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PROPOFOL ADMINISTRATION FOR THE PREVENTION OF EMERGENCE AGITATION IN PEDIATRIC ANESTHESIA

by

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An Independent Study

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Abstract

**Title:** Propofol Administration for the Prevention of Emergence Agitation in Pediatric Anesthesia

**Background:** Emergence delirium or emergence agitation is a common occurrence in the pediatric population following general anesthesia. The halogenated agents, sevoflurane and desflurane, used during general anesthesia have been linked with the increased occurrences of emergence agitation in children. This phenomenon impacts children by rendering them inexpressible, irritable, uncooperative, crying, and incoherent. In addition, many of these children are unable to recognize familiar people and objects which leads to further paranoid ideations. Although its effects are short-lived, it can result in harm or injury to the child.

As anesthesia care providers, the goal is to provide comfort and safety to all patients. The use of propofol in the pediatric population has shown promise in the reduction of emergence agitation. Propofol is a short acting sedative that is administered intravenously and produces a rapid loss of consciousness, along with a quick recovery. Propofol has many advantages and is vastly used in the anesthesia world. It can safely be given as an infusion or a single bolus perioperatively and has been widely studied for the prophylactic treatment of decreasing emergence agitation.

**Purpose:** The purpose of this independent project is to present a case study and perform an inclusive review of current evidence-based practice on the usage of propofol in the pediatric population undergoing general anesthesia as it relates to the decline in emergence agitation.

**Process:** A literature review was accomplished by searching the Cochrane Library, PubMed, and CINAHL databases. All were accessed via the School of Medicine and Health Science Library at the University of North Dakota. In addition, more articles were discovered by manually
searching the reference lists of the initially obtained articles. Each of the articles reviewed was evaluated for quality by using the Hierarchy of Evidence for Intervention Studies.

**Results:** The literature evaluated showed promise that the administration of adjunctive propofol at the end of inhalational general anesthesia in children reduced the incidence and severity of emergence agitation. Other multi-modal interventions should be added to the plan of care such as, pain control and anxiety reduction, in combination of propofol administration. Due to heterogeneity between studies, future research with more condensed evidence is needed to determine an effective and appropriate dose of propofol.

**Implications:** Propofol is a safe and effective sedative used throughout the anesthesia world, it has been widely studied for the prophylactic treatment of decreasing emergence agitation. The reduction in emergence agitation would lead to better patient outcomes, higher parental satisfaction scores and decreased healthcare costs.

**Keywords:** Children, pediatrics, propofol, emergence delirium, emergence agitation, and general anesthesia.
Propofol Administration for the Prevention of Emergence Agitation in Pediatric Anesthesia

Emergence agitation is a common phenomenon that occurs in pediatric patients post-operatively after general anesthesia. It was first defined in the early 1960s as a behavioral disorder that was characterized by restlessness, agitation, crying, moaning, incoherence, and disorientation, that occurred immediately during the recovery period (Jiang, Liu, Li, Ji & Liang, 2015). Although these behavioral changes are self-limiting, many complications can happen within this short time frame including harm to self or others, accidental removal of drains or dressings, surgical disruption and parental stress (Kim, Moon, Kim, & Lee, 2012). The cause of emergence agitation is not clearly understood, but some hypotheses are thought to be related to the volatile agents sevoflurane and desflurane, rapid emergence, post-operative pain, noisy environments, surgery type, pre-operative anxiety, type of induction, child temperament and personality, age, and adjunct medications (Nagelhout & Elisha, 2018).

In children, the overall occurrence of emergence agitation ranges from 10% to 80% (Nagelhout & Elisha, 2018). Key, Rich, DeCristofaro, & Collins (2010) explained that over the last few decades, there has been a positive relationship noted between the use of sevoflurane and desflurane and the incidence of emergence delirium. These newer agents have a lower blood-gas solubility which allows for a quicker awakening time. Unfortunately, sevoflurane is the halogenated agent of choice within the pediatric population due to its fast onset and decreased pungency (Key et al., 2010).

Costi et al. (2014) discussed different interventions suggested to decrease the likelihood and severity of emergence agitation which includes giving sedative agents at induction or right before emergence and using a total intravenous anesthesia (TIVA) technique. Propofol, dexmedetomidine, clonidine, fentanyl, and ketamine have all shown to decrease the rate of
emergence agitation (Costi et al., 2014). Since propofol can be safely administered perioperatively, it has been widely studied for the prophylactic treatment of decreasing emergence agitation. Along with its multiple usages, propofol is cost effective and readily available in most surgical centers and hospitals around the country (Hoff, O’Neill, Cohen, & Collins, 2015).

