RUTGERS

School of Nursing

Ketamine Gap Analysis and Toolkit Development to Increase its Use by Anesthesia Providers in the Perioperative Setting

Russell Lynn Memorial Student Lecture Series

Kevin Joseph BSN, CCRN & Steven Schwab BSN, CCRN

Rutgers, The State University of New Jersey

DNP Chair: Maureen McCartney Anderson DNP, CRNA/APN

DNP Team Member: Philip Huang DNP, CRNA/APN

Introduction

- Basic Overview

  - Ketamine has been in use since 1966 having been found to have both anesthetic and analgesic properties (Domino, Chodoff, & Corssen, 1965).

  - Despite its known efficacy and utility, ketamine remains rarely used as anesthesia providers are commonly in favor of other agents (Green, 2000).

- Intervention: Develop and introduce a ketamine workshop and toolkit for New Jersey Association of Nurse Anesthetists (NJANA) membership to use based on the data obtained from a pre-intervention gap analysis survey.

- Practice Change and Outcomes Implications

  - With a toolkit on ketamine, anesthesia providers may **increase** its use and **improve** patient outcomes.

Background and Significance

- Problem:
  - Ketamine has developed a stigma that has caused anesthesia providers to be biased against its use, despite research recommending its use (Kurdi, Theerth, & Deva, 2014).
  - Anesthesia providers, patients, and healthcare systems are affected.
- Ketamine Utility:
  - NMDA antagonism results in analgesic properties that allow ketamine to be included in opioid free or sparing techniques (Boysen, Pappas, & Evans, 2018).
  - Greater than 80% of patients undergoing surgery do not have their pain adequately managed leading to increased mortality, delay of recovery, and prolonged opioid use contributing to the opioid epidemic (Koepke et al., 2018).
  - Potentially useful in patients with chronic pain, whose health care costs based on health-care expenditure and lost productivity exceed the same costs associated with cancer, heart disease, and diabetes (Gan, 2017).
  - May serve as the prototype for new class of rapid acting antidepressants and those with treatment resistant depression (Vadivelu et al., 2016)

Implications

- Impact on Healthcare Quality and Safety:
  - Increased provider competency and comfortability
  - Potentially improve post-operative pain scores along with decreased post-operative opioid use (Barreveld et al., 2013)
  - Potentially combat the current opioid epidemic that is rampant in the United States
  - Explore other non-opioid drugs for the use in the clinical setting

Aim and Objectives

- Develop a ketamine workshop and readily accessible toolkit based on the needs of the NJANA membership.
  - Preform a **pre-intervention survey** to the NJANA membership
    - **Assess** gap in ketamine knowledge, barriers to use, comfortability and frequency of use among CRNAs and RRNAs.
    - **Determine** if the CRNAs and RRNAs are willing to implement ketamine into their anesthetic plan if provided with a toolkit for indications and usage.
    - **Assess** how CRNAs and RRNAs would prefer to have ketamine resources provided to them
  - **Provide** CRNAs and RRNAs knowledge on ketamine through a workshop and supplemental toolkit based on pre-intervention survey results at the NJANA fall symposium.
  - **Establish** a sustainable ketamine toolkit on the NJANA website for project sustainability.
  - **Evaluate** the efficacy of the ketamine toolkit, by assessing how many times the toolkit was accessed through NJANA website analytics.

