

A Comparison of Premedication Injections of Magnesium Sulfate, Ketamine and Lidocaine on the severity of Pain Induced by Intravenous Injection of Propofol

Masoum Khoshfetrat¹, Faranak Beirami¹, Forogh Safar Panah¹, Aliakbar Keykha^{2*}

Background: The pain induced by intravenous injection of propofol is controlled using a variety of methods, but there is no consensus in choosing the best effective method. Therefore, this study was conducted to compare premedication injections of magnesium sulfate, ketamine and lidocaine on pain induced by intravenous injection of propofol.

Methods: The present double-blind clinical trial was conducted on 150 patients with elective orthopedic surgery under general anesthesia. The patients were randomly assigned into three groups of 50; Group I: 2 cc magnesium sulfate 20%, Group II: 2 cc Ketamine at a dose of 0.1mg/kg and Group III: 2 cc lidocaine 2% at a dose of 0.05mg/kg. One minute after injecting the drugs, 2mg/kg intravenous propofol was injected in all groups and then a trained unaware expert evaluated the severity of subsequent pain using a Numeric Pain Rating Scale.

Results: The mean age of the patients was 39.3±12.3 years, and the mean weight was 67.4±11.5 kg. The patients consisted of 98 (65.4%) males and 52 (34.6%) females. Ten in the Group magnesium sulfate, eight in the Group ketamine and seven in the Group lidocaine complained of pain. The mean pain severity was 0.85±0.38 in the Group magnesium sulfate, 0.66±0.26 in the Group ketamine and 0.62±0.22 in the Group lidocaine (P=0.513).

Conclusion: The Group lidocaine showed further pain relief compared to other two groups, but there was no statistically significant difference.

Keywords: ketamine; lidocaine; magnesium sulfate; pain induced by injection of propofol

Propofol is one of the most widely used drugs for induction of anesthesia, whose common application is due to high clearance and fast awakening of patient [1]. Propofol-induced anesthesia is associated with adverse complications, including severe pain on injection, myoclonus, apnea, reduced blood pressure and rarely thrombophlebitis. The pain is one of the major side effects of propofol injection, and its incidence varies from 28% to 90% in adults [2-3]. The incidence of pain has been reported to be 80 to 90% in the case of injection in the back-of-hand vessels [4]. Many patients reported severe pain after drug injection and some of them stated unbearable pain [5]. The patients suffering from injection-induced pain may experience anxiety, fear, fatigue and ischemia or myocardial infarction [6]. Instead, reducing the injection-induced pain increases the patient's satisfaction and safety [3]. The injection-induced pain is attenuated through various

techniques, including injection of drugs at different rates and fluid injection at intervals, change in the temperature of the injectable fluid, or combination with other drugs [4,7]. One of the most accepted ways is using lidocaine as a premedication in angiocath (PVC) at the injection site of propofol [7]. However, studies have shown that this method does not relieve pain completely, and the patient's problem will continue [8]. Therefore, a combination therapy is proposed to solve this problem [9]. Other studies have suggested other methods for controlling pain, including the injection of low doses of narcotics such as sufentanil and butorphanol [10-11] injection in large vessels and lidocaine injection together with tourniquet closure [12], cold-warm propofol [13], propofol dilution and metoclopramide injection as a premedication [14], magnesium [15], beta blocker [16], midazolam injection to forget the pain on injection [17], 5-HT₃ receptor antagonists [18], or Alpha-2 agonists like dexmedetomidine [3]. Considering the contradictory results obtained in previous studies and the necessity of using propofol in short-term surgery, we decided to conduct the current study aiming to compare premedication injections of magnesium sulfate, ketamine and lidocaine on reducing the pain induced by intravenous injection of propofol.

From the ¹Department of Anesthesiology and critical care, Khatamolambnia hospital, Zahedan University of Medical Sciences, Zahedan, Iran.

²Community Nursing Research Center, Zahedan University of Medical Sciences, Zahedan, Iran.

Received: 28 May 2017, Revised: 19 Jun 2017, Accepted: 4 July 2017

The authors declare no conflicts of interest.

