

Ketamine and its Applications in the Clinical Setting

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Table of Contents

Abstract.....	3
Problem.....	4
Review of Literature.....	5
Project Description.....	10
Evaluation Plan.....	11
Results and Conclusions.....	11
References.....	14
Appendix A (Pre-Test/Post-Test).....	15
Appendix B (Informed Consent).....	17
Appendix C (PowerPoint).....	19

Abstract

The purpose of this research was to assess the level of understanding within the Adventist University student nurse anesthesia (SRNA) population regarding Ketamine. A lecture, as well as a pre-test and post-test to determine whether understanding of Ketamine increased, decreased, or remained the same. It is important that the anesthetist not only be familiar with all types of treatment modalities available, but proficient in them as well. As a result, this study looked to address any hesitancy for using Ketamine within the student nurse anesthesia population.

An extensive literature review was conducted on Ketamine. This review generated results that seemed to demonstrate a large gap between understanding and administration of Ketamine, indicating a need for increasing the knowledge base of SRNAs.

Upon review of the material, a PowerPoint presentation was administered to the student nurse anesthesia graduating cohorts of 2016 and 2017, informed consent was obtained, and a pre-test and post-test were administered. A paired t-test was conducted and the results of this indicated a significantly increased understanding regarding Ketamine and how to apply it in the clinical setting.

The purpose of this research and presentation was to clear any confusion regarding this medication, and teach a population of providers who will soon be delivering anesthetics as a career, that they have an additional option available to them to optimize patient outcomes. The pre-test and post-test results indicated a significant increase in understanding and the PowerPoint presentation may serve as a teaching tool for other SRNAs and CRNAs in the future.

Problem

Ketamine is a dissociative anesthetic whose use dates back to the 1970's when it was developed and used as a battlefield agent on patients in the Vietnam War. Ketamine has several advantageous physical, pharmacokinetic, and pharmacodynamics properties and can be used for anesthesia, analgesia, amnesia, and sedation (Haas & Harper, 1992). It can induce and maintain general anesthesia, maintain functional residual capacity (FRC), induce bronchodilation, and avoid cardiovascular depression (Haas & Harper, 1992). However, several side effects such as emergence hallucinations and cardiovascular excitement have been demonstrated that have prompted many newer anesthesia professionals to forgo its use in the operating room. This decreased use of ketamine has created a generation of anesthesia providers who are knowledgeable about the drug profile, but not necessarily comfortable with its use.

It is often said that an ideal anesthetic would have a rapid onset, be easy to titrate, have a predictable duration of action, and have a short elimination half-life while also producing analgesia, anesthesia, amnesia, and anxiolysis, all with minimal cardiovascular and respiratory depression (Haas & Harper, 1992). Ketamine displays several properties of this ideal anesthetic, and it does this by working on more than one receptor. Ketamine main site of action is the N-methyl-D-aspartate (NMDA) receptor, and inhibition of this receptor produces the catalepsy often found after ketamine administration (Haas & Harper, 1992). Ketamine also binds primarily to mu receptors in the brain and spinal cord to produce analgesia, as well as interaction muscarinic cholinergic receptors to potentiate the effects of neuromuscular blocking drugs (Haas & Harper, 1992).

As part of a growing profession, the nurse anesthesia provider attends to more complex cases than in the past. Since the anesthesia provider may be faced with more complex issues within these cases, it is important to have a thorough understanding of these issues as well as different medications such as ketamine available to treat them. The lack of knowledge and subsequent lack of utilization of this drug within the student nurse anesthesia educational process is a problem this study seeks to investigate.

Review of Literature

Pain is an uncomfortable and undesired sensation a person experiences during or after a surgical procedure. Pain control presents a difficult challenge for anesthesia providers in multiple surgical settings, and it continues to be one of the main components patients use to judge the success of their surgical experience upon. Throughout the years, many different drugs and treatment modalities have been developed to prevent the feeling of pain caused by such surgical procedures. Opioid-based analgesia control has been beneficial, but has also been shown to cause undesirable side effects in patients such as hypotension, nausea, bradycardia, apnea, constipation, urinary retention, itching and in some cases even death. The undesired side effects caused by opioids have led to the exploration and implementation of multimodal analgesia by anesthesia providers. Several studies have been completed with the implementation of ketamine's use in a multimodal approach with positive results.

