ORIGINAL ARTICLE

Assessment of the effects of ketamine-fentanyl combination versus propofol-remifentanil combination for sedation during endoscopic retrograde cholangiopancreatography

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Background: Endoscopic retrograde cholangiopancreatography (ERCP) as a diagnostic and treatment procedure is used in most biliary tract and pancreatic. Either sedation or general anesthesia could be considered for this procedure. Combining a sedative with an opioid agent can provide effective moderate sedation. This study compared the impact of ketamine-fentanyl (KF) versus propofol-remifentanil (PR) on sedation scale in patients undergoing ERCP. **Materials and Methods:** As a double-blinded randomized clinical trial, 80 patients selected by convenient sampling, allocated randomly into two groups. KF group received ketamine 0.5 mg/kg body weight intravenously over 60 s and then fentanyl 1 mcg/kg body weight intravenously. PR group received propofol l mg/kg body weight intravenously over 60 s and then remifentanil 0.05 mcg/kg body weight/min intravenously. Intravenous (IV) infusion of propofol was maintained by 50 mcg/kg body weight/min throughout ERCP. Ramsay Sedation Score, vital signs, oxygen saturation (SpO_2), recovery score (modified Aldrete score) and visual analog scales of pain intensity, and endoscopist's satisfaction were considered as measured outcomes. All analysis were analyzed by SPSS Statistics version 22 and using *t*-test, Chi-square and repeated measured ANOVA and Mann-Whitney tests for data analysis. **Results:** Respiratory rate and SpO_2 level during the time intervals were lower in PR group ($P < 0.001$). Sedation score at intervals was not significantly different ($P = 0.07$). The frequency of apnea in PR group was significantly higher than the KF group ($P = 0.003$). The percentage of need to supplemental oxygen in PR group was 35.1% that was also significantly higher than 8.8% in the KF group ($P = 0.008$), but the dosage frequency was significantly higher in KF group ($P < 0.001$). The KF and PR groups average length of stay in the recovery room were 50.71 standard deviation (SD = 9.99) and 42.57 (SD = 11.99) minutes, respectively, indicating a significant difference ($P = 0.003$). The mean severity of nausea in KF and PR groups was, respectively, 2.74 confidence interval (CI = 1.68-3.81) and 0.43 (CI = 0.11-0.75), that was significantly higher in KF group ($P < 0.001$). The average score of surgeon satisfaction in both KF and PR groups were 7.69 (CI = 7.16-8.21) and 8.65 (CI = 8.25-9.05), respectively, which was higher in KF group ($P = 0.004$), but the average level of patients satisfaction in KF group was 8.86 (CI = 8.53-9.19) and in PR group was 8.95 (CI - 8.54-9.35) that were not significantly different ($P = 0.074$). **Conclusion:** There is no statistically significant difference between KF and PR combinations in sedation score, but PR combination provides better pain control, with less nausea and shorter recovery time while causing more respiratory side effects, that is, apnea and need to oxygen.

Key words: Endoscopic retrograde cholangiopancreatography, fentanyl, ketamine, propofol, remifentanil

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INTRODUCTION

Over the last decade, the number of gastrointestinal endoscopic procedures carried out worldwide has increased significantly.[1] Endoscopic retrograde cholangiopancreatography (ERCP) not only as a diagnostic procedure, but also as a treatment can be used in most biliary tract and pancreatic diseases which include removal of common bile duct stones, stenting of biliary stricture, and resolution of pancreatic duct disruption.[2,3]

For the completion of the ERCP procedure, there are two basic choices of anesthesia available, sedation and general anesthesia.[2,4] According to the American Society of Anesthesiologists (ASA), sedation is defined as a continuum of progressive impairment in consciousness ranging from minimal to moderate, deep sedation and general anesthesia.[5] The goals of sedation are to achieve a balance between the benefits of sedation against potentially preventable risks. Sedation reduces pain, discomfort and stress, and can produce amnesia in patients undergoing unpleasant and prolonged

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procedures such as ERCP. On the other hand, there are adverse effects in sedation which we are trying to avoid such as patient aggravation, deep unarousable state, absence of purposeful response to physical and verbal stimulation, loss of protective airways reflexes, inability to maintain patent airway, hypoxemia/hypercarbia, and cardiovascular instability (arrhythmia or hypotension).

