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Dexmedetomidine for Prevention of Emergence Delirium in Pediatric Anesthesia

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DEXMEDETOMIDINE FOR PREVENTION OF EMERGENCE DELIRIUM IN PEDIATRIC ANESTHESIA

by

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Abstract

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Background: Since the introduction and wide use of Sevoflurane, an inhaled volatile anesthetic, in pediatric anesthesia, postoperative behavioral disturbances referred to as emergence agitation (EA) or emergence delirium (ED) has been identified as a common occurrence and problem in pediatric anesthesia. The terms ED and EA will be used interchangeably throughout this independent project. Desflurane has also been associated with this known phenomenon. Emergence delirium may result in self harm, delayed discharge times, and dissatisfied care from the parents. Delirium following anesthesia poses a barrier to quality patient care. Dexmedetomidine (DEX) is a newer selective alpha2-adrenergic receptor agonist. The safety and efficacy of DEX in the pediatric population is not completely clear, and it has not been approved by the United States Food and Drug Administration (FDA) for use in patients under 18 years of age. However, the use of DEX in pediatrics has been widely reported in clinical research with a high safety profile.

Purpose: The purpose of this independent project is to present a case report and comprehensive review of the evidence based literature regarding the use and effects of DEX in the pediatric population.

Process: An extensive literature review was conducted utilizing the Cochrane Library, PubMed, and CINAHL databases, all of which were accessed from the University of North Dakota's Health Sciences Library. Other related literature sources were acquired through the bibliographies of the articles that were initially found. All literature retrieved was evaluated utilizing the Oxford Centre for Evidence-Based Medicine (OCEBM) evidence leveling system for quality.

Results: The evidence-based literature verified that DEX reduced the incidence of early EA and overall agitation scores, reduced pain scores, decreased the need for postoperative painkillers, and diminished the occurrence of nausea and vomiting. No serious side effects on the circulatory or respiratory system were noted in any of the studies. In addition, a trend of fewer overall adverse events were noted in the DEX groups.

Implications: DEX can safely be utilized in pediatric anesthesia and has the properties to improve the awakening quality following general anesthesia. The literature search revealed various routes and forms of administration of DEX in pediatrics with similar successful results and safety profiles.

Keywords: Dexmedetomidine, emergence delirium, emergence agitation, and pediatric anesthesia.

Dexmedetomidine for Prevention of Emergence Delirium in Pediatric Anesthesia

Dexmedetomidine (DEX), also referred to as Precedex, is a relatively newer anesthetic adjuvant. It is a highly selective alpha2-adrenergic receptor agonist with analgesic, sedative, and anti-sympathetic properties with limited to no respiratory inhibition (Jin-hui et al., 2013). Dexmedetomidine has been approved for the use in adults, however, U.S. FDA has yet to provide an approved label application for implications for use in pediatric anesthesia (Hauber et al., 2015). However, DEX has reportedly been used in pediatrics for various uses such as: premedication, sedation in pediatric intensive care units, adjuvant to inhaled anesthetics, and as a drug for prophylaxis and treatment of emergence delirium following general anesthesia (Hauber et al., 2015).

Pediatric behavioral disturbances in the postoperative phase known as emergence agitation (EA) or emergence delirium (ED) have been identified as an issue in pediatric anesthesia after receiving a volatile agent such as Sevoflurane or Desflurane (Costi et al., 2014). Emergence delirium in children was first discussed in the early 1960s. It is characterized by a dissociated state of consciousness where the child becomes inconsolable, uncooperative, agitated, and at times even aggressive (Amorim et al., 2017). This experience is self-limiting, but still proves as a traumatic event for the child, parents, and even healthcare professionals (Amorim et al., 2017). A child who experiences ED postoperatively is at risk to injure themselves or others. This phenomenon can cause them to disrupt the surgical site or dislodge indwelling catheters and drains necessary for their care. In addition, they can experience delayed recovery times, discharge times, and less patient satisfaction from the parents (Amorim et al., 2017). The prevalence of agitation in literature varies from 25%-85% depending on criteria chosen by the authors. Different anesthetic techniques and drugs utilized can influence the

agitation. A variety of different classes of drugs such as benzodiazepines, ketamine, opioids, and alpha2-agonists have been trialed for their efficacy in prevention and treatment of agitation upon emergence, with varying success rates. This has led to a demand for more studies to examine and improve perioperative care to the pediatric population (Amorim et al, 2017).

A global and national agreement must be established on the appropriate label uses, safety profile, and efficacy of DEX uses in pediatric anesthesia. This consensus must be obtained following an extensive review of the evidenced based literature exploring the risks and benefits of DEX in children. A case report of a pediatric patient undergoing general anesthesia who was administered an intraoperative prophylactic bolus of DEX to prevent ED will be discussed in the following pages.

Purpose

The purpose of this independent project is to present a successful case report of a pediatric patient undergoing general anesthesia who was safely administered a prophylactic bolus dose of DEX intraoperatively and monitored for effects postoperatively. In addition, research based evidence from literature will be presented confirming DEX can safely and effectively be administered in pediatric anesthesia to prevent and treat ED as well as decrease rescue opioid use, nausea and vomiting, and improve patient care and satisfaction.

Case Report

A 2-year-old, 12 kilogram (kg), 84 cm, male presented for inguinal hernia repair. His past medical history was negative with the exception of passive smoke exposure. He had no past surgical or anesthetic history. No family history of problems with anesthesia. He was on no medications and had no known allergies. The patient had been NPO for 8 hours. No labs were

drawn preoperatively. Using the American Society of Anesthesiologists (ASA) system, the patient was classified as an ASA one.