Propofol is a 2, 6-diisopropyl phenol which exerts its effect on the gamma-aminobutyric acid (GABA) receptor. Propofol directly stimulates these receptors, actively allowing chloride ions to move through the ligand gated channels which results in hyperpolarization and inhibition of neuronal cell excitation (Nagelhout & Elisha, 2018). It is administered intravenously and produces a rapid loss of consciousness, along with a quick recovery. Propofol has many advantages and is vastly used in the anesthesia world. With this being said, a literature search on propofol related to emergence delirium in pediatric patients undergoing general anesthesia could lead to improved patient outcomes and support changes in clinical practice.

**Purpose**

The purpose of this independent project is to present a case report of a pediatric patient that was successfully given a prophylactic dose of propofol at the end of general anesthesia without noting any adverse reactions. This paper will also include a comprehensive review of current evidence-based literature that will inform the anesthesia provider of propofol usage in the pediatric population undergoing general anesthesia as it relates to the decline in emergence agitation. Reduction in emergence agitation rates results in higher satisfaction scores in patients, parents, and nursing staff, potential cost savings, and lower incidences of patient injury.
**Case Report**

A 4-year-old female, 21.9 kilograms (kg), 118 centimeters (cm) presented for dental restorations with multiple dental caries. Past medical history was negative. Anesthesia history included bilateral ear pressure equalization tube insertions with no complications. No family history of anesthetic problems. She had a medication allergy to amoxicillin. Current medication list included a pediatric multi-vitamin. The patient had been NPO for over 8 hours. No labs were ordered or drawn pre-operatively. She was classified as an ASA one according to the American Society of Anesthesiologists (ASA) system.

An airway assessment of this patient revealed a Mallampati class I, a thyromental distance of greater than three fingerbreadths, and full neck range of motion. Preoperative vital signs were blood pressure of 97/59 mmHg, heart rate of 79 beats per minute, respiratory rate of 20 breaths per minute, temperature of 36.6 degrees Celsius, and oxygen saturation (SpO2) of 99% on room air. Physical assessment included, clear, bilateral breath sounds and normal S1 and S2 heart sounds with a regular rate and rhythm.

After the preoperative assessment, the child was brought to the operating room (OR) on a cart. The OR staff helped the child on to the operating table. At this time, a pulse oximeter monitor, blood pressure cuff and a three-lead electrocardiogram (EKG) was placed prior to induction. Current vitals were blood pressure of 102/55 mmHg, heart rate of 88 beats per minute, respiratory rate of 22 breaths per minute, and SpO2 of 100% on room air. An inhalational induction was performed with a 5 liter (L) nitrous oxide and 3L oxygen mixture with sevoflurane slowly being titrated to effect. Once the patient was sedated, a 22-gauge intravenous (IV) catheter was placed in the left upper forearm and secured with tape and gauze dressing. Fluids were initiated after buretrol tubing was primed with Lactated Ringer and connected to the IV
catheter. The eyelids were carefully taped after a loss of eyelash reflex. Soon after, the patient was given 20 micrograms (mcg) of fentanyl IV, 40 milligrams (mg) of propofol IV, and one spray of 0.25% Neo-Synephrine to the right nare. A 5.0 nasal RAE endotracheal (ET) tube was placed into the right nare and advanced through the nasopharynx, into the oropharynx. With the use of a Magill’s forceps and MAC 2 blade, the ET tube was inserted through the vocal cords and into the trachea without difficulty. Confirmation of tube placement was determined by clear, bilateral breath sounds and positive end-tidal CO2 (ETCO2). Anesthesia was maintained with an expired concentration of sevoflurane 2.8% in an O2 0.6 L/min and air 0.4 L/min mixture. Spontaneous respirations and adequate oxygenation were maintained throughout the case. The patient required an additional 10 mcg of IV Fentanyl about 15 minutes into the procedure due to an increase in respirations. Prior to emergence, the patient was given 3mg IV Zofran and 4 mg IV Decadron for anti-emetic properties. In addition, a 22mg IV bolus of propofol was given 3 minutes prior to removing the ET tube with no adverse effects noted. After an oral airway was placed, the ET tube was removed from the trachea. An oxygen mask was placed by the patient’s face with an O2 concentration of 100%. Once stabilized, she was transferred to a cart and brought to the post-anesthesia recovery unit (PACU).

In the PACU, the patient woke up calm and directable. No additional medications were needed. Vital signs remained unremarkable, and the patient was discharged from PACU and brought to her parents in the same day unit 20 minutes later.