Suitable drugs and their dosage for sedation have been debated, and a variety of different drugs have been used around the world, consequently search for appropriate sedation regimen continues.[1,2,4]

Available agents for sedation include benzodiazepines (midazolam, diazepam), narcotics (fentanyl, meperidine), propofol, neuroleptic tranquilizers (droperidol), antihistamines (diphenhydramine), and dopaminergic receptor antagonists (promethazine).[1,6]

Ketamine, a synthetic phencyclidine derivative, has been pronounced as a safe and effective sedative agent. Ketamine produces a dissociative state, combination of analgesia, amnesia, and sedation at subanesthetic dose, with minimal effects on the airway and vital reflexes. Fentanyl, a short-acting opioid, is useful for upper gastrointestinal endoscopic procedures and produces analgesia and sedation.[2,7] The study has shown a shorter recovery period for patients undergoing endoscopy if fentanyl and midazolam are used compared with the use of pethidine and midazolam, and there was no difference in pain perception.[1] Remifentanil is another short-acting opioid that is able to permitting a rapid transition from intense analgesia to minimal residual effect. Propofol with rapid recovery profile produces sedation and amnesia and has been increasingly used worldwide as a sedative agent for standard endoscopy.[8-14]

As mentioned, combining a sedative with an opioid can provide effective moderate sedation, and most patients receive a combination of medications.[5,15]

Despite using different drugs and variant combinations of medications, still searching for the best drug combination with the minimum side effects is continued; accordingly, the purpose of this study was to compare between two combined drugs, ketamine-fentanyl (KF) and propofol-remifentanil (PR) for sedation in patients undergoing ERCP.

MATERIALS AND METHODS

This was a double-blinded randomized clinical trial study that after getting permission from Ethical Committee was performed in St. Alzahra hospital, Isfahan, Iran in 2013-2014. The target population was patients who underwent ERCP in this center and consented to participate in this study. They were selected by a convenient sampling method and then were randomly allocated into two groups in a ratio of 1:1, using Excel software random number generation. KF group received KF combination, and PR group received PR combination.

Inclusion criteria included patients at age between 25 and 70 years, ASA physical status I and II, without anatomic airway abnormalities, without severe cardiovascular and respiratory disease, without severe psychological problem, who are not pregnant, who are not smoker or addict and patients without history of previous ERCP. Furthermore, exclusion criteria included occurring severe ERCP complications such as perforation and bleeding, ERCP procedural failure or changing the sedation plan to the general anesthesia. According to the range of drug dosages in the authentic sources and principal investigator's opinion, the medication doses were chosen.[16]

Ketamine-fentanyl group received loading dose of Ketamine (Rotexmedica, Germany) 0.5 mg/kg body weight intravenously over 60 s and then Fentanyl (Mylan, USA) 1 mcg/kg body weight intravenously. PR group received Propofol (Claris Lifesciences Ltd., India) 1 mg/kg body weight intravenously over 60 s and then Remifentanil (GlaxoSmithKline, Italy) 0.05 mcg/kg body weight/min intravenously. IV infusion of propofol was maintained by 50 mcg/kg body weight/min throughout ERCP. To ensure the blindness of the study, the same infusing pumps and syringes were prepared and covered for both groups. All parameters were collected by the assistant, who was blinded to group allocation. All the nurses involved in the procedure and all the endoscopists were blinded to group allocation.

During preprocedural assessment, every patient underwent thorough physical examination with ASA classifications. Total sedation procedure was explained to every patient, and informed consent was taken for sedation. A baseline pulse, systolic blood pressure (SBP) and diastolic blood pressure (DBP), respiratory rate, and peripheral capillary oxygen saturation (SpO_2) were recorded. After 5 min, the patient was taken to the operation room.

Before administrating the IV drugs, oxygen 6 l/min was given to all patients with nasal cannula. Necessary monitoring such as an electrocardiogram, blood pressure (BP), and pulse oximetry were doing during the procedure.

An independent blinded nonphysician assistant observed and recorded patient's heart rate, respiratory rate, BP, and SpO_2 every 5 min during the first 15 min of the procedure and then every 15 min until the end of the operation. The whole sedation process was done under an anesthesiologist's supervision who instructed the assistant in administrating

sedation to these patients according to their conscious level, movement, and vital signs. Side effects during sedation and recovery such as desaturation (SpO_2 <93%), hypertension (SBP >30% of baseline record), hypotension (SBP <90 mm of Hg), bradycardia (heart rate <60 beat/min), tachycardia (heart rate >120 beat/min), frequency of retching, and frequency of apnea (the cessation of respiratory activity for >10 s by observation) were observed, recorded, and managed in both groups.

