



A Comparative Study of the Effect of Midazolam-Ketamine and Midazolam-Propofol in Children 1 to 10 years old

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A Comparative Study of the Effect of Midazolam-Ketamine and Midazolam-Propofol in Children 1 to 10 years old

Anahid Maleki *¹, Ebrahim Spahbodi¹, Ali Reza Ebrahim Soltani¹ Abbas Ostad Alipour¹, Mehrdad Goudarzi¹Alireza Takazare¹

1. Tehran University of Medical Sciences- Children's Medical Center Hospital, A-Maleki@tums.ac.ir

ABSTRACT

Objective: The aim of this study was to evaluate the effect of midazolam-ketamine and midazolam-propofol in children aged 1 to 10 years under endoscopy.

Materials and Methods: This cross-sectional study was performed on 60 children aged 1 to 10 years old who were non-emergency candidates for upper gastrointestinal tracheal endoscopy who referred to the pediatric medical center hospital. The samples were randomly divided in quadruple blocks into two groups of midazolam-ketamine and midazolam-propofol. Both groups were injected 0.05 mg / kg of midazolam and group one received 2 mg / kg of ketamine and the second group received 2mg / kg of propofol and oxygen was administered to the patient. Age, sex, weight of referral time, duration of patient's stay in recovery, mean endoscopic time, respiratory state based on saturation, gagging condition and presence of nausea and vomiting, recovery time after endoscopy, until complete waking, apnea, laryngospasm and insufficiency level of anesthesia was recorded by a third person on the checklist. Data were analyzed using SPSS version 20 and Chi-square and independent t-test.

Results: The mean age, mean endoscopy duration in minutes, mean of weight, frequency of sex, gag reflux rate, and incidence of insufficiency anaesthesia in two groups were not significantly different. But the average recovery time in minutes was significantly different in the two groups. The incidence of nausea and vomiting in the midazolam-ketamine group (33.3%) was more than midazolam-propofol (10%) ($P = 0.05$). The incidence of apnea in the midazolam-ketamine (0%) group was less than midazolam-propofol (23.3%) ($P = 0.005$). The incidence of laryngospasm was negative in all patients. The incidence of o_2Sat less than 90 in the midazolam-ketamine (3.3%) group was less than midazolam-propofol group (23.3%) ($P = 0.02$).

Conclusion: Pain and restlessness during children's endoscopy necessitate the use of medication for sedation during endoscopy.

Keywords: children, children one to ten, endoscopy, propofol, ketamine, midazolam



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1. INTRODUCTION

The use of upper gastrointestinal endoscopy (UGE) has been increasingly used to diagnose and treat children. Unlike adults, children need a deep relaxation (1). Various drug interventions, such as the use of propofol, ketamine, clonidine, and narcotics, are used effectively to soothe children, and benzodiazepines and narcotics are most commonly used (1-5). But with the presence of an anesthetist, a different drug regime can be used, including hypnosis. But these drugs include complications such as delayed waking up from anesthesia, excessive sleepiness, and other complications such as nausea and vomiting and hemodynamic disorders that limit the use of these drugs. Given that endoscopy and outpatient surgeries are being performed today without general anesthetic and using certain medications, there is evidence of restlessness during the above operations (surgeries) that occurs in many children and is raised as a common complaint by the doctor (physician) during endoscopy. Pain and restlessness during children's endoscopy necessitate the use of medication for endoscopic analgesia. Several drugs have been used to reduce the pain and restlessness of patients during endoscopy. Ketamine is one of the oldest medications for sedation outside the operating room, which is also valuable for maintaining a patient's breathing, but problems such as spasm and airway and movements during endoscopy and unpleasant feelings after anesthesia are its problems. Therefore, other endoscopic drugs are used to provide both immobility and calm for the patient, and because of low side effects the patient has appropriate cooperation during endoscopy and have a short recovery (6-11). In this study, the effect of two sedation methods and two drugs of propofol-midazolam and ketamine-midazolam on sedation in the upper gastrointestinal endoscopy were studied.

