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Research Article

Comparison Effect of Clonidine and Magnesium Sulfate on Bleeding Volume during Septorhinoplasty: A Double-Blind, Randomized Clinical Trial

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ABSTRACT

Background: Control of hemodynamic changes and blood loss is a daily challenge in general anesthesia for patients undergoing septorhinoplasty. This study aimed to evaluate the effects of magnesium sulfate and clonidine on the control of hemodynamic factors and bleeding volume during this procedure.

Methods: This double-blind, randomized clinical trial study was conducted on 60 patients undergoing septorhinoplasty at 5th Azar Medical & Educational Centre of Gorgan in 2021-2022. Patients were divided into two intervention groups (50 mg/kg of magnesium sulfate) and control group (5 µg/kg of clonidine) with permutation random block allocation. All patients underwent induced hypotension. Before induction of anesthesia and every 5 minutes afterwards, blood pressure was recorded. Blood loss volume was calculated at the end of the surgery.

Results: In the magnesium group, 36 individuals were evaluated, while in the clonidine group, 24 individuals were examined. There were no statistically significant differences in baseline characteristics of patients in the two groups and the duration of surgery. Both drugs were equally effective in inducing hypotension, however blood pressure changes in magnesium group were more trivial than clonidine group. The bleeding volume in the magnesium sulfate and clonidine groups was 139.44 ml and 141.25, respectively and this difference was not statistically significant (p-value=0.634).

Conclusion: The results of this study showed that magnesium sulfate can be effectively used as an alternative to clonidine in controlling hemodynamic changes and ultimately reducing blood loss volume during septorhinoplasty surgery. In addition, magnesium is at least as effective as clonidine in stabilizing hemodynamic changes.

Introduction

Septorhinoplasty is a surgical procedure aimed at correcting the appearance of the nose (rhinoplasty) and improving breathing through the nose (septoplasty). This surgery on the bones and cartilages, straightens the septum, and gives the nose a better shape [1]. One of the most common complications during rhinoplasty surgery is bleeding [2]. Bleeding during surgery could be caused by damage to large and small blood vessels in the subcutaneous network. It leads to edema of the operation area, lack of the proper vision of the surgeon, and an increased risk of errors during the procedure [3]. Several methods are available to control bleeding during surgery and one of the best methods is hypotension induction. In this method, the surgeon usually reduces the systolic blood pressure to 80-90

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mmHg or the mean arterial pressure (MAP) to 50-65 mmHg. Furthermore, the MAP could be reduced to 30% compared to the patient's baseline MAP to achieve induced hypotension [4]. Induced hypotension increases the visualization of the surgical site and reduces the amount of bleeding during surgery, the duration of the surgical procedure, and edema and ecchymosis around the eyes after surgery [5].

To achieve induced hypotension, clonidine could be used. Clonidine is a centrally and peripherally acting antihypertensive drug that acts on alpha-2 adrenergic receptors, leading to a reduction in sympathetic activity and an increase in vagal tone. Therefore, it can lower the patient's blood pressure and reduce bleeding during surgery [6]. In fact, clonidine is prescribed for hemodynamic stability during surgery [7].

Previous studies also indicated the magnesium sulfate as a suitable drug for reducing blood pressure [8]. Magnesium sulfate led to decrease blood presser via inhibiting calcium channel blockade and also inhibiting the norepinephrine release from nerve terminals [9]. Magnesium sulfate could be reducing the production and secretion of prostacyclin and, consequently, reduce the activity of angiotensin-converting enzyme and cause vascular vasodilatation [9]. Moreover, it has a small dose-dependent depressant effect on the myocardium, which could lead to a decrease in cardiac contraction [10]. Preoperative and intraoperative intravenous administration of magnesium sulfate has been approved as an accepted drug to stabilize hemodynamic parameters during surgery, especially by reducing blood pressure and cardiac rhythm, as well as minimizing side effects of hemodynamic responses [11].

Considering the mentioned information, it appears that magnesium sulfate has multifunctional properties and, based on several studies, provides a great hemodynamic stability during surgery. Therefore, in this study we aimed to compare the effects of magnesium sulfate with one of the most approved antihypertensive drugs, clonidine, on controlling bleeding and hemodynamic factors during septorhinoplasty surgery.

Methods

Study design

This study is a double-blind randomized clinical trial which was conducted on patients in 5th Azar Medical & Educational Centre of Gorgan in 2021-2022. In this study, candidates for septorhinoplasty surgery were admitted to the ENT department of the hospital. On the day preceding the surgical procedure, patients underwent a comprehensive preoperative assessment by an anesthesiologist. Following a detailed presentation regarding the forthcoming surgery and elucidation of the study's objectives, informed consent was obtained from each patient, thereby facilitating their inclusion in the research investigation. The research plan of this study was reviewed and approved by the ethics committee of the university before implementation (IR.GOUMS.REC.1399.177). In addition, the proposal of this project was registered and approved in Iran's randomized clinical trial site (IRCT20170413033408N4).