Ramsay Sedation score (RSS), 6-point sedation scale, was used to assess the baseline sedation level during ERCP in. The details of RSS are described in Table 1.[17] The blinded assistant recorded the RSS every 5 min during the first 15 min of the procedure and then every 15 min until the end of the operation.

In RSS1 and RSS2, the initial sedation was inadequate and the repeated dose was necessary to accomplish the procedure, additional incremental dose of ketamine 0.2 mg/kg body weight was given intravenously to patient in KF group and IV infusion of propofol was increased up to 100 μg/kg body weight/min to patient in PR group. The frequency of dose repeats in each case was recorded by an assistant. In SpO_2 ≤93%, additional oxygen was given with nasal cannula.

After the procedure, vital signs, SpO_2, and recovery score (modified Aldrete score) were recorded at the entrance to the recovery room and after first 15 min. Parameters of modified Aldrete score are described in Table 2.[18]

At 60 min postprocedure, patient's pain intensity and nausea and satisfaction were evaluated by the assistant. A 10-point visual analog scale (VAS) was used to measure the pain intensity. The VAS scale is 10 cm wide and marked with integers, with 0 representing "no pain," and 10 representing "worst possible pain." The patient marked the scale. The location of the mark was measured to determine a VAS score from 0 to 10. The nausea was also assessed by a VAS, in which 0 representing "none" and 10 representing "retching or vomiting." The patient's satisfaction was similarly evaluated by a VAS, 0: Unsatisfied and 10: Satisfied and the patient marked the scale and the location of the mark was measured to determine a VAS score from 0 to 10.[19]

Table 1: RSS[17]

Score	Clinical description
1	Patient is anxious and agitated or restless or both
2	Patient is cooperative, oriented and tranquil
3	Patient responds to commands only
4	Patient exhibits brisk response to light glabellar tap or loud auditory stimulus
5	5 patient exhibits a sluggish response to light glabellar tap or loud auditory stimulus
6	Patient exhibits no response

RSS = Ramsay Sedation Score

The patient was discharged when the modified Aldrete score is 9-10 points.

The endoscopist's satisfaction was also assessed by a VAS, with 0 demonstrating unmanageable, many interruptions or terminated procedure and 10 demonstrating excellent sedation, no interruptions. The endoscopist marked the VAS scale at the end of each case. The location of the mark was measured to determine a VAS score from 0 to 10.

Results are expressed as mean (standard deviation [SD] and confidence interval [CI]) or percentage (%), as appropriate. Comparison of sex and age between two groups was conducted with Chi-square and *t*-test, respectively. A repeated measured ANOVA test was performed to comparisons of SBP and DBP, heart rate, respiratory rate, and the level of SpO_2 among two groups. The difference between groups was evaluated by the Mann-Whitney test for the frequency of retching and nausea. Data of participants were analyzed by SPSS version 20 (SPSS Inc., Chicago, IL, USA).

RESULTS

Eighty-five of the possible 104 participants acquired the inclusion criteria and were enrolled in the study. Five patients refused to participate. The most common reason for refusal was the lack of interest in research participation. In all, 80 patients were selected and randomly divided into two groups of 40 individuals in order to be investigated. Nine patients (including 6 patients of KF group and 3 of PR group) were excluded during the study [Figure 1].