Untreated postoperative pain can evolve into chronic pain, which can have major effects on an individual's quality of life. An appropriate approach to treat perioperative and postoperative pain is the implementation of a multimodal analgesia regimen that combines opioids with non-opioid analgesics. Multiple mechanisms are involved in causing postoperative pain, and a multimodal analgesia regimen using opioids and non-opioids such as ketamine and

gabapentinoids can provide pain relief, reduced opioid consumption, less adverse effects and the prevention of hyperalgesia. The literature is decisive in that the use of ketamine perioperatively leads to more effective and longer lasting analgesic effect (Weinbroum, 2012). At low doses, ketamine is capable of reducing short-term postoperative pain, opioid consumption, and an infusion during general anesthesia is effective in providing long-term analgesia (Weinbroum, 2012).

In an article by Ahern et al. (2014) a study was conducted to describe the safe clinical use of ketamine in an emergency department for treatment of acute pain. This article explains how now days more than ever, emergency physicians are exploring and implementing alternative medications such as ketamine along with nonsteroidal anti-inflammatory drugs (NSAIDS) and opioids to achieve multimodal analgesia in this clinical setting. The objective of the article was to describe the clinical and safe use of Ketamine at low doses for pain management in an emergency department. The study was conducted at an urban Emergency Department between 2012 and 2013 where five hundred thirty patients received low dose Ketamine for pain. Two physicians from the Emergency Department reviewed records during these two years to determine indication, dose, route, disposition, occurrence of adverse events, and demographics using a standardized data abstraction form. Adverse effects for this study were categorized as minor and major events. Minor events consisted of emesis, psychomimetic or dysphoric reactions, and transient hypoxia. Major events included apnea, laryngospasm, hypertensive emergency, and cardiac arrest (Ahern et al, 2014). The results of the study are very encouraging regarding the use of Ketamine and the desired effects it may cause. The results of the study indicate that 55% of the populations studied were women. The preferred route of administration was intravenously (93%), and 92% of the patients received a dose of 10 to 15mg of Ketamine.

Comorbid diseases found during the study included hypertension, psychiatric disorders, obstructive airway disease and coronary artery disease. An interesting finding is that there were no changes in heart rate or systolic blood pressure in any of the subjects in the study. Out of five hundred and thirty patients in the study, only thirty patients (6%) of the total sample met criteria for adverse events. Eighteen patients (3.5%) experienced psychomimetic or dysphoric reactions, none of which were lasting or led to long-term changes in patients. Seven patients (1.5%) experienced hypoxia within one hour of Ketamine administration, but four of these patients had also received concomitant opioids. All but one of the patients responded quickly to nasal cannula oxygen. Only five patients (1%) developed emesis. Most of these patients with adverse events improved without intervention or after reassurance by nurse or physician. According to the study, there were no cases of serious adverse events.

The authors concluded that the results of this study confirm the results of prior smaller studies of low dose Ketamine showing that psychomimetic reactions are mostly mild in nature and rarely alter a patient's clinical course. It is also noted that the rate of mild dysphoric events is much lower than described in previous studies. The study concludes that the side effects of Ketamine found during this study such as emesis and hypoxia are equally or less common than reported with opioids. Minor psychomimetic side effects were observed during the study but easily managed by emergency department personnel. The use of low dose ketamine in an emergency department for the treatment of acute pain is feasible, safe, and effective when combined with other drugs such as NSAIDs and opioids. (Ahern et al., 2014).

In a study conducted by Elvir-Lazo and White (2010), the authors examined the use of opioids versus nonopioids analgesic drugs for the prevention of pain after ambulatory surgery. In this article, the authors explain how opioid-based analgesics used to be considered the standard

approach to treating acute postoperative pain are now being replaced by a multimodal approach to prevent and treat pain after ambulatory surgeries. Opioids cause side effects that in many occasions prevent the patient from being rapidly discharged after a procedure at an ambulatory center or are experiencing unacceptable levels of pain when they return home after surgery despite receiving standard analgesic drugs during and/or after the procedure.

Over the years, the volume and complexity of elective surgeries being performed at ambulatory centers have increased dramatically. The use of opioids based intravenous drugs, patient controlled analgesia and central neuraxial analgesia techniques are not practical for perioperative and post op pain management for patients at ambulatory settings. Patients in the ambulatory setting need an aggressive multimodal approach that provides quick and effective pain relief with minimal side effects, and results in little postoperative pain that can be safely managed either by the patient or family members at home.