Airway assessment of the child was limited due to cooperation. The patient appeared to have an adequate thyromental distance for his age and height, Mallampati class I, mouth opening of three fingerbreadths, and neck range of motion did not appear restricted. Preoperative vital signs presented as a blood pressure of 87/38 mmHg, heart rate of 112 beats per minute, respiratory rate of 22 breathes per minute, temperature 37 degrees Celsius, and oxygen saturations (SpO2) of 100% on room air. Auscultation of his heart and lungs revealed clear bilateral breath sounds and a regular heart rate and rhythm without murmur.

The patient was transported to the operating room (OR) on a cart accompanied by his mother. The OR staff assisted the child to the operating table. The child was calm and cooperative which allowed the application of standard monitors, which included: a pulse oximetry monitor, and blood pressure cuff. A three-lead electrocardiogram (EKG) was placed following induction. An inhalational induction was performed with three liters of oxygen and six liters of nitrous oxide, whilst titrating sevoflurane to desired effects. A 22-gauge intravenous (IV) peripheral catheter was placed in the left hand after the patient was adequately under general anesthesia. The IV was secured with a dressing. Normal saline fluids were initiated with the use of buretrol safety tubing. The patient was given 20 milligrams (mg) of propofol IV, and 5 micrograms (mcg) of fentanyl IV. Once no eyelid reflexes were noted, tape was carefully placed over the patient's eyelids to prevent corneal abrasions. With the use of a tongue blade, a size two laryngeal mask airway (LMA) was successfully placed and sealed with adequate tidal volumes and no air leak noted. Confirmation of placement was assessed by auscultation of clear, equal bilateral breath sounds, a positive end-tidal CO2 (ETCO2), equal chest rise, and a maintained

SpO2 of 99%. The LMA was taped securely in place. A nasopharyngeal temperature probe was placed in the right nare for continuous temperature monitoring during case. A total of 10 mcg of fentanyl IV was given in increments of 5 mcg for analgesia. Dexamethasone 3 mg, and Ondansetron 1.8 mg, were administered IV for prophylactic treatment of nausea and vomiting postoperatively. Supportive ventilation was administered until the spontaneous return of respirations occurred. The patient maintained adequate tidal volumes and respiratory pattern throughout the case. When closing of the incision began, the patient was given a slow 6 mcg (0.5mcg/kg) IV bolus of DEX. No negative hemodynamic side effects were noted. The patient was extubated deep with an expired sevoflurane concentration of 1.3%. An oral airway was placed, and a blow by oxygen mask was placed near the child's airway. There were no issues upon removal of the LMA or placement of the airway, good airway exchange was noted without spasm, and SpO2 was maintained at 98% or higher. Transfer to the post-anesthesia recovery unit (PACU) was completed without any complications. The patient woke up in the PACU crying for his mother, and was easily calmed and re-directed. The rest of the child's short stay in the PACU proved to be uneventful. He did not require any rescue opioid or sedation. He did not experience postoperative nausea or vomiting. No hemodynamic issues such as hypotension or bradycardia were noted. His stay in the PACU was not delayed, and he was successfully transferred to the day unit for discharge home.

Literature Search

To conduct an appropriate and precise literature search, a PICO question was formulated to accurately search the relevant literature. The PICO process is a technique used to frame and answer a health care related issue in evidence based practice. The purpose of a PICO question is to concisely construct a specific research question in order to perform an effective search of the

literature. The PICO acronym stands for (P) the patient, problem, or population, (I) intervention, (C) comparison, control or comparator, and (O) outcome. A properly constructed PICO question can facilitate a more efficient search of the literature (Stillwell, Fineout-Overholt, Melnyk, & Williamson, 2010). The following PICO question was formulated: among surgical pediatric patients undergoing general anesthesia(P), does administration of DEX (I/C), decrease the incidence of emergence delirium (O)?

Inclusion and exclusion criteria was established prior to the literature search. Articles were evaluated based on level of evidence, bias, and reliability of sources. The Oxford Centre for Evidence-Based Medicine (OCEBM) provides an evidence-leveling system to offer consistency with other health organizations and incorporates a user-friendly diagram. This evidence grading hierarchy was implemented to evaluate each article discovered. The OCEBM hierarchy of evidence categorizes evidence from strongest to weakest, level 1 being the highest level including systematic reviews of randomized trails, and level 5 including the lowest level of evidence involving mechanism-based reasoning (OCEBM Levels of Evidence Working Group, 2011). A majority of the articles used for the purposes of this independent project were categorized in the highest level of evidence.

Databases

After the PICO question was finalized, an extensive literature review was conducted. The University of North Dakota Health Sciences Library was used to access the Cochrane Library, PubMed, and CINAHL databases. In addition, the Chester Fritz library was also used to search various databases. According to Stillwell et al. (2010) the Cochrane reviews are considered to have the highest level of evidence for research questions due to their thorough study designs. The Cochrane Database of Systematic Reviews (CDSR) and the Database of Abstracts of Reviews of

Effects (DARE) both contain systematic reviews and meta-analyses of randomized controlled trials, the highest level of evidence (Stillwell et al., 2010). Since these databases include literature in nursing, medicine, and science they were appropriate for the purpose of this independent project and directly relevant to the PICO question.