Inclusion and exclusion criteria

In terms of the inclusion criteria, all eligible participants were required to contribute to this study within the age range of 15 to 45 years and possess the ASA I (American Society of Anesthesiologists). Additionally, they needed to be candidates for septorhinoplasty surgery. Conversely, for the exclusion criteria, individuals with known neuromuscular disorders, a history of neuropathic conditions, extreme obesity (defined as a BMI exceeding 35), coagulation disorders, a prior second-stage rhinoplasty procedure, a history of taking calcium channel blockers, anti-epileptic medications, non-steroidal anti-inflammatory drugs (NSAIDs), or a documented allergic reaction to anesthesia-related pharmaceuticals were not considered eligible for participation in this study.

Study protocol

Patients were randomly assigned to either the intervention group (magnesium sulfate, n=36) or control group (clonidine, n=24). Because we don't have the injectable type of clonidine in Iranian pharmacopeia, we used the oral tablets of clonidine in this study. Initially, the clonidine tablets were softened and dissolved in distilled water to form a homogenous mixture, and the amount of drug was selected based on the patient's weight (5 µg/kg). In the control group, a uniform mixture was given to the patient, and these mixtures were administered to the patient by the ward nurse one hour before entering the operating room. In the operating room, in the magnesium sulfate group, an appropriate amount was administered as an infusion (50 mg/kg) in a volume of 100 ml of normal saline crystalloid prior to induction over a period of 20 minutes, and in the control group, the same volume of crystalloid was infused over 20 minutes.

Before induction of anesthesia for all of the patients, 15 mg/kg tranexamic acid with 3ml/kg normal saline was administered. Then we used 0.05 mg/kg midazolam as premedication in operating room. After that 20-40 mg intravenous lidocaine was injected before propofol injection for anesthetizing the vein. We induced the anesthesia with 1mg/kg propofol, 2µg/kg remifentanil and 0.5mg/kg atracurium. After confirming adequate muscle relaxation with post-tetanic count (PTC = 0), patients were intubated with appropriate endotracheal tube. Anesthesia was maintained with 100-200µg/kg/min propofol infusion, 0.25-0.5µg/kg/min remifentanil infusion and N2O/O2 combination (70%/30%). We maintained mean arterial pressure (MAP) in the range of 60-70 mm Hg with these drugs. If we could not achieve

targeted blood pressure with our protocol, we could use bolus doses of 10mg labetalol. Maximum dose of administered labetalol for a patient, was 200mg.

Cardiac and respiratory monitoring was performed during surgery. All patients were positioned in the reverse Trendelenburg position at 30°. Baseline hemodynamic factors were recorded and monitoring were continued every 5 min. We continued fluid therapy during surgery with normal saline infusion at the rate of 5ml/kg/h. Right before osteotomy, to maintain optimal analgesia, a bolus dose of 0.5-1µg/kg remifentanil was prescribed for all patients. To reduce bleeding, a 2% lidocaine solution with epinephrine with a concentration of 1.100,000 was administered by surgeon for local injection in the perichondral and periosteal areas. Also, a mesh impregnated with epinephrine with a concentration of 1.1000 was used to create a tampon at the minute 5 of surgery to reduce mucosal congestion. The amount of bleeding was estimated by the anesthesiologist at the end of the surgery, by measuring the amount of suctioned blood. The patient's pharyngeal pack was weighed with an electronic scale. Hypotension and bradycardia as complications of Induced Hypotension, were assessed in patients. In case of blood pressure and heart rate decrement (MAP<60 mmHg & HR<55) we used atropine and phenylephrine respectively (Figure 4).

Sample Size

Based on the results of a preliminary study based on blood values, with a confidence level of 0.95 and a test power of 0.80, and using the sample size formula for two groups with heterogeneous variances, the sample size was determined to be 36 in the magnesium group and 24 in the clonidine group.

$$SD_M = 5.54$$

$$SD_C = 4.63$$

$$\mu_M - \mu_C = 3.76$$

$$\frac{n_M}{n_C} = 1.46$$

Randomization

Due to the imbalanced sample size, we needed to have blocks of five with three letters M and two letters C, such as MCMMC. Using a random mechanism, a total of 12 blocks of five were generated and written as a random sequence. Participants were randomly assigned a number from 1 to 5 upon entering the operating room and were allocated to one of these five-letter blocks. The clonidine group received a dose of 5 µg/kg and the magnesium group received magnesium sulfate with a dose of 50 mg/kg.

Blinding

The primary investigator and evaluator had no knowledge of how patients were assigned to the groups, and all stages of preparation and drug administration were performed by an anesthesiologist specialist who had no intervention in data measurement and collection.