2. MATERIALS AND METHODS

This cross-sectional study was performed on 60 children aged 1 to 10 years old who were candidates for non-emergency upper gastrointestinal tracheal endoscopy who referred to the pediatric center (pediatric medical center hospital). The sample size was determined using the sample size formula for both groups and the previous study. This study was registered with the Code of Ethics and compliance with the Helsinki Treaty was observed for all patients. Before the start of the study, the goal of the study was described for the parents of the patient children and an implied consent was received from them and



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patients whose parents did not agree were excluded. The samples were randomly divided in quadruple blocks into two groups of midazolam-ketamine and midazolam-propofol. Both groups were injected 0.05 mg / kg of midazolam and group one received 2 mg / kg of ketamine and the second group received 2mg / kg of propofol and oxygen was administered to the patient. Age, sex, weight of referral time, duration of patient's stay in recovery, mean endoscopic time, respiratory state based on saturation, gagging condition and presence of nausea and vomiting, recovery time after endoscopy, until complete waking, apnea, laryngospasm and insufficiency level of anesthesia was recorded by a third person on the checklist. Data were analyzed using SPSS version 20 and Chi-square and independent t-test.

3. FINDINGS

The sex frequency in the group of midazolam-ketamine was 12 girls (40%) and 18 boys (60%) and in the midazolam-propofol group 14 girls (46.67%) and 16 boys (53.33%) and there was no significant difference in terms of gender in two groups ($p = 0.8$). The mean (SD) age in the midazolam-ketamine group was 5.3 (2.645) years and in the midazolam-propofol group 4.9 (2.474) years, there was no significant difference in mean age in the two groups ($p = 0.6$). The mean (SD) of the endoscopy time in minutes was 7.5 (3.58) in the group of midazolam-ketamine and in the midazolam-propofol group was 7.6 (3.486) in terms of minutes and there was no significant difference in mean endoscopy duration per minute in both groups ($p = 0.9$). Mean (SD) of recovery time after endoscopy end to full awakening in the midazolam-propofol group was 30.1 (1515) minutes and in midazolam-ketamine group 46.3 (12.21) minutes, and there was no significant difference in the mean recovery time after endoscopy end to full awakening in minutes in two groups ($p = 0.03$).

The mean (SD) of the weight in the midazolam-ketamine group was 19.1 kg (6.386) and in the midazolam-propofol group 17.1 (5.750) and there was no significant difference in mean weight in the two groups ($p = 0.2$). There were no significant differences in terms of gag reflexes between the two groups ($P = 0.3$) (Fig. 1). The incidence of nausea and vomiting in the midazolam-ketamine (33.3%) group was significantly more than midazolam-propofol (10%) ($P = 0.05$) (Figure 2). The incidence of apnea in the midazolam-ketamine (0%) group was significantly less than midazolam-propofol



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(23.3%) ($P = 0.005$) (Figure 3). The incidence of laryngospasm was negative in all patients. The incidence of insufficiency anaesthesia in the midazolam-ketamine (10%) group was not significantly different with midazolam-propofol (13.3%) ($P = 0.6$) (Figure 4). The incidence of o_2Sat less than 90 in the midazolam-ketamine group (3.3%) was less than midazolam-propofol group (23.3%) ($P = 0.02$) (Figure 5).