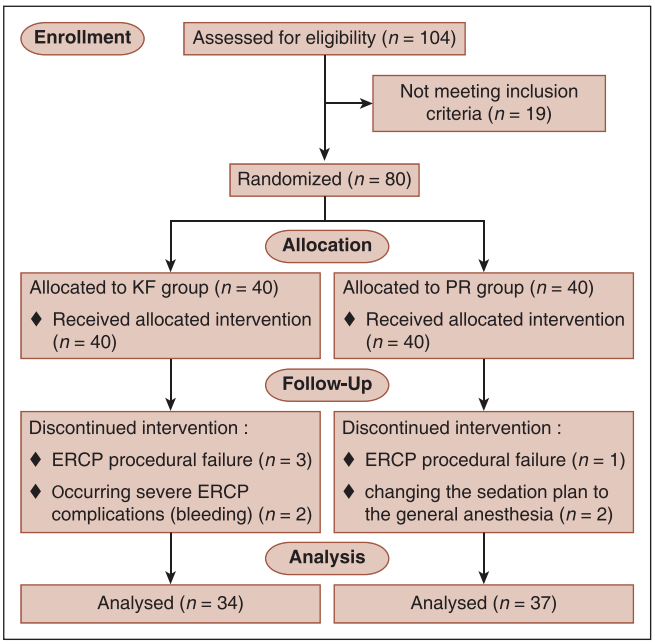

Figure 1: CONSORT trial flow diagram

The average age of two groups of patients using KF and PR was 55.3 (SD = 15.1) and 54.5 (SD = 11.1) years, respectively. According to *t*-test results, there was not any significant difference between two groups (P = 0.79). In addition, KF and PR groups population compromised of 18 and 18 male participants, respectively (%52.9 vs. %48.6) and 16 and 19 were female (%52.9 vs. %48.6). Whereas, Chi-square test indicated no significant difference between the groups (P = 0.72). In the present document, the hemodynamic parameters were measured in the operating room at 0, 5, 10, 15, 30, 45, and 60 min and also in the recovery room at 0 and 15 min. Figures 2-6 indicate the average rate of changes over a given period. ANOVA test along with repeated data observations revealed no significant difference among the groups due to SBP and DBP range and also heart rate ($P > 0.05$). However, respiratory rate per minute and SpO_2 level during the time intervals exhibited

Table 2: Modified aldrete score[18]

Parameter	Description of patient	Score
Activity	Moves all extremities voluntarily	2
	Moves two extremities	1
	Unable to move extremities	0
Respiration	Breathes deeply and coughs freely	2
	Dyspneic, shallow or limited breathing	1
	Apneic	0
Circulation	BP+20 mm of preanesthetic level	2
	BP+20-50 mm of preanesthetic level	1
	BP+50 mm of preanesthetic level	0
Consciousness	Fully awake	2
	Arousable on calling	1
	Not responding	0
SpO_2	SpO_2>92% on room air	2
	Supplemental O_2 require to maintain SpO_2>90%	1
	SpO_2<92% with O_2 supplementation	0

BP = Blood pressure; SpO_2 = Oxygen saturation

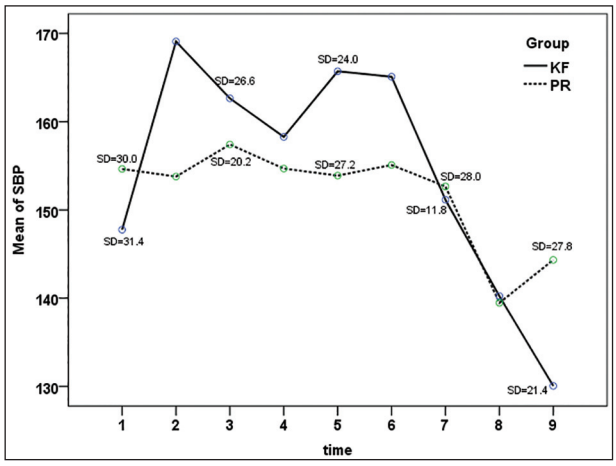

Figure 2: The average rate of systolic blood pressure changes before the surgery until the recovery 15 min in two groups (P = 0.57). Time intervals 1-9 present the time of measuring the variables: Every 5 min during the first 15 min of the procedure and then every 15 min until the end of the operation and then at the entrance to the recovery room and after first 15 min

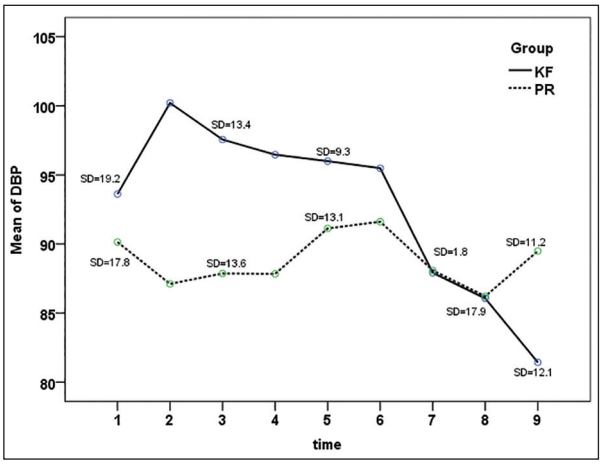

Figure 3: The average rate of diastolic blood pressure changes before the surgery until the recovery 15 min in two groups (P = 0.12). Time intervals 1-9 present the time of measuring the variables: Every 5 min during the first 15 min of the procedure and then every 15 min until the end of the operation and then at the entrance to the recovery room and after first 15 min