**Literature Search**

According to Stillwell, Fineout-Overholt, Melnyk, & Williamson (2010), a PICO question must be formulated to determine the appropriate literature to review and guide the search process. Construction of a clinical question in PICO format allows for an efficient search
in a concise manner leading to a quick and enhanced process. PICO stands for population (P), intervention (I), comparison (C), and outcomes of interest (O) (Stillwell et al., 2010). The following PICO question was developed to determine if the administration of propofol can lead to decreased rates of emergence agitation. In pediatric patients undergoing general anesthesia (P), will the administration of 0.5-1mg/kg IV propofol (I), compared with holding the administration of propofol (C) prior to emergence, decrease the incidence of emergence delirium (O)?

**Databases**

Stillwell et al. (2010) recommended searching more than one database because this decreases the likelihood of missing relevant information related to the PICO question. Databases suggested, are the Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Review of Effects (DARE), PubMed, and CINAHL. The articles found in the Cochrane Library are considered the highest level of evidence because they contain systematic reviews and meta-analyses of randomized, controlled trials (Stillwell et al., 2010). For this specific literature search, the Cochrane Library, PubMed, and CINAHL were all accessed via the School of Medicine and Health Science Library at the University of North Dakota. These databases were chosen because they included medical, life science, nursing, and allied health literature pertinent to the PICO question.

**Vocabulary and Limits**

Stillwell et al. (2010) explained that it is important to use keywords and their synonyms from the PICO question while searching for evidence. The following keywords and synonyms were identified: children, pediatrics, propofol, emergence delirium, emergence agitation, and general anesthesia. Within the Cochrane Library, the terms children, propofol, emergence delirium, and general anesthesia were entered into the advanced search browser with “all text”
selected and using the Boolean connector “AND”. This produced six articles in which one was relevant to the PICO question.

Two different searches were done using PubMed. First, the MeSH database was searched for the keyword “emergence agitation”. This was a direct match to one MeSH term “emergence delirium”. Emergence delirium was selected and searched with two articles found and neither were applicable to the PICO question. Next, PubMed’s advanced search builder was utilized. The terms children, propofol, emergence delirium, and general anesthesia were entered separately using the Boolean connector “AND” with “all fields” selected. This resulted in fifty-one articles. To further narrow the results, the limits “full text,” “within ten years,” “English,” and “humans” were selected, leading to twenty-nine articles with three related to the PICO question.

Within the CINAHL database, the advanced search option was used including the Boolean phrase “AND.” The terms added in the search field were propofol, children, and emergence agitation with limitations of “full text,” “English,” and “within the last ten years.” This search resulted in three articles pertaining to the PICO question.

Additional Search Means

In addition to the prior search methods, two more articles were found by reviewing the reference lists of the four meta-analyses which had already been evaluated. Identification of the key terms proved to be more efficient than the use of controlled vocabulary within the healthcare databases for this specific literature search. In the end, a total of eight articles were found after an extensive search within the Cochrane Library, PubMed, CINAHL, and reference lists of the systematic reviews and meta-analyses.
Grading of Evidence

The Hierarchy of Evidence for Intervention Studies that was developed by Melnyk & Fineout-Overholt (2011) was utilized to evaluate the articles reviewed for this literature search. Melnyk & Fineout-Overholt (2011) developed a rating and hierarchies’ system that grades the strength and quality of evidence which includes quantitative, qualitative, descriptive, and expert opinion studies. The Hierarchy of Evidence for Intervention Studies categorizes evidence from strongest to weakest, ranging from level I to VII. Level I is the highest rank in evidence which is comprised of systematic reviews and meta-analyses of randomized controlled studies, whereas level VII is the lowest level and includes expert opinions. All eight of the articles used in this literature review are categorized as level I (systematic reviews and meta-analyses) and level II (Randomized Control Trials) which are considered the strongest level of evidence within this hierarchy system.

Review of Literature

To appropriately evaluate the literature regarding emergence agitation and the administration of propofol in children, it would be imperative to comprehend the physiochemical properties, pharmacokinetics, and pharmacodynamics that propofol possesses. Likewise, understanding the pathophysiology of delirium and the concepts of emergence agitation and how it affects children will aid in the evaluation. In the upcoming section, these topics will be discussed followed by a review on the current literature related to the administration of propofol in the pediatric population associated with declining rates and severity of emergence agitation.

Delirium

The exact pathophysiology of pediatric delirium is unknown and complex, but a few pathways are suspected resulting from a combination of factors. Patel, Bell & Traube (2017)
highlighted three possible hypotheses that are thought to play an important role in pediatric delirium: the neuroinflammatory hypothesis, neurotransmitter hypothesis, and oxidative hypothesis.