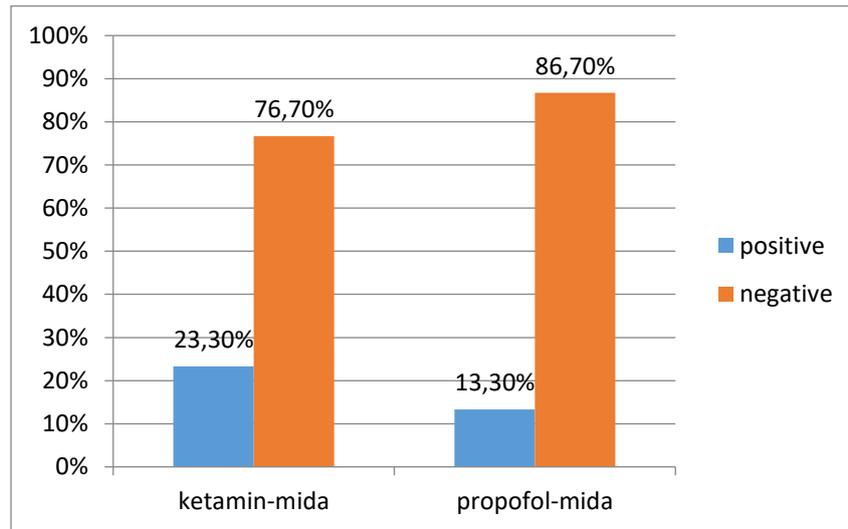


Figure 1 The gag reflex rate in the group

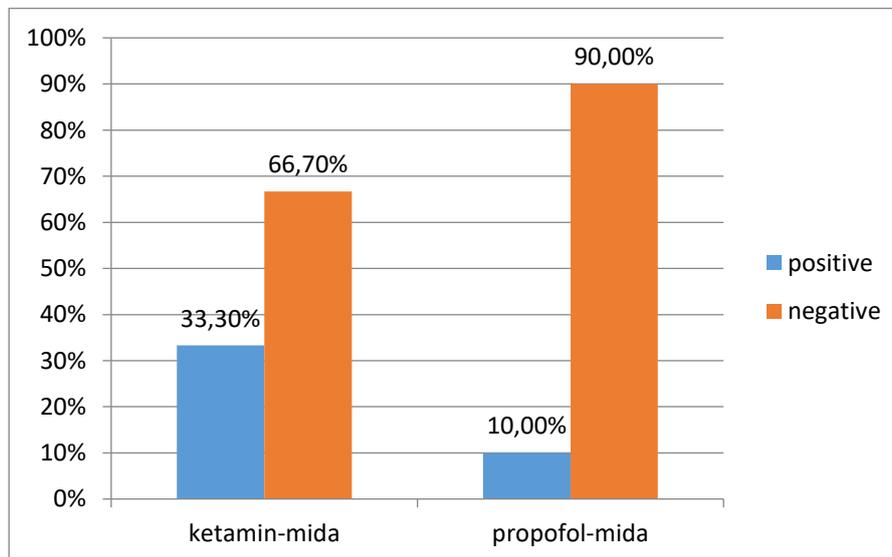


Figure 2 Incidence of nausea and vomiting in 2 groups



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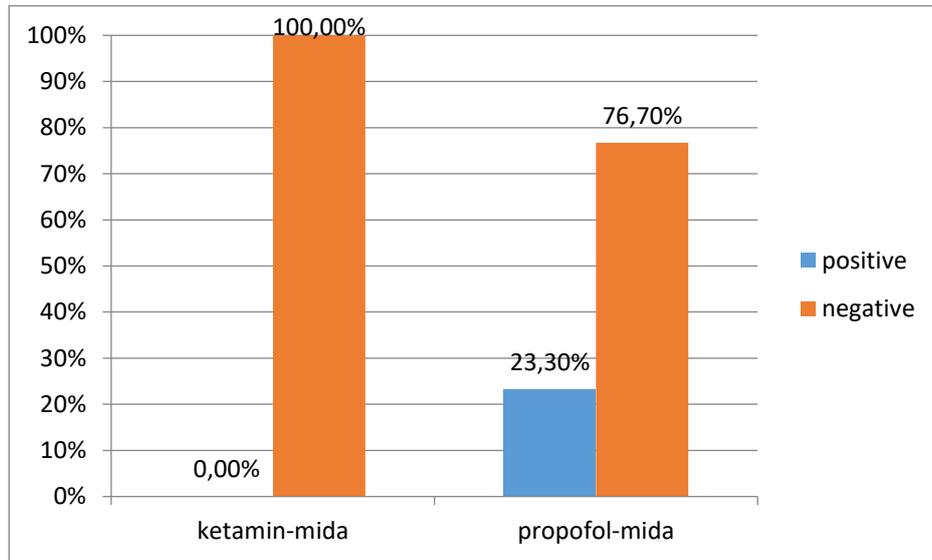