Vocabulary and Limits

Stillwell et al. (2010) suggest using keywords directly from the PICO question. The following keywords were identified: Dexmedetomidine, emergence delirium, emergence agitation, and pediatric anesthesia. Within the Cochrane database the terms "Dexmedetomidine" and "emergence delirium" were input into search browser. This search generated two pertinent articles. Emergence Delirium was input into the medical subject headings (MeSH) search engine, this search resulted in nineteen articles, of which seven were applicable to the PICO question.

A total of three searches were conducted using the PubMed database. Two of these searches performed using the Medical Subject Heading (MeSH) terms within the PubMed database. The use of MeSH terms finds all articles related to the keywords, resulting in the most comprehensive search of the literature. The first search used the key terms: "dexmedetomidine" and "emergence delirium" input together in the advanced search bar within PubMed. This resulted in 69 articles. The search was further refined by adding the search filters "free full text", "within ten years", and "humans." This decreased the search results to 14 articles, seven of which were directly relevant to the PICO question.

The second search utilized the MeSH terms "dexmedetomidine" and "emergence delirium" in all fields. This resulted in four articles. Three of these articles were pertinent and therefore used in this independent project. The third search using PubMed was performed using

the MeSH terms “pediatrics”, “emergence delirium” in all fields. This search produced three results. Two of these articles were directly related to the topic of interest.

CINAHL was the next database chosen for the literature search. A total of two searches were conducted using the CINAHL database. First, the search words “dexmedetomidine”, “emergence delirium” and “pediatric” were used with the all text option. This search yielded 16 results. Published date was adjusted to journal articles published within the last ten years. In addition, the “peer reviewed” box was also checked to narrow the search for higher quality articles. The application of these limits resulted in twelve articles, six of which were saved for review.

The second search within the CINAHL database employed the search words “dexmedetomidine” and “pediatric anesthesia” in all fields. This search generated 58 results. The search was further refined by adding the search filters “free full text”, “within ten years”, “academic journals” and “peer reviewed.” This decreased the search results to 32 articles. Five articles were directly relevant to the PICO question.

From the University of North Dakota’s website, a search of the Chester Fritz Library was completed. A variety of databases are included within this website. To maintain continuity, the same key phrases used throughout this literature search were input into the search bar. From this search, six relevant articles were found and used for the purposes of this independent research project.

Additional Search Means

An additional search strategy was employed following the initial search of the databases previously addressed. Once relevant articles were identified the reference list of said articles were searched to discover related evidence based literature. From this search method five

applicable journal articles were discovered and used. Within initial databases employed direct links such as "citations, cited by, and related articles" options were also employed to discover more related articles. Repeated and controlled use of the same specific vocabulary and search criteria within trustworthy and credible healthcare databases led to a successful and comprehensive review of the literature.

Review of Literature

To better understand and evaluate the results of the literature search regarding the effects DEX has on ED in children, it is important to first understand the pathophysiology of the ED phenomenon and how it is evaluated. In addition, it is essential to have an understanding of DEX in regard to: class of drug, mechanism of action, side effects, and other important aspects of the drug itself. The literature found regarding these topics will be covered first followed by a discussion involving the results of studies completed involving DEX and its success rate alleviating emergence delirium in the pediatric population.

Emergence Delirium

Emergence delirium is a complex of psychomotor agitation and perceptual disturbances that occurs mostly in preschool-aged children early in the postanesthetic phase (Moore & Anghelescu, 2017). Sikich and Lerman (2014) defined EA as "A disturbance in a child's awareness of and attention to his or her environment with disorientation and perceptual alterations, including hypersensitivity to stimuli and hyperactive motor behavior in the immediate post-anesthesia period" (p. 1138). The incidence of EA varies from 25% to 85% depending on the study, and is perceived as a troublesome event by 42% of anesthesia providers (Moore & Anghelescu, 2017). Children who experience ED are at risk for harming themselves and others as well as removing necessary surgical drains and/or dressings directly affecting

patient care and safety (Kanaya, 2016). In addition, witnessing a child undergo this unpleasant experience can prove to be difficult for the parents and/or caregivers. These events can lead to upset and dissatisfied parents (Kanaya, 2016). This has led to numerous studies and research to discover an anesthetic that provides an uneventful and smooth emergence from general anesthesia in the pediatric population.

Emergence delirium was first described early in the 1960s (Nagelhout & Plaus, 2014). Halothane, a volatile inhaled anesthetic, commonly used in general anesthesia during this time was not observed to be directly correlated with ED. It wasn't until the introduction and wide use of sevoflurane and desflurane that ED was noted of significance (Nagelhout & Plaus, 2014). Numerous studies done on desflurane and sevoflurane have reported direct correlation with the use of these volatile anesthetics and the increase of ED in pediatric anesthesia (Kanaya, 2016).

To minimize the measurement error in the assessment of ED, health care providers require a consistent tool they can use that is reliable and valid. The Pediatric Anesthesia Emergence Delirium Scale (PAED) is a newly validated tool for clinicians to assess emergence delirium in children (Sikich & Lerman, 2004). Behavior categories include: eye contact, purposeful action, awareness of surroundings, restlessness, and if the child is consolable. Frequency of behavior is divided into five categories: not at all, just a little, quite a bit, very much, and extremely. The total PAED is the sum of scores for the five behaviors indicated. If the child scores above 10, it is indicative they are experiencing ED (Sikich & Lerman, 2004).

