Hypnosedative and Analgesic Drug Choice for Pediatric Procedural Sedation: a Review of Recent Literature

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Aim

Various hypno-sedative and analgesic drugs are available in the setting of pediatric procedural sedation and analgesia outside the operating room. The aim was to perform a systematic internet based literature review to investigate sedative drug choices and associated clinical outcomes in pediatric population.

Materials and Methods

A search was made in the Pubmed Database with the specific term 'pediatric procedural sedation' to find associated prospective randomized clinical trials. We analyzed the data regarding sedo-analgesic drug choices, dosages, route of administrations, type of procedure, the data regarding physicians' who manage sedation procedures, adverse events, patient demographics and outcome, and publishing characteristics include journal type and country of medical center.

Results

Fifty-nine prospective randomized controlled trial that were published between 1989-2019 was found. Eleven of them were extracted from evaluation due to incompatible characteristics. Midazolam, Propofol, Ketamine, Fentanyl, and Dexmedetomidine were the most common hypno-sedative agents that were used either alone or in various combinations. Most common route of administrations were oral and intravenous routes. There was not any drug dosage information in 4 manuscripts. Distribution and range of patient population age were too large and different particularly from classic pediatric age scale. Among 23 different invasive procedure, orthopedic interventions such as fracture bone reduction and manuplation/repositioning of joint dislocation were the most common. Sedation process were managed by anesthetists in 8 of 48 trial. There were not any information regarding airway management in 28 studies. Nausea, vomiting, apnea, hypoxia and desaturation, and hemodynamic side effects such as bradycardia, hypo/hypertension were the frequently seen adverse events. Most of the studies were published in emergency medicine and pediatric journals. United States of America was the leading country according to the research centers.

Conclusion

Hypno-sedative anesthetic medications have been used for various indications and purposes outside the operating room by different specialists other than anesthesiologists.

Keywords: *Procedural sedation, analgesia, anesthesia, children, invasive and non-invasive procedures*

Introduction

'Sedation and analgesia' allows patients to endure painful invasive/non-invasive procedures without deterioration in hemodynamic and respiratory functions while maintaining ability to respond to verbal and tactile stimulation (1). Performance of invasive and painful procedures without sedation and/or anesthesia can be not only problematic but also impossible in some

cases for clinicians, patients and their parents. The comfort and convenience that anesthesia brings is increasingly noticeable over the past twenty years.

Procedural sedation and analgesia in children has been gradually implemented outside the operating room in intensive care units, emergency and radiology departments, and medical and dental offices (2-5). According to the variability of the procedure and department, different clinicians who are not specialists in anesthesiology such as intensivists, emergency physicians, pediatricians and nurses have been taken responsibilities in the sedation process. Various different hypno-sedative and analgesic drugs are available in the setting of procedural sedation and analgesia outside the operating room. With the contribution of advanced monitoring technology, many different sedative and analgesic drug options are available to perform procedural sedation and analgesia in children.

In this research the aim was to perform a systematic internet based literature review to investigate sedative drug choices and associated clinical outcomes in pediatric population undergoing invasive and/or non-invasive procedures under sedation.

Materials and Methods

A search was made in the Pubmed Database with the specific term 'pediatric procedural sedation' to find associated prospective randomized clinical trials. The data was analyzed in terms of sedo-analgesic drug choices, dosages, route of administrations, type of procedure, the data regarding physicians' who manage sedation procedures, adverse events, patient demographics and outcome, and publishing characteristics include journal type and country of medical center. Article types other than 'randomized controlled trial' such as case reports, comments, editorials, letters, guidelines, meta-analysis, and observational studies were not evaluated.

Results

Fifty-nine prospective randomized controlled trials published between 1989-2019 were found. Eleven of them were extracted from evaluation due to incompatible characteristics such as testing the effectiveness of a new sedation scale, observation of the effect of listening music during procedure, or determining the effect of adding capnography to standard monitoring, etc and limited data regarding procedural sedation process. Midazolam, Propofol, Ketamine, Fentanyl, and Dexmedetomidine were the most common hypno-sedative agents which were used either alone (in 20 studies) or in various combinations (in 39 studies). Most common route of administrations were oral and intravenous routes and apart from these, intramuscular, intranasal, inhaler, subcutaneous, and transmucosal routes were used. Drug dosage information were given in all studies except 4 studies. Distribution and range of patient population age were too large and different particularly from classic pediatric age scale. Among 23 different invasive procedures, orthopedic interventions such as fracture bone reduction and manipulation/repositioning of joint dislocation in the pediatric emergency departments were the most common. Sedation process were managed by anesthetists in 8 of 48 trial. There was not any information regarding airway management in 28 studies. Nausea, vomiting, apnea, hypoxia and desaturation, and hemodynamic side effects such as bradycardia, hypo/hypertension were the frequently seen adverse events. Most of the studies were published in emergency medicine and pediatric journals. United States of America was the leading country according to the research centers.

