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The Effect of Isometric Exercises and lidocaine 2% on Pain Relief during Intravenous Propofol Injection: A Randomized Clinical Trial

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Abstract

Background: One of the most common adverse effects of propofol is pain during intravenous injection.

Aim: This study was performed aimed to compare the effect of isometric exercises and lidocaine 2% on pain relief during intravenous propofol injection.

Method: This randomized clinical trial (RCT) study was performed in 2020 on 106 patients who were candidates for general anesthesia for different surgical treatments in Neyshabur 22 Bahman Hospital. The subjects were randomly allocated into three groups by permuted block randomization. Group A received propofol 1% with 40 mg lidocaine 2%, group B received pure propofol 1%, and group C completed 5 cycles of isometric exercises before injection of 1% pure propofol. Data collection tools consisted of a demographic information questionnaire and Ambesh four-point scale. Data were analyzed by SPSS software (version 16) and Fisher's exact test, Mann-Whitney U test, and analysis of variance (ANOVA). $P<0.05$ was considered statistically significant.

Results: In this study,. The majority of patients underwent general surgery,. There was no significant difference between pain intensity in groups A and C, but group B reported significantly higher pain intensity than the intervention groups ($P<0.001$).

Implications for Practice: The use of both lidocaine 2% and isometric exercises reduces the pain intensity of propofol injection. Therefore, the use of these two methods is recommended.

Keywords: Isometric exercises, Lidocaine 2%, Pain, Intravenous injection, Propofol

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Introduction

Propofol seems to be the most commonly used venous anesthetic medication for induction and maintenance of anesthesia in the operating room (1). Since its introduction as an anesthetic medication in the 1980s, due to its numerous applications and advantages, propofol was regarded not only in the operating room but also in other departments (2, 3).

Propofol produces anesthesia by increasing GABA receptor activation (4). In general anesthesia, the induction dosage of propofol is 2.5 mg/kg, inducing anesthesia within 90-100 seconds (5). One of the benefits of propofol is that faster recovery from anesthesia, while reducing nausea and vomiting (6). However, like any other chemical medication, some complications may be associated. Pain on injection, apnea, low blood pressure (7), and thrombophlebitis in the vein used to infuse propofol are regarded as the complications of propofol (8). According to observations, one of the most important features of propofol is pain on injection that produces discomfort for patients (9). Researchers have discovered two major sources of discomfort after propofol injection. First, phenol may cause local pain immediately by stimulating topical intravenous administration. Second, the indirect release of Kininogens from endothelial cells may stimulate pain at the nerve endings close to the vessel (10). In general, the incidence of pain on propofol injection is high (11). Shoaibi et al. showed that 45-75% of intravenous propofol injections resulted in pain (12). Another research found that the incidence of pain in adults after anesthesia with pofol injection ranged from 28% to 90%, although it might be greater (13). Many factors influence the intensity of pain on propofol injection, including injection speed, the size of the vessel, the concentration of propofol in the aqueous phase, and the effect of buffer solution (14). Since pain during intravenous propofol injection is one of the most prevalent adverse effects of this drug, the management and alleviation of pain is helpful during anesthesia induction process (8). Therefore, many solutions have been proposed, including lidocaine injection (15), pre-warming the drug (16), pre-cooling injection site (17), injecting ketamine before propofol injection (18), dexamethasone (19), and injection into larger vessels (20), that the most commonly used method is lidocaine injection (21). Lidocaine is a local anesthetic which decreases pain by blocking peripheral neural pathways via impacting the excitable membranes. It is used as pre-treatment before propofol injection or as a lidocaine–propofol admixture (22). Since chemical drugs have some adverse effects and are expensive, nowadays, non-pharmacological methods are emphasized to be used for treatment of diseases and medical disorders (23-25). Isometric exercises are one of the non-pharmacological methods (26).