Current evidence suggests that improvements in patient outcomes related to pain control can be best achieved using a combination of preventive analgesic techniques, involving both centrally and peripherally acting analgesic drugs (Ahern et al., 2014). Many multimodal analgesia regimens continue to be tested to improve outcomes after surgery. According to Elvir-Lazo and White, outpatient surgery analgesia can be sustained through the use of dexamethasone, local anesthetic surgical site infiltration, and the continuous use of NSAIDs or more selective COX-2 inhibitors for 3-5 days after ambulatory surgeries. Non-opioids analgesics are being used at an increasingly rate before, during, and after surgery to facilitate the recovery process after ambulatory surgery because of their anesthetic and analgesic sparing effects, also their ability to reduce post-operative pain, and reduction of opioid related side effects such as gastrointestinal and bladder dysfunction thus reducing the duration of hospital stay.

Elvir-Lazo and White concluded that using a combination of drugs available including Ketamine, provides multiple benefits for the ambulatory patient including pain relief, less side effects, decreased duration of stay after a procedure, and high quality recovery for the patient undergoing day case surgery. It is also worth noting that the authors believe that with the current amount of analgesic medications and wide spectrum of pharmacological and non-pharmacological techniques that a “pain free” recovery after ambulatory surgery procedures could be possible in the near future (Elvir-Lazo & White., 2010).

Propofol and fentanyl are often used for anesthesia in outpatient procedures such as in diagnostic laparoscopies. However, propofol can cause various cardiovascular effects such as decreased cardiac output, cardiac index and arterial pressure. In a randomized trial, 60 healthy women undergoing diagnostic laparoscopies were given ketamine shortly after receiving fentanyl and versed and propofol was subsequently used for maintenance of anesthesia. According to the authors, the use of low dose ketamine during these diagnostic procedures caused less pain during propofol infusion, lowered the dose of propofol used during the procedure and lowered the incidence of hemodynamic changes (Atashkhoyi et al., 2012).

Gritsenko et al. (2014), sought out to review the current evidence for multimodal analgesic options used in common surgical procedures today, and in particular during the perioperative period. Numerous amounts of multimodal analgesia techniques have been utilized in the perioperative period in order to control pain in short and long term for better patient outcomes. Different surgical specialties have adopted different analgesic choices with the hope of phasing in multimodal analgesia regimens into daily patient care. The authors focused their review on recent evidence of perioperative analgesic options on selected surgical procedures and specifically in general surgery, orthopedic surgery, OB/GYN, and cardiothoracic surgery. The

researchers found that for all surgeries the use of a multimodal approach using different combinations of agents and analgesic techniques are effective at reducing opioids consumption and reducing postoperative pain. Ketamine proved to be effective intraoperatively and postoperatively as well by attenuating opioid and volatile anesthetic induced hyperalgesia. (Gritsenko et al., 2014).

Project Description

An extensive literature review was performed in regards to Ketamine. The literature review included recent research articles from within the past 10 years. Within these articles, the focus was on the background information, indications, and side effects of Ketamine and how it compares to more frequently chosen anesthesia drugs with a cleaner side effect profile. The literature review also determined how ketamine could be utilized in conjunction with common anesthetic agents for a more extensive coverage regarding multimodal analgesia.

A PowerPoint presentation and pre-test and post-test were administered and completed by the sample population, consisting of a convenience sample of 43 SRNAs from Adventist University of Health Sciences. This presentation introduced Ketamine and explained how this drug can be more utilized within the clinical setting. The subjects were administered a pre-test and post-test. Before the presentation, a pretest was administered to determine the subjects' knowledge base on the topic prior to PowerPoint presentation. Prior to administering the pre-test, a voluntary consent was administered notifying the subject that they are not obligated to take this test. Anonymity was obtained by using a number system for both the pre-test and post-test. After the presentation, a post-test was administered to determine if the subjects' understanding on the topic increased, decreased, or remained the same. The data obtained was statistically analyzed

and included within the scholarly paper and poster presentation. A poster presentation was completed and will be displayed in the annual Capstone Project Poster Presentation day.

