

# Studying Outbreak of Pain Relieving by Three Drugs Including Alfentanil, Magnesium Sulfate and Ketamine during Intravenous Injection of Propofol

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## ABSTRACT

**Purpose:** Propofol is one of the most common drugs used in anesthesia induction and the pain during its intravenous injection is one of the most important side effects that it has. Therefore, many methods and drugs have been examined so far to reduce or eliminate this side effect. In this study a lot the effects of Alfentanil, Magnesium Sulfate and Ketamine drugs on reducing the pain during intravenous injection of Propofol are investigated.

**Materials and Methods:** This study was performed on 220 patients who underwent orthopedic surgeries in Poursina hospital in 2010. The intensity of Propofol intravenous injection pain is measured after using premedication by Visual Analogue Scale (VAS). The results are analyzed using Chi square and Post hoc tests.

**Results:** According to the gathered data and analysis of variance statistic tests, we found that after Propofol injection there is a meaningful difference in quantity of VAS score among the studied groups (Chi square = 49.78 and  $df = 3$  and  $P = .0001$ ). According to Post hoc test the VAS score in Magnesium Sulfate group has a meaningful difference in comparison to other groups, while there is no meaningful difference among other groups ( $P = .05$ ).

**Conclusion:** Despite the reduction the Propofol intravenous injection pain in three studied drugs in this thesis, there is no preference among them.

**Keywords:** analgesics; non-narcotic; therapeutic use; anesthetics, intravenous; adverse effects; pain; pain management; methods; propofol; administration & dosage; adverse effects; prospective studies.

AMHSR 2015;13:108-111  
www.journals.ajau.ac.ir

## INTRODUCTION

Today Propofol is one of the most common drugs that are used through an intravenous injection.<sup>1</sup> In 1977, the use of Propofol for anesthesia was first approved. It is an insoluble substance in water; it is used for induction and maintenance of anesthesia and sedation both inside and outside the operating room.

Induction of anesthesia with Propofol associates with severe side effects, including severe pain during injection, myoclonus, apnea, hypotension and thrombophlebitis in the vessel.

Injection pain is less or equal to Etomidate, equal to Methohexital and more than Thiopental. Injection pain can

be lessened by selecting large vessels, and adding Lidocaine to Propofol or the solution formulation of Propofol. Pretreatments with small amounts of Propofol, Esmolol, Metoprolol, Magnesium, Clonidine with Ephedrine, Dexamethasone and Metoclopramide accompanied by light have been used in order to reduce the pain, which led to different results. Foss Propofol causes less injection pain but unpleasant tingling sensation in perineal areas equal to Propofol. Myoclonus injectionis the second most common side effect after injection of Propofol and is more common than Thiopental, but its occurrence, after Propofol, is less than Thiopental and Methohexital injection. Whereas, occurrence of apnea is 30 times more common than

Propofol. The most common complication of systemic hypotension is induced by Propofol, which is prescribed as narcotics escalate. The pain during intravenous infusion of Propofol is one of the major side effects and its prevalence varies from 28 to 90 percent in adults.<sup>2</sup>

There is also some other methods such as addition of Lidocaine, hot or cold, injecting the Propofol infusion into a large vein; also prescribing the medicines such as Ephedrine, Ondansetron and Thiopental is applied. Although Lidocaine is used as the most common drug to reduce the pain associated with Propofol injection, this method has been reported between 13% to 32% useless.<sup>3,4</sup>

Since reducing the pain of Propofol injection has beneficial effects in the process of anesthesia induction, the use of available drugs, cheap and good efficacy, contraindicates another drug that can be used as a replacement, which leads to a plan. A comparative study of the effects of Ketamine, Magnesium Sulfate, Alfentanil, used to reduce the pain associated with intravenous Propofol was examined.

## MATERIALS AND METHODS

This study was done as a randomized clinical trial in Poursina hospital for six months beginning in 2010 in Rasht. This study complies with ethical requirements and permissions in form of informing consent of patients. A sum of 220 patients who are candidates for orthopedic surgery of the lower or upper limbs was recruited. The control group of the study, in case of occurrence of any problems with drugs and environmental conditions, can reduce the amount of pain compared with the other groups. Since we have a lot of medical care before injection of Propofol, a control group is morally justified. This procedure was used to select patients in the operation

room; they are candidates for surgery and the research project. A nurse receptionist named patients randomly from a box containing cards labeled A, B, C, or D. A card for each enrolled patient was chosen based on block randomization. Groups include:

