Original Article

A comparison between the effects of propofol–fentanyl with propofol–ketamine for sedation in patients undergoing endoscopic retrograde cholangiopancreatography outside the operating room

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ABSTRACT

Background: The efficient and secure techniques of anesthesia and sedation have always been needed for. One of these procedures is endoscopic retrograde cholangiopancreatography (ERCP), due to its painfulness and long duration, has high sensitivity. We compare the effects of propofol–fentanyl (PF) with propofol–ketamine (PK) to sedate patients undergoing ERCP.

Methods: In this clinical trial, patients were divided into two groups of 49 people. A group received a pharmaceutical combination of PK, and another group received a pharmaceutical combination of PF. Vital signs of patients, Ramsey Sedation Score, and pain of patients were assessed. The total dosage of used propofol was also recorded.

Results: There was no significant difference seen in the patients’ hemodynamic characteristics in both groups. Pain at the end of surgery and an hour after it in the PK group was less that was not statistically significant. By Ramsey Sedation Score also significant differences were not seen between groups (p = 0.68). By using total dose of propofol used also a significant difference was not observed between the two groups (p = 0.36). Rate of apnea in PK group was 32% and in the PF group was 63%, which this difference was statistically significant (p < 0.05).

Conclusion: A comparison between the two drugs combination shows that although in terms of hemodynamic and sedation criteria both groups were similar, but because of the lower amount of pain and apnea in the PK group, this combination may generally in the ERCP procedure is more efficient and safer.

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At a glance commentary

Scientific background

In 2012 Khutia et al. compared a combination of Propofol and fentanyl infusion with Propofol and ketamine infusion in the pediatric short-term procedures. In their study, in the propofol-fentanyl group more hypotension was seen compared with the propofol-ketamine group that was statistically significant as well, and this result is different with our study because hemodynamically differences was not observed in our study.

What this study adds to the field

By this study we will have guidelines about effective and with less side effects combination of drugs for sedation in ercp patients. The distinction between our study with other studies is that while comparison between the two medicinal compound has been applied in the studies of children limited studies have investigated its application in the endoscopic procedures of adults.

According to the multitude of surgical procedures outside the operating room, efficient and secure anesthesia techniques appreciably are required [1].

Sedation is a technique in which prescription of a tranquilizer medication leads to analgesia or without analgesic effects, creates a situation in which procedure can be tolerated while maintaining cardio-respiratory function [2].

One of these procedures is endoscopic retrograde cholangiopancreatography (ERCP), and because it is painful and also has long duration, ERCP needs more attention and is sensitive.

Sedation technique that used for these procedures should be in such a way that, despite to create analgesia and prevent cough, maintaining the spontaneous breathing and hemodynamic stability. Many drugs individually or in combination with each other, including benzodiazepines, opioids, propofol, and ketamine, can be used to create sedation [3].

Due to favorable features such as fast start and end of its effect, the short length of effects and quiet awakening, propofol is popular among certain outpatient procedures [4]. However, because it does not have analgesic effects in the painful procedures, large doses are used that may increase the risk of respiratory depression and hemodynamic consequences; for this reason the use of analgesic medicine in combination with propofol becomes essential [5].

Among the opioid drugs, fentanyl could lead to reducing the dosage of propofol and reduce its complications [6]. While it has been reported that alfentanil and remifentanil cause to worsen the cardio-respiratory depression effects of propofol [7].

Ketamine, a derivative of phencyclidine, has a noteworthy ability to create analgesia without respiratory depression that is considered beneficial compared to the opioids. Another advantage of it is sympathomimetic effects that can create the hemodynamic stability when using propofol. In addition to this, it can decrease the pain of propofol injection by local anesthesia effects [8–10].

On the other hand, the probability of occurrence of complications such as the increased blood pressure, the elevated intraocular pressure and or disorders, such as the bad dreams, will limit the usage of this medicine alone; as a result, it seems that better results can be achieved with a combination of propofol and ketamine by reducing the side effects of each other.

According to the lack of extensive studies about the combination of propofol and ketamine in endoscopic procedures, in this study we compared the effects of propofol–fentanyl (PF) with effects of propofol–ketamine (PK) for patients sedating undergoing ERCP outside the operating room.

Methods

After obtaining a written permission from the Ethics Committee (2013, 286, IRCT2014031316976N1), and the Pain Research Center (pain 2013–05), in this double-blind clinical trial, a total of 98 patients between 18 and 65 years old, who were referred to hospital during 2013–2014 to perform the ERCP (with a length of time of <45 min), were selected as inclusion criteria and were divided into two groups of 49 patients randomly (using odd and even numbers). Furthermore, in this study, the exclusion criteria were patients with allergies to medications, eggs, and soy, age <18 or more than 65 years, renal or hepatic failures, the difficult airway, ASA classes III and IV, having contraindications for propofol, ketamine, or fentanyl.