Causes and Risk Factors

A specific cause and underlying mechanism of action for ED has yet to be identified, although several factors are thought to be involved (Nagelhout & Plaus, 2014). Those of preschool age have been reported to have a higher incidence of ED when compared to those of

school-age, however gender does not seem to be an independent variable (Kanaya, 2016). Martini (2005) explained that a child's brain is more susceptible to delirium following general anesthesia due to a decline in norepinephrine, acetylcholine, dopamine, and y-aminobutyric acid (GABA). Children who are diagnosed with a social or behavioral disorder have been found to show a higher incidence of ED (Kanaya, 2016). Anxiety pre-operatively has also been linked to experiencing higher rates of emergence delirium following general anesthesia (Kanaya, 2016). Pain has been found to be another variable that can influence ED (Kanaya, 2016). Agitation is more likely to occur if pain has not been adequately controlled (Kanaya, 2016). In addition, the surgical procedure has been identified as a variable that contributes to ED (Nagelhout & Plaus, 2014).

As discussed earlier, sevoflurane and desflurane have been reported to be a contributing factor to the cause of emergence delirium. It has been suggested that this is related to the fact that awakening from these anesthetics occurs at a rapid pace, and sevoflurane has an excitatory effect on the central nervous system (Kanaya, 2016). It has been hypothesized that emergence delirium is caused due to the different clearance rates of the volatile anesthetics from the central nervous system, leading to varying recovery rates at different sites of brain function following anesthesia (Voepel-Lewis, Malviya, & Tait, 2003). Cognitive function of the brain is slow to return in comparison to locomotion, sensibility, and audition, leading to confusion (Voepel-Lewis, Malviya, & Tait, 2003). Continued research is needed to fully establish the definitive cause of ED.

Dexmedetomidine

Dexmedetomidine is an alpha-2 adrenergic agonist (Mason & Lerman, 2011). It works by binding with pre and postsynaptic alpha-2 receptors, causing a decrease in norepinephrine levels

resulting in sedative and analgesic effects. Its sedative effect is similar to physiological sleep (Cao, Pei, Wei, & Zhang, 2016). In 1999 the United States FDA approved the use of DEX in the intensive care unit (ICU) for sedation of intubated adults (Mason & Lerman, 2011). In 2008, DEX was approved for sedation outside of the ICU for medical procedures on adults who were not intubated (Mason & Lerman, 2011). Despite the fact that DEX does not have an approved label indication for the its use in the pediatric population, the use for its sedative, analgesic, and anxiolytic properties in children have been widely reported (Hauber et al., 2015). Dexmedetomidine use in children has yet to be approved in any country. However, dexmedetomidine has been employed for an anesthesia adjuvant both inside and outside operating rooms, and on both adults and children (Mason & Lerman, 2011).

Throughout the past ten years the uses for DEX has been increasing. Dexmedetomidine has been used as a premedication prior to surgery, as an adjunctive drug both intraoperatively and postoperatively, to lessen ED, shivering, and pain during surgery and for sedation, analgesia, and airway management in the ICU (Mason & Lerman, 2011). Clear implications and use of DEX has not been fully outlined in all these settings, including the use in children. There is limited research on the pharmacology, pharmacodynamics, and physiologic effects of DEX in children (Mason & Lerman, 2011). Cardiovascular effects of dexmedetomidine have been well documented. Hypertension, hypotension, and bradycardia can occur to varying degrees depending on the age of the child and the rate of administration (Mason & Lerman, 2011). The safety record of DEX indicates that if the cardiovascular effects are closely monitoring and managed, DEX can indeed be administered safely and effectively in the pediatric population (Mason & Lerman, 2011).

Dexmedetomidine for Emergence Delirium in Children

This extensive review of the literature generated a substantial amount of high level evidence-based research that led to the conclusion that DEX can safely be administered in children, and has significant effects on alleviating ED. Hauber et al. (2015) found that the bolus administration of DEX in children did in-fact decrease the incidence of ED post-operatively. In addition, children who received DEX required less rescue doses of opioids in the postoperative phase and experienced less adverse side effects (Hauber et al., 2015).

Hauber et al. (2015) conducted a randomized double-blind study involving 400 patients ages 4 to 10 years of age undergoing a tonsillectomy with or without adenoidectomy, with or without myringotomy, and/or insertion of ear tubes (Hauber et al., 2015). A standardized anesthetic regimen was employed for all patients. The patients were divided into two treatment groups. One group received DEX while the other received the placebo, saline. Five minutes before the surgery ended, the patients in the DEX group were administered a 0.5mcg/kg IV bolus of DEX, whereas the patients in the placebo group were given an equivalent dose of saline at the same time (Hauber et al., 2015). In the postanesthesia care unit, ED was evaluated utilizing the PAED, vitals were recorded, and opioid use and complications were documented. Emergence delirium incidence was significantly lower in than DEX group compared to the placebo group. The placebo group also required a greater amount of supplemental opioids, and experienced more adverse effects compared to the DEX group. Patients in the DEX group did experience a greater hemodynamic response, however no treatment was required (Hauber et al., 2015).

A meta-analysis of the literature was completed by Jin-hui et al. (2013). The meta-analysis which entailed 27 randomized trials and 1882 children showed that DEX was largely adventitious and effective in reducing emergence agitation postoperatively. From this search of

the literature, Jin-hui et al. (2013) also discovered evidence that DEX decreased pain scores, need for opioids, postoperative nausea and vomiting, and occurrence of bucking during emergence. However, it was discovered that children who received DEX had longer discharge and recovery times related to sedation post-operatively. No serious respiratory or circulatory side effects were noted in any of the included studies (Jin-hui, 2013).