Exercise with all of its proven benefits, positively affects the body's health. In fact, it strengthens the muscles and impacts the cardiovascular system, respiratory system, and bone density. In addition, by affecting nerves isometric exercises can harness stress and generate a sense of peace and vitality. Some studies demonstrated that patients may experience pain relief after performing isometric exercises (27, 28). The study by Ozkahraman suggested that isometric exercises increase intravenous carrier fluid and the diameter of forearm veins. The mechanism may be related to that the involved stretching exercises may increase blood supply to the organs and improve arterial compliance; moreover, it could increase the body’s oxygen supply through aerobic exercise, thus reduce blood viscosity and relieve the hypercoagulation state of the serum. Also, through relaxing and contracting muscles (29), it could accelerate the rate of blood flow, and enhancing the elasticity of the blood vessel wall (30). As a result, isometric exercises reduce pain intensity by influencing the mechanisms that affect the pain intensity caused by propofol injection.

Considering to the importance of reducing pain on propofol injection and the resulting problems, it is important to provide solutions for reducing pain on propofol injection with minimum complications. Therefore, this study was performed aimed to compare the effect of isometric exercises and 2% lidocaine on the intensity of pain during intravenous propofol injection in patients referred to Neyshabur 22 Bahman Hospital.

Methods

This three-group randomized clinical trial study was conducted with a parallel pretest-posttest design in 2020 on 106 patients who were candidates for general anesthesia for different surgical treatments in 22 Bahman Hospital Neyshabur, Iran. The subjects were randomly allocated into three groups by permuted block randomization. Group A received propofol 1% with 40 mg lidocaine 2%, group B received pure propofol 1%, and group C completed 5 cycles of isometric exercises before injection of

1% pure propofol. The sample size was estimated based on the study of Ozkaraman et al. (30) using G*Power software. The sample size was considered 34 in each group with a 95% confidence level, 0.95 % test power and 0.4 Effect size. However, due to the probability of 20% loss to follow up, 40 participants were considered for each group (total sample size= 120). A total of 14 participants were excluded from the study due to non-cooperation in pain reporting (Figure 1).

Inclusion criteria were the patient aged 20-60 years, American Anesthesia Association Class I, II, lack of sensitivity to the studied drugs, minimum academic literacy, ability to communicate with the research team, and no drug addiction. Exclusion criteria were neuromuscular disorders, difficulty in communicating with the researcher, chronic disorders such as heart disease, seizures, end stage renal failure, severe neurological and mental disorders, Class III and IV of the American Anesthesia Association, emergency patient's admission, breastfeeding and pregnancy, thrombophlebitis, taking sedatives and drugs, allergy to propofol, alcoholic patients, and need to rapid sequence intubation.

Initially, the study units were selected based on inclusion and exclusion criteria. Written informed consent was obtained from the research units. Then, the samples were randomly allocated to three groups of isometric exercise, lidocaine, and control by permuted block randomization method. Group A received Propofol injection with 40 mg of lidocaine 2%, group B received 1% pure propofol injection, and 1% pure propofol injection was given to group C after 5 cycles of isometric exercises and then received 1% pure propofol injection. Each course of isometric exercises in Group C consisted of 20 seconds of exercise and 5 seconds of rest. During the 20 seconds of exercise, the researcher pressed the patients' fingers with his four fingers, and the patients attempted to grip the researcher's hand in the opposite direction and closed their fingers toward their face. In the operation room, intravenous (IV) access was inserted with 20-gauge catheter in suitable vein on the dorsum of the patient for drug injection.