Based on previous studies, the sample size with a confidence level of 95% and a test power of 90% in each group were estimated to be 49, where 40% of the patients in both groups were women, and the remaining 60% were men.

At the beginning of a visit, the written consent was obtained for inclusion. Monitoring of patients, including systolic and diastolic blood pressure, heart rate, percentage of blood oxygen saturation and capnography, was measured and recorded in an interval time of each 5 min until the end of the procedure.

In the beginning, both groups of patients in the supine position received 0.05 mg/kg of intravenous midazolam (Chemie Tehran, Iran) and then, in the first group, 0.5 mg/kg of propofol (Claris, India) and 1 μg/kg of fentanyl (Caspian Tamin, Iran) were injected; also, in the second group, 0.5 mg/kg of propofol was injected and 0.5 mg/kg of ketamine (Rotex, Germany) was used for bolus injection, and after 90 s sedation level, the patient was assessed and recorded based on the criteria for Ramsey (1). A Ramsey score of five or six was considered as a desirable limit of sedation and score less than five was considered as insufficient rate of sedation. If the insufficient rate of sedation in a patient was seen, a bolus dose of propofol 0.5 mg/kg was prescribed. Then, if necessary, the dose can be repeated every 60 s. (1). The patient’s respiration was controlled during a procedure with a bag and a mask.

At the end of surgery, patients were evaluated using Aldrete criteria (Aldrete postanesthetic recovery scoring) and time for reaching them to a score equal or more than eight was recorded.

The patients then were transferred to the postanesthesia care unit and were monitored with the help of a pulse and noninvasive blood pressure monitoring, and complications such as oxygen saturation percentage drop, systolic blood pressure, and heart rate increase were investigated. Also, the endoscopic procedure was performed by a skilled endoscopist.
pressure drop, or nausea and vomiting, psychiatric side effects, optical side effects, shivering, and vertigo were recorded. During this study, none of the patients were excluded from the study. After obtaining the scores equal to or greater than 9 based on the scoring system criteria for exit from monitoring care unit, patients were discharged, and the duration of hospitalization in recovery was also recorded.

At the start of a procedure, at the end of a procedure and an hour after finishing the procedure the amounts of pain assessed based on patients response to the Ambesh score [11]. Furthermore, all amount of propofol used, rate of nausea and vomiting, and apnea in both groups were recorded.

**Statistical analysis**

The data has been reported based on mean ± standard deviation. After assessing normal data distribution, by using the Kolmogorov–Smirnov test as well as the consistency of the variance using Loon test, to compare groups the independent t-test was used and if the data distribution is abnormal or ranked parameters, the Mann–Whitney U-test was used. Alpha at a level of 0.05 was considered statistically significant. All statistical analyses were performed using SPSS version 16 (SPSS Inc., Chicago, IL, USA).

**Results and discussion**

Demographic characteristics of participants as well as the duration of anesthesia and surgery are displayed in [Table 1]. In each group, participants were 49 people, who did not have a significant difference with each other in terms of age, weight, gender, and time spent for doing procedure.

**Table 1 – Demographic characteristics of participants.**

| Procedure time (min) | Height (m) | Weight (kg) | Age (years) | Groups | p value |
|----------------------|------------|-------------|-------------|--------|---------|
| 162.18 ± 4.41        | 26.34 ± 3.23 | 66.09 ± 7.12 | 42.22 ± 7.10 | PF group |
| 163.65 ± 4.27        | 27.36 ± 2.26 | 67.94 ± 6.24 | 41.18 ± 5.98 | PK group |
| p = 0.88             | p = 0.52 | p = 0.67 | p = 0.54 | Significance |
showed that a combination of ketamine—propofol is more acceptable than propofol [18] and or an assessment of recovery time in a study showed that the combination of PK compared with a combination of PF, has longer recovery time [14].

When talking about ERCP its complications also should be detected, an important problem, which might not be considered. The patient’s pain during ERCP is important because studies show that pain while performing ERCP has a great relationship with its complications such as the occurrence of pancreatitis, as the most common complication of ERCP.

Hence, preparing a proper diet for pain control as a factor that causes side effects [19] is an important component of the sedation [20]. In this study, the pain of patients was studied; according to data analysis, a combination of PK is more appropriate in controlling the pain, and also the amount of apnea is less by this combination, so it can be concluded that a combination of PK generally is more efficient and safer in the ERCP procedure.

**Conclusion**

A comparison between the two drugs combination shows that while both groups were similar in terms of the hemodynamic and sedation criteria, because of the lower amount of pain and apnea in the PK group, the mentioned combination generally in the ERCP procedure is more efficient and more secure.

In the end, the broader spectrum studies are recommended for investigating and comparing other medicinal combinations and their effects to perform more secure sedation.