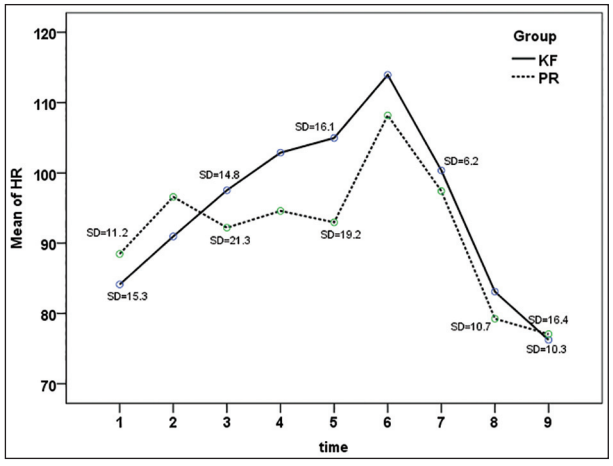

Figure 4: The average rate of heart beat changes before the surgery until the recovery 15 min in two groups (P = 0.28). Time intervals 1-9 present the time of measuring the variables: Every 5 min during the first 15 min of the procedure and then every 15 min until the end of the operation and then at the entrance to the recovery room and after first 15 min

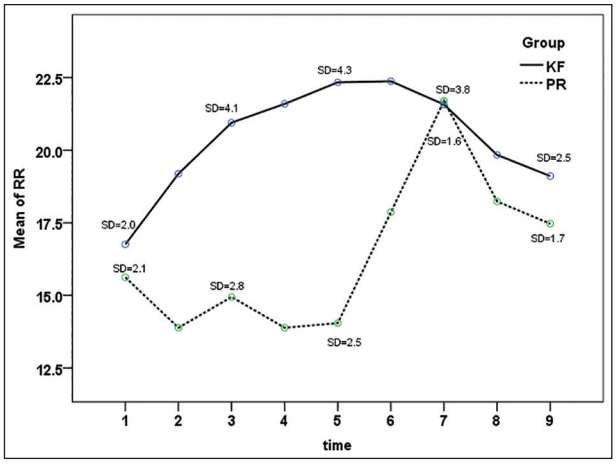

Figure 5: The average rate of respiratory changes before the surgery until the recovery 15 min in two groups (P < 0.001). Time intervals 1-9 present the time of measuring the variables: Every 5 min during the first 15 min of the procedure and then every 15 min until the end of the operation and then at the entrance to the recovery room and after first 15 min

a significant difference between two groups ($P < 0.001$). The average of both criteria in PR group was lower than the alternative one. Moreover, sedation score was measured at 0-60 min in the operating room and also at 0-15 min in the recovery room which was not significantly different ($P = 0.07$) [Figure 7].

Table 3 shows the frequency of endoscopic complications in two groups of patients using KF and PR. This table represented that the frequency range of retching in KF group was almost higher than the other group, while according to the Mann-Whitney test, the difference between two groups was not significant ($P = 0.58$). In addition, the frequency of apnea in PR group was higher than the KF group which is represented as a significant difference through the mentioned test ($P = 0.003$). Moreover, PR group needed oxygen more often than the alternative ($P = 0.008$). The dosage frequency was significantly higher in KF group than PR group ($P < 0.001$).

Table 3: Distribution of endoscopic complications in two groups

Complications	Groups level	KF ($n = 34$) (n [%])	PR ($n = 37$) (n [%])	P
Frequency of retching	0	8 (23.5)	17 (45.9)	0.58
	1	16 (47.1)	7 (18.9)	
	2	7 (20.6)	4 (10.8)	
	3	3 (8.8)	9 (24.3)	
Frequency of apnea	1	30 (88.2)	21 (56.8)	0.003
	2	4 (11.8)	12 (32.4)	
	3	0 (0)	4 (10.8)	
Frequency of receiving repeated dose of ketamine in KF group and propofol in PR group	0	3 (8.8)	8 (21.6)	<0.001
	1-2	16 (47.1)	29 (78.4)	
	□3	15 (44.1)	0 (0)	
Need to supplemental oxygen by mask or intranasal	Yes	3 (8.8)	13 (35.1)	0.008
	No	31 (91.2)	24 (64.9)	