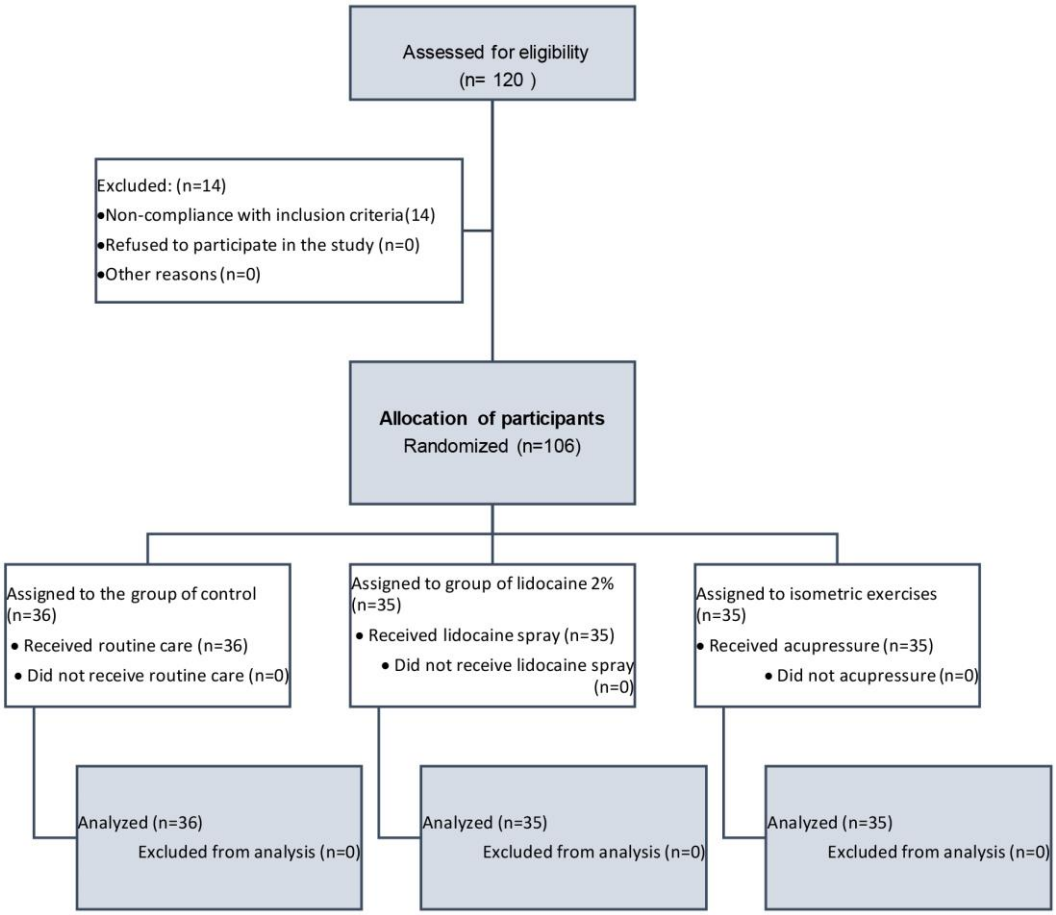

Figure 1. Consort Flow Diagram

All patients were monitored by electrocardiogram, non-invasive management of blood pressure, pulse oximeter, and heart rate assessment. No premedication was used before the study. One-fourth of the calculated dose of propofol was injected over 5 s and 15 s later, the patient was assessed for pain during propofol injection. In all patients, induction of anesthesia was performed with 0.2 mcg/kg of fentanyl, 2 mg/kg of propofol and 0.5 mg/kg of atracurium. After induction, the patients were intubated and maintained with atracurium and propofol infusion. Patients were inquired about the pain intensity rate during the injection till they lost consciousness. The person completing the checklist was blind about the type of intervention the patient received.

Data were collected using demographic questionnaire including age, gender, body mass index, and educational level and parameteres such as systolic blood pressure, diastolic blood pressure, SPO2 and etc. The other collection tool was a four-point Ambesh scale, which uses verbal and behavioral answers concerning frowning, hand pulling, or lacrimation. The patients answered questions about whether the injection was accompanied by pain at the administration site. The scoring method of pain intensity due to intravenous propofol injection was based on four point likert scale including: no pain = 0, mild pain = 1, moderate pain = 2, and severe pain or lack of limbs' and muscles' movement = 3 (10, 12, 31). Data were analyzed by SPSS software (version 16) and Fisher's exact test, Mann-Whitney U test, and analysis of variance (ANOVA). $P< 0.05$ was considered statistically significant.

This study protocol was approved by the research ethics committee of Sabzevar University of Medical Sciences and registered at Iranian Registry of Clinical Trials.