*Corresponding author: Aliakbar Keykha, MSc. Community Nursing Research Center, Zahedan University of Medical Sciences, Zahedan, Iran. E-mail: aliakbar.keykha@gmail.com

Copyright © 2017 Tehran University of Medical Sciences

Methods

The present double-blind clinical trial was conducted on 150 patients undergoing elective orthopedic surgeries referring to Khatam-ol-Anbia Hospital after approval by the Research and Technology Deputy of Zahedan University of Medical Sciences, Iran, obtaining approval from the Ethics Committee of the university and receiving informed consent from the patients or legal guardian. The sample size was considered to be 150 according to previous studies and the formula for calculating the sample size [19-21]. Inclusion criteria were ages 18-60 years, Class I and II American Society of Anesthesiology (ASA), no history of known skin disease and severe burns in the organs, lack of diabetes or heart, liver and kidney disorders, no history of known allergy to used drugs, no history of addiction to alcohol and oral or injectable drugs. Exclusion criteria included drug sensitivity, dissatisfaction of patients and their caregivers to continue the study process and the need for opiate injection before surgery. The patients were randomly divided into three groups of 50 after enrolment in the study. In order to randomize, 150 colour cards were made in the three groups of red (the Group of magnesium sulfate), blue (the Group ketamine) and yellow (the Group lidocaine). Each patient received a card. Then the venipuncture was performed from the left antecubital fossa with angiocath number 20 (pink) (venipuncture was performed from the right hand only if surgery on the left hand). Then cardiac monitoring, vital signs control, pulse oximetry, and Ringer serum infusion of 5 cc/kg were applied for all the patients. Prior to induction of anesthesia, Group I received 2 cc magnesium sulfate 20%, Group II took 2 cc Ketamine at a dose of 0.1 mg/kg and Group III received 2 cc lidocaine 2% at a dose of 0.05 mg/kg. The researcher prepared drugs in the syringe, and

then presented to an anaesthetist who was unaware of the type of drug and the patient in the group.

One minute after injecting the drugs, 2mg/kg intravenous propofol was injected in all groups and then the same trained-unaware expert evaluated the severity of subsequent pain in the injection site using a numeric pain rating scale ranging from zero to ten. The anaesthetic process continued for all patients in the same way. First, ventilation with masks and oxygen was performed and then, 1 µg/kg of intravenous remifentanyl and 0.1 mg/kg pancuronium bromide and 3 lit/min of nitric oxide gas as well as intubation and mechanical ventilation. Throughout the period, the patients were examined for the incidence rate of adverse effects from drugs and recorded in a pre-prepared form for each patient in case of occurrence. Data were analyzed by SPSS software using descriptive statistics, one-way ANOVA and Chi-square.

Results

The mean age of the patients was 39.3 ± 12.3 years, and the mean weight was 67.4 ± 11.5 kg. The patients consisted of 98 (65.4%) males and 52 (34.6%) females. The patients in the Group magnesium sulfate included 29 (58%) males and 21 (42%) females. The patients in the Group ketamine had 36 (72%) males and 14 (28%) females. In the Group lidocaine group, 33 (66%) were males and 17 (44%) females. There was no significant difference in the gender between the groups according to Chi-square test ($P = 0.337$). The lowest mean score of pain was observed in the Group lidocaine. However, there was no significant difference in the mean score of pain in three groups based on ANOVA test. The results in terms of the number of patients who experienced the pain are presented in (Table 1).

Table 1- Comparison of the number of patients and their pain in the three groups

Groups receiving Premedications	Number	Number of people experiencing pain after injection	P	Mean score of pain \pm SD	P
Magnesium sulfate	50	10 (20%)	0.715	0.85 \pm 0.38	0.513
Ketamine	50	8 (16%)		0.66 \pm 0.26	
Lidocaine	50	7 (14%)		0.62 \pm 0.22	

The level of side effects from the drugs were different in the studied groups; 24% in the Group magnesium sulfate (4 (8%) had rigidity and 8 (16%) had flushing), 6% in the Group ketamine (3 (6%) patients with psychological complications) and the lowest level in the Group lidocaine group including only one person with hypotension