A: Magnesium Sulfate (20%), made in Iran

B: Fentanyl (one mL containing 500 µg/kg), made in Germany

C: Ketamine 1%, made in Germany

D: Physiological saline, made in Iran

Before the arrival of the patient to the operation room, he has been informed about the studied plan, the style of the project profile (Appendix A), and finally, and the consent (Annex II) was obtained. After entering the operating room and the placing the patient on the operating room table, an intravenous cannula (IVC) (20 gauge) with the ringer volume requirements was inserted in peripheral vein on the back of the hand (preferably non-dominant hand), while monitoring non-invasive blood pressure (BP), electrocardiography (ECG), and oxygen saturation. In order to achieve the same volume of 5 mL, the drugs, studied by anesthesia technician, were diluted at the room temperature with normal saline serum. Then the group names were labeled on each syringe mostly in the form of A, B, C, or D. The group labels are as follow:

Group A: Magnesium Sulfate for the amount of 2 mL diluted with saline to 5 mL

Group B: Alfentanil for the amount of 10 µg/kg and diluted with saline to 5 mL

Group C: Ketamine for the amount of 0.2 mg/kg of body weight diluted with saline serum to 5 mL/kg

Group D: Saline serum for the amount of 5 mL

Each group is informed by the researcher or the anesthesiologist about the type of drug (as in case of any complication can act to treatment), then is injected within 5 seconds, and after 30 seconds the Propofol 1% (made in India by Claris factory) is injected for the amount of 3 mL (equivalent to 30 mg) at a rate of 5 mL/s into the vein. After administrating the anesthesia by residents other than the researcher (who is not aware of the type of drug injected), the patient is asked for the pain or discomfort at the injection site clearly and the answer Yes or No is determined; if there is any pain, its severity is evaluated based on the Visual Analogue Scale (VAS) in the questionnaires. Then, continuation of the process of induction means anesthesia with Propofol for the amount of 2 mg/kg made masks followed by ventilation of the lungs, and if necessary anesthetic inhalation or other opioids were used. Also in case of complications such as stiffness, nerve defects, nausea, vomiting and seizures,

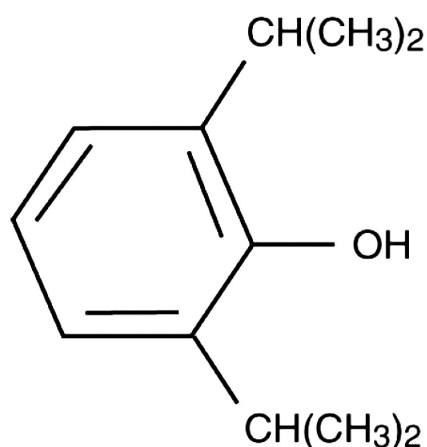


Figure 1. The biochemical structure of propofol

the data were recorded by the researcher. After gathering information from the first incidence of pain by (p1, p2, p3, p4) and 95% confidence interval (CI) (p1, p2, p3, p4), the ratio of K-square test was used to reduce the pain significantly according to the groups studied.

Four levels of success among three groups of drugs were compared according to the volume sampling formula with certainty of 95% and test ability of 80% for maximum sample at each group, which consists of 55 persons making a total number of 220 persons in 4 groups (P1 = 85, P2 = 60, P3 = 65)

$$n = \frac{\left( Z_{1-\frac{a}{2}} + Z_{1-b} \right)^2 \left[ P_1(1-P_1) + P_2(1-P_2) \right]}{(P_1 - P_2)^2}$$

### RESULTS

A study on 4 groups of 55 members (total of 220 patients) was done. Population findings (including age,

**Table 1.** The basic characteristics of the patients into 4 groups

Variables	Number	Percent
Age groups		
20<=	53	24/1
21 – 30	61	27/7
31 – 40	31	14/1
41 – 50	30	13/6
51 >=	45	20/5
Age (years)		
SD (Standard deviation) ± Average	14/29 ± 34/88	
Weight (kg)		
SD (Standard deviation) ± Average	11/60 ± 67/46	
gender		
Male	151	68/8
Female	69	31/4
Class of Anesthesia		
I	189	85/9
II	31	14/1

**Table 2.** Distribution of pain after injections of propofol in 4 groups.

Group of pain	Magnesium Sulfate		Alfentanil		ketamine		Normal saline		Pluralization	
	Member	percent	Member	percent	Member	percent	Member	percent	Member	percent
pain	8	14/5	6	10/9	7	12/7	46	83/6	67	30/5
No pain	47	85/5	49	89	48	87/3	9	16/4	153	69/5
pluralization	55	100	55	100	55	100	55	100	220	100