Results

Out of 106 participants, 50.94% were male and 49.06% were female. Also, 37.7% of them had Associate's degree. The majority of patients underwent general surgery, and 76 participants had no history of smoking. In terms of pain intensity, 46.22% of participants had no experience of pain during propofol injection (Table 1).

Table 1. Correlation between participating groups with gender variables, degree, type of anesthesia, type of surgery, smoking

Variable		Number in each group			p-value
		Isometric exercises	No intervention	Lidocaine 2%	
Sex	Male	18	16	20	P=0.563
	Female	17	20	15	
Level of Education	Illiterate	8	1	1	P=0.072
	Intermediate Education	2	2	4	
	Diploma	3	5	8	
	Associate Degree	10	15	15	
	Bachelor's degree and higher	12	13	7	
Intensity of pain	No Pain	21	9	19	P<0.001
	Mild	10	7	13	
	Moderate	3	12	3	
	Severe	1	8	0	
Type of anesthesia	Class I	16	27	23	P=0.160
	Class II	13	7	11	
	Class III	4	2	1	
Type of surgery	Orthopedics	11	14	10	P=0.658
	general	17	17	16	
	ENT	3	0	3	
	Urology	4	5	6	
Smoking	No	25	28	25	P=0.642
	Yes	10	8	10	

According to the Chi-Square test, no significant relationship was found between the groups (lidocaine 2%, no intervention, and isometric exercises) and the variables such as gender, educational level, ASA, and the techniques of surgical treatment. There was no significant difference between pain intensity in groups A and C, but group B reported significantly higher pain intensity than the intervention groups (P<0.001) (Table 2).
Based on repeated measures analysis, method of treatment did not affect the vital signals of patients (Table 3).

Table 2. Comparison of patients' pain intensity in the studied groups

Variable		Number in each group			P-Value
		Isometric exercises	No intervention	Lidocaine 2%	
Intensity of pain	No Pain	21	9	19	P<0.001
	Mild	10	7	13	
	Moderate	3	12	3	
	Severe	1	8	0	

Table 3. Relationship between the type of treatment and vital signs of research participants based on time factor

Vital signs in groups	Total frequency	Total M±SD	P-Value
HR Pre operation	106	84.55±15.19	p=0.924
HR Post operation	106	78.94±16.12	p=0.556
HR 15 min Post operation	106	76.24±14.46	p=0.310
HR In recovery	106	80.59±13.04	p=0.835
HR out of recovery	106	79.89±12.38	p=0.886
BP-high Pre operation	106	132.60±36.36	p=0.364
BP-high Post operation	106	110.70±19.71	p=0.292
BP-high 15 min Post operation	106	112.33±14.40	p=0.196
BP-high In recovery	106	120.23±12.42	p=0.544
BP-high out of recovery	106	121.32±18.58	p=0.101
BP-low Pre operation	106	80.28±63.14	p=0.908
BP-low Post operation	106	69.30±15.81	p=0.693
BP-low 15 min Post operation	106	69.36±13.32	p=0.747
BP-low In recovery	106	74.97±11.76	p=0.314
BP-low out of recovery	106	78.59±9.73	p=0.373
SPO2 Pre operation	106	98.36±1.79	p=0.743
SPO2 Post operation	106	98.92±1.63	p=0.069
SPO2 15 min Post operation	106	99.34±1.06	p=0.370
SPO2 In recovery	106	97.42±8.81	p=0.493
SPO2 out of recovery	106	98.41±1.90	p=0.888

Discussion

This comparative study aimed to evaluate the impact of isometric exercises and lidocaine 2% on the pain intensity during intravenous propofol injection in patients referred to Neyshabur 22 Bahman Hospital for surgical treatment. The results of the present study showed that the pain intensity during propofol injection was significantly higher in the control group, which had no intervention during propofol injection than in two intervention groups which received lidocaine 2% and the isometric exercises. In other words, lidocaine 2%–propofol admixture injection and completing isometric exercises before the propofol injection decrease the injection pain intensity. This result is consistent with the results reported in the studies conducted by Shabana (2013), Sing et al. (2014), and Hanala et al. (2019), the purpose of which was to determine the effect of lidocaine on pain relief after propofol injection. Their results showed that lidocaine 2% decreases the pain of propofol injection (18, 32, 33). Bojan et al. (2019) also conducted a comparative study to examine the effect of lidocaine and ketamine on propofol injection pain. They found that lidocaine has the same effect as ketamine in reducing pain on propofol injection (22). These results are consistent with the results of the current study, based on which lidocaine reduces the pain on propofol injection. Alizadeh et al, (2014)