Survey

RUTGERS
School of Nursing

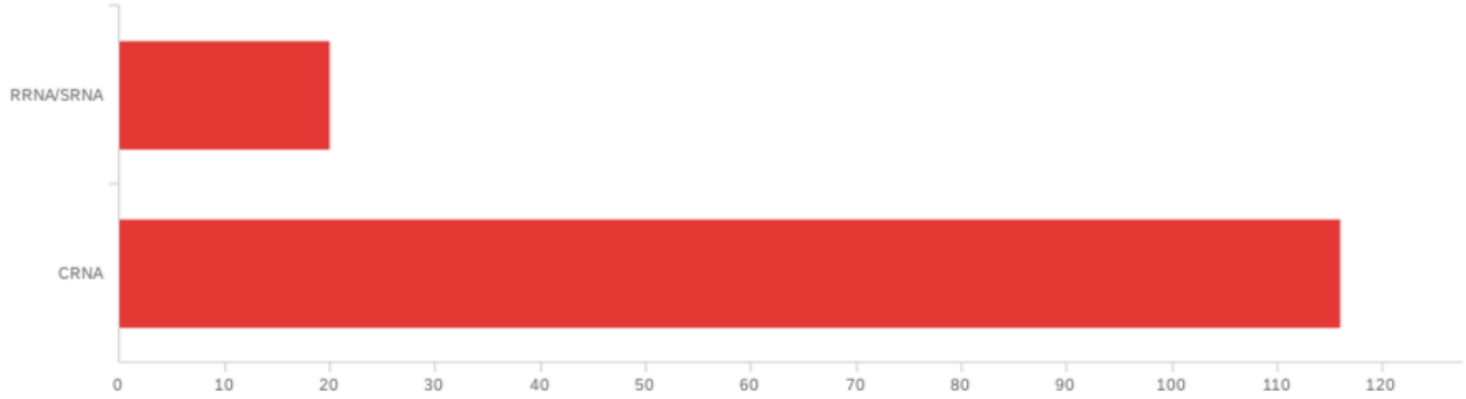
Ketamine Gap Analysis and Toolkit Development to Increase its Use by Anesthesia Providers in the Perioperative Setting

Pre-Intervention Survey	
Are you a RRNA or CRNA?	RRNA/SRNA CRNA
What region of NJ do you primarily practice?	o Northern New Jersey o Central New Jersey o Southern New Jersey
What is your primary practice setting?	o Hospital o Ambulatory Surgery Center o Office Based o Endoscopy Center o Pain Management Clinic o Other: _____
Are you **currently working** in the clinical setting?	Yes No
Indicate the number of years of experience you have in clinical practice.	o Less than 1 year o 1-4 years o 5-10 years o Greater than 10 years o Resident/Student in clinical training o Resident/Student not in clinical training
1=Strongly Disagree 2=Disagree 3=Neutral 4=Agree 5=Strongly Agree	
I feel comfortable with my current knowledge, indications, dosages, benefits and contraindications about the drug ketamine and its uses in the clinical setting?	o 1 2 3 4 5
I frequently implement ketamine in my anesthetic plan.	o 1 2 3 4 5
I have used ketamine in the clinical setting, other than for induction of anesthesia. (Subanesthetic doses)	o 1 2 3 4 5
A ketamine workshop and toolkit will be helpful to increase knowledge, comfortability and frequency of use.	o 1 2 3 4 5

What are the barriers preventing you from utilizing ketamine in your clinical practice? (Select all that apply)	o Institutional Policy o Undesired side effects o Lack of knowledge o Lack of comfortability/confidence o Lack of supply o Use is not recommended by peers o Unfavorable effect in past use o Other:
What form of delivery of the ketamine toolkit would best suit you to retain knowledge and sustain use of ketamine in the clinical setting?	o Printable Badge Buddy o One-page highlight sheet o PowerPoint slides o Infographic o Other:

Data Collected

- Survey
  - Our survey was published in July 2020 and was open to the members of the NJANA to complete until September 21st, 2020.
  - Various email reminders and social media posts by the NJANA were sent to encourage member participation.
  - **136** participants completed the survey.