Statistical analysis

Given the repeated measurements of variables such as MAP, SYS, DYS, HR, and the conditions of the data, the Marginal model in the GEE (Generalized Estimating Equation) method was used. Normality of data was determined by Shapiro-Wilk test. Comparison of the mean of continuous variables at the beginning of the study was done with independent t-test and Mann-Whitney U test. Categorical data was compared using Chi-square test. GEE is used to determine whether or not there is a statistically significant difference between the means of 25 time points. Statistical analysis was done using R v4.3.1software. P value <0.05 was considered as statistically ‘significant’

Results

Patient demographics

60 patients undergoing septorhinoplasty were included in this study (Magnesium Sulfate=36 and Clonidine=24). The baseline characteristics of patients from the two groups are shown in the (Table1,2). Both groups were comparable with respect to age, sex, body weight, and duration of surgery. The mean age of patients was approximately 27 years old (15 to 45 years old). The mean weight of patients was 66.49 kg. Time of surgery was similar in two groups (P value=0.131) and the mean time was approximately 107.84 minutes. Baseline arterial pressures of patients are documented in (Table 1). 66.7% of patients in the magnesium group and 75% of patients in the clonidine group were women, but the gender distribution was similar between the two groups (p value= 0.490).

Induced hypotension and alterations in hemodynamics

With using propofol and remifentanil, we could manage to decrease and maintain the MAP of patients to 30% of baseline MAP. For those patients that did not achieve targeted MAP, we used labetalol. 8 patients from magnesium group (210 mg labetalol) and 5 patients from clonidine group (115 mg labetalol) received various labetalol doses. This difference was not statistically significant (p value = 0.261).

The trend of average blood pressure parameters in the studied patients is shown in Figure 1. According to the results, although the average MAP and SBP did not have a significant statistical difference at the beginning of the study in both groups, overall baseline parameters in the clonidine group showed relatively lower blood pressure, which was not unpredictable considering the prescription

of pre-operation clonidine in these patients. In fact, the average of the two baseline parameters (HR and DBP) was significantly lower in the clonidine group compared to the intervention group.

The results of implementing the Marginal model in the GEE method showed that the interaction effect between drug type and time on the MAP variable is not significant (p value = 0.562). The average MAP in both groups decreased significantly in the first ten minutes, with a greater decrease observed for Clonidine group, reaching its lowest value at minute 25. However, in the Magnesium group, there have been slight changes from minute 10 onwards. In both groups approximately after 90 minutes, MAP has been increased. The results indicate that the group effect in the first 10 minutes has been approximately significant on MAP changes (p value = 0.059). (Figure 1) is demonstrated the trends of MAP between two groups of study.

Moreover, the results of implementing the model showed that the interaction effect between drug type and time on the Systolic blood pressure variable is not significant (P-Value=0.956). The average Systolic blood pressure in the first 10 minutes has been lower in Clonidine group. The results indicate that the group effect is almost significant (p value = 0.071). (Figure 2) indicates the trends of SBP between two groups of study.

Additionally, the results of implementing the model showed that the interaction effect between drug type and time on the Diastolic blood pressure variable is not significant (p value = 0.538), and the average Diastolic blood pressure in the first 10 minutes has been lower in Clonidine group. The results indicated that the group effect is approximately significant (p value= 0.077). (Figure 3) illustrated that the trends of DBP between two groups of study.

As it is hallmarked the highest rate of blood pressure reduction in all three parameters (MAP, SBP and DBP) was during the first 10 minutes of surgery and induction. Furthermore, it is clear the decrease in blood pressure in the clonidine group was parallel with time and reached its maximum at minute 25. After that, the pressure slightly increased with a slope until approximately minutes 90-95, where both groups had almost equal parameters. However, in the magnesium group, the peak of blood pressure reduction occurred at minute 10 and no significant changes in parameters were observed during minutes 10-95, and the mean pressure in this time interval was more stable in these patients. From approximately minute 90 in both groups, we observed a predictable increase in patients' blood pressure due to the end of osteotomy and septoplasty and no need for more controlled hypotension.

Volume of bleeding

Besides, the results of implementing the model showed that the interaction effect between drug type and time on the HR variable is not significant (p value = 0.852), and the average of HR even in the first 10 minutes of the operation, was approximately similar. The results indicate that the group effect is not significant (p value = 0.397). Regarding HR, although this parameter was almost lower in the clonidine group throughout the operation, this difference was very brief and not significant. Volume of bleeding in the Magnesium Sulfate group (139.44 ml) was more than the Clonidine group (141.25 ml), but this difference was not statistically significant (P-Value=0.634). the obtained results showed in (Figure 5).

Complications

We administered 4 mg atropine and 500 mcg phenylephrine in magnesium group although these drug doses in clonidine group were 2.5 mg atropine and 350 mcg phenylephrine. This difference was not statistically significant between two groups (p value = 0.312). We also analyzed the incidence of shivering between the two groups. 61.7% of patients experienced shivering but this parameter was not statistically different between the two groups (p value = 0.665). In both groups, the incidence of shivering was higher in male than in female, but the difference was not statistically significant (p value > 0.326). the obtained results are illustrated in (Table 2).