compared the pain on propofol injection in simultaneous lidocaine 2%–propofol admixture injection and propofol injection following the lidocaine injection. Their results showed that the pain intensity in the second group (Propofol injection after lidocaine injection) was less than the first group (mixed injection) (10). As a result, lidocaine 2% can be the main factor in reducing pain on intravenous propofol injection.

The current study found that isometric hand exercise lowers pain intensity induced by propofol injection. According to Ring et al. (2008), pain intensity decreased during isometric exercises. Their result is consistent with an arterial baroreceptor inhibition mechanism for exercise-induced hypoalgesia (34). Studd et al. (2005) conducted a study on fibromyalgia patients. They discovered that isometric exercises considerably decreased thermal pain ratings and enhanced mechanical pain threshold in topical areas in the control group; however, the reverse effects were reported in fibromyalgia patients (35). Another goal of their study was to evaluate whether there was a link between the intensity of pain induced by propofol injection and the participants' demographics. Their findings of the present study revealed no significant relationship between the interventions and demographic variables such as gender, educational level, general anesthesia, surgical treatment type, and smoking. In other words, these variables did not affect the intensity of the pain. In this regard, Alizadeh et al. discovered no significant relationship between participants' pain intensity and demographic variables. To put it simply, participants' demographic variables did not influence the type of intervention and pain intensity (10). Koltyn et al. found that isometric exercises increased pain perception in women but had no effect on men's pain perception (36). In another study conducted by the same researcher, it was discovered that isometric hand exercises prolong the effect of analgesic medications in women, but not in men (37). The reason for the difference in the results can be due to the different method of work.

In the present study, there was no statistically significant relationship between the type of intervention and vital signs, which was consistent with the findings of the study by Alizadeh et al. aimed to compare the severity of pain caused by propofol injection with three methods of a mixture of propofol and lidocaine, lidocaine and 1% pure propofol injection (10). Since the dose and condition of propofol injection were standard (5) in the present study, there was no difference in the patient's hemodynamic condition. Also, the results of the study conducted by Taloh et al. in 2018 that evaluated low dose ketamine pretreatment for alleviation of propofol injection pain showed that the type of intervention does not influence the heart rate in both groups (18). Moreover, shabana et al., in their study showed that heart rate was not statistically different before and after intubation in the two groups (32), which was consistent with the results of the present study. The results of the study conducted by Karbasi et al. indicated that heart rate in the two groups increased and had a statistically significant relationship with the type of intervention. The reason for this discrepancy can be the difference between the method and the type of intervention. The intervention in the present study was lidocaine injection and isometric exercise, while in the study of Karbasi et al., the intervention received was Dexamethasone injection to reduce the pain of propofol (9).

The important strength of this study was the use of a non-pharmacological method to reduce the pain of propofol injection.

The limitation of the present study was that some factors, such as social context, previous records of injections and pain tolerance threshold which can affect pain perception were not controlled. Therefore, future studies are recommended to be conducted with larger samples and consideration of genetic, ethnic and pain tolerance threshold in patients to increase the percentage of confidence in the generalization of the results.

Implications for practice

The results of the present study showed that the use of both lidocaine 2% and isometric exercise reduces the pain intensity of propofol injection. Therefore, the use of these two methods is recommended.

Acknowledgments

The present study is a research proposal approved by student research committee (97081) and ethics committee in biomedical research of Sabzevar University of Medical sciences (IR.MEDSAB. REC.1397.088), and the research project was registered on the Iranian Registry of Clinical Trials

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Conflicts of interest

The authors declared no conflict of interest.

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