Evaluation Plan

Submission to the Adventist University (ADU) Scientific Review Committee (SRC) and Institutional Review Board (IRB) were submitted and approved. The NAP Class of 2016 and 2017 was evaluated before and after the PowerPoint presentation. The evaluations included the same questions in the pretest and the posttest. The pretest and posttest were statistically analyzed to determine the difference between the scores. The evaluation determined if the PowerPoint presentation was effective in improving the subjects' understanding in regards to ketamine. The PowerPoint was presented in the fall of 2015.

Results and Conclusions

Results for the pre-test indicated that the students' knowledge of ketamine and its use in the clinical setting was appropriate, but there was room for improvement. The results for the pre-test showed the average score to be at 48.5% with a standard deviation of 23.48 and a standard error mean of 3.71. The standard deviation for the pre-test shows that there is a wide variety of scores among the students taking the pre-test and the standard error mean in the high side justifies the high scores of the standard deviation.

After the power point presentation concluded, the post-test was handed out to the anesthesia students present and the test was collected once the students completed the assessment. The results of the post-test showed an increase in average scores from 48.5% to 88.5% with a standard deviation of 8.92 and a standard error mean of 1.41. The standard deviation in the post-test indicates more similar scores among the students taking the post-test and the standard error mean concurs with the standard deviation by providing a smaller score of

1.41. The obtained t-value of this project is -11.647 with an associated p-value that is <.05 level of confidence, indicated the results were statistically significant upon analysis of the numbers provided by Dr. Lukman.

After carefully reviewing the results from the pre and post-test provided to the anesthesia students regarding the use of Ketamine in the clinical settings, taking into account the average percent scores increased from the pre-test to the post-test, it can be concluded that an increased understanding of the use of Ketamine had been achieved.

Capstone project data analysis:

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Pre-Test %	48.5000	40	23.48486	3.71328
	Post-Test %	88.5000	40	8.92993	1.41195

	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 %	-40.00000	21.72084	3.43437	-46.94666	-33.05334	-11.647	39	.000

The anticipated outcomes of the project were achieved. Results from the collection of data show an increased understanding within the population studied after the power point presentation. The evaluation also showed that the PowerPoint presentation was effective in improving the subjects’ understanding in regards to ketamine. The increases in the average scores from 48.5% to 88.5% also show that the anticipated outcome of improving understanding in anesthesia students regarding Ketamine and its use in the clinical setting was achieved.

This PowerPoint presentation can be useful in the future as a tool for providers interested in applying Ketamine to their clinical practice, by increasing the providers understanding of Ketamine and its applications.

References

- Ahern, T. L., Herring, A. A., Anderson, E. S., Madia, V. A., Fahimi, J., & Frazee, B. W. (2015). The first 500: Initial experience with widespread use of low-dose ketamine for acute pain management in the ED. *The American Journal of Emergency Medicine, 33*(2), 197-201. doi:10.1016/j.ajem.2014.11.010
- Atashkhoyi, S., Negargar, S., & Hatami-Marandi, P. (2013). Effects of the addition of low-dose ketamine to propofol-fentanyl anaesthesia during diagnostic gynaecological laparoscopy. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 170*(1), 247-250. doi:10.1016/j.ejogrb.2013.06.026
- Elvir-Lazo, O. L., & White, P. F. (2010). Postoperative pain management after ambulatory surgery: Role of multimodal analgesia. *Anesthesiology Clinics, 28*(2), 217-224. doi:10.1016/j.anclin.2010.02.011
- Gritsenko, K., Khelemsky, Y., Kaye, A. D., Vadivelu, N., & Urman, R. D. (2014). Multimodal therapy in perioperative analgesia. *Best Practice & Research Clinical Anaesthesiology, 28*(1), 59-79. doi:10.1016/j.bpa.2014.03.001
- Haas, D., & Harper, D. (1992). Ketamine: A review of its pharmacologic properties and use in ambulatory anesthesia. *Anesthesia Progress, 39*(3), 61-68.
- Weinbroum, A. A. (2012). Non-opioid IV adjuvants in the perioperative period: Pharmacological and clinical aspects of ketamine and gabapentinoids. *Pharmacological Research, 65*(4), 411-429. doi:10.1016/j.phrs.2012.01.002

Appendix A

Pre and Post Test

- 1) All of the following work on GABA receptors except?
 - a. Inhaled anesthetics
 - b. Etomidate
 - c. Ketamine**
 - d. Both A and C