Discussion

Levels of sedation/analgesia (minimal/ moderate/ deep) was defined by American Society of Anesthesiologists (ASA) according to the multiple parameters such as responsiveness of patient, requirement of any intervention to the airway, spontaneous ventilation status and

maintenance of cardiovascular functions and approved by the ASA House of Delegates in October 13, 1999 (1). Occasionally, predicting precise sedation level before sedative drug applications may be impossible due to inter-individual variation in the pharmacokinetics. Furthermore, in some cases, level of sedation becomes deeper than initially intended with lower dosages and undesirable complications such as hypotension, desaturation, and agitation can occur. In order to minimize associated risks while providing the advantages of sedation/ analgesia, there are several general principles and recommendations in practical guidelines for non-anesthesiologist clinicians particularly for moderate/ deep sedation.

Appropriate preprocedural patient evaluation and preparation is a well-accepted clinical practice for anesthesiologists. Although there is insufficient data to evaluate the impact of this practice on outcomes in procedural sedation, it is strongly recommended particularly in patients having special medical conditions such as extremes of age, ASA status III or higher, obstructive sleep apnea, respiratory distress syndrome, obesity, history of gastric bypass surgery, and cardiovascular disorders (6-8). ASA physical status classification system and preprocedural evaluation was mentioned in 23 of 59 studies and in all 8 studies conducted by anesthesiologists.

The pediatric population is divided into subcategories (preterm newborns, term newborns, infants, toddlers, children and adolescents) and the dose is selected according to a child's age. It was proven that categorizing dosing regimens by age ranges creates an artificial discontinuity in the dose–exposure relationship across each age group (9). Compared with adults, neonates and infants frequently require reduced hypno-sedative drug doses while children require increased doses in relation to their body weight (10). There was a large variability among 59 studies regarding age ranges and age groups. We found 41 miscellaneous age ranges in 59 studies that differ from classical pediatric age scale and in 8 studies newborn infants were evaluated with children. Furthermore, in 1 study children were evaluated with adults and the age range was varried from 1 month to 28 years (11). We found only 3 studies that the sedative drug dosages were given gradually variable according to age groups (12-14).

Detection of adverse systemic drug reactions with the help of using modern monitoring technology is crucial to avoid the complications associated with moderate/deep sedation and analgesia such as cardiovascular decompensation and cerebral hypoxia. Monitoring level of consciousness, ventilation and oxygenation with capnography and pulse oximetry, hemodynamic parameters such as blood pressure, heart rate, and electrocardiography and recording of these monitoring parameters were strongly recommended (15). We found that the data regarding cardiorespiratory monitoring was not presented in 7 studies and monitoring level of consciousness via BIS (Bispectral index) was reported only in 1 study (16). Unfortunately, we couldn't find any information regarding usage of continuous end-tidal carbon dioxide monitoring which is a useful adjunct in reducing the frequency of hypoxemic events during moderate/deep procedural sedation.

Lack of personnel experienced in airway management or advanced life support, or unfamiliarity with medications being administered for sedation and analgesia was accepted as an absolute contraindication (17). In 13 studies there was lack of information regarding the identity of personnel who conducted the sedation process. In the rest of 52 studies common liable consultants were pediatricians, anesthesiologists, and emergency physicians in 17, 8, and 4 studies, respectively. In most of the studies there was uncertainty regarding the qualification of clinicians who were responsible in sedation process.

Using supplemental oxygen during procedures with sedation was reported to be beneficial in reducing the rate of hypoxemia (18). Although there was satisfying information related to airway management and routine oxygen support in 14 studies, in some studies there was lack of information despite an airway and/or pulmonary complication.

Although recent studies suggest that pediatric procedural sedations performed outside of the operating room are safe and unlikely to yield serious adverse events, hypno-sedative drugs and

opioids have broad side effect potential (19,20). Nausea, vomiting, desaturation, and hypotension were the common reported adverse events. Central nervous system adverse effects such as hallucinations, dizziness, nightmares, agitation and dysmorphic emergence occurred more frequently with ketamine usage. In 9 studies no adverse events and side effects were reported. There wasn't any reported serious and/or life-threatening adverse event in all studies.

Conclusion

Hypno-sedative anesthetic medications have been used for various indications and purposes outside the operating room by different specialists other than anesthesiologists. We believe that published guidelines are important tools to increase effectiveness and quality of procedural sedation while reducing the likelihood of adverse effects.

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