The neuroinflammatory hypothesis proposes that the production of inflammatory mediators (cytokines and leukocytes) that occur in times of stress or acute illness in the combination of a compromised blood brain barrier plays a role in the development of delirium in children (Patel et al., 2017). The decreased integrity of the blood brain barrier allows for the passage of cytokines and leukocytes into the central nervous system, eventually leading to ischemia and apoptosis of neuronal cells. The damage to these cells leads to cognitive impairment (Patel et al., 2017).

The neurotransmitter hypothesis suggests that impaired cholinergic function, excess dopamine, and dysregulation of melatonin, glutamate, norepinephrine, serotonin, histamine, and GABA may be contributing factors in the development of delirium (Patel et al., 2017). Specifically, children are dependent on the cholinergic system as it controls attention and orientation. Past studies have shown delirium often follows the administration of certain medications such as anticholinergics that can impair these neurotransmitter functions (Patel et al., 2017).

The oxidative stress hypothesis implies that hypoxia is a determining factor in the development of delirium. Reactive oxygen species are produced when oxygen delivery is decreased initiating the development of central nervous system dysfunction (Patel et al., 2017). Patel et al. (2017) also discussed that hypoxia leads to increased dopamine levels because catechol-o-methyl transferase is inhibited. Catechol-o-methyl transferase is oxygen dependent
and is involved in the conversion of dopamine to norepinephrine. Evidence in the literature indicates excess dopamine levels are linked to hyperactive delirium (Patel et al., 2017).

In the end, all the hypotheses discussed above result in altered neurotransmission. Changes in these pathways will result in integration and process failure of the central nervous system, ultimately leading to behavioral and emotional changes, reduced awareness and mental confusion (Patel et al., 2017).

**Emergence Agitation**

Emergence agitation is a common condition occurring in children emerging from general inhalational anesthesia that was first described in the 1960s (Nagelhout & Elishia, 2018). This phenomenon can be seen in all ages but most frequently occurs in young children, ages 3 to 7 years old, because of their inability to reorient upon awakening (Whitman, 2018). It is defined as “a mental disturbance during the recovery from general anesthesia consisting of hallucination, delusions, and confusion manifested by moaning, restlessness, involuntary physical activity, and thrashing about in bed” (Sikich & Lerman, 2004, p. 1138). The overall occurrence of emergence agitation ranges from 10% to 80% (Nagelhout & Elisha, 2018). Behavioral changes linked with emergence agitation not only impacts children negatively but also the parents and providers taking care of the child (Whitman, 2018). Common injuries and psychological effects to the child include harm to self or others, accidental removal of drains or dressings, surgical disruption, hematoma formation, infection, nightmares, separation anxiety, eating problems and increased fear of physicians (Kim et al., 2012; Whitman, 2018). Financial burdens become a concern as well. According to Faulk et al., (2010) extra staff is required to care for patients experiencing emergence agitation and the average length of time spent with these patients was greater leading to additional costs for the hospital.
Identifying and distinguishing emergence agitation from pain can be difficult (Mason, 2017). Key et al. (2010) indicated that there are 18 different scales that have been used to assess emergence agitation in children but not all are validated. In recent years, the Pediatric Anesthesia Emergence Delirium (PAED) scale has become the leading validated scale used in emergence agitation research (Key et al., 2010). The PAED scale was developed by Sikich and Lerman (2004) to measure the presence of emergence agitation. It is a four-point scale to measure five different behaviors - eye contact, purposeful actions, awareness, restlessness, and inconsolability. Each item is scored from 0 to 4 with reverse scoring in the restlessness and inconsolability categories. Scores are then totaled and if the score is 10 or greater it indicates the presence of emergence agitation. Although this scale is most commonly used, drawbacks include subjectivity of the assessor, high false-positive rates, and difficulty distinguishing between behaviors of emergence agitation and other negative postoperative outcomes such as pain (Mason, 2017).

The exact cause of emergence agitation is not clearly understood, but some hypothesize it is related to the volatile agents such as sevoflurane and desflurane, time to awakening, postoperative pain, noisy environments, surgery type, pre-operative anxiety, type of induction, child temperament and personality, age, and adjunct medications (Nagelhout & Elisha, 2018). As stated above, children between the ages of 3 and 7 tend to be most vulnerable with boys experiencing emergence agitation more than girls at 2:1 ratio (Whitman, 2018). Emergence agitation was originally recognized with the use of cyclopropane and ether but has become more prevalent over the last 30 years after the development of modern inhalational agents (Mason, 2017). Nagelhout & Elishia (2018) explained that sevoflurane is commonly used for the induction of general anesthesia within this age group because it produces a rapid induction and emergence, along with a decrease in airway irritation. Because of their high pungency, both
Propofol and Emergence Agitation

Isoflurane and desflurane are not recommended for induction but can safely be administered following initiation of general anesthesia. These newer halogenated agents have low blood-gas solubility, causing quicker awaking times, making the child more susceptible to emergence agitation (Nagelhout & Elishia, 2018).

