

Clinical evaluation of intravenous sedation in pediatric endoscopic procedures: A retrospective observational study

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ABSTRACT

Objective: The main benefits of sedation are to reduce the patient's anxiety and discomfort, to improve their tolerability. The aim of study was evaluate intravenous sedation for pediatric gastrointestinal endoscopic procedures

Materials and Methods: We analyzed patients' data, who underwent gastrointestinal endoscopic procedures in our pediatric endoscopy unit, retrospectively. All gastrointestinal endoscopic procedures were performed by a pediatric gastroenterologist and sedations were managed by an anaesthesia team, including two staff anesthesiologists.

Results: During the study period, 530 gastrointestinal endoscopic procedures were performed. 461 (87%) were esophagogastroduodenoscopy, 56 (10.6%) were both esophagogastroduodenoscopy and colonoscopy and 13 (2.5%) were percutaneous endoscopic gastrostomy. Propofol was given all of the patients either as a single drug (6 patients, 1%) or in combinations (77.4% with midazolam; 12.3% with ketamine and 9.2% with fentanyl). Overall adverse event rate due to sedation was 19.6%, but no serious side effects were documented. The most frequent side effects were injection pain (10.4%), and nausea (7.5%). Allergic reactions were experienced in 1.3% patients and resolved with methylprednisolone and antihistaminic medications. Respiratory depression was observed in only two girls (3 and 17 years old) and did not need advanced interventions to control the problem. Seven patients' gastroscopies were interrupted by gastroenterologist due to gastric content in order to prevent vomiting and aspiration.

Conclusions: Intravenous sedation for pediatric gastrointestinal endoscopic procedures can be applied safely and successfully with a trained team and organized endoscopy unit.

Keywords: child, anaesthesia, intravenous agents, sedation, endoscopic procedures

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INTRODUCTION

Anesthesia procedures outside the operating room have increased as a result of increasing number and kind of procedures in the other fields of the medicine. Sedation is often used during gastrointestinal endoscopic procedures (GEP) for the diagnosis and management of the patients. The main targets of sedation are to reduce the patients' anxiety and discomfort, to improve their tolerability. Additionally, in children it is important to modify behavior to provide immobility to allow the safe completion of the procedure.

Different combinations of medications have been used for pediatric sedation including propofol, ketamine, midazolam, fentanyl, and pethidine (1). In our pediatric endoscopy unit, midazolam, ketamine, propofol and fentanyl have been used as alone or in combinations. In this study, we aimed to evaluate our intravenous sedation (IVS) administrations for pediatric GEP and based on these evaluations, to discuss the issue in the light of current literature.

MATERIAL and METHODS

This is a retrospective observational study. This study was approved by the institutional non-invasive clinical research ethics committee (Approval Date and Number: 26.06.2019, 2011-KAEK-25 2019/06-04). Informed consent was obtained from the parents of all children prior to endoscopy, and the study was conducted according to the tenets of the Declaration of Helsinki.

Patients

A total of 530 pediatric patients, given IVS, between 1.10.2018 and 1.6.2019 were included in the study. Patients' data were collected from anaesthesia records and hospitals software database. Patients' age, gender, American Society of Anesthesiologists (ASA) status, type of procedure, anaesthesia time, procedural time, recovery time, medications were recorded. Adverse events were also recorded from anaesthesia complication charts, including respiratory depression (defined as SpO₂ <90%), allergic reactions, injection pain, nausea and vomiting. Serious adverse event means that a deep sedation not easily treated with basic interventions, causes hypoventilation, laryngospasm, pulmonary aspiration, and needs to antidotes or endotracheal intubation.

Anaesthetic procedures

According to routine operating procedures in our clinic anaesthetic procedures were managed by two anaesthesiologists. Patients were evaluated for the risks of anaesthesia before any procedural intervention and obtained a written consent from patients and/or parents. In elective cases patients and/or parents informed about gastric emptying time, but in urgent or emergent situations where complete gastric emptying is impossible, we did not delay sedation based on fasting time alone. There was no premedication prior to the procedure.

In line with our clinical follow-up protocol, all medications were given to achieve moderate to deep sedation as defined by ASA (2). Patients monitoring included continuous electrocardiogram, heart rate and oxygen saturation. All patients received supplemental oxygen at 2 L/min via nasal cannula according to ASA recommendations. After the procedure, patients were observed and monitored by an anaesthesia nurse in the recovery room until they are near their baseline level of consciousness and no longer at cardiac risk for cardiorespiratory depression according to ASA guideline (2).

An emergency kit which contains the necessary age and size-appropriate equipment, emergent medications and antidotes of the sedation drugs for managing unintended deeper sedation, was always ready in the endoscopy unit and checked before every procedure.