- 2) In addition to the NMDA receptor, what other receptors does Ketamine interact with to produce its effect?
 - a. Nicotinic receptors
 - b. Muscarinic receptors
 - c. Opioid receptors
 - d. Non-NMDA glutamate receptors
 - e. All of the above**

- 3) Which of the following patients would you avoid the administration of Ketamine?
 - a. A 15 year-old avid Call Of Duty gamer who presents with severe asthmatic bronchoconstriction
 - b. A 49 year-old Fibromyalgia patient who complains of severe post-operative pain after previous surgeries unrelieved by opioids
 - c. An 81 year-old patient scheduled for a pericardial window who presents with cardiac tamponade
 - d. A 35 year-old s/p motor vehicle accident patient with a suspected traumatic brain injury**

- 4) What is the drug of choice in a hypotensive and tachycardic patient?
 - a. Thiopental
 - b. Ketamine**
 - c. Propofol
 - d. None of the above

- 5) Select two of the following medications that are compatible with somatosensory evoked potential monitoring (SSEP)
 - a. Sevoflurane
 - b. Ketamine**
 - c. Nitrous Oxide
 - d. Propofol**

- 6) What is mostly responsible for the metabolism of Ketamine?
- Kidneys
 - Liver**
 - Bile
 - Lungs
- 7) After a smooth intraoperative anesthetic, your patient awakens with agitation and hallucinations after administration of Ketamine. What is the following step you should take?
- Talk the patient through this as you know the effects of Ketamine are short-lived
 - This is a severe reaction to Ketamine and the patient should be tagged as allergic and not administered Ketamine again
 - This can be a side effect of Ketamine especially if the anesthetist did not pre-treat with a benzodiazepine, administer Versed**
 - Induce the patient with Propofol and keep them on an LMA until you believe the side effect has worn off
- 8) What is the correct IV dose of Ketamine for induction of anesthesia?
- 1-2 mcg/kg
 - 1-2 mg/kg**
 - 1-2 mcg/kg/min
 - 1-2 mcg/kg/hr
- 9) Which of the following is not a measurable outcome of Ketamine administration?
- Increased heart rate
 - Increase blood pressure
 - Increased bronchoconstriction**
 - Increased oropharyngeal secretions
- 10) Ketamine is contraindicated in a patient with traumatic head injury
- True**
 - False

Appendix B

ADU NAP CAPSTONE PROJECT – INFORMED CONSENT

Our names are **John Todorovic & Frank Cardenas**, and we are MSNA students in the Nurse Anesthesia Program (NAP) at Adventist University of Health Sciences (ADU). We are doing a Capstone Project called **Quantitative Study Examining Student Nurse Anesthesia Knowledge Regarding Ketamine And Its Application In The Clinical Setting**. This project is being supervised by **Steve Fowler, DNP, CRNA**. 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 increase awareness and medical understand of multimodal analgesia with Ketamine

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 specific pharmacology of ketamine, clinical applications, and misnomers regarding the use of this anesthetic. Your participation by attendance at the presentation and completion of the survey is anticipated to take approximately **30 minutes**.

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.

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 Ketamine and its use in multimodal analgesia

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 by using a randomized numbering system that includes the same numerical identification for the pre-test, as well as the post-test. By using a numerical identification system instead of participant names, 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 **40 minutes** of your time, but will require no monetary cost on your part. You will not be paid to participate.

VOLUNTARY CONSENT

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, please feel free to contact **John**

Todorovic or Frank Cardenas by email using Bojan.Todorovic@my.adu.edu or Fr.J.Cardenas@my.adu.edu. If you have concerns about the project process or the investigators, please contact the Nurse Anesthesia Program at (407) 303-9331.

Participant Signature

Date

Participant Name (PRINTED LEGIBLY)

Appendix C

ADU NAP CAPSTONE PROJECT – POWERPOINT PRESENTATION

1/8/2016

Quantitative Study Examining Student Nurse Anesthesia Knowledge Regarding Ketamine And Its Application In The Clinical Setting

John McCann, RN, DPA
 Heidi Cardenas, RN, DPA
 Christy Annley, DPA, DNP
 Walter George Salazar, DO

Why Ketamine?