Table 1- Baseline characteristics of patients.

		Mean	Std. Deviation	P value
Age (year)	Magnesium	27.69	5.29	0.856*
	Clonidine	27.71	6.73	
Weight (Kg)	Magnesium	67.94	12.17	0.375**
	Clonidine	65.04	12.57	
S.T (min)	Magnesium	111.11	24.35	0.131*
	Clonidine	103.54	19.53	
B.L (ml)	Magnesium	139.44	92.03	0.634*
	Clonidine	141.25	79.19	
MAP (mmHg)	Magnesium	93.818	12.53	0.057**
	Clonidine	86.89	14.91	
SBP (mmHg)	Magnesium	123.33	16.04	0.236**
	Clonidine	117.75	19.92	
DBP (mmHg)	Magnesium	79.06	11.92	0.029**
	Clonidine	71.46	14.19	

HR (b/min)	Magnesium	92.06	15.53	0.023**
	Clonidine	82.67	14.84	

* Mann-Whitney U test ** Independent t-test. S.T: Surgery Time, B.L: Blood Loss, MAP: Mean Arterial Pressure, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, HR: Heart Rate.

Table 2- Distribution of drug side effect.

Type of Drug	shivering		P value
	Yes Count (%)	No Count (%)	
Magnesium	23 (63.9)	13 (36.1)	0.665*
Clonidine	14 (58.3)	10 (41.7)	

* Chi square test

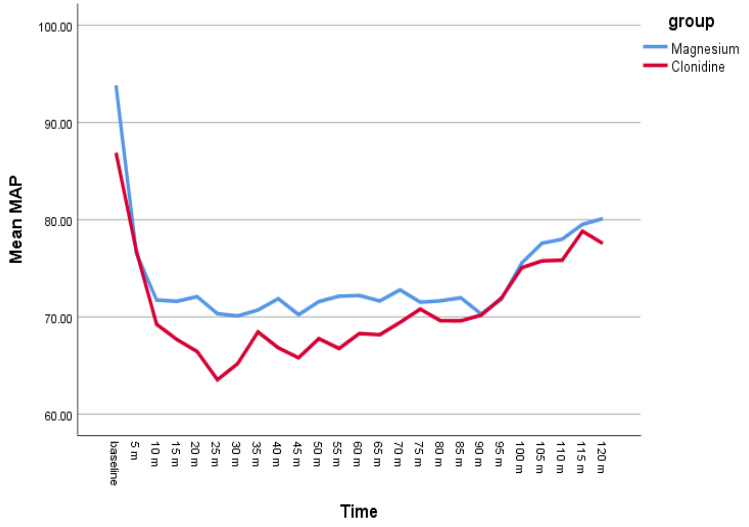

Figure 1. Trends of MAP between both groups.

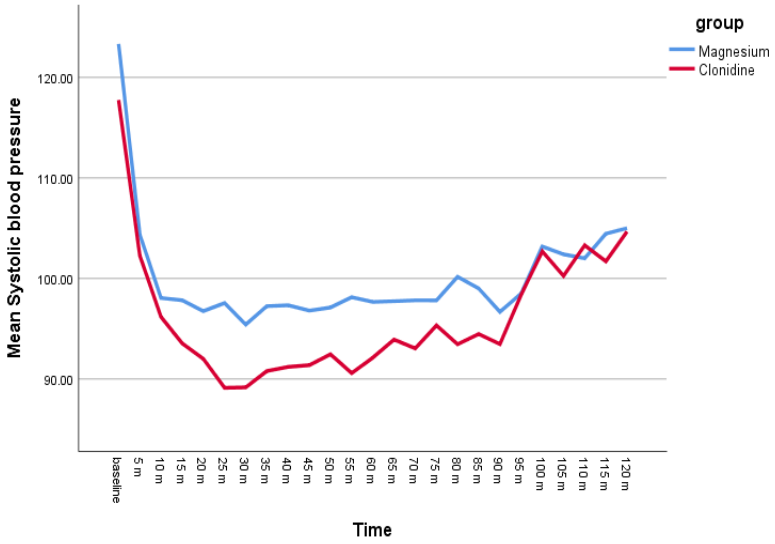

Figure 2. Trends of SBP between both groups.

Figure 3- Trends of DBP between both groups.

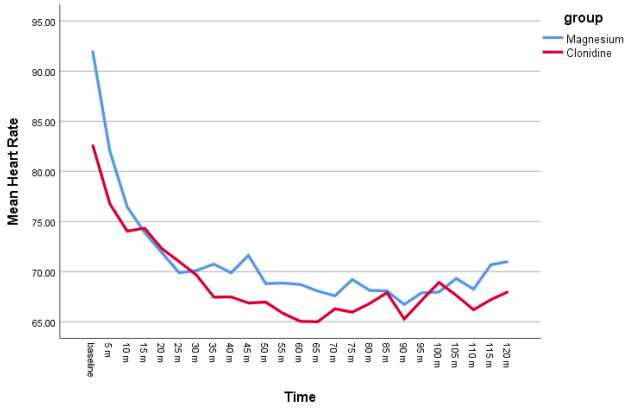

Figure 4- Trends of HR between both groups.

