexamethasone and the reduction of PONV. PONV has also been shown to contribute to the overall discomfort of the patient in the postoperative period. For this reason, the practitioner should still consider using dexamethasone as part of a multimodal approach to patient management. Further research in the form of a randomized, prospective study should be implemented that could control factors such as the surgeon performing the procedure, anesthetic

technique, the administration of NSAIDs, local anesthetics, and intravenous acetaminophen, and other limitations that the present study was unable to control.

CONCLUSION

In this study, the administration of a single 4-8 mg dose of dexamethasone intraoperatively was not associated with lower VAS pain score upon admission or discharge from the PACU or total PACU opioid consumption in patients undergoing laparoscopic cholecystectomy in the outpatient setting.

REFERENCES

American Society of Anesthesiologists, [ASA]. (2017). *ASA Physical Classification System.* Retrieved August 21, 2017 from http://www.asahq.org/Home/For-Members/Clinical-Information/ASA-Physical-Status-Classification-System

Barash, P. G., Cullen, B. F., Stoelting, R. K., Cahalan, M. K., Stock, M. C., & Ortega, R. (2013). *Clinical Anesthesia* (7th Edition ed.). Philadelphia, PA: Lippincott Williams & Wilkins.

Bisgaard, T. (2006). Analgesic treatment after laparoscopic cholecystectomy *Anesthesiology, 104*(4), 835-846. doi:10.1016/j.acpain.2006.08.039

Bisgaard, T., Klarskov, B., Kehlet, H., & Rosenberg, J. (2003). Preoperative dexamethasone improves surgical outcome after laparoscopic cholecystectomy. *Annals of Surgery, 238*(5), 651-655. doi:doi.org/10.1097/01.sla.0000094390.82352.cb

Breivik, H., Borchgrevink, P. C., Allen, S. M., Rosseland, L. A., Romunstad, L., Hals, E. K. B., . . . Stubhaug, A. (2008). Assessment of pain. *British Journal of Anesthesia, 101*(1), 17-24. doi:10.1093/bja/aen103

Centers for Disease Control and Prevention [CDC]. (2017). *Body Mass Index.* Retrieved August 21, 2017 from http://www.cdc.gov/healthyweight/assessing/bmi/

Charleston Area Medical Center [CAMC]. (2017a). *CAMC Hospital & Centers.* Retrieved August 20, 2017 from http://camc.org/hospitals-centers

Charleston Area Medical Center [CAMC]. (2017b). *CAMC General Hospital.* Retrieved August 20, 2017 from http://camc.org/gh

ClinCal. (2017). *Equivalent Opioid Calculator*. Retrieved from http://clincalc.com/opioids/

Cooney, M. F. (2016). Optimizing acute pain management in the obese patient: Treatment and monitoring considerations. *Journal of PeriAnesthesia Nursing, 31*(3), 269-276. doi:10.1016/j.jopan.2015.12.008

Flood, P., Rathmell, J. P., & Shafer, S. (2015). *Stoelting's Pharmacology & Physiology in Anesthetic Practice* (5th Edition ed.). Philadelphia, PA: Wolters Kluwer Health.

Garimella, V., & Cellini, C. (2013). Postoperative pain control. *Clinics in Colon and Rectal Surgery, 26*(3), 191-196. doi:10.1055/s-0033-1351138

Hermans, V., Pooter, F. D., Groote, F. D., Hert, S. D., & Linden, P. V. d. (2012). Effect of dexamethasone on nausea, vomiting, and pain in paediatric tonsillectomy. *British Journal of Anesthesia, 109*(3), 427-431. doi:10.1093/bja/aes249

Karaman, K., Bostanci, E. B., Aksoy, E., Ulas, M., Yigit, T., Erdemli, M. O., . . . et al. (2013). Effects of dexamethasone and pheniramine hydrogen maleate on stress response in patients undergoing elective laparoscopic cholecystectomy. *The American Journal of Surgery, 205*(2), 213-219. doi:doi.org/10.1016/j.amjsurg.2012.05.010

Kehlet, H., Jensen, T., & Woolf, C. (2006). Persistent postsurgical pain: Risk factors and prevention. *The Lancet, 367*(9522), 1618-1625. doi:10.1016/s0140-6736(06)68700-x