- Increase student nurse anesthesia knowledge regarding ketamine
- Review the beneficial uses of ketamine and how it differs from other anesthetics
- Understand the background of ketamine and why it is not used more frequently
- Understand the properties of ketamine including pharmacokinetics, pharmacodynamics, and respiratory
- Encourage application of ketamine in the clinical setting when appropriate



"It is often said that an ideal anesthetic would have a rapid onset, be easy to titrate, have a predictable duration of action, and have a short elimination half-life while also producing analgesia, anesthesia, amnesia, and anxiolysis, all with minimal cardiovascular and respiratory depression"

History and Background of Ketamine

- 1951 First synthesized by American Scientist Calvin Stevens at Parke-Davis Laboratories
- Initially named Orbits and developed as a derivative of PCP
- Ketamine began as a recreational anesthetic for PCP which caused long lasting and severe hallucinogenic effects
- Not suitable for humans because it presented people with symptoms such as delirium, delirium, and even psychosis
- 1957 Identified in Belgium and used as intravenous anesthetic
- 1958 Testing with humans began and it was found that ketamine had less respiratory and cardiovascular effects than PCP
- 1959 It was determined that ketamine could be safe for human use. The first human use of ketamine was by Prof. James Stewart in 1959. The chemical ketamine is a potent psychotropic drug for which it is termed as a "Dissociative Anesthetic"

History and Background of Ketamine

- 1950s Identified for human and animal use in the United States by Parke-Davis Laboratories
- 1950s Became available to general public in the form of ketamine hydrochloride under the name of Ketalar
- 1950s Official approval by human consumption by the United States Food and Drug Administration. Also approved in Canada during the Vietnam War as a field anesthetic
- 1960s began to interest scientific world for the use of ketamine as a recreational and therapeutic drug
- Argentina used it as a recreational therapy drug
- 1960s began using ketamine for animal anesthesia and anesthesia applications
- Pharmacology and Anesthesia researchers published findings regarding effects of ketamine in their papers and in clinical studies of ketamine use
- 1960s DEA filed a federal notice of its intent to place ketamine on the list as a Schedule II drug
- Early 80s Ketamine became increasingly available for illegal use in Australia, private clinics, private hospitals, and other medical settings

History and Background of Ketamine

- 1950s ingested effects were studied in ketamine in other effects. Examples of this include ketamine become part of the club scene
- 1972 Ketamine added to DEA's emerging drug list
- 1973 US Government classified ketamine as schedule II controlled substance
- 1980s Ketamine abuse was in Hong Kong where government had to name drug as a schedule II drug under the Dangerous Drug Ordinance
- 1980s Taiwan classified ketamine as a schedule II drug after a case in Taipei
- 1982 Classified as schedule I narcotic in Canada
- 1980s Ketamine classified as class C drug in United Kingdom
- Note: it is the history of ketamine abuse to report that in usage, availability, and danger that has prompted various countries to ban the drug for purposes other than professional, medical or medical reasons

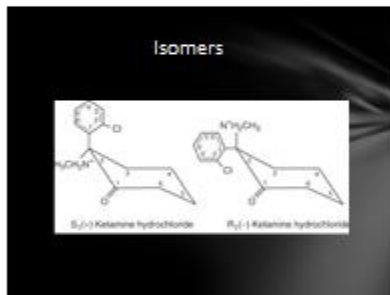
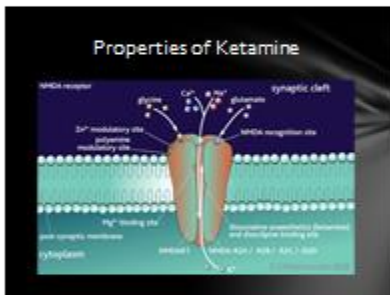
1/8/2016

Problem Statement

- As part of a growing profession, the anaesthetist provides a service to more complex cases than in the past.
- Because of the variety of issues the anaesthetist provides may encounter during these cases, it is increasingly important to have a thorough understanding of all medications available.
- The lack of knowledge in the student nurse anaesthetist community and subsequent lack of utilization of medications like ketamine is a problem this study seeks to investigate.