Sun and Guo (2014) also conducted a meta-analysis of randomized controlled trials involving DEX administration in children. As previously discussed, the efficacy and use of DEX in children remains a controversial issue. The meta-analysis was conducted to determine the effectiveness of DEX on the occurrence of sevoflurane-related EA. Sun and Guo (2014) completed a thorough search of the current research-based literature in order to compare DEX with a placebo in-relation to their effects on children and ED. A total of 15 randomized control trials made up the final analysis. Dexmedetomidine was received by 518 of the children, whereas 413 were given the placebo. Results were definitive, demonstrating a significant decrease in the incidence and severity of ED in the DEX groups as compared to the placebo.

Boku et al. (2016) conducted a prospective randomized controlled trial that aimed to test the hypothesis that the administration of DEX would decrease the incidence of ED following sevoflurane based anesthesia in infants who underwent a palatoplasty. The trial included 70 patients, ages 10-24 months. The infants were randomly distributed into two groups of 35, a DEX group and a saline group. In the DEX group, an infusion of dexmedetomidine 6mcg/kg/hr was administered approximately 10 minutes prior to the end of the case for approximately 10 minutes, followed by 0.4 mcg/kg/hr until 5 minutes following extubation. This was completed with the same approach and dosing in the saline group. The infant's behavior was observed and documented in the PACU. Emergence agitation and pain scores were both assessed using the

same rating scales at 30 minute intervals. Results of the study showed that EA and pain scores were meaningfully lower in the DEX group than in the saline group (Boku et al., 2016).

Due to the fact that ED is a common problem, various classes of drugs have been employed to attempt to lessen or deter it (Makkar, Bhatia, Bala, Dwivedi, & Singh, 2016). Opioids, midazolam, ketamine, propofol, and NSAIDs are among some of the medications used to prevent and/or treat the symptoms of emergence delirium (Makkar et al., 2016). Makkar et al., (2016) conducted a study comparing emergence characteristics in 100 children, undergoing infra-umbilical surgery, who were randomly placed in either a propofol, DEX, or saline group. Again, the PAED scale was used to assess ED. In the DEX group, ED occurred in 9.4% of the children, compared to 13.9% in the propofol group, and 62.5% in the saline or control group. It was also noted, however, sedation occurred for a longer period of time in the post anesthesia phase in the DEX group.

Discussion

The pediatric patient discussed in this independent project was at a high risk to experience postoperative ED based on his age and the use of sevoflurane during the case. He had no past medical or surgical history, no known allergies, and was undergoing a simple same day hernia repair. The patient received no premedication prior to surgery and proved to be a good candidate to receive a bolus dose of DEX intraoperatively to decrease ED in the PACU. The child experienced no cardiovascular side effects and remained stable throughout the entire intraoperative and postoperative phase. The patients PACU experience was uneventful. He did not show signs of ED or EA, required no opioids, and did not harm himself or others. His parents expressed satisfaction with the anesthetic and their child's care.

The literature search revealed that currently DEX does not have a clear approved label use in children. Additional clinical trials and research are needed for a more conclusive and definitive use of DEX in pediatric anesthesia. Statistically pediatric surgery generally involves smaller scale operations with shorter surgical times and length of stay (Jin-hui et al., 2013). Therefore, the incidence of postoperative complications and increased discharge times significantly influence the evaluation of pediatric anesthetic methods and outcomes (Jin-hui et al., 2013). As anesthesia providers, we need to construct an anesthetic plan that is safest and most appropriate for our patients, not only during the intraoperative phase, but in the preoperative and postoperative phase as well. It is our responsibility to strive to provide the most efficient anesthetic with a safe recovery profile to reduce the amount of postoperative complications. By altering our intraoperative anesthetic to strive for a smooth recovery phase, patients will experience shorter residence time in both the operating rooms and PACU, enhancing productivity, patient satisfaction, and safety.

Conclusion

In the pediatric population, ED continues to be a barrier for safe care faced by anesthesia providers. Although the pathophysiology of emergence delirium is not fully understood, the incidence in pediatric anesthesia continues to be prevalent. Commonly used volatile inhaled anesthetics sevoflurane and desflurane have been researched and reported to be a contributing factor in the cause of post-anesthesia delirium. Dexmedetomidine is a relatively new drug that continues to grow in popularity and use in the anesthesia community. Although not approved by the FDA for use in children, there are extensive reports of successful and safe use in pediatric anesthesia. Evidence-based research has been completed that concludes that DEX has repeatedly and successfully been administered in children to alleviate postoperative ED.

