Comparison of oral and intra venous midazolam for sedation in children undergoing upper gastrointestinal endoscopy

Original Article

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Abstract:

Background: Selecting the best medication for upper GI endoscopy in children is a challenging issue. The goal of this study was to compare the effects of oral and intravenous midazolam for upper gastrointestinal endoscopy (UGIE) on children.

Methods: In this randomized clinical trial study conducted in Amirkola Children's Hospital, 110 children were randomly assigned to oral or intravenous groups. An expert nurse recorded O2 saturation, heart rate before, during and 5 minutes after endoscopy for all patients. Sedation, separation from parents and child cooperation were recorded.

Results: Heart rate before and during endoscopy was not significantly different between two groups while heart rate was significantly lower in IV group after endoscopy. Cooperation during bite block was significantly better in oral group. Cooperation during endoscopy was not significantly different between two groups. Separation from parents in both male and female ones was significantly better in oral group. Complications were reported in 7 cases in oral group and 6 in IV group.

Conclusion: Oral midazolam in comparison with IV midazolam is better and may be a method of choice for pediatric UGIE purposes.

Key Words: Midazolam, Pediatric, Endoscopy

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Introduction:

The number of endoscopic procedures in children for diagnostic and therapeutic purposes is increasing in worldwide [1]. As this method is invasive, discomfort during the procedure is common, which makes it difficult for both the physician and the patient. In children, the proper sedation is challenging as inappropriate sedation will cause longer duration and increase risk of complications as the result of less cooperation [2]. To maximize cooperation, proper sedative agents to preserve consciousness are recommended [3]. There is controversy regarding to select the best sedative agent. Any agent with rapid onset of action, minimal side effects and rapid recovery are optimal. Midazolam is a benzodiazepine with rapid onset of action. It acts by GABA (Gamma Amino Butyric Acid) accumulation and occupation of benzodiazepine receptors [4]. It is used orally or intravenously in children settings for sedative purposes. The goal of this study was to compare the effects of oral and intravenous midazolam for upper gastrointestinal endoscopy (UGIE) in children.

Methods:

In this randomized clinical trial study conducted in Amirkola Children's Hospital (affiliated hospital of Babol university), 120 children with 6 months to 12 years old age were enrolled in 2014.

Inclusion criteria:

Patients with need for UGIE, class I or II ASA (American Society of Anesthesiologists) were selected. [5]

Exclusion criteria:

Patients with ASA class III or IV, pulmonary, cardiac, renal, psychological/mental disorders or infectious diseases, metabolic disorders, liver diseases, seizure history, previous endoscopy, hematologic diseases and fever, medical history including anti-epileptic drugs, narcotics and anti-arrhythmic agents were excluded.

All parents were asked to fill informed consent forms and the study had been approved by local ethics committee. All patients were NPO for 4-6 hours before UGIE. By means of computerized simple randomization, patients were randomly assigned to oral or intravenous midazolam group. 0.5 mg/kg oral midazolam with maximum dose of 20 mg was administered to oral group 20-30 minutes before endoscopy.

Oral midazolam prepared as solution (5mg/mL) from injectable midazolam (Dormicum, Roche) and 2 cc Dextrose Water 5%.

For intravenous (IV) group, 0.15 mg/kg intravenous midazolam (Dormicum, Roche) was administered 3-5 minutes before UGIE. An expert nurse recorded O2 saturation, heart rate before, during and 5 minutes after endoscopy for all patients. All endoscopies were performed using Pentax Gasrodeodenoscope (E110236 JAPAN).

Separation from parents and child cooperation were recorded. Separation from parents was scored as follow: 1; quiet, 2; restless

Child cooperation during bite block was scored as:
Good: no movement during UGIE
Moderate: movement control by another person
Poor: movement control by more than one person

Modified Ramsay sedation scoring was used to evaluate sedation. It is 1 to 6 point scales based on the level of the patient's cooperation and response [6].

Ramsey:
1: Anxious, agitated, restless
2: Cooperative, oriented, tranquil
3: Responsive to commands only
4: Brisk response to light glabellar tap or loud auditory stimulus
5: Sluggish response to light glabellar tap or loud auditory stimulus
6: No response to light glabellar tap or loud auditory stimulus

All cases were under observation for three hours after endoscopy to detect complications. All data were analyzed using SPSS version 20 (SPSS Inc., Chicago, IL, USA). Continuous variables were compared using the Student-t test and categorical variables were compared using the x2 test. P value less than 0.05 was considered significant.

Results:

One hundred and twenty children were enrolled. Five patients in each group were withdrawn from the study.

Table 1 shows demographic characteristics of patients. Heart rate before and during endoscopy was not significantly different between two groups while heart rate was significantly lower in IV group after endoscopy (table 2).

Separation from parents was more easily in oral group (table 3). Cooperation during bite block was significantly better in oral group (table 4).

Cooperation during endoscopy was not significantly different between two groups (table 5).

Separation from parents in both male and female ones was significantly better in oral group (table 6). Complications were reported in 7 cases in oral group and 6 in IV group (p=0.2).

In oral group, the complications were as follow: 3 (5.4%) transient diplopia, 2 (3.6%) vomiting and 2 (3.6%) hiccough and complications in IV group were as follow: 3 (5.4%) vertigo, 1 (1.8%) vomiting, 2 (5.4%) agitation.

