

Ketamine administration makes patients and physicians satisfied during gastro-enteric endoscopies

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Background: A suitable sedative status during gastro-enteric endoscopies results in better physicians' approach and more stable view of internal organs. Therefore, we evaluated the effect of ketamine for sedation in endoscopic procedures of adult patients. **Materials and Methods:** Patients who were candidates for gastro-enteric endoscopy during the years 2014-2015 were included into the study and divided into two groups of case (administered 5 mg/kg of oral ketamine half an hour before initiation of the procedure) and control (administered placebo in a same pattern). After endoscopy, patients and physicians' satisfaction of sedation was assessed. SPSS-22 was used for data analysis. **Results:** Eighty-six patients participated into the study of which divided into each groups. The pain and discomfort scores were 2.4 ± 1.8 and 5.81 ± 1.48 in case and control groups, respectively, ($P < 0.001$). Mann-Whitney test revealed statistical difference among groups about physician's satisfaction of sedation during endoscopy ($P < 0.001$). Patients who received ketamine had better sedative status ($P < 0.001$). None of the patients in the case group was completely awake but all of the patients in the control group were awake. The number of retching during endoscopy showed that individuals in the control group had more frequent retching episodes ($P = 0.04$). **Conclusion:** Low-dose oral administration of ketamine could make a satisfied sedation for gastro-enteric endoscopy.

Key words: Gastro-enteric endoscopy, ketamine, sedation

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INTRODUCTION

Endoscopy is the most accurate and beneficial way for the diagnosis of dyspepsia, peptic ulcers, and malignancies.^[1] Sedative drugs are used for both patient and physician satisfaction during the procedure; type of endoscopy, duration, degree of difficulty, and patients' physical status are the criteria which determine the suitable type of sedation for endoscopy.^[2] Although there are several drugs and techniques for the induction of sedation and reduction of pain during gastro-enteric endoscopies, there is no standardized method of sedation, and physicians

themselves choose the best method regarding their experience.^[3-6]

Benzodiazepines are mostly used for the goal of sedation,^[7,8] and among them, midazolam is the drug of choice. Opioids (including pethidine and fentanyl), propofol, ketamine, and droperidol are other sedative drugs used for the same purpose.^[9,10] Ketamine could be used as a substitute of opioids and benzodiazepines for sedation during endoscopy with a wide spectrum effects on pain, amnesia, anesthesia, and sedation which can be administered intravenous, intramuscular, or even oral and rectal. Dose of 0.2-0.5 mg/body weight (Kg) is usually used for reduction of pain and after 10-15 min, the full consciousness is returned. Delusion,

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auditory and visual hallucinations, and other side effects which may occurred in a period of 24 h after ketamine administration make some limitations for drug usage. A potential contractive effect on laryngeal muscles in unwell patients also would lead to significantly unpredictable decrease in blood pressure and cardiac output. Previous studies had worked on the combination of ketamine and midazolam for the induction of sedation in pediatric gastro-enteric endoscopy but there is no similar study on adults.^[12]

In some areas of the world, ketamine is mostly used in sedation for endoscopy for all ages due to lack of other medications.^[13] Ketamine is also used for the reduction of neuropathic pains such as postherpetic neuralgia, complex regional pain syndrome, malignancy, orofacial pain, and limb phantom pain.^[14] Due to lack of enough data about the effect of ketamine on endoscopic sedation, we designed this study to evaluate the mentioned purpose.

MATERIALS AND METHODS

This double-blinded, randomized clinical trial study was done by the grant of Isfahan University of Medical Sciences during the years 2014-2015 with the group of patients who were candidates for gastro-enteric endoscopy. Inclusion criteria were the following: Age between 18 and 65 years, absence of hypersensitivity or any contraindication for ketamine, absence of mental or physical retardation, and no history of hypertension, seizure, hyperthyroidism, immune deficiency, or increased intraocular pressure. Any patient who required emergent intervention or who showed drug sensitivity during the study was excluded from the study.

All the patients who had the inclusion criteria were informed about the study protocols and procedures and fulfilled a written consent, after that they were divided into two groups of case and controls by computer randomizing system meaning that every participant had a number categorized into case or control group by the computer.

A questionnaire including demographic data was fulfilled; patients in case group administered 5 mg/body weight (Kg) of ketamine,^[21,22] 30 min before the endoscopy and the control group received placebo in the same order. For complete blindness of the study, drug or placebo was solved in 10 cc of apple juice because of the bitter taste of ketamine and after that, medication was given to the patient by a nurse who was blinded about the study protocols. After finishing the procedure, pain severity, degree of sedation, and physicians' satisfaction of sedation were measured in both groups. Visual analog scale was used for pain assessment and physicians' satisfaction of

sedation was measured with the following scale: Very bad (scale 0), bad (scale 1), intermediate (scale 2), good (scale 3), and very good (scale 4). The sedation was also assessed with 1 = completely awake, 2 = awake but drowsy, 3 = asleep but responsive to verbal commands, 4 = asleep but responsive to tactile stimulus, and 5 = asleep and not responsive to any stimulus.