Discussion

The results obtained from the present study showed that all used drugs reduced the pain caused by propofol injection though the pain control was better in patients who received lidocaine but there was no statistically significant difference between the groups. In line with the current results, Safavi et al. compared ketamine, lidocaine, and magnesium with placebo and reported that all three mentioned drugs could reduce the propofol-induced pain. Unlike the present study, the incidence rate of injection-induced pain was 34% in the Group magnesium and 28% in the Group ketamine and 18% in the Group lidocaine, much higher than the incidence rate of pain in this study. It is worth noting that in the above

study, the amount of injectable drugs for all patients was 2.48 mM of magnesium, 10 mg of ketamine and 30 mg of lidocaine. In the present study, the dosage of the used drugs was different, based on the weight of each patient; this is probably one of the causes of difference in the pain level reported in two studies [22]. Koo et al. examined three different doses of ketamine (10, 50 and 100 µg/kg), with 2 cc of lidocaine 2%. They reported a reduction in injection-induced pain in all groups. However, this decrease in the Group 100 µg/kg ketamine and lidocaine was significantly different from the rest. They also claimed that the administration of 100 µg/kg ketamine along with oral midazolam before surgery had the least hemodynamic changes and the best effect [23]. Alizadeh et al. tested three routes of propofol injection, including propofol combination with 40 mg of lidocaine in the first group, the same amount of intravenous injection of lidocaine and then propofol in the second group, and only propofol injection in the third group. The highest reduction in pain was seen in the Group lidocaine administered prior to propofol injection. Although the type of drugs used in the two studies was not the same,

but their results were consistent with our results given that the lidocaine injection before propofol is the best way to control the pain [21]. Consistent with the results obtained in this study, Canbay et al. compared the effect of injectable acetaminophen with lidocaine to reduce propofol-induced pain, and reported that both drugs are effective to relieve the pain caused by the injection but lidocaine showed a better effect [24]. Mohammadzadeh et al. studied the effect of magnesium sulfate, alfentanil and ketamine on the reduction of propofol-induced pain versus control group. They reported that the incidence rate of pain in these groups was 14.5, 10.9, 12.7, respectively, while 83.6% in the control group. These differences were significant between the groups and the control group, but not significant between the groups themselves, similar to the current study. Although the Alfentanil group had the least pain, but the group lidocaine in our study showed the least pain. This suggests that opiates can also have a pain-reducing effect and they can be a good alternative to lidocaine if needed. Moreover, in line with this study, 14 (25.4%) patients suffered from rigidity in the group magnesium sulphate, and 13 patients (23.6%) had psychological complications and one had rigidity in the Group ketamine [25].

Conclusion

According to the present results and in line with other studies, the injection of lidocaine before propofol seems to be the best method for controlling pain caused by drug injection.

Acknowledgment

This article has been adopted from the Thesis written by Resident of Anesthesiology and Critical Care, approved and funded by Research and Technology Deputy of Zahedan University of Medical Sciences. The researcher would like to express own gratitude to the Research and Technology Deputy of the University and the staff and orthopedic surgery ward at the Khatam-ol-Anbia Hospital of Zahedan.