Table 1. Descriptive values (*min= minutes)

Variable	Overall (n= 530)
Age (year) (mean ± SD)	10.7 ± 5.2
Gender (male-female; %)	204-326 (38.5%-61.5%)
Timing (elective-emergency; %)	506-24 (95.5%- 4.5%)
ASA physical status (I, II, III, IV; %)	437, 83, 9, 1 (82.5, 15.7, 1.7, 0.2 %)
Duration of procedure (min*)	15.89± 6.7
Duration of recovery (min*)	21.01± 2.7

Statistical analyses

Statistical analyses were conducted with SPSS 22.0 (IBM Corporation, Armonk, New York, United States). Results with variable data were expressed as mean ± SD. Results with categorical data were expressed as percentage (%).

RESULTS

Out of 530 children underwent GEP with IVS, 326 (61.51%) were girls and 204 (38.49%) were boys. Patients' descriptive values were listed in (Table 1).

There were three main endoscopic procedure types: 461 (86.98%) patients underwent esophagogastroduodenoscopy (EGD), 56 (10.57%) both EGD and colonoscopy, and 13 (2.45%) percutaneous endoscopic gastrostomy (PEG).

Propofol, midazolam, ketamine, fentanyl and their combinations were used for sedation. Propofol was the main agent and used in all patients: Except six (1.13%) patients, propofol was used in combination with another drug. For 410 (77.35%) patients, midazolam was added to propofol, 65 (12.26%) ketamine, 49 (9.24%) fentanyl.

As for the side effects, only two (3 and 17 years old girls) patients, represented respiratory depression (0.37% of all patients) were given propofol plus midazolam combination. Fortunately, none of them was serious and controlled with basic intervention (encourage or physically stimulate to breathing deeply). The most frequent adverse event was injection pain (55 patients, 10.37%) and followed by nausea (40 patients, 7.54%). Allergic reactions, which were only represented with urticarial lesions, were seen in 7 (1.32%) patients. Methylprednisolone and antihistaminic medications were enough to control the situations in all cases (Table 2).

Patients were divided subgroups according to their ages, considering that age can change the side effect profile. Respiratory depression (1.36 %) was frequent in 0-3 age group. Injection pain, nausea and allergic reactions were recurring in 11-18 ages group (Table 3).

All of the procedures were completed successfully except for seven EGDs. In these seven patients, underwent EGD, the procedure was stopped due to gastric content, without any complication. Five of these seven procedures were elective, and the other two were emergent, but procedures were delayed in order to ensure gastric emptying time.

In this retrospective study, we did not find any document about other possible adverse events, like laryngospasm, hypersalivation, hemodynamic instability.

Table 2. Incidence of side effects

Side effects	n (%)
Injection pain	55 (10.37 %)
Nausea/ vomiting	40 (7.54 %)
Allergic reactions	7 (1.32%)
Respiratory depression	2 (0.37%)

Table 3. Incidence of side effects by age groups

Side effects	0-3 years old (n=73)	4-11 years old(n=170)	11-18 years old (n=287)
Injection pain	9 (12.3%)	15 (8.82%)	31 (10.80%)
Nausea/ vomiting	3 (4.10%)	16 (9.4%)	21 (7.31%)
Allergic reactions	1 (1.36%)	2 (1.17%)	4 (1.39%)
Respiratory depression	1 (1.36%)	0	1 (0.34%)

DISCUSSION

During the past 40 years pediatric GEPs have become important and effective procedures for the diagnosis and treatment of gastrointestinal tract and needed optimal sedation conditions. Especially young children can be uncooperative and tend to have psychological trauma as a result of separation from their parents and pain due to the procedure. Endoscopic sedation is intended to reduce patients' anxiety, minimize psychological trauma, maximize the potential for amnesia and improve tolerability with minimizing discomfort and pain. Of course it also provides optimal conditions for the endoscopist.

" Sedation and analgesia " comprise a continuum of states ranging from minimal sedation (anxiolysis) through general. Both American Academy of Pediatrics, American Academy of Pediatric Dentistry and ASA suggested that the practitioner must be sufficiently skilled to rescue a child with cardiorespiratory complications, a well-trained support personnel must be accompanied with him/her and must be preset in the room, as unintended level of sedation may be occurred (3,4). Studies demonstrated that, when a pediatric sedation team involving an anesthesiologist was attended, successful sedation rates were 100% and adverse events ranged 1.7-5% (5). In our hospital sedations were managed by anesthesiologists and support personals were well-trained anesthesiology nurses. Our pediatric endoscopy unit is well designed and fully equipped just in case.

To date, data are limited to have a conclusion about the best sedation regimen (6, 7, 8). Midazolam, propofol, ketamine and fentanyl are used alone or in combinations. As a first line sedative agent, midazolam is considered safe but midazolam alone often provides inadequate sedation so usually opioids or ketamine are used together (9). Midazolam also used as premedication in many anesthetic situations (10). Ketamine, a NMDA receptor antagonist, is in common use in pediatric patients as a safe and effective agent (11). Both propofol and midazolam are effective in reducing ketamine's hallucinogenic emergence reactions (12). Propofol is a rapid onset sedative-hypnotic agent and is commonly used to relieve anxiety and to sedate children who undergo therapeutic or diagnostic procedures such as cardiac catheterization, endotracheal intubation, emergency orthopedic procedures, dental procedures, and radiological imaging (13). Sunhee Kim et al. performed a systematic review and meta-analysis of randomized controlled clinical trials to evaluate propofol's safety for pediatric procedural sedation. They concluded that propofol sedation had advantages in recovery time compared with other drugs, without excessive adverse events and suggested propofol as a safe sedative for pediatric procedures as an option that is comparable to other alternatives (1).

