



Original Article

Effect of Oral Clonidine as a Premedication on Hemorrhage during Septorhinoplasty: A Double-Blind Randomized Clinical Trial

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ABSTRACT

Introduction: Intraoperative hemorrhage is one of the most important complications of septorhinoplasty surgery. Many techniques and drugs are used to reduce this problem. Accordingly, the present study was conducted to investigate the effect of oral clonidine as a premedication on hemorrhage during septorhinoplasty surgery.

Methods: In this double-blind randomized clinical trial, 53 patients undergoing septorhinoplasty at Motahari Hospital in Jahrom were studied. Patients were randomly divided into oral clonidine and placebo groups. Intraoperative hemorrhage was measured based on the blood in the suction. The data were analyzed in SPSS-21 and both descriptive and inferential statistical tests were computed.

Results: Both groups were homogenous in terms of demographic variables of age, weight, gender and the level of fluid received during the surgery. Mean hemorrhage ($P = 0.001$) and total duration of surgery ($P = 0.031$) in the clonidine group were significantly lower than the control group.

Conclusion: The results of the present study revealed that oral clonidine as a premedication for anesthesia can reduce hemorrhage and the duration of septorhinoplasty surgery. It is recommended that future studies be performed with a larger sample size and compare with other drugs.

GRAPHICAL ABSTRACT



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Introduction

Septorhinoplasty is considered as the most common plastic surgery in Iran [1]. The rate of septorhinoplasty in Iran is 180 cases per 100000 people [2], which is one of the highest rates of this surgery in the world [3]. One of the problems in the operating room for surgeons and anesthesiologists is intraoperative hemorrhage. Also, the surgeon needs a clear range of operation with minimum hemorrhage to perform delicate and sensitive operations. Additionally, the anesthesiologist wants to reduce intraoperative hemorrhage to maintain hemodynamic stability during the surgery [4]. Alpha-2 agonists have potentially beneficial effects. In addition to lowering blood pressure, they also have analgesic and sedative properties. They cause hemodynamic stability as a result of the central sympatholytic effect [5]. Clonidine is being used commonly as an adjunct in anesthesia in light of its sedative and anesthetic properties [6]. Also, its favorable effects on patient hemodynamics have been approved by anesthesiologists [7]. Clonidine is quickly absorbed in its oral administration, and its concentration reaches a maximum within 1.5 to 2 hours. Its half-life is about 8-12 hours [8]. Various studies have proven the effects of clonidine on reducing hemorrhage during septorhinoplasty [9-10]. Clonidine lowers arterial blood pressure without lowering postural blood pressure. It also reduces heart rate, reduces intraoperative hemorrhage in general, and reduces stress during surgery [11]. Since clonidine is one of the drugs studied extensively in recent years, the present study aimed to investigate the effect of oral clonidine as a premedication on hemorrhage during septorhinoplasty.

Material and Methods

Study design

The present study was a double-blind randomized clinical trial conducted over a three-month from February 2022 to April 2022 in patients who referred to the operating room of Motahari Hospital in Jahrom and underwent septorhinoplasty.

Ethical considerations

Before entering the patients in this study, the research process was explained and informed consent was obtained from them. During the study, researchers adhered to the principles of the Helsinki Declaration and the confidentiality of patient information. All costs of the project were provided by the researchers and no additional costs were incurred by the patients. This study was approved by the ethics committee of Jahrom University of Medical Sciences under the code of ethics of IR.JUMS.REC.1400.072.

Sampling

The statistical population of the present study included all patients undergoing septorhinoplasty surgery. The sample size was determined at 60 patient for each group assuming standard difference = 0.85 and 95% confidence level and power = 80% using the Altman nomogram and with considering 15% dropout in samples. Then, to have an equal chance of being in the intervention group or the control group, the samples were randomly assigned to study groups (30 patient in each group) using coin flipping. Subjects were randomly divided into two groups of clonidine or control (placebo) based on the inclusion and non-exclusion criteria. Sampling was continued up to the stage where two groups were homogenized in terms of underlying characteristics (Figure 1). Inclusion criteria were all subjects over 18 years of age, hemoglobin above 10, normal PT/ PTT/ INR, normal hemodynamics and heart rate above 60 beats per minute.

Exclusion criteria were patients with coagulation disorders, coronary artery disease, stroke, venous thrombosis and clonidine sensitivity.

Intervention

All patients who met the inclusion criteria at the time of study entered the study after obtaining their written consent and explaining the study conditions for them. They were randomly divided into clonidine and placebo groups by coin flipping method. Group A received oral clonidine at a dose of 0.2 Mg and Group B was treated with placebo. This study was designed in a double-blind method. It means that the patient, the

person giving the drug to the patient and the data analyst were not aware of the type of drug. Both groups received the drugs orally (with a small amount of water) two hours before induction of

anesthesia. Both groups of patients underwent septorhinoplasty by a surgeon. The level of intraoperative hemorrhage was estimated based on the rate of hemorrhage in the suction.