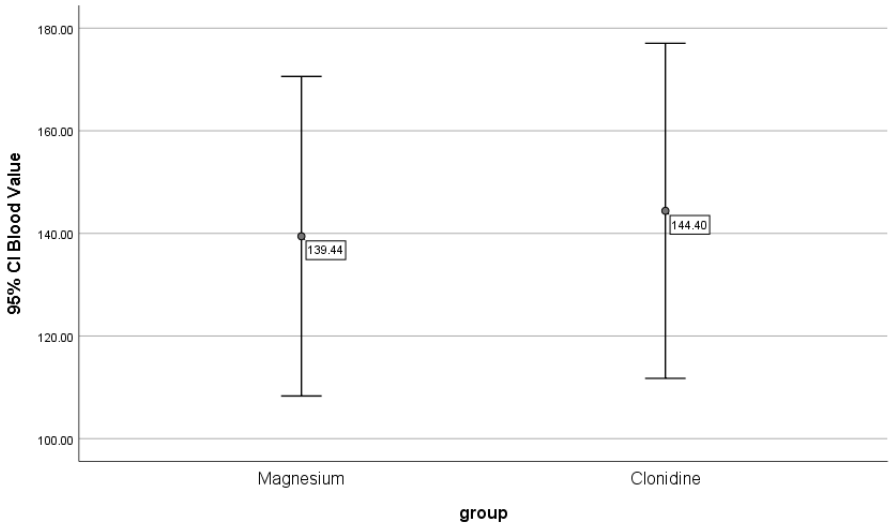

Figure 5- Comparison of the means and 0.95 confidence interval for bleeding volume in the two groups under investigation

Discussion

Numerous studies have investigated various methods and drugs to reduce intra-operative bleeding during septorhinoplasty surgery. The aim of this study was to compare the effects of magnesium sulfate and clonidine for control of hemodynamics and bleeding during this procedure; clonidine as an approved anti-hypertensive drug and magnesium sulfate as a multitasking agent with hypotensive properties.

Bleeding during surgeries like spine surgery and septorhinoplasty can cause poor surgical field visualization and weak surgical outcomes. Several studies and meta-analyses confirmed that hypotensive drugs with Inducing Hypotension can decrease blood loss and subsequently improve field visualization [12].

Several drugs such as Esmolol, Labetalol, Remifentanil, Clonidine, Magnesium sulfate, Dexmedetomidine, Nitroprusside, and Nitroglycerine are used to induce controlled hypotension and also to control of bleeding during surgery (12). Many different type of surgeries such as lumbar spine surgery [13], laparoscopic surgeries [14-15] and Cesarean Section [16] were assessed with the use of these hypotensive drugs.

Kim et al. in 2021 assessed the efficacy of hypotensive agents on intraoperative bleeding for nasal surgery in a meta-analysis study. In this study 37 trials were analyzed, consisting of six interventions (placebo, clonidine, dexmedetomidine, beta-blockers, opioids, and nitroglycerine). They indicated that the systemic use of dexmedetomidine was superior to the other five examined agents. The other agents were also superior to placebo in improving intraoperative bleeding. According to our research, we found two similar study about comparison the effects of dexmedetomidine and magnesium sulfate during rhinoplasty [14]. Furthermore, Rokhtabnak et al. in 2017 compared dexmedetomidine (1µg/kg bolus & 0.4-0.6 µg/kg/h infusion) with Magnesium Sulfate (40mg/kg bolus & 10-15 mg/kg/h infusion) in inducing controlled hypotension during rhinoplasty. Their results illustrated that the hypotension controlled was in both groups, whereas there was no significant difference in MAP between both groups, but heart rate was significantly lower in the Dex group ($P < 0.001$). Moreover, they found that dexmedetomidine was more effective than magnesium to achieve controlled hypotension, and provide a favorable surgical field condition. However, dexmedetomidine also heightened the risk of induced bradycardia and prolonged sedation [15]. In the study by Aboelsuod et al. in 2023 and his colleagues also analyzed dexmedetomidine (1µg/kg bolus & 0.4µg/kg/h infusion) with magnesium sulfate (30mg/kg bolus & 10mg/kg/h infusion) in inducing controlled hypotension during rhinoplasty. They revealed that dexmedetomidine has high effectiveness in attaining controlled hypotension in patients undergoing rhinoplasty but Magnesium sulfate requires extra nitroglycerine [16]. In regard to these investigations, we decided to disregard the dexmedetomidine (because of its side effects) and do an assessment with magnesium sulfate for the multitasking properties of this agent and clonidine because of its efficacy and easy use. In recent studies clonidine and magnesium sulfate have attracted increased attention. These drugs do a great job as adjuncts to both regional as well as general anesthesia. The most desired feature of an anesthetic adjuvant has been reduced anesthetic consumption while maintaining hemodynamic stability, and few studies have used clonidine and magnesium sulfate to fulfill this aim [13]. Majority of studies compared effect of these drugs in intubation, orthopedic, obstetric and laparoscopic surgeries, but in the study by Mireskandari et al. in 2015 demonstrated the effectiveness of intravenous magnesium sulfate for deliberate hypotension in rhinoplasty [17]. Additionally, Ghazipour et al. in 2013 demonstrated that clonidine as a pre-anesthetic drug decrease bleeding during rhinoplasty surgery [18]. Besides, Kosucu et al. (2020) analyzed the Effects of perioperative magnesium sulfate (30–50 mg/kg bolus & 10–20 mg/kg/h infusion) with controlled hypotension on intraoperative bleeding and postoperative ecchymosis and edema in open rhinoplasty. In the magnesium sulfate group, mean arterial pressure decreased during most of the perioperative period [19].