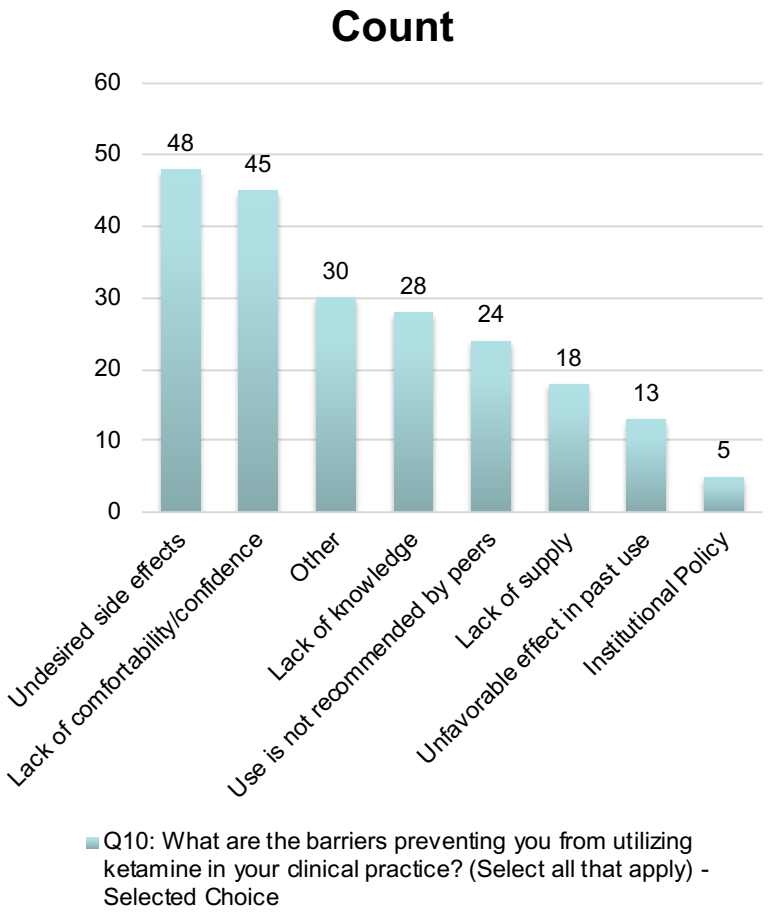
Data Analysis

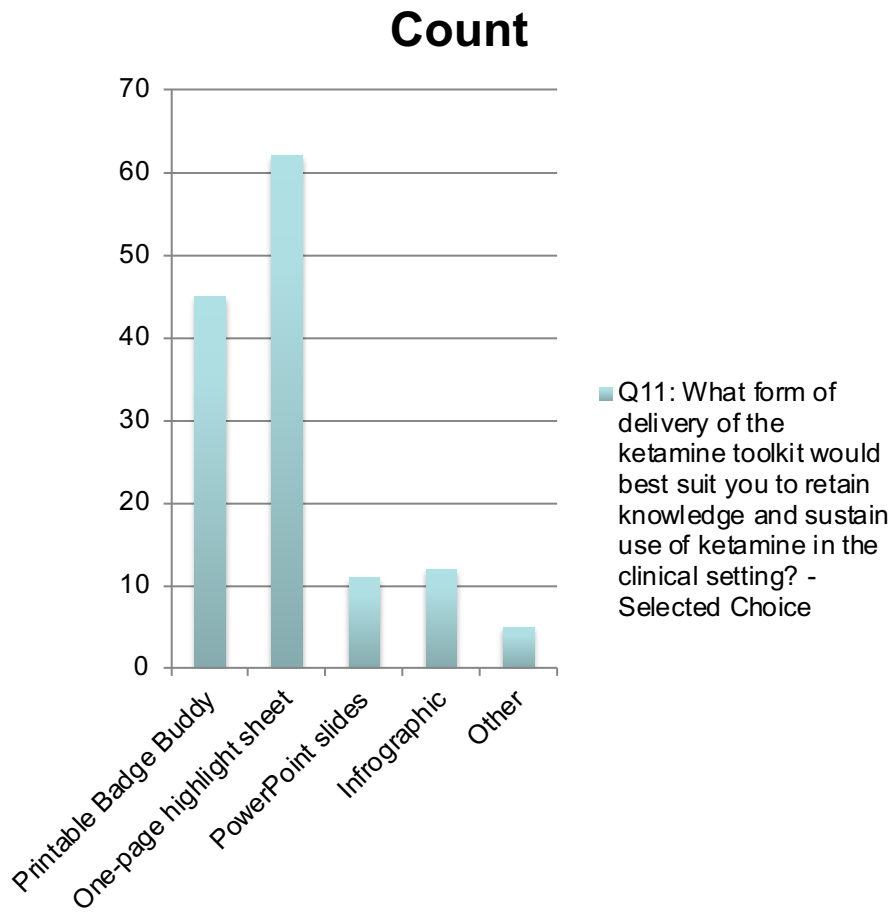
- When analyzing data obtained from the survey, the **Chi-Squared Test** was used to look for relationships.
- It was seen that there was a strong statistically significant relationship between people's comfort and knowledge of ketamine and how frequently they were to use it **$p<0.00001$.**
- There was a relationship between the number of years of practice and the comfort and knowledge of ketamine having a **$p = 0.001$**
- Another relationship was seen between the area of practice in New Jersey and the comfort level of using ketamine **$p =0.003$**
- A strong relationship was seen in the use of sub anesthetic doses and the comfort level of ketamine knowledge **$p<0.00001$**

Data Analysis (cont.)