KF = Ketamine-fentanyl; PR = Propofol-remifentanil

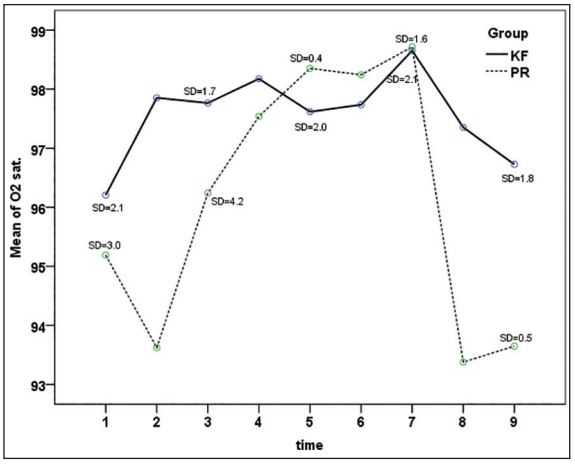

Figure 6: The average rate of oxygen saturation changes before the surgery until the recovery 15 min in two groups ($P < 0.001$). Time intervals 1-9 present the time of measuring the variables: Every 5 min during the first 15 min of the procedure and then every 15 min until the end of the operation and then at the entrance to the recovery room and after first 15 min

The KF and PR groups average length of stay in recovery room were 50.71 (SD = 9.99) and 42.57 (SD = 11.99) minutes, respectively, indicating a significant difference by independent samples t-test ($P = 0.003$).

In KF and PR groups, the patients' average pain intensity was, respectively, 3.77 (CI = 2.52-5.02) and 0.65 (CI = 0.20-1.09), which confirmed a significant difference according to independent samples t-test ($P < 0.001$). The mean severity of nausea in KF and PR groups was respectively 2.74 (CI = 1.68-3.81) and 0.43 (CI = 0.11-0.75), thus the difference between the two groups was also significant ($P < 0.001$).

The average score of surgeon satisfaction in both KF and PR groups was 7.69 (CI = 7.16-8.21) and 8.65 (CI = 8.25-9.05), respectively. Independent samples t-test results indicated that the difference between two groups was statistically significant ($P = 0.004$).

The average level of patients satisfaction in KF group was 8.86 (CI = 8.53-9.19) and in PR group was 8.95 (CI - 8.54-9.35) that were not significantly different ($P = 0.074$).

DISCUSSION

The general objective of the current study was to compare the impact of two-drug combination, that is, KF and PR on sedation scale in endoscopy procedure. In this study, 80 patients who had to have an endoscopy were randomly divided into two groups of 40 individuals. The groups were not significantly different in terms of demographical variables including age and sex distribution, therefore, destructive effect of the mentioned factors has been neutralized and obtained results are likely to be regarded as direct impact of drug combination used by two groups. Examination of hemodynamic criterion before endoscopy

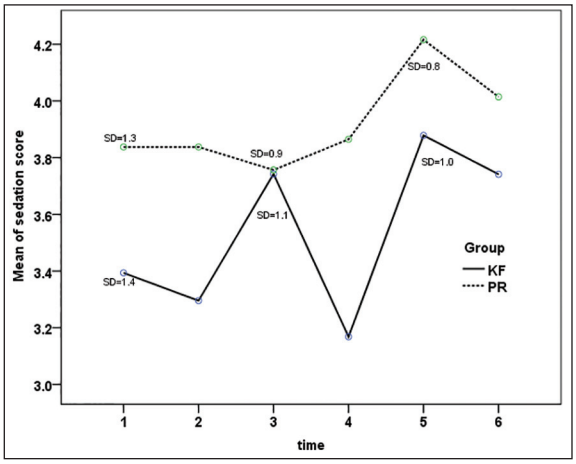

Figure 7: The average rate of sedation score changes before the surgery until the recovery 15 min in two groups ($P = 0.07$). Time intervals 1-6 present the time of measuring the variables: Every 5 min during the first 15 min of the procedure and then every 15 min until the end of the operation

until 15 min after the end of procedure showed that BP and heart rate changes were not different while the respiratory rate was significantly different between two groups as it was significantly higher in KF users than PR group. Moreover, SpO_2 changes among the groups involved significant which was more considerable at the beginning and the end of the procedure. There was no significant difference in terms of sedation score between two groups. The frequency range of retching was not significant, but respiratory depression and apnea frequency in PR group were significantly higher. KF users required more repeated dose of the drug compared with PR group which can be the result of the maintenance dose of propofol at PR group and no maintenance drug at the other group. Moreover, they had to stay more in the recovery room and suffered more from severe pain and nausea. To summarize the disadvantages of KF group, more repeated dose of drug, poor pain control, and more nausea should be mentioned, when some advantages were existed, such as less frequency of apnea and need to oxygen. On the other hand, PF users took some benefits, consisting better pain control, less nausea, shorter recovery time, and less repeated dose of drug, while higher apnea frequency and more need to oxygen and longer recovery time were some disadvantages.