**Table 3.** The mean pain score in patients when injected propofol into 4 groups.

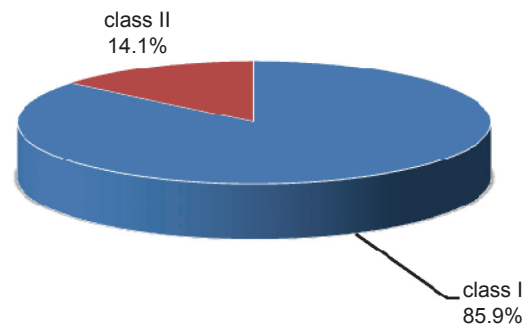
Group	Member	Average of VAS	SD (Standard deviation)	Amount of (F)	Statistical estimation
Magnesium Sulfate	55	/23	/71	49/78	P< .0001
Alfentanil	55	/23	/71		
ketamine	55	/2	/55		
Normal saline	55	1/69	1/01		

weight, sex, and physical class) did not show significant differences between the two groups, which is given in **Table 1**. According to the information obtained, the rate of pain in four groups had a statistically significant difference (P = .0001), so that the groups of Magnesium Sulfate, Alfentanil and Ketamine, respectively, had a value equal to 14.5% and 10.9% and 12.7 % in the incidence of pain; while the rate in the control group (receiving saline) was equal to 83.6%, which is given in **Table 2**. The difference in the incidence of pain was statistically significant between the first three groups (Magnesium Sulfate, Alfentanil and Ketamine) and the control group; while there was no such difference among the first three groups.

According to analysis of variance statistical test (ANOVA) the pain score (VAS) in four groups was not statistically identical (P = .0001) as the average amount of pain in Ketamine group (0.2 ± 1.01) was significantly lower than the other groups, while the greatest pain was recorded in saline serum group (1.69 ± 1.01), which are all listed in **Table 3** and **Table 4** comparing the effects of the four groups.

### DISCUSSION

The pain during intravenous infusion of Propofol is



**Figure 2.** Frequency distribution of anesthesia classes in the study group

**Table 4.** Distribution frequency of side effects of injected drugs were distributed in 4 groups.

Type of complication	Magnesium Sulfate		Alfentanil		Ketamine		Normal saline		Pluralization	
	Member	Percent	Member	Percent	Member	Percent	Member	Percent	Member	Percent
Rigidity	14	25/4	0	0	1	1/8	0	0	15	6/8
Psychological	0	0	0	0	13	23/6	0	0	13	5/9
Hypotension	0	0	1	1/8	0	0	0	0	1	/4
Red heat	11	20	0	0	0	0	0	0	11	5

one of the most important and common side effects in studies such as the study of by Picard and Tramèr<sup>5</sup> and Miller and colleagues,<sup>6</sup> in which from 28% to 90% of adults have been reported.

In this study, factors such as age and gender were compared in groups and were known as a confounding factor. In a study on 100 patients by Memis and colleagues (including Magnesium Sulfate and saline groups), the pain in the Magnesium Sulfate group was 8%<sup>7</sup> and the amount of Magnesium in the study group was 14.5 %, which represents a higher incidence. In another study performed by Iyilikci and colleagues about reducing the pain of intravenous Propofol by Alfentanil a rate of 10.6% was reported<sup>8</sup> and this rate in our study on Alfentanil group was 10.9%, which confirms the previous studies.

Koo and colleagues studied the effects of Ketamine in 100 patients aged 15 to 63 years old and the incidence of pain was reported in the group receiving Ketamine as 14%,<sup>9</sup> while in our study the rate of 12.7% was represented in the same group. In the final review on the incidence of pain in the first three groups (receiving Magnesium Sulfate, Alfentanil and Ketamine) compared with the control group (receiving saline), the result has been significant and confirms the previous findings on the effectiveness of these drugs,<sup>9</sup> which is to reduce pain caused by intravenous injection of Propofol. Although the incidence of pain in the group receiving Alfentanil and Ketamine had lower rates than the Magnesium Sulfate group, this difference was not statistically significant in this study and therefore Alfentanil can't be a better choice.

## CONCLUSIONS

According to this study, it seems that using Magnesium Sulfate, Alfentanil and Ketamine medications were effective in reducing the pain associated with intravenous Propofol, and any priority among these three drugs to reduce the pain associated with intravenous Propofol does not exist.

## ACKNOWLEDGMENTS

The authors express thankful regards to the research

department of AJA University of Medical Sciences. Last but not the least, they express their gratitude to all the patients who cooperated in conducting this research.

## CONFLICT OF INTEREST

None declared.

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Received July 2015

Accepted August 2015