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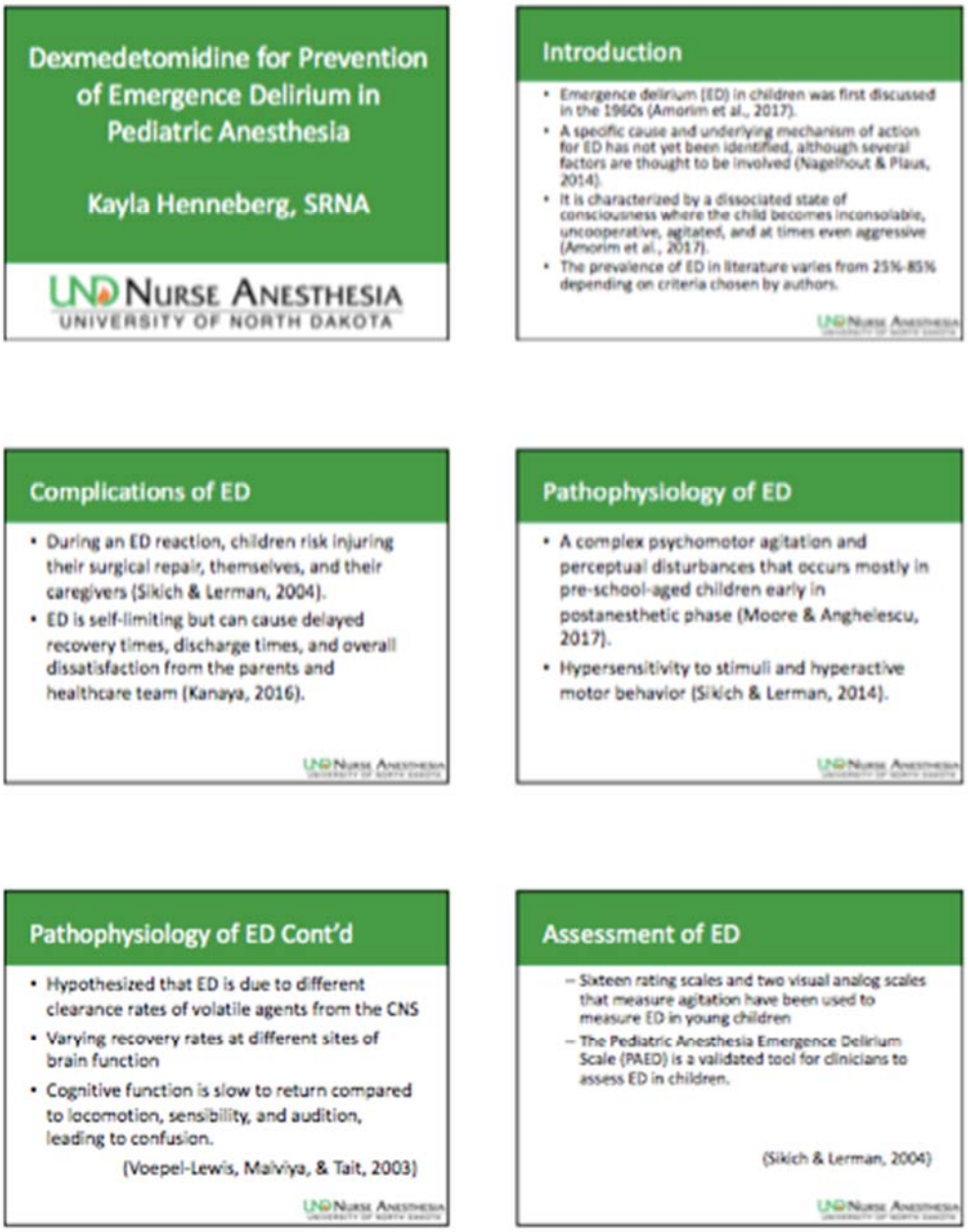
Appendix A


Dexmedetomidine for Prevention of Emergence Delirium in Pediatric Anesthesia
Kayla Henneberg, SRNA
UND Nurse Anesthesia
University of North Dakota
Introduction
• Emergence delirium (ED) in children was first discussed in the 1960s (Amorim et al., 2017).
• A specific cause and underlying mechanism of action for ED has not yet been identified, although several factors are thought to be involved (Nagelhout & Plaus, 2014).
• It is characterized by a dissociated state of consciousness where the child becomes inconsolable, uncooperative, agitated, and at times even aggressive (Amorim et al., 2017).
• The prevalence of ED in literature varies from 25%-85% depending on criteria chosen by authors.
Complications of ED
• During an ED reaction, children risk injuring their surgical repair, themselves, and their caregivers (Sikich & Lerman, 2004).
• ED is self-limiting but can cause delayed recovery times, discharge times, and overall dissatisfaction from the parents and healthcare team (Kanaya, 2016).
Pathophysiology of ED
• A complex psychomotor agitation and perceptual disturbances that occurs mostly in pre-school-aged children early in postanesthetic phase (Moore & Anghelescu, 2017).
• Hypersensitivity to stimuli and hyperactive motor behavior (Sikich & Lerman, 2014).
Pathophysiology of ED Cont'd
• Hypothesized that ED is due to different clearance rates of volatile agents from the CNS
• Varying recovery rates at different sites of brain function
• Cognitive function is slow to return compared to locomotion, sensibility, and audition, leading to confusion.
(Voepel-Lewis, Malviya, & Tait, 2003)
Assessment of ED
– Sixteen rating scales and two visual analog scales that measure agitation have been used to measure ED in young children
– The Pediatric Anesthesia Emergence Delirium Scale (PAED) is a validated tool for clinicians to assess ED in children.
(Sikich & Lerman, 2004)

PAED Scale

- Behavior categories include: Eye contact, purposeful action, awareness of surroundings, restlessness, and if the child is consolable.
- Frequency of behavior is divided into five categories: Not at all, just a little, quite a bit, very much, and extremely.
- The total PAED is the sum of scores for the five behaviors indicated
- Score above 10 is indicative of ED (Sikich & Lerman, 2004)

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Dexmedetomidine (DEX)

- An alpha-2 adrenergic agonist
- Commonly used intraoperatively as an adjuvant for sedation and analgesia (Mason & Lerman).
- Binds with pre and postsynaptic alpha-2 receptors, causes a decrease in norepinephrine levels resulting in sedative and analgesic effects.
- Its sedative effect is similar to physiological sleep (Cao, Pei, Wei, & Zhang, 2016)