In oral group, Ramsey score in 41 (74.5%) was 1 and in 14 (25.4%) was 2 while in IV group, Ramsey score were 1, 2 and 4 in 34 (61.8%), 20 (36.3%) and 1 (1.8%), respectively (table 7).

Table 1: Demographic characteristics of patients

		Oral	Intravenous	P value
Age (year)		4.5±2.5	4.6±3.2	0.6
Sex	Male	33(58.2%)	27(49.1%)	0.08
	Female	23(41.8%)	28(50.9%)	

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Table 2: Heart rate and O2 saturation before (B), during (D) and after (A) endoscopy (E).

	Oral	Intravenous	P value
Heart rate BE	117.9±14.3	114.4±18.2	0.09
O2 saturation BE (%)	97.1±1.1	96.9±1.1	0.4
Heart rate DE	148.5±18.7	150.8±19.4	0.5
O2 saturation DE (%)	90.8±4.4	89.6±4.4	0.1
Heart rate AE	143±19	132±19.9	0.005
O2 saturation AE(%)	97.03±1.3	97.3±0.9	0.1

Table 3: Separation from parents before UGIE

		Oral N(%)	Intravenous N(%)	P value
Quiet		47(85.4)	29(52.7)	<0.001
Restlessness	Mild	3(5.5)	16(29.1)	
	Moderate	2(2.6)	7(12.7)	
	Severe	3(5.5)	3(5.5)	

Table 4: Cooperation during bite block

	Oral N(%)	Intravenous N(%)	P value
Good	39(70.9)	27(49.1)	0.02
Moderate	14(25.5)	26(47.3)	
Poor	2(3.6)	2(3.6)	

Table 5: Cooperation during endoscopy

	Oral N(%)	Intravenous N(%)	P value
Good	11(20)	7(12.7)	0.1
Moderate	39(70.9)	39(70.9)	
Poor	5(9.1)	9(16.4)	

Table 6: Separation from parents

		Oral N(%)	Intravenous N(%)	P value
Male	Quiet	28(87.5)	16(56.3)	0.04
	Restless	4(12.5)	11(40.7)	
Female	Quiet	19(82.6)	13(46.4)	0.03
	Restless	4(17.4)	15(53.6)	

Table 7: Ramsey score in two groups:

Score	Oral N(%)	Intravenous N(%)	P value
Score 1	41 (74.5)	34 (61.8)	0.14
Score 2	14 (25.4)	20(36.3)	
Score 3	0	0	
Score 4	0	1(1.8)	
Score 5	0	0	
Score 6	0	0	

Discussion:

The result of current study showed that oral midazolam is as effective as IV midazolam for sedation before UGIE in children and oral midazolam was superior medication in separating children from their parents. As the number of endoscopic procedures increases for pediatrics, the need for proper sedations increases, too. These procedures could be done in operating rooms or endoscopy rooms [7]. Nevertheless, the best sedation protocol has not been established up to now [1]. Due to different strategies and protocols in different hospitals, different medications are used for this purpose [8].

Different sedative agents have been used for sedation such as Benzodiazepines (eg, midazolam, lorazepam, diazepam), opioids (eg, morphine, fentanyl, meperidine), and sedative-hypnotics (eg, chloral hydrate, ketamine). Inhaled agents (sevoflurane and nitrous oxide) and IV propofol also have been used [9-11]. In most pediatric units, IV midazolam is a sedative choice. Midazolam is a short-acting benzodiazepine, which acts during 5 minutes and reaches to peak effect within 3-5 minutes [12]. It is used as anxiolytic, muscle relaxant, and anticonvulsant agent [13]. It applies most of its effects by interacting with inhibitory neurotransmitter receptors as GABA receptors [14].

In the present study, we compared oral and IV midazolam for sedation before UGIE. The results showed that heart rate after endoscopy was significantly lower in IV group while separation from parents was easier in oral group. Lamireau et al.'s found that heart rate and blood pressure increase during endoscopy with IV midazolam sedation in comparison with general anesthesia [15]. Ramsey score one was more reported in oral group than intravenous group while there was no statistically significant difference between Ramsey scores of two groups.

The results of current study also showed that cooperation during bite block was significantly better

in oral group than IV group. Separation from parents in both males and females was significantly better in oral group than IV group. Feld et al.'s reported that ease of separation from parents is associated with the use of oral midazolam [16]. In a previous study, Kaviani et al.'s suggested that separation from parents was significantly better in oral midazolam group than control group in children who were referred to dentist [17]. In another study, Rafeey et al.'s evaluated 30 children in oral midazolam group and 31 in IV midazolam group who underwent upper GI endoscopy [18]. They investigated that ease of separation from parents, ease of ability to monitor the patient during the procedure, heart rate, systolic arterial pressure, or respiratory rate were not significantly different between two groups. However, oxygen saturation was significantly lower in the IV group than the oral group while in this study, oxygen saturation in different time was similar in both groups.

In the current study, the rate of complications was not significantly different between two groups while diplopia was the most common complication in oral group and vertigo was the most complication in IV group. In the study of Oh et al.'s the nausea was the most common complication in IV midazolam group while in Hulland's study, vomiting was the most common complication in oral midazolam group [1, 19].

Oral midazolam in comparison with IV midazolam is better choice for pediatric UGIE purposes.

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