According to alternative studies, ketamine is categorized as the type of anesthetic drugs with immediate effect which sedation impact duration and depth is lower than propofol.[18] Providing patients with peaceful situation and reducing pain is among the key factors in performing the procedure successfully,[20] thus it is rather recommended to use PR combination than KF exception in patients who have pulmonary diseases who oxygen desaturation and apnea are harmful for them and every patient who has low respiratory rate for any reason, so lower respiratory rate is harmful for him/her. Since the frequency of apnea in PR group was higher than the KF group as a preventive approach for apnea, it is advised to administer high oxygen via mask with reservoir rather nasal cannula. In 2012, Fabbri *et al*. conducted a similar study assessed ketamine, propofol and low dose remifentanil versus propofol and remifentanil for ERCP, indicating that respiratory depression was more frequent in patients who used PR. In addition, the average length of stay in the recovery room was significantly lower in the ketamine group which received ketamine-PR. Remifentanil with extremely rapid clearance and offset of effect has a very short half-life, ranging between 3 and 5 min. In the Fabbri *et al*. study, it is administered in both groups.[21] But in our study, remifentanil is just administered in the PR group which can be the result of lower length of stay in the recovery room versus the other group.

In one study that done by Angsuwatcharakon *et al*., Cocktail sedation containing propofol provides faster recovery time and better patients' satisfaction for patients undergoing ERCP.[22] Furthermore, the results of Amornyotin study showed that sedation for gastroesophageal endoscopy procedure can be safely and effectively performed with a multi-drug IV regimen utilizing anesthesiologist or nonanesthetic personnel with appropriate monitoring. However, comprehensive presedation assessment and proper patient selection and preparation as well as availability of skilled professionals for sedation administration are key components to provision of quality patient care.[23] Also in Triantafillidis *et al*. study, the same results were achieved.[24] In 2013, Gül *et al*. compared fentanyl and remifentanil combination impact on children endoscopy in Turkey. According to this study, the frequency and duration of apnea in patients receiving remifentanil were significantly higher than the group receiving fentanyl. In this study, similar to the present study, respiratory rate and the duration of stay in the recovery room in remifentanil group procedure was significantly lower than the fentanyl group.[25] The main limitation of our study is that the study duration was short and there was no follow-up after discharge and also the duration of ERCP is not assessed in our study.

CONCLUSION

Ketamine-fentanyl and PR combinations are not significantly different in sedation score, but PR combination provides better pain control with less nausea, as well as shorter recovery time. On the other hand, it causes more respiratory side effects, that is, apnea and need to oxygen. While this study has its own limitations, more investigations with larger sample sizes and longer follow-up periods as well as using other combinations are suggested to determine the best choice for sedation prior to ERCP.

AUTHOR'S CONTRIBUTIONS

SMH carried out the design and coordinated the study, participated in most of the experiments and participated in manuscript preparation. PL provide assistance in the design of the study, coordinated and carried out all the experiments, analyzed and interpreted the data, and prepared the manuscript. All authors have read and approved the content of the manuscript.