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Dexmedetomidine Adverse Effects

- Cardiovascular effects of DEX have been well documented.
  - Hypertension
  - Hypotension
  - Bradycardia
- Despite substantial case reports of the safe use of DEX in pediatric anesthesia, DEX has not been approved for use in children by U.S. Food and Drug Administration (FDA) (Mason & Lerman, 2011)

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Case Information

- Inguinal hernia repair
- 2 years old
- 84 cm
- 12 kg
- Male
- ASA 1

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Pre-operative Evaluation

- Past Medical History: Passive smoke exposure. NKA
- Surgical History: Negative
- Pre-op VS: BP 87/38 mm Hg, HR 112/min, RR 22/min, SpO2 100% on room air, Temp 99 degrees F
- No abnormal pre-op labs or studies
- Airway evaluation was unremarkable

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Anesthetic Course

- Patient did not receive pre-operative oral midazolam
- Escorted to OR with mother
- SpO2, BP, 3-lead EKG monitors applied
- Inhalation induction with 3L of O2 and 6L nitrous oxide, whilst titrating sevoflurane to desired effect
- 22-gauage IV placed in left hand
- NS fluids initiated with buretrol tubing
- Induced with 20 mg of propofol IV and 5 mcg fentanyl IV

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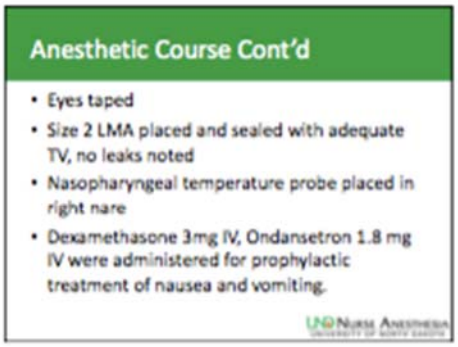
Anesthetic Course Cont'd
• Eyes taped
• Size 2 LMA placed and sealed with adequate TV, no leaks noted
• Nasopharyngeal temperature probe placed in right nare
• Dexamethasone 3mg IV, Ondansetron 1.8 mg IV were administered for prophylactic treatment of nausea and vomiting.
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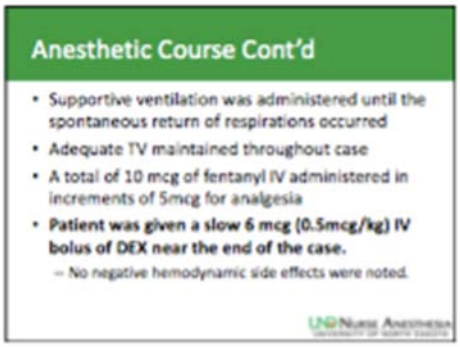
Anesthetic Course Cont'd
• Supportive ventilation was administered until the spontaneous return of respirations occurred
• Adequate TV maintained throughout case
• A total of 10 mcg of fentanyl IV administered in increments of 5mcg for analgesia
• Patient was given a slow 6 mcg (0.5mcg/kg) IV bolus of DEX near the end of the case.
– No negative hemodynamic side effects were noted.
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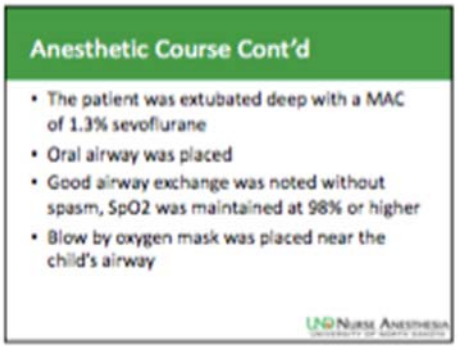
Anesthetic Course Cont'd
• The patient was extubated deep with a MAC of 1.3% sevoflurane
• Oral airway was placed
• Good airway exchange was noted without spasm, SpO2 was maintained at 98% or higher
• Blow by oxygen mask was placed near the child's airway
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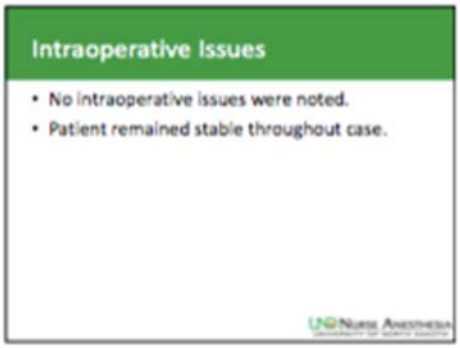
Intraoperative Issues
• No intraoperative issues were noted.
• Patient remained stable throughout case.
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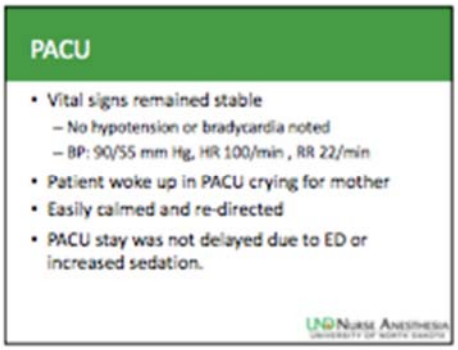
PACU
• Vital signs remained stable
– No hypotension or bradycardia noted
– BP: 90/55 mm Hg, HR 100/min , RR 22/min
• Patient woke up in PACU crying for mother
• Easily calmed and re-directed
• PACU stay was not delayed due to ED or increased sedation.
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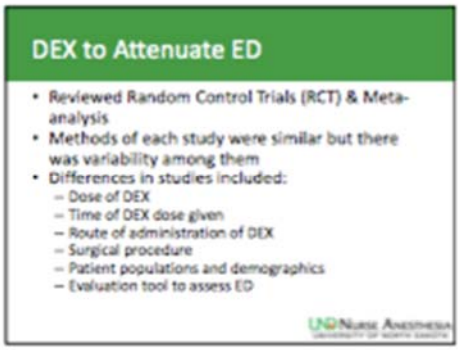
DEX to Attenuate ED
• Reviewed Random Control Trials (RCT) & Meta-analysis
• Methods of each study were similar but there was variability among them
• Differences in studies included:
– Dose of DEX
– Time of DEX dose given
– Route of administration of DEX
– Surgical procedure
– Patient populations and demographics
– Evaluation tool to assess ED
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DEX to Attenuate ED Cont'd