- When using ketamine in an anesthetic plan it appears there is a very strong relationship with its use in sub anesthetic doses $p<0.00001$.
- There was no relationship seen with the primary area of practice and, frequency of use of ketamine $p = .861$ or comfort level of current ketamine knowledge $p = .638$
- 82.2% of respondents Agreed or Strongly Agreed that a ketamine workshop and tool kit would be helpful.

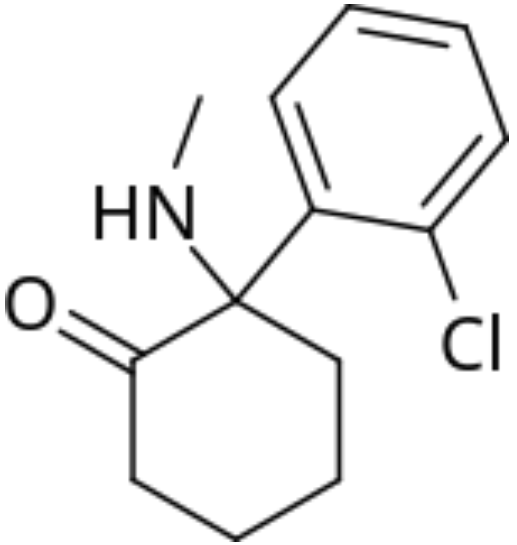
Data Analysis





What is Ketamine?

- **Phencyclidine derivative** found in the 1960s.
- Antagonist action at the **N-methyl-D-aspartate (NMDA)** receptors throughout the CNS.
- Metabolized in the **liver.**
  - active metabolite is **norketamine**.
  - Metabolites are then **excreted renally**.
- Routes of administration:
  - **IV, IM**, oral, transnasal, and rectal



Standard Doses and Facts

- Ketamine does not cause hypotension or severe respiratory depression
  - Useful in trauma and patients with hypovolemia
- **Bronchodilator**
- Onset: 30 seconds
- **Induction**:
  - 1-2mg/kg IVP for adults and pediatrics
  - 4-6mg/kg IM
- **Obstetrics**:
  - 10mg IVP per dose PRN
- **Maintenance (adjunct with TIVA)**:
  - 0.25-0.35mg/kg loading dose, followed by infusion up to 1mg/kg/hr
- **Sedation**:
  - 2.5-15mcg/kg/min IV
  - 1-2mg/kg IV over 2 minutes, repeat 0.5-1 mg/kg q15min
    - 0.25-0.5 mg/kg if you have concomitant sedation
- **Intranasal (acute pain)**:
  - 0.2-1mg/kg, given in divided dose in each nostril
- **Rectal (pediatrics >1)**:
  - 1.5-3mg/kg

Review of Literature

- Reducing Post-Operative Opioid Use
  - Kaur, Saroa, and Aggarwal (2015) demonstrated that 0.2mg/kg bolus and infusion of 0.1mg/kg/h at start of surgery and stopped at the end of the case, results in **reduced** pain scores and opioid requirements.
  - Patients undergoing C-section under general anesthesia given 0.5mg/kg bolus and 0.25 mg/kg/h infusion resulted in **significantly decreased** morphine use 24 hours post-operatively (Haliloglu et al., 2016)
  - Low dose ketamine was found to **significantly reduce** total opioid use and pain scores at 24 and 48 hours post-operatively in painful orthopedic surgery (Riddell et al., 2019).
- Psychomimetic Events
  - Occurrence may be dose dependent and correlated with the lack of a benzodiazepine or other hypnotic agent. Bolus dose of <0.5mg/kg **do not** typically result in psychotic reactions (Gorlin et al., 2016).
  - Incidence of psychomimetic events appear **rare** with sub-anesthetic does given intra-operatively (Cohen et al., 2018).