Other factors associated with emergence agitation are pain, preoperative anxiety, and baseline child temperament. Although pain reduction does not eliminate emergence agitation completely, the literature shows a correlation between the two (Key et al., 2010; Makkar, Bhatia, Bala, Dwivedi, & Singh 2016). Preoperative anxiety and temperament prove to be indications on whether a child will experience post-operative behavioral problems. Interventions such as medication adjuncts, providing a quiet environment, music therapy, allowing loved ones to accompany the child to the OR, and bringing familiar objects from home should be initiated for calming measures with the aim of stress reduction (Key et al., 2010). Anesthetic techniques and medications can be tailored appropriately if one acknowledges these pre-existing conditions are linked to the prediction of emergence agitation (Mason, 2017).

**Propofol**

Propofol is a 2, 6-diisopropyl phenol which exerts its effect on the GABA(a) receptor and inhibitory GABA neurotransmitter (Key et al., 2010). Propofol directly stimulates the GABA receptors by decreasing the rate of dissociation of the GABA neurotransmitter from the receptor (Flood, Rathmell, & Shafer, 2015). By doing this, the ligand gates remain open, actively allowing chloride ions to move through the channels which results in hyperpolarization and inhibition of neuronal cell excitation (Nagelhout & Elisha, 2018). It is administered intravenously with a fast on-set and short duration of action, and recovery is normally characterized as a calm and euphoric state (Jiang et al., 2015). This is a highly lipophilic and
insoluble agent that requires a lipid vehicle for emulsification. Flood et al. (2015) explained that the major metabolic pathway of propofol is through the hepatic oxidative cytochrome P450 enzyme. The benzene ring of propofol undergoes hydroxylation by CP450 forming the metabolite 4-hydroxypropofol. This metabolite, which has one-third the activity of propofol, is glucuronidated or sulfated and forms the glucuronide and sulphate conjugates. These conjugates are mainly eliminated by the kidneys.

Propofol is a sedative that is vastly used throughout the anesthesia world, including inpatient and outpatient procedures (Hoff et al., 2015). Multiple usages of propofol include induction of anesthesia, maintenance of anesthesia, short-term sedation for intensive care patients, antiemetic effects, antipruritic effects, anticonvulsant activity, and decreasing bronchoconstriction (Flood et al., 2015). Relatively, it is safe to use, but some side effects include possible delayed awaking, hypotension, bradycardia, apnea, the risk of infection, and pain on injection (Hoff et al. 2015). Because propofol is cost effective, safe to use and has multiple indications, it has been studied for the prophylactic treatment of decreasing emergence agitation in pediatric patients with promising results.

**Propofol for Emergence Agitation in Children**

There is a substantial amount of evidence that supports the use of low dose propofol at the end of general inhalational anesthesia to decrease the incidence and severity of emergence agitation in children (Abu-Shahwan, 2008, 2013; Aouad et al., 2007, Costi et al., 2014; Jiang et al., 2015; Hoff et al., 2015; Key et al., 2010; Kim et al., 2012; Makkar et al., 2016). Although heterogeneity was found in three of the level I studies (Costi et al., 2014; Jiang et al., 2015; Hoff et al., 2015), they still indicated that propofol would be reasonable and safe to add as an adjunct medication in children undergoing general anesthesia. Costi et al. (2014) specifically noted that
other multi-modal interventions should be considered such as pain control and anxiety reduction in combination of propofol administration to further decrease the risk of emergence agitation.

Kim et al. (2012) preformed a randomized, double-blind study that compared the administration of propofol 1mg/kg, fentanyl 1mcg/kg or saline in pediatric patients at the end of general anesthesia. The study involved 222 children, ages ranging from 18-72 months, that were having an inguinal hernia repair under general anesthesia with sevoflurane. Exclusions included children with developmental delays, abnormal airways, reactive airway disease, psych or neuro disorders, severe agitation at induction, laryngospasm, or an inadequate caudal block. Each child was randomly assigned by an internet program to either propofol (74), fentanyl (74) or saline group (74). The agents were wrapped in foil by a person not involved in the process. Each child was blindly given the medication they were assigned to prior to emergence. In addition, every patient received a caudal block with 1.2 ml kg of 0.5% lidocaine after induction but prior to the start of the operation. After surgery, each patient was brought to PACU and cared for by two nurses and an anesthesiologist. Assessment scales used were the PAED, Aonos, and Five-Step Emergence Agitation scales. Delayed discharges, adverse events, delayed voiding, nausea and vomiting were also recorded by the anesthesiologist. Of the 265 patients assessed for the study, 205 completed the study. The PAED scores in the propofol and fentanyl group were significantly lower than the saline group (P < 0.001). Both the Aonos scale and Five-Step scale showed a decline in emergence agitation compared to the saline group. Time to awakening was longer in both the fentanyl and propofol groups and incidences of nausea and vomiting were higher in the Fentanyl group (Kim et al., 2012).