Figure 3 The incidence of apnea in 2 groups

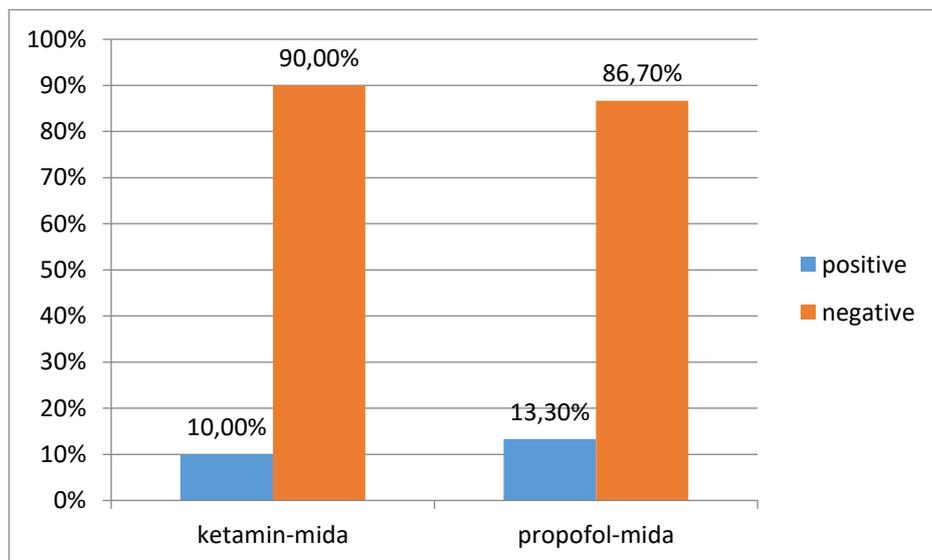


Figure 4 Incidence of insufficiency anaesthesia in 2 groups



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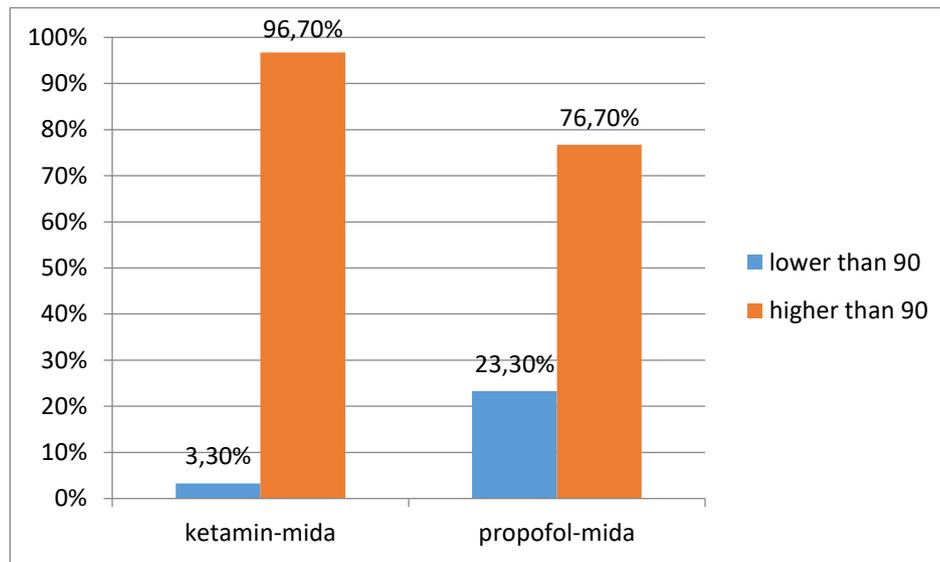


Figure 5 The incidence of o₂Sat is less than 90 in 2 groups

4. DISCUSSION

Today, opioids have a special role in creating relaxation reducing the sympathetic output through their central effects in many outpatient procedures, and there are various guidelines for advanced countries in this regard (1-10). And of course, there is a need for more care, which will prolong recovery and hospitalization (11-19). In the present study, 60 patients were evaluated in 2 groups. The incidence of nausea and vomiting in the midazolam-ketamine group was 33.3% and in the midazolam-propofol group was 10% ($P = 0.05$). The incidence of vomiting was apparently higher in the ketamine group, which is a complication of ketamine. Propofol has an anti-nausea and vomiting effect, and it is natural that it is less common in the propofol group. Our study indicated that the incidence of apnea in the midazolam-ketamine group was 0% and in the midazolam-propofol group was 23.3% ($P = 0.005$). The combination of midazolam-propofol appears to increase the incidence of apnea while administering it and there also was a significant difference in this regard. There were no cases of apnea in the ketamine group, but in the propofol group, about 20% of the patients had apnea, and in this respect it would seem reasonable that this drug should be administered more slowly or at a lower dose. A study by Motamed et al. (2012) on the combination of midazolam and ketamine in order to achieve a moderate



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overall relaxation has been shown to be effective and safe in children with oral ketamine and IV midazolam (4).