Finally, all the gathered data were analyzed using SPSS-20 software (SPSS Inc., Chicago, Illinois, USA); *t*-test, independent *t*-test, Mann-Whitney test, and Chi-square test were used for data analysis and $P < 0.05$ was considered statistically significant.

RESULTS

Eighty-six patients (43 in case group and 43 in control group) who were candidates for gastro-enteric endoscopy were included into this study; of which 43 (50%) individuals were males and 43 (50%) were females. As seen in Table 1, no differences were seen among groups regarding age, sex, and level of academic degree. Most of the patients had high school education in both groups.

Table 2 shows that the mean number of pain severity and discomfort during endoscopy were 2.4 ± 1.8 and 5.81 ± 1.48 in case and control groups, respectively, which showed significant differences among groups ($P < 0.001$) [Figure 1].

As seen in Table 2, none of the patients in the case group had severe nausea and pain otherwise there were five individuals in the control group who had severe nausea and pain. Overall, regarding categorization of pain and nausea in both groups, there was difference among groups. Endoscopist's satisfaction measurement showed that most of the patients in the case group were categorized as "completely satisfaction" (32 patients; 74.4%), but most of the patients in the control group were in "relatively

Table 1: Demographic and educational data of case and control group

| Variables | Groups | Case (ketamine) | Control (placebo) | P |
|--------------------|----------------|-----------------|-------------------|------|
| Mean±SD age (year) | | 42.7±12.3 | 47.6±15.5 | 0.11 |
| Sex n (%) | Male | 24 (55.8) | 32 (74.4) | 0.07 |
| | Female | 19 (44.2) | 11 (25.6) | |
| Education (%) | Illiterate | 9 (20.9) | 15 (34.9) | 0.33 |
| | Primary school | 2 (4.7) | 5 (11.6) | |
| | Prehigh school | 5 (11.6) | 2 (4.7) | |
| | High school | 19 (44.2) | 14 (32.6) | |
| | University | 8 (18.6) | 7 (16.3) | |

SD = Standard deviation

satisfaction" group (13 patients; 30.2%). Mann-Whitney test revealed statistical difference among groups about physician's satisfaction of sedation during endoscopy ($P < 0.001$) [Figure 2].

The sedation score was assessed in both groups, and patients who received ketamine had better sedative status (Mann-Whitney test; $P < 0.001$). None of the patients in the case group was completely awake, but all of the patients in the control group were awake. The number of retching during endoscopy showed that individuals in the control group had more frequent retching episodes [Table 2].

Fifteen patients in the case group showed complications including nausea (four patients), nausea and vomiting (three patients), tachycardia (six patients), and deep sedation (one patient). One patient in the control group

had severe nausea. Ketamine-induced sedation had more complications in comparison with those administered with placebo ($P < 0.001$).

DISCUSSION

The main goal of this study was to find a response to a question that is whether low-dose oral ketamine administration can ameliorate patients' pain and discomfort and also increase physicians' satisfaction during gastro-enteric endoscopy. Our data revealed that low-dose administration of ketamine, 30 min before initiation of the endoscopy, can significantly decrease patient's pain and discomfort. We also found that physicians reported better satisfaction of sedation in patients who received ketamine comparing with those who received placebo.

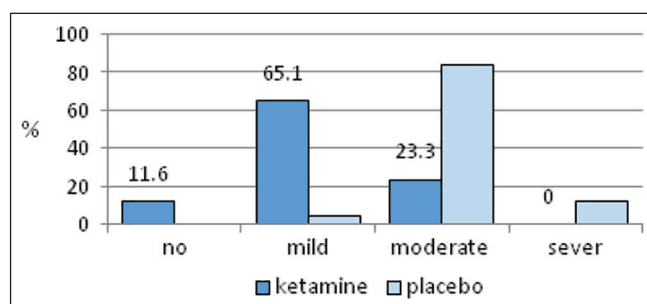


Figure 1: Severity of pain and nausea in case and control groups

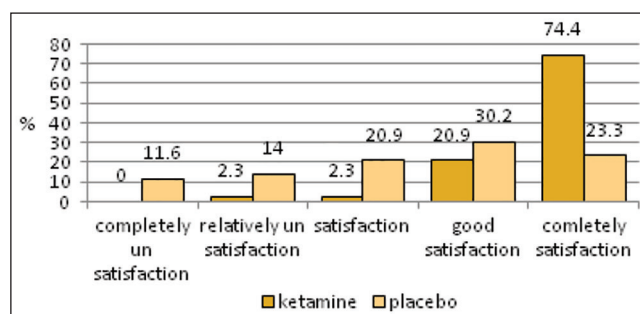


Figure 2: Endoscopist's satisfaction of sedation during endoscopy in case and control groups