Review of Literature

- Immune Response
  - Incorporating subanesthetic doses of ketamine (0.15mg/kg/IV bolus) prior to anesthetic induction can **decrease alterations in immune function** in the early post-operative period (Beilin et al., 2007).
    - Patients who received ketamine prior to induction were noted to have **significantly lower IL-6 and TNF-alpha markers** at 4 hours post-operative mark, compared to the control group
  - Patients who received ketamine immediately prior to surgery or intraoperative had a **decreased IL-6 inflammatory response** (Dale et al., 2012).
- Sepsis
  - Ketamine (2mg/kg/IV) was deemed a **safe and valuable induction agent** in the setting of a critically ill septic patient requiring rapid sequence intubation (Jabre et al., 2009).
    - **No significant differences in intubation conditions and morbidity rates** were noted in septic patients who received a single dose of ketamine or etomidate at induction.
    - Septic patients often are hypotensive due to cytokine release, however with ketamine adequate vascular tone is maintained

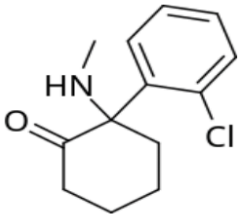
Review of Literature

- Neurological Benefits
  - Ketamine 0.5mg/kg/IV bolus given during anesthesia induction was found to **reduce incidences of post-operative cognitive dysfunction** in patients undergoing cardiac surgery (Hudetz et al., 2009).
    - Data showed that patients who received ketamine at induction had **lower levels of c-reactive protein**, which is associated with systemic inflammation and elderly cognitive deterioration, post-operatively compared to the control group.
  - Ketamine 0.5mg/kg/infusion over 40 minutes can help **decrease explicit suicidal cognition and nonsuicidal-related depressive symptoms** in patients who are resistant to treatment (Price et al., 2014).
    - Treatment resistant depression is defined as patients who are on 3 or more antidepressants with no improvement.

Ketamine Review

- **Standard Induction** Dose: 1-2mg/kg
  - **Sepsis** dose: 2mg/kg/IV
- Give adequate dose of benzodiazepine or hypnotic agent with ketamine to **reduce psychomimetic events**
  - Bolus dose of <0.5mg/kg **does not** typically result in psychotic reactions
- **Reduction in post-op opioid use** dose:
  - 0.2mg/kg bolus followed by infusion at 0.1mg/kg/hr
- Decrease alterations in **immune function**:
  - 0.15mg/kg IV bolus prior to induction **decreased IL-6 and TNF-alpha markers** post operatively
- Neurological benefits:
  - 0.5mg/kg/IV bolus during induction **reduced incidences of post-operative cognitive dysfunction**
  - 0.5mg/kg infusion over 40 minutes **decreased suicidal cognition and nonsuicidal-related depressive symptoms**

KETAMINE TOOLKIT



Easy toolkit with standard doses, drug facts and pertinent information

WHAT IS KETAMINE?

- Is a **phencyclidine** derivative
- **N-methyl-D-aspartate receptor antagonist** throughout the CNS
- Metabolized in the liver (**nor-ketamine is active metabolite**), **caution** in patients with **liver disease**
- **Renally** excreted
- Does not cause severe hypotension or severe respiratory depression
- **Increases CO, HR, BP and ICP**
- Great drug of choice for induction in trauma cases, without suspicion of head injury/trauma, and patients with hypovolemia and **sepsis (1-2mg/kg IVP)**
- **Bronchodilation** properties
- Patient can have **psychomimetic events**
- **Side Effects**: prolonged emergence, delirium, confusion, hallucinations, irrational behavior, increased salivation

HOW CAN IT BE ADMINISTERED?