Over and above that, Kalra et al. indicated 50mg/kg magnesium sulfate can produce hemodynamic stability comparable to 1µg/kg Clonidine, although Clonidine in doses of 1.5µg/kg more effectively blunts the hemodynamic response to pneumoperitoneum [20]. Altan et al. in 2005 demonstrated both magnesium sulfate (10mg/kg/h infusion following 30mg/kg bolus) and clonidine (2µg/kg/h infusion following 3µg/kg bolus) lowered the hemodynamic response to intubation in patients undergoing spine surgery, but clonidine was more effective in attenuating the sympathetic response. They found more bradycardia and hypotension in the clonidine group than in the other groups [21]. Ray et al. analyzed the effect of magnesium sulfate (10mg/kg/h infusion following 30mg/kg bolus) and clonidine (1µg/kg/h infusion following 3µg/kg bolus) on hemodynamics and postoperative recovery in upper limb orthopedic surgery. They both attenuated the hemodynamic response to tracheal intubation and caused bradycardia and hypotension [22]. Rajabi et al. in 2020 demonstrated that Intravenous infusion of either magnesium sulfate (30mg/kg) or clonidine (3µg/kg) would stabilize hemodynamic parameters in the setting of cesarean section [23]. In this study we examined the effects of 50mg/kg intravenous magnesium sulfate versus 5µg/kg oral clonidine during septorhinoplasty. despite of most of articles and with combination of remifentanil-propofol-tranexamic acid, we used only bolus doses of

magnesium and clonidine. Obviously, this study is the first one that assess the effects of clonidine and magnesium sulfate during septorhinoplasty surgery. The results from this study indicates that both drugs had been able to reduce the MAP below 75 mmHg. Not only we do agree with Kalra [20], Altan [21], Ray [22] and Rajabi [23] that magnesium can produce an effective controlled hypotension, but also, we revealed that the magnitude of blood pressure changes and fluctuations was higher in the clonidine group during the 10-90 minutes interval of the operation. In the other hand we noticed that the mean blood pressure parameters were more stable in the magnesium group than clonidine group at the same interval.

The most important part of our study was comparing bleeding volume between two drugs. For this purpose, we distinct to use multimodal approach. In fact, we found numerous studies about efficacy of tranexamic acid as an antifibrinolytic agent in bleeding control during rhinoplasty. McGuire [24], de Vasconcellos [25], Ping [26] and Motazedian [27] and their colleagues in the systematic review and meta-analyze revealed the positive role of tranexamic acid in this issue. We used 15 mg/kg tranexamic acid before surgery in all patients.

Rokhtabnak et al. indicated that dexmedetomidine was more effective than magnesium to achieve controlled hypotension, and provided a favorable surgical field condition [15]. Moreover, Jouybar et al. in 2022 [28] compared the effects of remifentanil and dexmedetomidine in rhinoplasty. They concluded that dexmedetomidine was associated with decreased intraoperative bleeding and greater surgeon satisfaction.in the study by Kosucu et al. illustrated that magnesium could decrease intraoperative bleeding [19]. In the present study, although the volume of bleeding in the Magnesium Sulfate group (139.44 ml) was trivially more than in the Clonidine group (141.25 ml), but the difference was not statistically significant (P-Value=0.634). Briefly, our results our findings align with Kosucu et al. that magnesium is a good agent for control of bleeding during septorhinoplasty. Besides, Vyas in 2018 confirmed that clonidine could control postoperative shivering [29]. Further, Kosucu et al. also indicated that magnesium can decrease postoperative shivering in comparison to placebo [19]. Our findings confirmed the effects of both mentioned drugs on this issue. Although incidence of shivering in men & magnesium group was slightly higher but we found that there is no significantly difference between these two drugs (p-value= 0.665) and gender in incidence of shivering after operation. In the other hand there is no preference between magnesium sulfate and clonidine in control of hemodynamic and bleeding volume during septorhinoplasty surgery. In this regard with the absence of injectable clonidine in Iranian pharmacopeia and drug’s side effects such as dry mouth and orthostatic hypotension, magnesium sulfate can be a better choice for control of bleeding in these patients.