Table 2: Distribution of pain and discomfort, endoscopist's satisfaction, sedation score, and retching in case and control groups

| Variables | Groups | Ketamine | Placebo | P |
|----------------------------|---|-----------|-----------|--------|
| Pain and discomfort | Mean±SD | 2.4±1.8 | 5.8±1.5 | <0.001 |
| | No | 5 (11.6) | 0 (0) | <0.001 |
| | Mild | 28 (65.1) | 2 (4.7) | |
| | Moderate | 10 (23.3) | 36 (83.7) | |
| | Sever | 0 (0) | 5 (11.6) | |
| Endoscopist's satisfaction | Completely unsatisfaction | 0 (0) | 5 (11.6) | <0.001 |
| | Relatively unsatisfaction | 1 (2.3) | 6 (14) | |
| | Satisfaction | 1 (2.3) | 9 (20.9) | |
| | Relatively satisfaction | 9 (20.9) | 13 (30.2) | |
| | Completely satisfaction | 32 (74.4) | 10 (23.3) | |
| Sedation score | Mean±SD | 3.56±0.67 | 1.14±0.64 | <0.001 |
| | Completely awake | 0 (0) | 43 (100) | <0.001 |
| | Awake but drowsy | 2 (4.7) | 0 (0) | |
| | Asleep but responsive to verbal commands | 17 (39.5) | 0 (0) | |
| | Asleep but responsive to tactile stimulus | 22 (51.2) | 0 (0) | |
| | Asleep and not responsive to any stimulus | 2 (4.7) | 0 (0) | |
| Retching | Mean±SD | 0.77±0.2 | 1.84±0.39 | 0.017 |
| | No | 28 (65.1) | 24 (55.8) | 0.049 |
| | 1-2 | 10 (23.3) | 5 (11.6) | |
| | 3-4 | 4 (9.3) | 7 (16.3) | |
| | 5 and + | 1 (2.3) | 7 (16.3) | |

SD = Standard deviation

Studies and experiences suggested that a successful gastro-enteric endoscopy can be done with a moderately potent sedative medication. A previous meta-analysis revealed that a moderate sedation can increase patient and physician's satisfaction. Although propofol is growing to be used as a moderate sedative medication, midazolam plus one opioid is considered as a standardized sedative method.^[11]

There are several studies worked on the effect of ketamine on pain reduction^[17-20] and most of them are focused on the intravenous injection of ketamine and its effect on some special pains such as neuropathic pains.^[14] Moharari *et al.* found that injection of 10 cc lidocaine plus 2 cc of ketamine into the urethra can significantly decrease pain during cystoscopy, especially in the first 5 min of the procedure.^[15] Another study designed to find a suitable sedative method for pediatric gastro-enteric endoscopy revealed that combination of oral ketamine with intravenous injection of midazolam is a perfect way to decrease pain and induction of sedation; however, further episodes of vomiting were reported due to oral administration of ketamine.^[16] Khademi *et al.* in a 2011 study on 78 pediatric patients showed that peritonsillar infiltration of ketamine (0.5 mg/kg) leads to reduced pain and postsurgery vomiting after adenotonsillectomy.^[17] Another study on 180 patients aged 18-60 and candidates for cholecystectomy revealed that subcutaneous injection of 2 mg/kg of ketamine or intravenous injection of 1 mg/kg of ketamine 15 min before initiation of the surgery can decrease postsurgery pain.^[18] Combination of ketamine (0.25 mg/kg) and meperidine (5 mg) had been shown to have effects on pain reduction and decreased need to opioids after major abdominal surgeries in patients aged 15-60 years.^[19] Results of a recent investigation by Shavakhi *et al.* revealed that sublingual administration of alprazolam resulted in better sedative status, decreased anxiety, and increased patient's satisfaction during endoscopic procedures compared with oral route of administration.^[23] Lack of measurement of awaking time and ending time of procedure can be mentioned as our study limitation. As we searched, there was no study which compared the effect of ketamine compared with placebo, so we did not compare the effect of ketamine with other sedative agents.

CONCLUSION

Our data showed that a low-dose oral administration of ketamine could make a suitable sedation for gastro-enteric endoscopy. Patients experienced less pain and less frequent retching and physicians had greater satisfaction of sedation compared with those placebo-treated group. We would like to suggest using ketamine as a suitable medication for the induction of sedation during gastro-endoscopic procedures if there is no contraindication.

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Conflicts of interest

There are no conflicts of interest.

AUTHOR'S CONTRIBUTION

SM contributed in the conception of the work, revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work. AK contributed in the conception of the work, revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work. MK contributed in the conception and design of the work, drafting and revising the draft, and agreed for all aspects of the work. SD contributed in the drafting and revising the draft, approval of the final version of the manuscript, and agreed for all aspects of the work. PA contributed in the conception and design of the work, drafting and revising the draft, and agreed for all aspects of the work. MM and RK contributed in the conception and design of the work and agreed for all aspects of the work.

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