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**Conflicts of interest**

There are no conflicts of interest.

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**References**

[1] Akin A, Esmaglu A, Tosun Z, Gulcu N, Aydogan H, Boyaci A. Comparison of propofol with propofol–ketamine combination in pediatric patients undergoing auditory brainstem response testing. Int J Pediatr Otorhinolaryngol 2005;69:1541–5.
[2] Krauss B, Green SM. Sedation and analgesia for procedures in children. N Engl J Med 2000;342:938–45.
[3] Joo JD, In JH, Kim DW, Jung HS, Kang JH, Yeom JH, et al. The comparison of sedation quality, side effect and recovery profiles on different dosage of remifentanil patient-controlled sedation during breast biopsy surgery. Korean J Anesthesiol 2012;63:431–5.
[4] Akcaboy ZN, Akcaboy EY, Albayrak D, Altinoren B, Dikmen B, Gogus N. Can remifentanil be a better choice than propofol for colonoscopy during monitored anesthesia care? Acta Anaesthesiol Scand 2006;50:736–41.
[5] Lichtenbelt BJ, Mertens M, Vuyk J. Strategies to optimise propofol-opioid anaesthesia. Clin Pharmacokinet 2004;43:577–93.
[6] Dima N, Astuto M, Rizzo G, Rosano G, Naso P, Aprile G, et al. Propofol sedation with fentanyl or midazolam during oesophagogastroduodenoscopy in children. Eur J Anaesthesiol 2005;22:848–52.
[7] Moerman AT, Stryu MM, Vereecke HE, Herregods LL, De Vos MM, Mortier EP. Remifentanil used to supplement propofol does not improve quality of sedation during spontaneous respiration. J Clin Anesth 2004;16:237–43.
[8] Koo SW, Cho SJ, Kim YK, Ham KD, Hwang JH. Small-dose ketamine reduces the pain of propofol injection. Anesth Analg 2006;103:1444–7.
[9] Akhondzadeh R, Runassi N. Evaluation of analgesic effect of the ketamine on pain injection of propofol in patients undergoing general anesthesia 2014;3:72–5.
[10] Akhondzadeh R, Pipelzade MR, Gousheh MR, Sarrafan N, Mahmoodi K. Comparison of the analgesic effect of intra-articular and extra-articular injection of morphine and ketamine compound in arthroscopy lower limb surgery under spinal anesthesia. Pak J Med Sci 2014;30:942–5.
[11] Li L, Chen HZ, Long B, Meng LX. Preventive function of remifentanil to propofol injection pain. Pract Pharm Clin Remedies 2009;12:175.
[12] Friedberg BL. Propofol–ketamine technique: dissociative anesthesia for office surgery (a 5-year review of 1264 cases). Aesthetic Plast Surg 1999;23:70–5.
[13] Hui TW, Short TG, Hong W, Suen T, Gin T, Plummer J. Additive interactions between propofol and ketamine when used for anesthesia induction in female patients. Anesthesiology 1995;82:641–8.
[14] Khutia SK, Mandal MC, Das S, Basu SR. Intravenous infusion of ketamine–propofol can be an alternative to intravenous infusion of fentanyl–propofol for deep sedation and analgesia in pediatric patients undergoing emergency short surgical procedures. Indian J Anaesth 2012;56:145–50.
[15] Andolfatto G, Abu-Laban RB, Zed PJ, Staniforth SM, Stackhouse S, Moadebi S, et al. Ketamine–propofol combination (ketofol) versus propofol alone for emergency department procedural sedation and analgesia: a randomized double-blind trial. Ann Emerg Med 2012;59:504–12.
[16] David H, Shipp J. A randomized controlled trial of ketamine/propofol versus propofol alone for emergency department procedural sedation. Ann Emerg Med 2011;57:435–41.
[17] Phillips W, Anderson A, Rosengeen M, Johnson J, Halpin J. Propofol versus propofol/ketamine for brief painful procedures in the emergency department: clinical and bispectral index scale comparison. J Pain Palliat Care Pharmacother 2010;24:349–55.
[18] Shah A, Mosdossy G, McLeod S, Lehnhardt K, Peddle M, Rieder M. A blinded, randomized controlled trial to evaluate ketamine/propropofol versus ketamine alone for procedural sedation in children. Ann Emerg Med 2011;57:425–33.e2.
[19] Nesioonpour S, Mokmeli S, Vojdani S, Mohtadi A, Akhondzadeh R, Behaeen K, et al. The effect of low-level laser on postoperative pain after tibial fracture surgery: a double-blind controlled randomized clinical trial. Anesth Pain Med 2014;4:e17350.
[20] Vandervoorst J, Soetikno RM, Tham TC, Wong RC, Ferrari Jr AP, Montes H, et al. Risk factors for complications after performance of ERCP. Gastrointest Endosc 2002;56:652–6.