Tosun et al. (2007) evaluated the effect of two propofol-Ketamine compounds with propofol-fentanyl in 90 children (1-16 years) in anesthesia for endoscopy of the upper gastrointestinal tract and concluded that both compounds have anesthetic effect in endoscopy, but the combination of propofol-ketamine, despite more complications, results in deeper anesthesia and a more stable hemodynamic (19). Khutia et al. (2012) studied the effect of two propofol-ketamine compounds with propofol-fentanyl in 100 children (3-14 years) in anesthesia to carry out mini emergency procedures, they concluded that the combination of low-dose ketamine with propofol compared to propofol-fentanyl is more safe and more anesthetized and more pain-resistant than analgesics, resulting in lower hemodynamic and lower apnea (20).

Goyal et al. (2012) assessed the effect of two propofol-ketamine compounds with propofol-fentanyl in 60 patients aged 18-50 years in anesthesia for small surgical procedures and concluded that the combination of propofol-ketamine results in more stable hemodynamic and less complications during and after surgery compared to propofol-fentanyl (21). The study by Akbulut et al. (2015) on the use of low dosage of midazolam and ketamine in performing UGIE in children showed that minor complications during the procedure were about 39% and most commonly reported were oral secretions. There was no major and considerable complication. The average recovery time was about 22 minutes. The complications created during recovery were reported to be about 60%. The most common major complication during recovery was double vision (Strabismus) (1).

The final conclusion was that the process was completed with a high level of success and no significant major complication occurred in this study. This means that the combination of these two drugs is a proper relaxation protocol for children during UGIE (1). Our study has shown that laryngospasm has been reported negative in all patients. The incidence of insufficiency-anaesthesia in the midazolam-ketamine group was 10% and in the midazolam-propofol group was 13.3% ($P = 0.6$). In both groups, some patients needed re-administration of the drug during the endoscopy, but there was no significant difference between the two groups and this only slightly was more in the propofol group,



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which is also explained by the shorter duration of the propofol effect. Singh et al., (2013) evaluated the effect of two combinations of propofol - ketamine with propofol fentanyl on 100 patients aged 45-45 years in anesthesia for tubectomy through laparoscopic method was evaluated and concluded that patients receiving the combination of propofol-fentanyl compared to propofol-ketamine group had faster recovery and early leave (22). Akin et al. (2005) evaluated the effect of two combinations of propofol-ketamine with propofol-fentanyl in 40 female patients (38-61 years) who underwent endometrial biopsy and concluded that due to hemodynamic changes and anesthesia depth, both drugs can be safely administered, although due to the side effects of the drug and the patient's satisfaction, the combination of propofol fentanyl is preferable (23). Disma et al. (2005), studied the effect of sedation of propofol in combination with fentanyl or midazolam during the UGI endoscopy in children and showed propofol, in combination with fentanyl or midazolam, has a more relaxed effect and allows for easier and endoscopic process (5). Our review also indicated that the incidence of SpO_2 less than 90 in the midazolam-ketamine group was 3.3% and in the midazolam-propofol group was 23.3% ($P = 0.02$). In terms of saturation drop is also due to the high prevalence of sleep apnea in propofol, it is natural that its incidence is higher in the group propofol. 23.5% in the propofol group versus 3.5% in the ketamine group and it seems that the use of propofol -midazolam combination compared to Ketamine-midazolam seems to need more care and attention. Akin et al. (2005) evaluated the effect of two compounds of propofol - ketamine with propofol for 60 children (1 month to 13 years) undergoing cardiac catheterization and found that the combination of propofol with low dose of ketamine compared with propofol resulted in a better arterial pressure (24). The results of this study suggest that this medication regime is relaxing, safe and effective, and it significantly reduces the anxiety of children and parents to perform diagnostic and therapeutic procedures. Complications such as delay in waking up from anesthesia, excessive sleepiness, and other complications, such as nausea and vomiting and hemodynamic disorders, should be considered in other studies. It is recommended that this study be carried out with a higher sample size and different drug combinations in patients undergoing endoscopy of the upper gastrointestinal tract.

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