Lau, H., & Brooks, D. (2001). Predictive factors for unanticipated admissions after ambulatory laparoscopic cholecystectomy. *Archives of Surgery, 136*(10), 1150. doi:10.1001/archsurg.136.10.1150

LeResche, L. (2011). Defining gender disparities in pain management. *Clinical Orthopaedics and Related Research, 469*(7), 1871 to 1877. doi:10.1007/s11999-010-1759-9

Lim, S. H., Jang, E. H., Kim, M.-H., Cho, K., Lee, J. H., Lee, K. M., . . . et al. (2011). Analgesic effect of preoperative versus intraoperative dexamethasone after laparoscopic

cholecystectomy with multimodal analgesia. *Korean Journal of Anesthesiology, 61*(4), 315-319. doi.org/10.4097/kjae.2011.61.4315

Lombana, W. G., & Vidal, S. E. G. (2012). Pain and gender differences: A clinical approach. *Colombian Journal of Anesthesiology, 40*(3), 207-212. doi:10.1016/j.rcae.2012.05.006

Manworren, R. C. B. (2015). Multimodal pain management and the future of a personalized medicine approach to pain. *Association of periOperative Registered Nurses Journal, 101*(3), 307-318. doi:10.1916/j.aorn.2014.12.009

McKesson Corporation. (2017). *Hospital Information Systems.* Retrieved August 20, 2017 from http://www.mckesson.com/en_us/McKesson.com/For%2BHealthcare%2BProviders/Hospitals/Hospital%2BInformation%2BSystems/Hospital%2BInformation%2BSystems.html

Mohtadi, A., Nesioonpour, S., Salari, A., Akhondzadeh, R., Rad, B. M., & Aslani, S. M. M. (2014). The effect of single-dose administration of dexamethasone on postoperative pain in patients undergoing laparoscopic cholcystectomy. *Anesthesiology and Pain Medicine, 4*(3), 1-4. doi.org/10.5812/aapm.17872

Mossey, J. M. (2011). Defiing racial and ethnic disparities in pain management. *Clinical Orthopaedics and Related Research, 469*(7), 1859-1870. doi:10.1007/s11999-011-1770-9

Moyano, J., Garcia, M., & Caicedo, M. (2016). Analgesic effect of dexamethasone after arthroscopic knee surgery: A randomized controlled trial. *Pain Research and Management, 2016,* 1-6. doi:10.1155/2016/4216469

Murphy, G. S., Szokol, J. W., Avram, M. J., Greenberg, S. B., Shear, T., Vender, J. S., . . . et al. (2014). The effect of single low-dose dexamethasone on blood glucose concentrations in the perioperative period: A randomized, placebo-controlled investigation in gynecologic

surgical patients. *Anesthesia & Analgesia, 118*(6), 1204-1212. doi:10.1213/ane.0b013e3182a53981

Nagelhout, J. J., & Plaus, K. L. (2010). *Nurse anesthesia*. St Louis, Missouri: Saunders Elsevier.

Oliveria, G. S. D., Almeida, M. D., Benzon, H. T., & McCarthy, R. J. (2011). Perioperative single dose systemic dexamethasone for postoperative pain. *Anesthesiology, 115*(3), 575-588. doi:10.1097/aln.0b013e31822a24c2

Rezonja, K., Mars, T., Jerin, A., Kozelj, G., Pozar-Lukanovic, N., & Sostaric, M. (2016). Dexamethasone does not diminish sugammadex reversal of neuromuscular block - clinical study in surgical patients undergoing general anesthesia. *BMC Anesthesiology, 16*(1). doi:10.1186/s12871-016-0254-6

Schulz, K., & Grimes, D. (2002). Case-contol studies: Research in reverse. . *Lancet, 359*(9304), 431-434. doi:doi.org/10.1016/s0140-6736(02)07605-5

Seleem, M. I., Gerges, S. S., Shreif, K. S., Ahmed, A. E., & Ragab, A. (2011). Laparoscopic cholecystectomy as a day surgery procedure: Is it safe? - An Egyptian experience. *Saudi Journal of Gastroenterology, 17*(4), 277-279. doi:10.4103/131903767.82584

Srivastava, A., & Niranjan, A. (2010). Secrets of safe laparoscopic surgery: Anaesthetic and surgical considerations *Journal of Minimal Access Surgery, 6*(4), 91-94. doi:10.4103/0972-9941.72593