- **IV, IM**, Oral, transnasal, and rectal

DOSES

- **Induction**:
  - 1-2mg/kg/IVP for adults and pediatrics
  - 4-6mg/kg IM
- **Maintenance** (adjunct to TIVA):
  - 0.25-0.35mg/kg loading dose, followed by an infusion up to 1mg/kg/hr
- **Obstetrics (questionable neuraxial)**:
  - 10mg IVP per dose PRN
- **Sedation:**
  - 2.5-15mcg/kg/min IV
  - 1-2mg/kg IVP over 2 minutes repeat if necessary 0.5-1mg/kg IVP q15min
    - 0.25-0.5mg/kg if you have concomitant sedation
- **Intranasal (acute pain):**
  - 0.2-1mg/kg, given in divided doses in each nostril
- **Rectal (pediatrics >1 yr)**
  - 1.5-3mg/kg
- **Reducing post-operative opioid use**:
  - 0.2mg/kg bolus followed by an infusion of 0.1mg/kg/hr at start of surgery
- **Immune Response**:
  - 0.15mg/kg IV bolus prior to anesthetic induction was shown to decrease alterations in immune function in the early post-operative period
    - Shown to significantly **reduce IL-6 and TNF-alpha markers**
- **Neurological benefits**:
  - 0.5mg/kg/IV bolus given during anesthesia was found to **reduce incidences of post-op cognitive dysfunction** in patients undergoing cardiac surgery
  - 0.5mg/kg infusion over 40 minutes was found to help **decrease explicit suicidal cognition and nonsuicidal-related depressive symptoms**.

HOW CAN YOU REDUCE PSYCHOMIMETIC EVENTS?

- Give **adequate dose of benzodiazepine (versed) or hypnotic agent (Propofol)** to reduce psychomimetic events
- Recommended to give **glycopyrrolate** to reduce salivation

References

Barreveld, A. M., Correll, D. J., Liu, X., Max, B., McGowan, J. A., Shovel, L., Wasan, A. D., & Nedeljkovic, S. S. (2013). Ketamine decreases postoperative pain scored in patients taking opioids for chronic pain: Results of a prospective, randomized, double-blind study. Pain Medicine, 14(6), 925-934. https://doi.org/10.1111/pme.12086

Beilin, B., Rusabrov, Y., Shapira, Y., Roytblat, L., Greemberg, L., Yardeni, I. Z., & Bessler, H. (2007). Low-dose ketamine affects immune response in humans during the early postoperative period. British Journal of Anaesthesia, 99(4), 522-527. https://doi.org/10.1093/bja/aem218

Boysen, P. G., 2nd, Pappas, M. M., & Evans, B. (2018). An Evidence-Based Opioid-Free Anesthetic Technique to Manage Perioperative and Periprocedural Pain. The Ochsner journal, 18(2), 121-125. doi:10.31486/toj.17.0072

Butterworth, J. F., Mackey, D. C., & Wasnick, J.D. (Eds.). (2013). *Morgan & Mikhail's clinical anesthesiology* (5th ed.). New York, NY: McGraw-Hill Education.

Cohen, S. P., Bhatia, A., Buvanendran, A., Schwenk, E. S., Wasan, A. D., Hurley, R. W., Viscusi, E. R., Narouze, S., Davis, F. N., Ritchie, E. C., Lubenow, T. R., & Hooten, W. M. (2018). Consensus Guidelines on the Use of Intravenous Ketamine Infusions for Chronic Pain From the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists. Regional Anesthesia & Pain Medicine, 43(5), 521-546. doi:10.1097/AAP.000000000000080

Dale, O., Somogyi, A. A., Li, Y., Sullivan, T., & Shavit, Y. (2012). Does intraoperative ketamine attenuate inflammatory reactivity following surgery? A systematic review and meta-analysis. Anesthesia & Analgesia, 115(4), 934-943. https://doi.org/10.1213/ANE.0b013e3182662e30

Domino, E. F., Chodoff, P., & Corssen, G. (1965). Pharmacologic effects of CI-581, a new dissociative anesthetic, in man. Clinical Pharmacology & Therapeutics, 6(3), 279-291. doi:10.1002/cpt196563279

Gan, T. J. (2017). Poorly controlled postoperative pain: prevalence, consequences, and prevention. Journal of pain research, 10, 2287-2298. doi:10.2147/JPR.S144066 Gales, A., & Maxwell, S. (2020). Ketamine: Recent Evidence and Current Uses. Update in Anaesthesia, 35, 43-48.