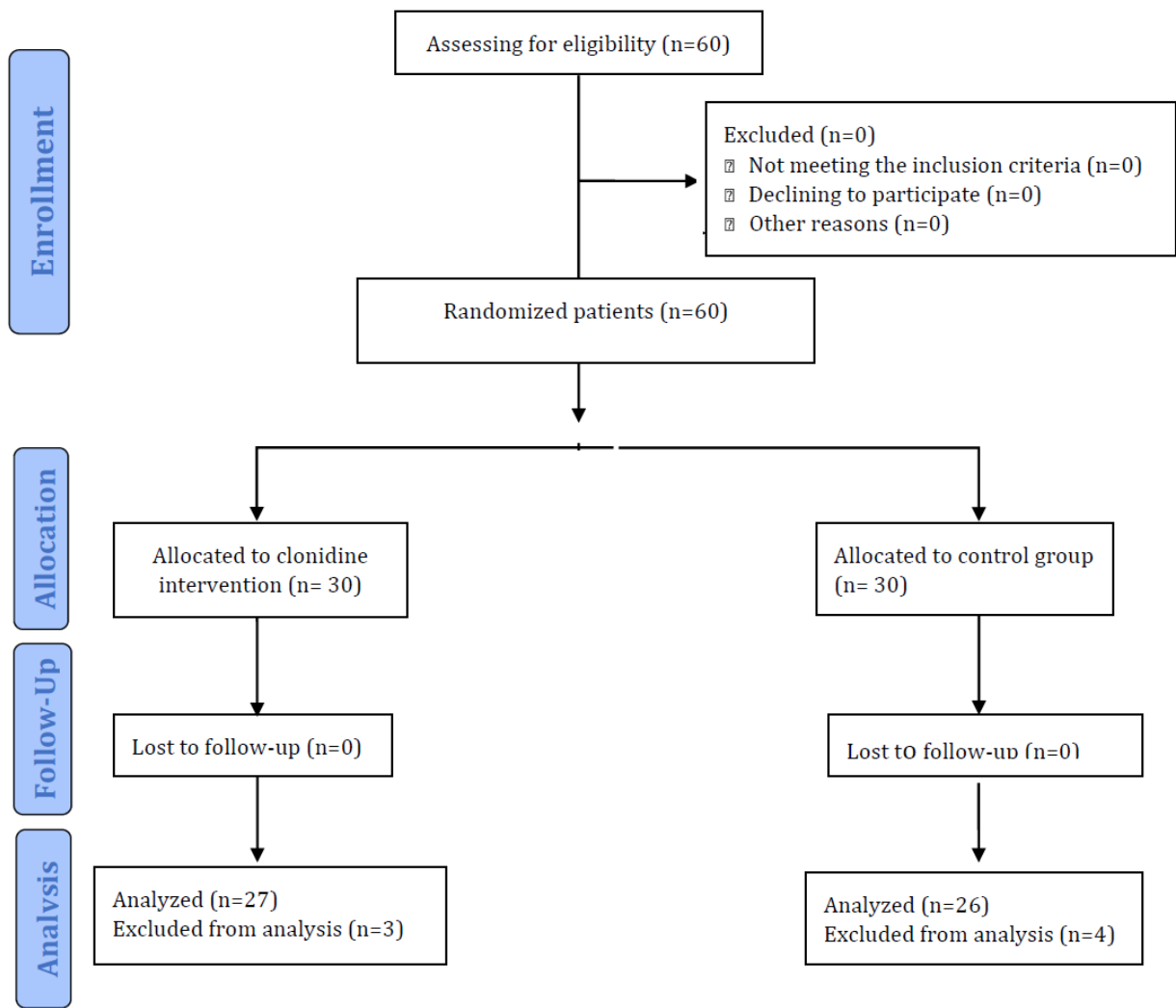


Figure 1: The consort flow diagram of the study

Data collection

A checklist designed by the researcher included age, gender, weight, amount of fluid received during the surgery and the rate of intraoperative hemorrhage. Intraoperative hemorrhage was measured based on the blood in the suction.

Data analysis

Data were analyzed using SPSS-21 software and descriptive statistics including mean and standard deviation as well as inferential statistical tests including t-test, Fisher and Mann-Whitney were computed at a significant level of $P < 0.05$.

Result and Dissection

Sixty patients aged 18 to 44 years (in two groups of 30) with ASA I, II who underwent septorhinoplasty were evaluated. Finally, the data of 27 patients in the clonidine group and 26 patients in the control group were evaluated. Twenty-one patients (77.8%) in clonidine group and 23 patients (88.5%) in control group were female. The results in Table 1 show that the study groups were homogeneous in terms of demographic variables of age, weight, gender and the amount of fluids received during the surgery ($p < 0.05$) (Table 1).