Stewart, L. (2014). Iatrogenic biliary injuries: Identification, classification, and management *Surgical Clinics of North America, 94*(2), 297-310. doi:10.1016/j.suc.2014.01.008

Stoicea, N., Russell, D., Weidner, G., Dudra, M., Joseph, N. C., Yu, J., & Bergese, S. D. (2015). Opioid-induced hyperalgesia in chronic pain patients and the mitigating effects of gabapentin. *Frontiers in Pharmacology, 6*(104), 1-6. doi:10.3389/fphar.2015.00104

Sugrue, M., Sahebally, S. M., Ansaloni, L., & Zielinski, M. D. (2015). Grading operative findings at laparoscopic cholecystectomy - A new scoring system. *World Journal of Emergency Surgery, 10*(1). doi.org/10.1186/s13017-015-0005-x

Waldron, N. H., Jones, C. A., Gan, T. J., Allen, T. K., & Habib, A. S. (2013). Impact of perioperative dexamethasone on postoperative analgesia and side-effects: systematic review and meta-analysis. *British Journal of Anesthesia, 110*(2), 191-200. doi:10.1093/bja/aes431

White, P. F. (2008). Pain management after ambulatory surgery - Where is the disconnect? *Canadian Journal of Anesthesia, 55*(4), 201-207. doi:10.1007/bf03021503

Wilkerson, R. G., Kim, H. K., Windsor, T. A., & Mareiniss, D. P. (2015). The opioid epidemic in the United States. *Emergency Medicine Clinics of North America, 34*(2), e1-e23. doi:10.1016/j.emc.2015.11.002

Yamanaga, S., Posselt, A. M., Freise, C. E., Kobayashi, T., Tavakol, M., & Kang, S.-M. (2017). A single perioperative injection of dexamethasone decreases nausea, vomiting, and pain after laparoscopic donor nephrectomy. *Journal of Transplantation, 2017*, 1-8. doi:10.1016/j.acpain.2008.01.023

APPENDICES

Appendix A: Collection Tool 1

Patient Study Number	Patient Identification Number
1	
2	
3	
4	
5	
…	
200	

Appendix B: Data Collection Tool 2

Patient #	Age (years)	ASA (I-III)	Height (cm)	Weight (kg)	BMI (kg/m^2)	Dexamethasone (Y=1, N=0)	Gender (F=1, M=0)	Dose (mg)	Pain Score Admission (0-10)	Pain Score Discharge (0-10)	LOS – (min)	Total Intraop Opioids (morphine equiv.)	Total PACU Opioids (morphine equiv.)
1													
2													
3													
4													
5													
…													
200													

Appendix C: IRB Approval Certification

New study by expedited review: Approved

CAMC INSTITUTE
RESEARCH AND GRANTS
ADMINISTRATION
Institutional Review Board • Institutional Scientific Review Board
Charleston Area Medical Center | Robert C. Byrd Health Sciences Center

July 20, 2017

School of Nurse Anesthesia
3110 MacCorkle Avenue, SE
Charleston, WV 25304

RE: Initial Review Submission Packet 07/18/2017 10:11:02 AM EDT regarding study number 17-361 The Association Between Intraoperative Single Dose Dexamethasone and Postoperative Pain in Patients Undergoing Laparoscopic Cholecystectomy

Dear Priscilla Walkup:

Your request for expedited approval of the new study listed above has been reviewed. This type of study qualifies for expedited review under FDA and DHHS (OHRP) regulations.

This is to confirm that your application is approved. The following items are approved:

Submission Components			
Form Name	Version	Outcome	
Study Document			
Title	Version #	Version Date	Outcome
COI	Version 1.0	07/17/2017	Approved
IRB Submission - Sara Hatfield FINAL	Version 1.0	07/13/2017	Approved

The accrual goal is 200. You must submit a request to the IRB to increase enrollment beyond the approved accrual goal.

You are granted permission to conduct your study as described effective immediately. The study is subject to continuing review on or before 07/19/2018, unless closed before that date.

Please note that any changes to the study as approved must be promptly reported and approved prior to implementation. Some changes may be approved by expedited review; others require full board review.

Also, serious and/or unanticipated adverse events must also be reported as required by law and in accordance with CAMC/WVU Charleston Division IRB policies. Contact CAMC / WVU Charleston Division

3110 MacCorkle Ave. SE, Room 3283 Charleston, WV 25304 (304) 388-9970 Fax (304) 388-9976