Gorlin, A. W., Rosenfeld, D. M., & Ramakrishna, H. (2016). Intravenous sub-anesthetic ketamine for perioperative analgesia. Journal of anaesthesiology, clinical pharmacology, 32(2), 160-167. doi:10.4103/0970-9185.182085

Green, S. M. (2000). Modern Anesthesiologists Receive Limited Training with Ketamine: Implications for Emergency Medicine. Academic Emergency Medicine, 7(7), 839-840. doi:10.1111/j.1553-2712.2000.tb02284.x

Haliloglu, M., Ozdemir, M., Uzture, N., Cenksoy, P. O., & Bakan, N. (2016). Perioperative low-dose ketamine improves postoperative analgesia following Cesarean delivery with general anesthesia. The Journal of Maternal-Fetal & Neonatal Medicine, 29(6), 962-966. doi:10.3109/14767058.2015.1027190

References

Hudetz, J. A., Patterson, K. M., Iqbal, Z., Gandhi, S. D., Byrne, A. J., Hudetz, A. G., Warltier, D. C., & Pagel, P. S. (2009). Ketamine attenuates delirium after cardiac surgery with cardiopulmonary bypass. Journal of Cardiothoracic and Vascular Anesthesia, 23(5), 651-657. https://doi.org/10.1053/j.jvca.2008.12.021

Jabre, P., Combes, X., Lapostolle, F., Dhaouadi, M., Ricard-Hibon, A., Vivien, B., Bertrand, L., Beltramini, A., Gamand, P., Albizzati, S., Perdrizet, D., Lebail, G., Chollet-Xemard, C., Maxime, V., Brun-Buisson, C., Lefrant, J. Y., Bollaert, P. E., Megarbane, B., Ricard, J. D., . . . Adnet, F. (2009). Etomidate versus ketamine for rapid sequence intubation in acutely ill patients: A multicentre randomised controlled trial. The Lancet, 374(9686), 293-300. https://doi.org/10.1016/S0140-6736(09)60949-1

Kaur, S., Saroa, R., & Aggarwal, S. (2015). Effect of intraoperative infusion of low-dose ketamine on management of postoperative analgesia. Journal of natural science, biology, and medicine, 6(2), 378-382. doi:10.4103/0976-9668.160012

Koepke, E. J., Manning, E. L., Miller, T. E., Ganesh, A., Williams, D. G. A., & Manning, M. W. (2018). The rising tide of opioid use and abuse: the role of the anesthesiologist. Perioperative Medicine, 7(1), 16. doi:10.1186/s13741-018-0097-4

Kurdi, M. S., Theerth, K. A., & Deva, R. S. (2014). Ketamine: Current applications in anesthesia, pain, and critical care. Anesthesia, essays and researches, 8(3), 283-290. doi:10.4103/0259-1162.143110

Price, R. B., Iosifescu, D. V., Murrough, J. W., Chang, L. C., Al Jurdi, R. K., Iqbal, S. Z., Soleimani, L., Charney, D. S., Foulkes, A. S., & Mathew, S. J. (2014). Effects of ketamine on explicit and implicit suicidal cognition: A randomized controlled trial in treatment-resistant depression. Depression & Anxiety, 31(4), 335-343. https://doi.org/10.1002/da.22253

Riddell, J. M., Trummel, J. M., & Onakpoya, I. J. (2019). Low-dose ketamine in painful orthopaedic surgery: a systematic review and meta-analysis. British Journal of Anaesthesia, 123(3), 325-334. doi:10.1016/j.bja.2019.05.043

Stetler, C. B. (2001). Updating the Stetler Model of research utilization to facilitate evidence-based practice. Nursing Outlook, 49(6), 272-279. doi:https://doi.org/10.1067/mno.2001.120517

Vadivelu, N., Schermer, E., Kodumudi, V., Belani, K., Urman, R. D., & Kaye, A. D. (2016). Role of ketamine for analgesia in adults and children. Journal of anaesthesiology, clinical pharmacology, 32(3), 298-306. doi:10.4103/0970-9185.168149