Propofol also has antiemetic effects, explained by its interactions with the

dopaminergic and the serotonergic systems (15,16). Fentanyl is a potent lipid-soluble analgesic with sedative properties. It is often combined with propofol or midazolam to provide sedation for outpatient procedures (17). However, studies showed that propofol based sedation provides a safe sedation profile (14,18), combinations with midazolam, ketamine or fentanyl are used in order to provide effectiveness and quality (8, 19, 20, 21).

The use of more than two drugs has been identified as a risk factor, the addition of fentanyl or midazolam to propofol significantly reduced the individual dosage of drugs and minor adverse events were observed. Our retrospective analyses demonstrated that propofol is the main drug for our team to provide sedation. Safety and efficacy level of propofol alone are satisfactory and reported with rare complications. Only six patients were given propofol alone, which refers to combinations were preferable. In that context, the most popular combination drug was midazolam, which was followed by ketamine and fentanyl (22).

The incidence of respiratory problems is predominant in pediatric patients compared to cardiovascular adverse events. Apnea, laryngospasm, bradycardia, hypotension, aspiration and vomiting are also described. Younger age, higher ASA status, female sex and intravenous sedation have been reported as the main risk factors for procedural sedation (22). In our study, only two children represented respiratory depression, controlled with basic interventions, and this is account for 0.37% of the patients. Both of them have ASA III physical status and this finding is consistent with previous data.

The most frequent adverse event was injection pain, which is more likely to be with propofol injection and can be controlled with lidocaine or opioid injection before propofol (23). Unfortunately, our team did not prefer this intervention. Nausea was seen 7.54% of the patients and none of them experienced vomiting, the patients whose procedure stopped because of the gastric content, not excepting. We attributed this rare and light emesis complication to the antiemetic properties of propofol. Urticarial lesions were significantly rare and could be handled with medications. In our study, overall adverse event rate was 19.62 %. In the literature, adverse events in various rates were reported (8, 14, 24, 25). Therefore, it is more important to compare serious adverse events. Amorniyotin et al. reported 0.6% serious adverse effects in a cohort study (24). Also, in a study performed by Barbi et al., desaturation was 3%, and major desaturation was 0.7% (25).

Although we used pulse oximetry, it is not sufficient enough to detect the respiratory complications for sedation (5). End-tidal carbon dioxide may be used for early detection of hypoventilation and apnea, but it was not an opportunity for our team. We believe that close clinical monitoring of the breathing pattern is the best way to detect such complications.

In our clinical practice all patients were ordered according to ASA practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration (2). Nevertheless, in seven patients, gastroenterologist saw gastric content during endoscopy and then stopped procedure, in order to prevent vomiting and aspiration. This finding indicates that one should be careful about gastric residual volume, even if preoperative fasting period is over. Pre-procedural gastric ultrasonography may be suggested as a solution. Fortunately, these patients did not experienced vomiting, the procedure ended without any complication.

The results of the publications, described the use of propofol for paediatric sedation by providers other than anesthesiologists are contradictory, due to definition differences, especially (26, 27, 28). For example, Wehrmann and Riphaut(27) showed lower incidence of adverse events, but they restricted the definition of adverse events, bag-mask ventilation, intubation and intensive care administration. In this study, definitions of adverse events are undisputably more delicate. Although propofol was administered by specially trained pediatricians, Barbi E et al. (28) pointed out that, constant and immediate availability of anesthesiological support continues to be mandatory. The work of Amornyotin S et al. (24) also high lightened that pediatric GEP procedures could be safely and effectively performed with anesthesiologist and basic monitoring.

The limitations of the present study were as become a retrospective study and there were some data collection deficiencies because of improper chart documentations for example, it was not possible to obtain the total drug doses from the records. Drugs were given with titration to achieve the target sedation level. In addition, as a consequence of our clinical practice, in which, one member of the team continuously palpate radial pulse and observe the patients' respiratory pattern, the data did not contain blood pressure, so we could not demonstrate hypo/ hypertension.

CONCLUSIONS

In conclusion, although we used different combinations, propofol and fentanyl became more favorable regimen and IVS for pediatric GEP can be applied safely and successfully by the well- trained team with an anesthesiologist and a well-designed, fully- equipped endoscopy unit.

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Ethical approval: This is a retrospective observational study. This study was approved by the institutional non-invasive clinical research ethics committee (Approval Date and Number: 26.06.2019, 2011-KAEK-25 2019/06-04). Informed consent was obtained from the parents of all children prior to endoscopy, and the study was conducted according to the tenets of the Declaration of Helsinki.

Conflict of interest: Nondeclared.

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