Conclusion

The study's results demonstrate that intravenous Magnesium sulfate at a dosage of 50 mg/kg, similar to 5µg/kg oral Clonidine, effectively induces controlled hypotension and reduces bleeding volume during septorhinoplasty surgery. Notably, Magnesium sulfate usage does not appear to elicit common Clonidine-related side effects like dry mouth or orthostatic hypotension in these patients. Furthermore, despite a potentially greater blood pressure reduction in the clonidine group, Magnesium sulfate achieved bleeding reduction by maintaining stable blood pressure and minimizing hemodynamic fluctuations, resulting in a lesser drop in blood pressure. This capacity to sustain controlled blood pressure can be particularly advantageous for high-risk patient groups, such as those with controlled blood pressure or diabetes, and Magnesium sulfate may offer a viable solution in this regard.

Study limitations

Unfortunately, due to the lack of injectable clonidine in the Iranian pharmacopeia, we were unable to use the injectable form of the drug, and therefore, the oral form of the drug was used with an increased dosage. Although necessary measures were taken to standardize conditions for both groups, the use of injectable form of the drug could have reduced unintended errors caused by incomparable pharmacokinetics in the two groups during the study.

Declarations

Ethical Approval for this study was obtained from the Ethics and Research committee of Golestan University of Medical Sciences (IR.GOUMS.REC.1399.177). In addition, the proposal of this project was registered and approved in Iran's randomized clinical trial site (IRCT20170413033408N4). Before registration, all participants read and sign the informed written consent form. A copy of the signed consent form is given to the participant. The guidelines on research involving the use of human subjects (beneficence, non-maleficence, veracity, confidentiality, and voluntarism) were strictly adhered to according to the Helsinki Declaration. Participants did not incur any cost by participating in this study and there was no financial inducement.

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Availability of data and material

The data used to support the findings of this study are available from the corresponding author upon request.

References

[1] Ishii LE TT, Basura GJ, Rosenfeld RM, Abramson PJ, Chaiet SR, Davis KS, et al. Clinical Practice Guideline: Improving Nasal Form and Function after Rhinoplasty. Otolaryngol Head Neck Surg 2017; 156:1-30.

[2] Ors S OM. Late postoperative massive bleeding in septorhinoplasty: A prospective study. Plast Surg (Oakv). 2016; 2:96-8.

[3] Tuncel U TA, Bayraktar MA, Erkorkmaz U, Kostakoglu N. Efficacy of dexamethasone with controlled hypotension on intraoperative bleeding, postoperative oedema and ecchymosis in rhinoplasty. J Craniomaxillofac Surg. 2013; 41:124-8.

[4] Giovannitti JA Jr TS, Crawford JJ. Alpha-2 adrenergic receptor agonists: a review of current clinical applications. Anesth Prog. 2015; 62(1): 31-9.

[5] Jabalameli M HM, Soltani H, Hashemi J. Oral Clonidine Premedication Decreases Intraoperative Bleeding in Patients Undergoing Endoscopic Sinus Surgery. Journal of Research in Medical Sciences. 2005; 1:25-30.

[6] Elsharnouby NM EM. Magnesium sulfate as a technique of hypotensive anaesthesia. Br J Anaesth. 2006; 96(6):727-31.

[7] Shimosawa T TK, Ando K, Fujita T. Magnesium inhibits norepinephrine release by blocking N-type calcium channels at peripheral sympathetic nerve endings. Hypertension. 2004; 44:897-902.

[8] Soave PM CG, Costa R, Arcangeli A. Magnesium and anaesthesia. Curr Drug Targets. 2009; 10: 734-43.

[9] Razavi M NM, Ahmadi M, Kashani I. Comparison of Labetalol and Nitroglycerine,s Effects on Deliberate Hypotension in Septo-Rhinoplasty Ssurgery, a Randomized Clinical. Rev Clin Med. 2020;7(4):176-9.

[10] Reena, Vikram A. Comparative evaluation of clonidine and magnesium sulfate infusions upon intraoperative hemodynamics and anesthetic consumption, and postoperative recovery profile in lumbar spine surgery: a prospective, randomized, placebo controlled, double-blind study. Acta Anaesth Belg. 2017; 68:31-8.

[11] Aparna B, Krusha Suresh S, Spoorti P, Tanya G, Chandrakala S. Comparison of Effect of Clonidine and Magnesium Sulfate on Attenuation of Haemodynamic Response to CO2 Pneumoperitoneum in Patients undergoing Laparoscopic Surgeries- A Randomised Clinical Study. Journal of Clinical and Diagnostic Research. 2022; 16(6).

