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SHORT COMMUNICATION

The effect of oral clonidine premedication on blood loss and the quality of the surgical field during endoscopic sinus surgery: a placebo-controlled clinical trial

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Abstract Bleeding during functional endoscopic sinus surgery (FESS) remains a challenge for both surgeons and anesthesiologists despite several modalities available for improving the surgical field. This study was conducted to evaluate the effect of oral clonidine premedication on blood loss and the quality of the surgical field in FESS. In a placebo-controlled clinical trial, a total of 84 American Society of Anesthesiologists (ASA) physical status I–II patients undergoing endoscopic sinus surgery for chronic sinusitis were randomly allocated to receive either oral clonidine 0.2 mg or identical-looking placebo tablets 90 min before arrival at the operating room. Blood loss in the clonidine group was 214 ± 67 ml on average and that in the placebo group was 276 ± 78 ml (mean ± SD, $p < 0.01$). The median (range) bleeding score in the clonidine group was significantly lower than that in the placebo group (2 (1–3) vs. 2.5 (2–4), $p < 0.0001$). Accordingly, the surgeon was more satisfied with the surgical field in the clonidine group than with that in the placebo group (median score, 4 (3–5) vs. 3 (1–5), $p < 0.001$). In conclusion, premedication with oral clonidine 0.2 mg can effectively reduce bleeding during FESS.

Keywords Clonidine · Endoscopy · Otorhinolaryngologic surgical procedure · Paranasal sinuses · Hemorrhage

Bleeding during functional endoscopy sinus surgery (FESS) remains a challenge for both surgeons and anesthesiologists despite several modalities available for improving the surgical field [1]. Although major blood loss during FESS is rare, maintaining an optimal surgical field is crucial for the surgeon, in that even a small amount of blood may disturb the endoscopic view, increasing the likelihood of complications as well as lengthening the operative procedure and possibly resulting in incomplete surgery [2].

Several techniques have been suggested to improve the surgical field in sinus surgery. Bipolar diathermy, topical vasoconstrictors, and induced hypotension are among the most commonly used [2, 3]. Of these, diathermy may result in local tissue damage and subsequent bleeding [2]. Topical vasoconstrictors may result in hemodynamic instability, especially in patients with a history of hypertension or ischemic heart disease. Induced hypotension with volatile agents or narcotics exposes the patients to more anesthetic drugs and consequently their side effects. Furthermore, none of these techniques have consistently provided a desirable bloodless field for the surgeon.

Clonidine has gained popularity as an adjuvant drug in anesthesia for its sedative and analgesic effects [4], as well as for its favorable effects on the hemodynamic profile of patients [5]. It has been used to reduce intraoperative bleeding in major abdominal and orthopedic surgeries through its hypotensive effects [6, 7]. Clonidine as an α-agonist constricts peripheral blood vessels [8], and has been suggested to reduce nasal mucous blood flow in animal models [9]. Therefore, clonidine may reduce the bleeding associated with paranasal sinus endoscopy and other surgeries with similar vascular-rich environments. To our knowledge, no earlier study has evaluated the effects of clonidine on blood loss and the quality of the surgical field in FESS.

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Between June 2008 and February 2009, a total of 84 American Society of Anesthesiologists (ASA) physical status I–II patients, aged 23–57 years, undergoing endoscopic sinus surgery for chronic sinusitis were enrolled. Patients receiving anticoagulants or having a bleeding diathesis were excluded. Exclusion criteria were significant heart disease that contraindicated the use of controlled hypotension, medically important liver or kidney dysfunction, known allergy to clonidine, systolic blood pressure (SBP) >160 mmHg, diastolic blood pressure (DBP) >90 mmHg, or pulse rate <50 beats/min at the time of the preoperative visit. Also, patients receiving anticoagulants, beta blockers, calcium channel blockers, or digoxin were not included. The patients were randomly allocated to receive either oral clonidine 0.2 mg (Tolidaru, Tehran, Iran) or identical-looking placebo tablets 90 min before arrival at the operating room. This prospective study was approved by the regional ethics committee, and written informed consent was obtained from all patients.