Makkar et al. (2016) preformed a randomized, double-blind study that compared the administration of dexmedetomidine 0.3 mcg/kg, propofol 1mg/kg or saline in children
undergoing an infra-umbilical surgery with a single-shot caudal block of 0.75 ml/kg 0.25% bupivacaine. Exclusions included developmental delay, neurological disease, previous general anesthesia, and allergies to the drugs being used. A total of 100 patients, ages 2 to 8, were randomly assigned into one of the three groups by a random computer-generated number table. The agents were wrapped in foil by a person not involved in the process and the children were blindly given the medication they were assigned. After surgery, once the child had resumed spontaneous respirations, they were brought to the PACU. Assessment of emergence agitation was done by the PAED scale. According to Makkar et al. (2016), “emergence agitation occurred in 9.4% of children in the dexmedetomidine group compared with 13.9% in the propofol group and 40.6% in the control group” (p. 50). A prolonged stay in the PACU was also noted in the dexmedetomidine and propofol groups, but greater in the dexmedetomidine group (Makkar et al., 2016).

Jiang et al. (2015) conducted a meta-analysis of randomized controlled trials to determine the effects of adjunct propofol in reducing the incidence of emergence agitation in the pediatric population. A comprehensive literature search was done in accordance with the Cochrane Handbook for Systematic Reviews of Interventions and found 11 randomized controlled trials with 897 children. Jiang et al. (2015) concluded that the addition of prophylactic propofol before emergence can reduce the incidence of emergence agitation after sevoflurane and desflurane anesthesia in children without prolonging the length of stay. Due to heterogeneity between studies and small sample sizes, future research with more condensed evidence was recommended to determine an effective and appropriate dose of propofol (Jiang et al., 2015).

Hoff et al. (2015) performed a systematic review and meta-analysis of randomized controlled trials following the recommendations in the Preferred Reporting Items for Systematic
Review and Meta-Analysis. The goal of this systematic review was to determine if the administration of low dose propofol prior to emergence influenced the incidence and severity of emergence agitation in children undergoing general anesthesia with inhalational agents. A total of 9 randomized controlled studies with 997 children were looked at. Hoff et al. (2015) found that heterogeneity existed between studies but implied that a single dose of 1mg/kg of propofol at the end of general inhalational anesthesia can decrease the incidence and severity of emergence agitation in children without increasing recovery time (Hoff et al., 2015).

Even though there is a considerable amount of current evidence supporting the use of prophylactic propofol in decreasing emergence agitation, future studies are recommended (Costi et al., 2014; Jiang et al., 2015; Hoff et al., 2015; Key et al., 2010; Kim et al., 2012). Some limitations noted in the literature were multiple assessment scales used to measure emergence agitation (Key et al., 2010), heterogeneity between studies (Costi et al., 2014; Jiang et al., 2015; Hoff et al., 2015), and small trials (Jiang et al., 2015). If further research is done addressing these limitations, more reliable and strengthened information would help justify the use of prophylactic propofol in the prevention and reduction of emergence agitation in children.

Discussion

The patient discussed in this case study was at an increased risk of experiencing behavioral and emotional changes, reduced awareness and mental confusion following her dental procedure due to her age and the use of sevoflurane. The patient had no past medical history, was calm and easily directable prior to initiation of anesthesia. She was recognized and selected as a potential candidate for the administration of 1 mg/kg of propofol at the end of anesthesia and prior to emergence to decrease emergence agitation postoperatively. After the propofol was administered, the patient continued to maintain spontaneous respirations and no adverse
hemodynamic issues were noted. Her stay in PACU was unremarkable. She was evaluated with PAED scale and did not show any signs of emergence agitation. Pain was adequately controlled, with no additional medications required. Total time spent in PACU was around 20 minutes. Later, she was transferred to the same day unit where her parents were waiting for her. The patient and both parents were all satisfied with the anesthesia and progression of her care.