[12] Mohamed Ali HS ea. A comparative study of clonidine and magnesium sulfate premedication on perioperative hormonal stress responses, hemodynamic stability and postoperative analgesia in patients with gallbladder diseases undergoing laparoscopic cholecystectomy. A randomized, double-blind, controlled study. Egyptian J Anaesthesia. 2022; 38(1).

[13] Rajabi M RM, Hamidi-Shad M, Tabasi Z, Akbari H, Hajian A. Magnesium Sulfate and Clonidine; Effects on Hemodynamic Factors and Depth of General Anesthesia in Cesarean Section. Anesth Pain Med. 2020;10(5).

[14] Kim DH LJ, Kim SW, Hwang SH. The Efficacy of Hypotensive Agents on Intraoperative Bleeding and Recovery Following General Anesthesia for Nasal Surgery: A Network Meta-Analysis. Clin Exp Otorhinolaryngol. 2021; 14(2):200-9.

[15] Rokhtabnak F DMS, Ghodraty M, Pournajafian A, Maleki Delarestaghi M, Tehrani Banihashemi A, Araghi Z. Controlled Hypotension During Rhinoplasty: A Comparison of Dexmedetomidine with Magnesium Sulfate. Anesth Pain Med. 2017; 7(6).

[16] Aboelsuod M SS. Dexmedetomidine versus magnesium sulfate for controlled hypotension during rhinoplasty surgeries: A prospective randomized comparative study. Egyptian J Anaesthesia. 2023; 39:657-64.

[17] Mireskandari SM ea. The effectiveness of intravenous magnesium sulfate for deliberate hypotension in rhinoplasty. Arch Anesth & Crit Care. 2015; 1(4):112-5.

[18] Ghazipour A AK, Sarafraz M, Abshirini H, Akbari N. Can clonidine as a pre-anaesthetic drug decrease bleeding during rhinoplasty surgery?. Indian J Otolaryngol Head Neck Surg. 2013; 65(2):301-3.

[19] Kosucu M TE, Arslan E, Omur S, Livaoglu M. Effects of perioperative magnesium sulfate with controlled hypotension on intraoperative bleeding and postoperative ecchymosis and edema in open rhinoplasty. Am J Otolaryngol. 2020; 41(6).

[20] Kalra NK VA, Agarwal A, Pandey H. Comparative study of intravenously administered clonidine and magnesium sulfate on hemodynamic responses during laparoscopic cholecystectomy. J Anaesthesiol Clin Pharmacol. 2011; 27(3): 344-8.

[21] Altan A TN, Yildiz F, Türkmen A, Ustün H. Effects of magnesium sulfate and clonidine on propofol consumption, haemodynamics and postoperative recovery. Br J Anaesth. 2005; 94(4):438-41.

[22] Ray M BD, Hajra B, Pal R, Chatterjee N. Effect of clonidine and magnesium sulfate on anaesthetic consumption, haemodynamics and postoperative recovery: A comparative study. Indian J Anaesth 2010; 54(2):137-41.

[23] Rajabi M RM, Hamidi-Shad M, Tabasi Z, Akbari H, Hajian A. Magnesium Sulfate and Clonidine; Effects

on Hemodynamic Factors and Depth of General Anesthesia in Cesarean Section. Anesth Pain Med. 2020; 10(5).

[24] McGuire C NS, Samargandi OA, Bezuhly M. Role of Tranexamic Acid in Reducing Intraoperative Blood Loss and Postoperative Edema and Ecchymosis in Primary Elective Rhinoplasty: A Systematic Review and Meta-analysis. J. AMA Facial Plast Surg. 2019; 21(3):191-8.

[25] de Vasconcellos SJA dN-JE, de Aguiar Menezes MV, Tavares Mendes ML, de Souza Dantas R, Martins-Filho PRS. Preoperative Tranexamic Acid for Treatment of Bleeding, Edema, and Ecchymosis in Patients Undergoing Rhinoplasty: A Systematic Review and Meta-analysis. JAMA Otolaryngol Head Neck Surg. 2018; 144(9):816-23.

[26] Ping WD ZQ, Sun HF, Lu HS, Li F. Role of tranexamic acid in nasal surgery: A systemic review and meta-analysis of randomized control trial. Medicine (Baltimore). 2019; 98(16).

[27] Motazedian G SM, Jahromi M S S, Ghaedi M. Bleeding Management In Rhinoplasty Surgery: A Systematic Review Study On Clinical Trial Studies Conducted In Iran. Int J Med Invest. 2021; 10(4):32-4.

[28] Jouybar R NM, Asmarian N. Comparison of the effects of remifentanil and dexmedetomidine on surgeon satisfaction with surgical field visualization and intraoperative bleeding during rhinoplasty. BMC Anesthesiol. 2022; 22(1).

[29] Vyas V GR, Dubey P. Comparative Efficacy and Safety of Intravenous Clonidine and Tramadol for Control of Postspinal Anesthesia Shivering. Anesth Essays Res. 2018; 12(3):663-8.