Properties of Ketamine

- Ketamine is an (1S,2S)-2-oxo-1,2,3,4-tetrahydroquinazolin-4(1H)-one, separating it from many anaesthetic induction agents as it is not an GABA receptor.
- Works directly in the brain to suppress afferent signals of pain generated from the thalamus nuclei to the thalamus and cortex.
- Ketamine has been shown to enhance regional blood analysis and prevent hypoxemia.
- Multiple sites of action including:
 - Glutamate Receptors
 - Glutamate Receptors
 - Calcium Channels
 - Non-NMDA Receptors



Properties of Ketamine

- Rapidly metabolized through hepatic metabolism.
- Derived as ketamine through amphetamine and currently utilized primarily as analgesic.
- Pharmacokinetics of ketamine:
 - Barbiturate (Class of ketamine is ketamine)
 - Ketamine also gets converted into the brain convert to metabolism in peripheral compartments.
 - Multiple actions.



Properties of Ketamine

- Ketamine is a dissociative anaesthetic.
 - "Dissociative" means:
 - In dissociative cases, the patient is conscious, the eyes remain open, pupils are dilated as light, normal reflexes, tachycardia, and no bradycardia, and sensory input continues to increase.
 - Clinical effects, which may include: amnesia, analgesia, sedation, and dissociation.
- After an induction dose, reorientation to person, place, and time can happen in as little as 15-30 minutes.
- Usually used in combination with Propofol for ESSED sedation, as well as conscious sedation.
- OPR is increased with ketamine leading to a potential increase in OPR and this should be avoided in Trauma/Intra-aortic.

1/8/2016

Properties of Ketamine

- Cardiovascular Effects**
 - Ketamine is a direct sympathomimetic, in that it acts as a thalidomide administration in **hypertension, tachycardia, and increased CO**
 - As a result, ketamine serves as an anesthetic for patients in situations where there are **hypertensive and arrhythmias**
- Respiratory Effects**
 - Ketamine has very positive effects on the lungs including:
 - Increased pulmonary compliance
 - Decreased pulmonary resistance
 - The **airway reflexes** (larynx, epiglottis, and the signs of choice in acute airway obstruction) **suppress**
 - It acts through bronchial smooth muscle relaxation

Pretreat?

- One common anesthetic practice is the **pretreatment** of patients prior to ketamine administration
- Why Opioid?**
 - Increased analgesic, bronchodilator, and cardiovascular effects
 - Prevents muscle pain and prevents airway reflexes from being
- Why Benzodiazepine?**
 - Incidence of emergence reactions is **less**
 - Administration of a benzodiazepine has been shown to reduce this to **nearly 0%**



Emergence Reactions

- Disorienting effects**
- Associated with **psychic disturbances** including visual, auditory, perceptual, and confusion
- Incidence is influenced by age, dose, gender, and psychological predisposition

Emergence Reactions

- Resolves within a few hours with full return of orientation, person, place, and time
- Important to note this is **not** associated with repeated administration, high-dose anesthesia doses, and improper pretreatment
- Be sure to **interpret this information**

Applications of Ketamine

- Induction in High-Risk populations**
 - Stroke
 - Hypertension
 - Trauma
 - Benzodiazepine
- CR induction**
 - Stroke hypotension
 - Local Hemorrhage
 - Pain relief

Applications of Ketamine

- Local Anesthetic Analgesia**
 - Superior regional anesthesia
 - Incidence is similar to general anesthesia
 - Efficacy
- Outpatient Surgery/Out of OR**
 - For both diagnosis and therapeutic procedures
 - MCOs
 - Used for minor procedures
 - Outpatient

1/8/2016

To use or not to use, that is the question

- Volume: Heart Disease
- Uncontrolled Hypertension
- Neurosurgery
- African-American population
- Patient taking TGA's
- Diabetic injury/Diabetes

Case Scenario

- 21 year old patient in the pre-operative area awaiting exploratory laparotomy
- Presents with history of multiple abdominal surgeries, severe back and neck pain related to fibromyalgia
- On multiple medications including opioids and muscle relaxants
- States providers have tried multiple anesthetic regimens and he wakes up with increased pain after each surgery

What did we do?