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REFERENCES

1. Thomson A, Andrew G, Jones DB. Optimal sedation for gastrointestinal endoscopy: Review and recommendations. J Gastroenterol Hepatol 2010;25:469-78.
2. Chowdhury IH, Maruf AA, Lateef KA, Reza SM, Hye MA. Sedation for ERCP-comparison between ketamine diazepam combination with propofol fntanyl combination. J Bangladesh Soc Anaesthesiol 2009;20:45-50.
3. Mazzon D, Germanà B, Poole D, Celato M, Bernardi L, Calleri G, *et al.* Conscious sedation during endoscopic retrograde colangiopancreatography: Implementation of SIED-SIAARTI-ANOTE guidelines in Belluno Hospital. Minerva Anestesiol 2005;71:101-9.
4. Chainaki IG, Manolaraki MM, Paspatis GA. Deep sedation for endoscopic retrograde cholangiopacreatography. World J Gastrointest Endosc 2011;3:34-9.
5. American Society of Anesthesiologists Task Force on Sedation and Analgesia by Non-Anesthesiologists. Practice guidelines for sedation and analgesia by non-anesthesiologists. Anesthesiology 2002;96:1004-17.
6. Khajavi M, Emami A, Etezadi F, Safari S, Sharifi A, Shariat Moharari R. Conscious sedation and analgesia in colonoscopy: Ketamine/propofol combination has superior patient satisfaction versus fentanyl/propofol. Anesth Pain Med 2013;3:208-13.
7. McQuaid KR, Laine L. A systematic review and meta-analysis of randomized, controlled trials of moderate sedation for routine endoscopic procedures. Gastrointest Endosc 2008;67:910-23.
8. Varadarajulu S, Eloubeidi MA, Tamhane A, Wilcox CM. Prospective randomized trial evaluating ketamine for advanced endoscopic procedures in difficult to sedate patients. Aliment Pharmacol Ther 2007;25:987-97.
9. Javid MJ, Hajijafari M, Hajipour A, Makarem J, Khazaeipour Z. Evaluation of a low dose ketamine in post tonsillectomy pain relief: A randomized trial comparing intravenous and subcutaneous ketamine in pediatrics. Anesth Pain Med 2012;2:85-9.
10. Kongkam P, Rerknimitr R, Punyathavorn S, Sitthi-Amorn C, Ponauthai Y, Prempracha N, *et al.* Propofol infusion versus intermittent meperidine and midazolam injection for conscious sedation in ERCP. J Gastrointestin Liver Dis 2008;17:291-7.
11. Rex DK. Review article: Moderate sedation for endoscopy: Sedation regimens for non-anaesthesiologists. Aliment Pharmacol Ther 2006;24:163-71.
12. Ellett ML. A literature review of the safety and efficacy of using propofol for sedation in endoscopy. Gastroenterol Nurs 2010;33:111-7.
13. Pournajafian A, Rokhtabnak F, Kholdbarin A, Ghodrati M, Ghavam S. Comparison of remifentanil and fentanyl regarding hemodynamic changes due to endotracheal intubation in preeclamptic parturient candidate for cesarean delivery. Anesth Pain Med 2012;2:90-3.
14. Farnad I, Mahmoud-Reza A, Zahra TA, Hamid-Reza FS. Use of remifentanil and alfentanil in endotracheal intubation: A comparative study. Anesth Pain Med 2011;1:61-5.
15. Berzin TM, Sanaka S, Barnett SR, Sundar E, Sepe PS, Jakubowski M, *et al.* A prospective assessment of sedation-related adverse events and patient and endoscopist satisfaction in ERCP with anesthesiologist-administered sedation. Gastrointest Endosc 2011;73:710-7.
16. Barash PG. Clinical anesthesia. Philadelphia, PA 19106 US: Lippincott Williams & Wilkins; 2009.
17. Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedation with alphaxalone-alphadolone. Br Med J 1974;2:656-9.
18. Aldrete JA. The post-anesthesia recovery score revisited. J Clin Anesth 1995;7:89-91.
19. Mortero RF, Clark LD, Tolan MM, Metz RJ, Tsueda K, Sheppard RA. The effects of small-dose ketamine on propofol sedation: Respiration, postoperative mood, perception, cognition, and pain. Anesth Analg 2001;92:1465-9.
20. Imani F, Faiz HR, Sedaghat M, Hajiashrafi M. Effects of adding ketamine to fentanyl plus acetaminophen on postoperative pain by patient controlled analgesia in abdominal surgery. Anesth Pain Med 2013;4:e12162.
21. Fabbri LP, Nucera M, Marsili M, Al Malyan M, Becchi C. Ketamine, propofol and low dose remifentanil versus propofol and remifentanil for ERCP outside the operating room: Is ketamine not only a "rescue drug"? Med Sci Monit 2012;18:CR575-80.
22. Angsuwatcharakon P, Rerknimitr R, Ridtitid W, Kongkam P, Poonyathawon S, Ponauthai Y, *et al.* Cocktail sedation containing propofol versus conventional sedation for ERCP: A prospective, randomized controlled study. BMC Anesthesiol 2012;12:20.
23. Amornyotin S. Sedation-related complications in gastrointestinal endoscopy. World J Gastrointest Endosc 2013;5:527-33.
24. Triantafillidis JK, Merikas E, Nikolakis D, Papalois AE. Sedation in gastrointestinal endoscopy: Current issues. World J Gastroenterol 2013;19:463-81.
25. Gül R, Hizli Ş, Kocamer B, Koruk S, Şahin L, Kilinçaslan H, *et al.* The safety and efficacy of remifentanil compared to fentanyl in pediatric endoscopy. Turk J Med Sci 2013;43:611-6.

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