- Hauber et al. (2015) conducted a randomized double-blind study
  - 400 patients ages 4 to 10 years
  - Tonsillectomy with or without adenoidectomy, with or without myringotomy, and/or insertion of ear tubes
  - All received a standardized anesthetic regimen
  - Divided into a DEX group and saline group

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DEX to Attenuate ED Cont'd

- 5 minutes prior to surgery ending
  - DEX group was administered 0.5mcg/kg IV bolus, saline group given equivalent dose at same time
  - ED evaluated using PAED
  - Results: ED was significantly lower in DEX group
  - Placebo group: required greater amount of rescue opioids, and experienced more adverse effects

(Hauber et al., 2015)

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DEX to Attenuate ED Cont'd

- Meta-analysis of 27 randomized trials involving 1882 children
  - DEX was largely adventitious and effective in reducing ED
  - DEX also decreased pain scores, PONV, opioid use, and occurrence of bucking during emergence.
  - DEX groups had longer discharge time due to sedation

(Jin-hui et al., 2013)

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DEX to Attenuate ED Cont'd

- Meta-analysis of RCT to determine the effectiveness of DEX on the occurrence of sevoflurane-related ED.
  - 15 RCT
  - DEX received by 518 children, 413 were given saline
  - Results demonstrated a significant decrease in the incidence and severity of ED in DEX groups

(Sun & Guo, 2014)

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DEX to Attenuate ED Cont'd

- Boku et al. (2016) conducted a prospective RCT
  - Evaluated sevoflurane based anesthesia in infants who underwent a palatoplasty
  - 70 patients, ages 10-24 months
  - Two group of 35 (DEX and saline)
  - DEX group received an infusion of DEX at 6mcg/kg/hr for about 10 minutes prior to the end of case, followed by 0.4mcg/kg/hr until 5 minutes following extubation.
  - Completed in same approach with saline group.
  - ED scores were significantly lower in the DEX groups.

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DEX to Attenuate ED Cont'd

- A randomized control trial by Makkar et al. (2016) compared the use of DEX to propofol and saline
  - 100 children undergoing infra-umbilical surgery
  - 3 groups (DEX, propofol, saline) 5 minutes before end of case:
    - DEX group: 0.3 mcg/kg IV DEX bolus diluted in 10 ml saline
    - Propofol group: 1mg/kg bolus of propofol
    - Saline group: 10 ml of saline
  - PAED scale used to assess ED
  - ED occurred in 9.4% of the DEX group, compared to 13.9% in propofol group, and 62.5% in the saline group

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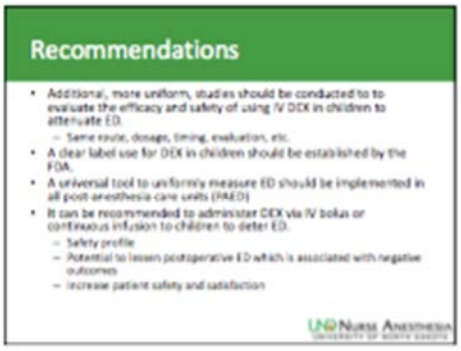
Recommendations
• Additional, more uniform, studies should be conducted to to evaluate the efficacy and safety of using IV DEX in children to attenuate ED.
– Same route, dosage, timing, evaluation, etc.
• A clear label use for DEX in children should be established by the FDA.
• A universal tool to uniformly measure ED should be implemented in all post anesthesia care units (PACU)
• It can be recommended to administer DEX via IV bolus or continuous infusion to children to deter ED.
– Safety profile
– Potential to lessen postoperative ED which is associated with negative outcomes
– Increase patient safety and satisfaction
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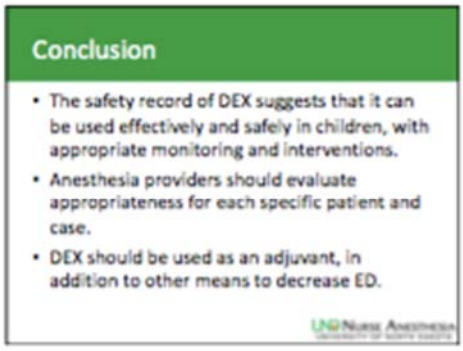
Conclusion
• The safety record of DEX suggests that it can be used effectively and safely in children, with appropriate monitoring and interventions.
• Anesthesia providers should evaluate appropriateness for each specific patient and case.
• DEX should be used as an adjuvant, in addition to other means to decrease ED.
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References
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Thank You
Are There Any Questions?
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