As previously discussed, it would be important to understand the predisposing factors related to emergence agitation as prophylactic treatment could improve patient outcomes and satisfaction scores. Current literature supports the administration of 0.5-1mg/kg of propofol into anesthesia practice before emergence to reduce the chances of emergence agitation. This specific case study coincides with the current literature and shows that 1mg/kg of propofol can be safely given to a pediatric patient 3 minutes prior to extubation, thereby reducing the likelihood of emergence agitation.

Conclusion

Emergence agitation continues to be a prevalent problem encountered in pediatric cases undergoing general inhalational anesthesia. If left untreated, it can result in harm to self or others, accidental removal of drains or dressings, surgical disruption and parental/caregiver stress (Kim et al., 2012). It is our goal and oath as anesthesia providers, to deliver safe and effective care to all our patients. By incorporating a prophylactic dose (0.5-1mg/kg) of propofol into our anesthetic plan at the end of general anesthesia, we could reduce the occurrence and severity of emergence agitation in children. The reduction of emergence agitation could lead to decreased healthcare costs, better patient outcomes, and higher satisfaction rates in patients, parents, and nursing staff. It would be important to consider the addition of other multi-modal interventions such as pain control and anxiety reduction in combination of propofol administration. Although
current research supports the use of prophylactic propofol, future studies are suggested with larger sample sizes and less heterogeneity.
References


Appendix A

Propofol Administration for the Prevention of Emergence Agitation in Pediatric Anesthesia

Casey Pesch, SRNA

Complications of Emergence Agitation

- Behavioral changes are self-limiting
- Common injuries and psychological effects:
  - Harm to self or others
  - Accidental removal of drains or dressings
  - Surgical disruption
  - Hematoma formation
  - Infection
  - Parental/Caregiver stress
- Other complications:
  - Financial burdens
  - Delayed discharges

Introduction

- Emergence agitation is a common phenomenon that occurs in pediatric patients postoperatively after general anesthesia that was first described in the 1960s.
- Characteristics include:
  - Restlessness
  - Agitation
  - Crying
  - Moaning
  - Disorientation
- The exact cause of emergence agitation is not completely understood but some ideas are thought to be related to:
  - Visceral agents
  - Rapid emergence
  - Pain
  - Child temperament and personality
  - Age
  - Adjunct medications
  - Surgery type
- The overall occurrence of emergence agitation ranges from 10% to 80%.

Pathophysiology

- Emergence agitation was originally recognized with the use of cyclopropane and ether but has become more prevalent over the last 30 years after the development of modern inhalational agents.
- The halogenated agents (sevoflurane, desflurane, isoflurane) have low blood-gas solubility, causing quicker awakening times, making the child more susceptible to emergence agitation.

Propofol

- 2,6-dichlorophenol which exerts its effect on the GABA(a) receptor and inhibitory GABA neurotransmitter
  - Chloride ions cause hyperpolarization and inhibition of neuronal cell excitation
- Sedative that is vastly used throughout the anesthesia profession
  - Inpatient/Outpatient procedures for induction and maintenance of anesthesia
  - Short-term sedation in the ICU
  - Antiemetic
  - Antipruritic
  - Anticonvulsant

(Paauw, Rasmussen, & Shaber, 2015; Koef et al., 2015; Kay et al., 2016; Nagayashiki & Ehrta, 2010)
Propofol Adverse Effects

- Possible delayed awaking
- Hypotension
- Bradycardia
- Apnea
- Pain on injection
- Risk of infection

Case Information

- Dental Restorations
- 4 years old
- 118 cm
- 21.9 kg
- Female
- ASA I

Pre-operative Evaluation

- Past Medical History: Negative
- Allergies: Amoxicillin
- Surgical History: Bilateral ear pressure equalization tube insertions with no complications.
- Medications: Pediatric multi-vitamin
- No labs ordered
- Pre-op VS
  - BP: 97/59 mmHg
  - Heart rate: 79 bpm
  - RR: 20 bmp
  - Temp: 36.6 °C
  - SpO2 99% on room air
- Airway evaluation
  - Mallampati class I
  - Thyromental distance >3 fingerbreadths
  - Full neck range of motion

Anesthetic Course

- Inhalational induction- 5L nitrous oxide and 3L Oxygen mixture with sevoflurane slowly added and titrated to effect.
- 22 gauge IV was placed to left upper forearm.
- Lactated ringer started via buretrol tubing.