References

- Kariman Majed M, Emadi S, Nasiri E, Farzin D. Comparison of the effects of different doses of ketamine propofol on haemodynamic changes of the patients during induction of anesthesia. *Journal of Mazandaran University of Medical Sciences*. 2006; 16(54):7-13.
- Tan C, Onsiang M. Pain on injection of propofol. *Anaesthesia*. 1998; 53(5):468-76.
- He L, Xu J-M, He T, Liu L, Zhu R. Dexmedetomidine pretreatment alleviates propofol injection pain. *Ups J Med Sci*. 2014; 119(4):338-42.
- Kwak K-H, Ha J, Kim Y, Jeon Y. Efficacy of combination intravenous lidocaine and dexamethasone on propofol injection pain: a randomized, double-blind, prospective study in adult Korean surgical patients. *Clin Ther*. 2008; 30(6):1113-9.
- Jeon Y. Reduction of pain on injection of propofol: combination of nitroglycerin and lidocaine. *J Anesth*. 2012; 26(5):728-31.
- Morishima T, Sobue K, Arima H, Tanaka S, So M, Ando H, et al. Profound pain due to propofol injection triggered myocardial ischemia in a patient with a suspected pheochromocytoma. *Anesth Analg*. 2003; 96(2):631.
- Picard P, Tramèr MR. Prevention of pain on injection with propofol: a quantitative systematic review. *Anesth Analg*. 2000; 90(4):963-9.
- Yamakage M, Iwasaki S, Satoh J-I, Namiki A. Changes in concentrations of free propofol by modification of the solution. *Anesth Analg*. 2005; 101(2):385-8.
- Fujii Y, Nakayama M. Prevention of pain due to injection of propofol with IV administration of lidocaine 40 mg+ metoclopramide 2.5, 5, or 10 mg or saline: a randomized, double-blind study in Japanese adult surgical patients. *Clin Ther*. 2007; 29(5):856-61.
- Ghai B, Makkar JK, Bala I, Wig J. Effect of parecoxib pretreatment and venous occlusion on propofol injection pain: a prospective, randomized, double-blinded, placebo-controlled study. *J Clin Anesth*. 2010; 22(2):88-92.
- Agarwal A, Raza M, Dhiraaj S, Pandey R, Gupta D, Pandey CK, et al. Pain during injection of propofol: the effect of prior administration of butorphanol. *Anesth Analg*. 2004; 99(1):117-9.
- Kim DH, Chae YJ, Chang HS, Kim JA, Joe HB. Intravenous lidocaine pretreatment with venous occlusion for reducing microemulsion propofol induced pain: Comparison of three doses of lidocaine. *J Int Med Res*. 2014; 42(2):368-75.
- Jeong M, Yoon H. Comparison of the effects of lidocaine pre-administration and local warming of the intravenous access site on propofol injection pain: Randomized, double-blind controlled trial. *Int J Nurs Stud*. 2016; 61:209-18.
- Chaudhary K, Gupta P, Gogia AR. A prospective, randomized, double-blind study to compare the efficacy of lidocaine+ metoclopramide and lidocaine+ ketamine combinations in preventing pain on propofol injection. *J Anesth*. 2013; 27(3):402-6.
- Sun J, Zhou R, Lin W, Zhou J, Wang W. Magnesium Sulfate Plus Lidocaine Reduces Propofol Injection Pain: A Double-blind, Randomized Study. *Clin Ther*. 2016; 38(1):31-8.
- Salman EA, Titiz L, Akpek E, Arslan G. Pretreatment with a very low dose of intravenous esmolol reduces propofol injection pain. *Agri*. 2013; 25(1):8-13.
- Boku A, Inoue M, Hanamoto H, Oyamaguchi A, Kudo C, Sugimura M, et al. Effective dosage of midazolam to erase the memory of vascular pain during propofol administration. *Anesth Prog*. 2016; 63(3):147-55.
- Wang W, Zhou L, Wu L-X, Wang T, Zhang C-B, Sun L. 5-HT3 receptor antagonists for propofol injection pain: A meta-analysis of randomized controlled trials. *Clin Drug Investig*. 2016; 36(4):243-53.
- Afhami M, Naghipour B, Hassanzadeh Salmasi P. Effect of Ephedrine on Reducing Pain Induced by Intravenous Injection of Propofol at the Time of Anesthesia Induction. *Armaghane danesh*. 2006; 10(4):1-11.
- Özkoçak I, Altunkaya H, Özer Y, Ayoğlu H, Demirel C, Çiçek E. Comparison of ephedrine and ketamine in prevention of injection pain and hypotension due to propofol induction. *Eur J Anaesthesiol*. 2005; 22(1):44-8.
- Alizadeh V, Kazemihaki B, Eftekhari J, Tizro P. Comparison of pain on propofol injection with three methods: mixed lidocaine with Propofol, propofol after lidocaine injection and purified one percent propofol injection. *Anesthesiology and Pain*. 2015; 4(3):30-7.
- Safavi M, Honarmand A. Magnesium sulfate pretreatment to alleviate pain on propofol injection: a comparison with ketamine or lidocaine. *Journal of Mazandaran University of Medical Sciences*. 2007; 17(60):30-8.
- Koo S-W, Cho S-J, Kim Y-K, Ham K-D, Hwang J-H. Small-dose ketamine reduces the pain of propofol injection. *Anesth Analg*. 2006; 103(6):1444-7.
- Canbay O, Celebi N, Arun O, Karagöz A, Sarıcaoğlu F, Özgen S. Efficacy of intravenous acetaminophen and lidocaine on propofol injection pain. *Br J Anaesth*. 2008; 100(1):95-8.
- Mohammadzadeh A, Haghghi M, Amir-alavi S, Naderi-nabi B, Nekoofard M, Abad M. A Comparison of Effects of Alfentanil, Magnesium Sulfate and Ketamin on Reduction of Pain during Propofol Injection. *Anesthesiology and Pain*. 2011; 2(5):52-8.