Table 1: Mean and standard deviation of demographic characteristics separately for clonidine and control groups

Demographic		Clonidine [27]	Control [26]	P-value	Test
		SD± Mean	SD± Mean		
Age (Year)		6.9±29	7.4±28.5	0.80	T-test
Weight (Kg)		12.3±67.5	10±64.3	0.34	T-test
		Frequency (%)	Frequency (%)		
Gender	Man	6(22.2)	3(11.5)	0.47	Fisher
	Woman	21(77.8)	23(88.5)		
The amount of fluid received during Surgery (cc)	700	2(10)	2(9.5)	0.66	Fisher
	800	2(10)	3(14.3)		
	1000	14(70)	16(76.2)		
	1500	2(10)	0(0)		

Mean hemorrhage (P = 0.001) and total duration of surgery (P = 0.031) in the clonidine group were significantly lower than the control group (Table 2).

Table 2: Mean and standard deviation of hemorrhage rate separately in the clonidine and control groups

	Clonidine [27]	Control [26]	P-value	Test
	SD± Mean	SD± Mean		
Bleeding (cc)	28.1±89.7	48.5±120.6	0.001	Mann-Whitney
Total duration of surgery (minutes)	27.6±229.6	33.3±206	0.03	Mann-Whitney

To reduce the rate of intraoperative hemorrhage, various methods and drugs are used [12-13], one of which is clonidine [14-15]. The results of studies indicate that clonidine reduces heart rate and blood pressure and sympathetic activity [16-18]. Clonidine lowers blood pressure by reducing heart rate and relaxation of vascular vessel. It also reduces the peripheral vascular resistance, which is usually associated with decreased renal vascular resistance and establishment of renal blood flow [19]. In the present study, the mean hemorrhage in the clonidine group was significantly lower than that of the control group (P = 0.001). The results of other studies in this area suggest the positive effects of clonidine in reducing hemorrhage. The results of these studies are in line with those of the present study. Zangouei *et al.* (2019) compared the effects of clonidine, promethazine and morphine on hemorrhage during rhinoplasty surgery. The results of this study showed that the mean hemorrhage in patients in the clonidine group was lower than that of other patients [20]]. Nadri *et al.* (2014) examined the effect of oral clonidine as a premedication before anesthesia on the rate of hemorrhage during tympanoplasty.

Pretreatment with clonidine reduces the rate of hemorrhage during tympanoplasty [21]. Tabrizi *et al.* (2014) examined oral clonidine premedication in reducing hemorrhage during rhinoplasty surgery. The results of this study showed that oral clonidine premedication may reduce preoperative hemorrhage during rhinoplasty surgery [10]. Ghazipour *et al.* (2013) examined the effect of clonidine as an anesthetic premedication in reducing hemorrhage during rhinoplasty surgery. The results of this study showed that oral clonidine as a pre-anesthetic drug can reduce hemorrhage during rhinoplasty surgery [9]. Mohseni *et al.* (2013) examined the effect of preoperative oral clonidine administration on the rate of surgical hemorrhage during sinus endoscopy. The results of the study revealed that oral administration of clonidine 0.2 mg before surgery effectively reduces hemorrhage during sinus endoscopic surgery [22]. In their study, Marchal *et al.* (2001) examined clonidine effect in reducing hemorrhage during middle ear microscopic surgery. The results of the mentioned study showed that premedication with clonidine reduced hemorrhage in middle ear

microscopic surgery [23]. In their research, Sadri *et al.* (2007) examined the role of clonidine in reducing hemorrhage during rhinoplasty surgery. They showed that pretreatment with oral clonidine 3 µg/kg of body weight reduces the rate of hemorrhage in rhinoplasty [24].

Examining the effect of clonidine on hemorrhage during middle ear microscopic surgery, Jafarieh *et al.* (2010) reported that clonidine can be useful as a premedication in creating a hemorrhage-free environment and improving vision at the surgical site during middle ear microscopic surgery [25]. In their study, Cardesin *et al.* (2015) compared clonidine and remifentanyl on the rate of hemorrhage during endoscopic sinus surgery. The results revealed that the use of clonidine reduced surgical field hemorrhage during FESS (26). Approaching the effect of oral clonidine as premedication in reduce intraoperative hemorrhage in patients undergoing sinus endoscopic surgery, Jabalameli *et al.* (2005) revealed that oral clonidine reduced hemorrhage in sinus endoscopic surgery [27]. The results of the present study and those of previously conducted in this area suggest the effectiveness of clonidine in reducing hemorrhage. Reducing the rate of hemorrhage improves the scope of surgery for the surgeon and shortens the duration of surgery.

Conclusion

The results of the present study revealed that oral clonidine as a premedication for anesthesia can reduce hemorrhage and the duration of septorhinoplasty surgery. It is recommended that future studies be performed with a larger sample size and compare with other drugs.

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Authors' contributions

All authors contributed toward data analysis, drafting and revising the paper and agreed to be responsible for all the aspects of this work.

Conflict of interest

There are no conflicts of interest in this study.

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