Anesthetic Course

- The patient required an additional 10 mcg of IV Fentanyl about 15 minutes into the procedure due to an increase in respirations
- 3mg IV Zofran and 4 mg IV Decadron was given for anti-emetic properties
- 22mg IV bolus of propofol was given 3 minutes prior to removing the ET tube
  - no adverse effects were noted
**Anesthetic Course**

- Oral airway placed
- Patient extubated deep
- Oxygen mask placed by the patient’s face with an O2 concentration of 100%
- Transferred to PACU once stabilized

**Intraoperative Issues**

- No intraoperative issues noted

**PACU**

- Vitals remained stable
  - BP 102/62
  - HR 77 bpm
  - RR 20 bpm
  - SpO2 100%
  - Temp 36.7
- Patient woke up calm and directable
- No signs of emergence agitation
- Brought to her parents in the same day unit 20 minutes later

**Propofol for Emergence Agitation in Children**

- Makkar et al. (2016) performed a randomized, double-blind study that compared the administration of dexametomidine 0.3 mcg/kg, propofol 1mg/kg or saline
  - 100 patients, ages 2 to 8
  - Infra-umbilical surgery
  - Each child was randomly assigned to either a propofol (36), dexametomidine (32) or saline group (32)
  - Emergence agitation occurred in 9.4% of children in the dexametomidine group compared with 13.9% in the propofol group and 40.6% in the control group
  - A prolonged stay in the PACU was also noted in the dexametomidine and propofol groups, but greater in the dexametomidine group

- Kim et al. (2012) performed a randomized, double-blind study that compared the administration of propofol 1 mg/kg, fentanyl 1 mcg/kg or saline in pediatric patients at the end of general anesthesia
  - 222 children, ages ranging from 18-72 months
  - Inguinal hernia repair
  - Each child was randomly assigned by an internet program to either propofol (70), fentanyl (74) or saline group (74)
  - The mean PAED scores in the propofol (4.3) and fentanyl (4.9) groups were significantly lower than the saline group (9.0).
  - Time to awakening was longer in both the fentanyl and propofol groups and incidences of nausea and vomiting were higher in the Fentanyl group

**Propofol for Emergence Agitation in Children**

- Jiang et al. (2015) conducted a meta-analysis of randomized controlled trials to determine the effects of adjunct propofol in reducing the incidence of emergence agitation in the pediatric population
  - 11 randomized controlled trials
  - 897 children
  - Concluded that the addition of prophylactic propofol before emergence can reduce the incidence of emergence agitation after sevoflurane and desflurane anesthesia in children without prolonging the length of stay
  - Future research was recommended due to heterogeneity between studies and small sample sizes
Propofol for Emergence Agitation in Children

- Hoff et al. (2015) performed a systematic review and meta-analysis of randomized controlled trials to determine if the administration of low dose propofol prior to emergence influenced the incidence and severity of emergence agitation in children undergoing general anesthesia with inhalational agents
  - 9 randomized controlled studies
  - 997 children
  - Heterogeneity existed between studies and future studies were recommended
  - Concluded that a single dose of 1mg/kg of propofol at the end of general inhalational anesthesia can decrease the incidence and severity of emergence agitation in children without increasing recovery time

Propofol for Emergence Agitation in Children

- Costi et al. (2014)
  - Systematic review
  - Propofol, halothane, alpha-2 agonists, opioids, and ketamine reduce the risk of emergence agitation
  - Other multi-modal interventions should be considered such as pain control and anxiety reduction in combination to further decrease the risk of emergence agitation
- Key et al. (2010)
  - Literature review
  - The use of propofol (TIVA or adjunctive) when combined with sevoflurane has advantages of decreasing emergence agitation in children
  - Future studies were recommended addressing limitations
    - Multiple assessment scales
    - Small sample sizes

Propofol for Emergence Agitation in Children

- Aouad et al. (2007)
  - Randomized controlled study
  - Showed that propofol as an adjunct decreased the incidence of emergence agitation to 19.5% compared to 47.2% in patients who received sevoflurane only
- Abu-Shahwan (2008)
  - Randomized double-blind study
  - In nonpainful procedures, the addition of 1 mg/kg of propofol can decrease the incidence of emergence agitation

Recommendations

- It would be safe to recommend the administration of 0.5-1 mg/kg of propofol into anesthesia practice before emergence to reduce the chances of emergence agitation
- Future studies are suggested addressing limitations
  - Larger sample sizes
  - Less heterogeneity between studies
  - Universal assessment scale
- Other multi-modal interventions should be considered such as pain control and anxiety reduction in combination of propofol administration

Conclusion

- By incorporating a prophylactic dose (0.5-1 mg/kg) of propofol into our anesthetic plan at the end of general anesthesia, we could reduce the occurrence and severity of emergence agitation in children
- This could lead to decreased healthcare costs, better patient outcomes, and higher satisfaction rates in patients, parents, and nursing staff

References

Thank You
Are There Any Questions?

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