Case Scenario

- Versed 5mg and 5mg Glycopyrrolate administered pre-op
- Ketamine/Propofol Induction using 0.5mg/kg Ketamine and 5mg Propofol followed by Propofol infusion and Ketamine supplementation in 0.5mg increments for TIVA
- BIS scored and Ketamine administered to keep bis 4.0-6.0
- Patient woke with "good anesthetic experience to date"

The first 500: Initial experience with widespread use of low dose Ketamine for acute pain management in ED

- Study to describe the initial use and effectiveness of low dose Ketamine (0.5mg/kg) for pain management in the Emergency Department
- Study was conducted at a Level II ED between 2008 and 2011 and 500 patients received low dose Ketamine over five year period
- A standardized data collection form was used to collect data. The physicians recorded patient's records to determine demographics, indication, dose, route, disposition, and occurrence of adverse events
- Adverse events were categorized as serious and minor. Minor events consisted of: nausea, palpitations, or dysphoria reactions, and transient hypoxia. Serious events consisted of: apnea, laryngospasm, hyperreflexia, emesis, and cardiac arrest. Additional parameters included HR and BP

- Results: Median age was 43 years old, 50% of patients were women
- Route of administration: 77% of patients, IM/IV route
- Over 90% of patients received a dose of 0.5mg/kg
- Demographics: 47% were male, psychiatric disorders were 10%, distribution of ethnicities: 50% were white, 30% black
- 22 patients (4%) had serious adverse events
- 48 patients (10%) experienced subjective or objective reactions. These reactions were mild and self-resolving. 10% of patients received 0.5mg/kg
- 1 patients (0.2%) developed transient hypoxia
- 2 patients (0.4%) had emesis
- There were no cases of serious adverse events reported
- Recommendations: Use of low dose Ketamine is an option in different patient populations. Monitor closely and be alert for potential for many different types of pain

1/8/2016

Conclusion

- Ketamine is an **NDMA Receptor antagonist**
- It also works on **opioid receptors**, which explains **opioid tolerance** and **opioid addiction**
- Ketamine increases **CBF** which can **decrease ICP** and should generally be **avoided in trauma** to brain injury patients
- Ketamine is an **excellent choice** for patients presenting with symptoms of shock including **hypotension, tachycardia, and tachypnea**
- During neurosurgeries that require **CBF** monitoring, **ketamine and Etomidate** are both **acceptable choices**

Conclusion

- Ketamine is eliminated by the kidneys, but it is **first metabolized by the liver**
- If your patient received prior general anesthesia treatment with **opioid** and **opioid antagonists**, **ketamine** should be used **cautiously** as an option to **break through** tolerance
- The **anesthetic induction dose of ketamine is variable**
- Ketamine produces an increase in **heart rate, blood pressure, bronchodilation, and analgesic** sensations

"It is often said that an ideal anesthetic would have a rapid onset, be easy to titrate, have a predictable duration of action, and have a short elimination half-life while also producing analgesia, anesthesia, amnesia, and anxiolysis, all with minimal cardiovascular and respiratory depression"

References

- Allen, T. L., Clarke, J. A., Anderson, C. E., Minto, V. A., Schell, J. J., & Dutton, G. V. (2010). The first 1000 responses and clinical use of ketamine: results of a survey of emergency medicine physicians. *Journal of Emergency Medicine*, 40(2), 107-111. <https://doi.org/10.1016/j.jemermed.2010.04.014>
- Anesthetics & Narcotics. (2016). *Textbook of Anesthesiology*. Elsevier. <https://www.sciencedirect.com/book/9780323328124>
- Clarke, T. L., & Allen, T. L. (2010). Ketamine: the forgotten analgesic. *Journal of Emergency Medicine*, 40(2), 107-111. <https://doi.org/10.1016/j.jemermed.2010.04.014>
- Chavakis, N., Nitsch, R., Nitsch, A. D., Nitsch, M., & Nitsch, R. S. (2010). Ketamine: a review of its pharmacology and clinical use. *Journal of Emergency Medicine*, 40(2), 107-111. <https://doi.org/10.1016/j.jemermed.2010.04.014>

References

- Hsu, C., & Marger, D. (1992). Ketamine: A review of its pharmacologic properties and use in ambulatory anesthesia. *Anesthesia Progress*, 21(2), 41-48.
- Westbrook, J. A. (2013). Ketamine: A review of its pharmacologic properties and use in ambulatory anesthesia. *Anesthesia Progress*, 21(2), 41-48. <https://doi.org/10.1016/j.jemermed.2010.04.014>
- Westbrook, J. A., & Paus, K. (2014). Ketamine: A history of discovery. In R. S. Clarke (Ed.), *Textbook of Anesthesiology* (pp. 1-14). St. Louis, MO: Elsevier Saunders.

QUESTIONS??