All patients were premedicated with oral oxazepam 10 mg 2 h before surgery, as well as fentanyl 4 μg/kg and intravenous lidocaine 1.5 mg/kg 3–5 min before intubation. After the application of 100% oxygen at 5 l/min for 5 min, anesthesia was induced with propofol 2 mg/kg and atracurium (0.5 mg/kg). After tracheal intubation, anesthesia and muscle relaxation was maintained with propofol 100 μg/kg/min, remifentanil 0.1 μg/kg/min, and atracurium. Controlled mechanical ventilation with an initial tidal volume of 10 ml/kg and respiratory frequency of 10 breaths/min was adjusted to maintain normocapnia. At the end of anesthesia, muscle relaxation was reversed with neostigmine 0.04 mg/kg and atropine 0.02 mg/kg. Before the induction of anesthesia all patients received isotonic crystalloids 3 ml/kg for volume expansion. During the surgery maintenance fluids were standardized for the patients, based on their weight, and blood losses were replaced with Ringer's lactate in a 3:1 ratio. None of the patients required transfusion of blood products.

All patients were placed in a 10° reverse Trendelenburg position during the surgery. The same anesthesia and surgical teams performed all the procedures with the same technique. Based on the study protocol, none of the patients received preoperative or intraoperative local vasoconstrictors. From a technical aspect, cutting forceps as well as grabbing instruments were used, while a microdebrider was not employed.

Intraoperative blood loss was estimated by the responsible anesthesiologist at the end of surgery by accounting for loss of blood and irrigation fluid into the 25 mL-graded suction canister, and nasopharyngeal packing (measured weight of packing on the electronic scale). Moreover, at the end of the surgery, the surgical field was graded in terms of bleeding by the surgeon, using the scale used by Boezaart and colleagues in 1995 [from no bleeding (0) to severe bleeding—constant suctioning required (5)] [10]. The satisfaction of the surgeon about the quality of surgical field was also asked, and responses were graded on a 5-point Likert scale (1: poor, 5: excellent). Hemodynamic parameters including systolic and diastolic arterial blood pressure and heart rate were recorded at 15-min intervals.

Randomization was performed by the hospital pharmacy by using a table of random numbers. The head nurse of the surgery ward provided the tablets to the patients. The patient, surgeon, and anesthetist were blinded to the nature of the assignments.

For statistical analyses, the baseline characteristics of the two groups were analyzed with Student's *t*-test for continuous data and the χ^2 test for categorical analysis. Differences in repeated measures of blood pressure and heart rate between the two groups were analyzed with general linear model repeated measurement of analysis of variance (GLM ANOVA). Ranked data, including bleeding and satisfaction scores, were compared between the two groups with the Mann–Whitney *U*-test; *p* values of <0.05 were considered statistically significant.

Blood loss in the clonidine group was 214 ± 67 ml and in the placebo group it was 276 ± 78 ml (mean ± SD, $p < 0.01$). By the surgeon's opinion, the median (range) bleeding score in the clonidine group was significantly

Table 1 Demographic data, coagulation profile, and outcome measurements in two groups

Variable	Clonidine	Placebo	*p* value
Age (years)	34 (12)	36 (13)	0.61
Male sex, *N* (%)	23 (54.7)	27 (64.2)	0.99
Platelet count ($1000/mm^3$)	231 (43)	269 (54)	0.81
PT (s)	12.3 (1.2)	12.1 (1.2)	0.83
PTT (s)	33.4 (2.8)	32.2 (3.1)	0.51
Duration of surgery (min)	104 (29)	96 (23)	0.28
Bleeding score, *N* (%)			<0.01
1	4 (9.4)	0 (0)	
2	29 (69.0)	23 (54.7)	
3	8 (19.0)	16 (38.1)	
4	1 (2.4)	3 (7.1)	
Satisfaction score, *N* (%)			<0.01
1	1 (2.4)	2 (4.8)	
2	3 (7.1)	4 (9.5)	
3	9 (21.4)	16 (38.1)	
4	20 (47.6)	16 (38.1)	
5	9 (21.4)	4 (9.5)	

Data are presented as means (standard deviation)

PT prothrombin time, *PTT* partial thromboplastin time

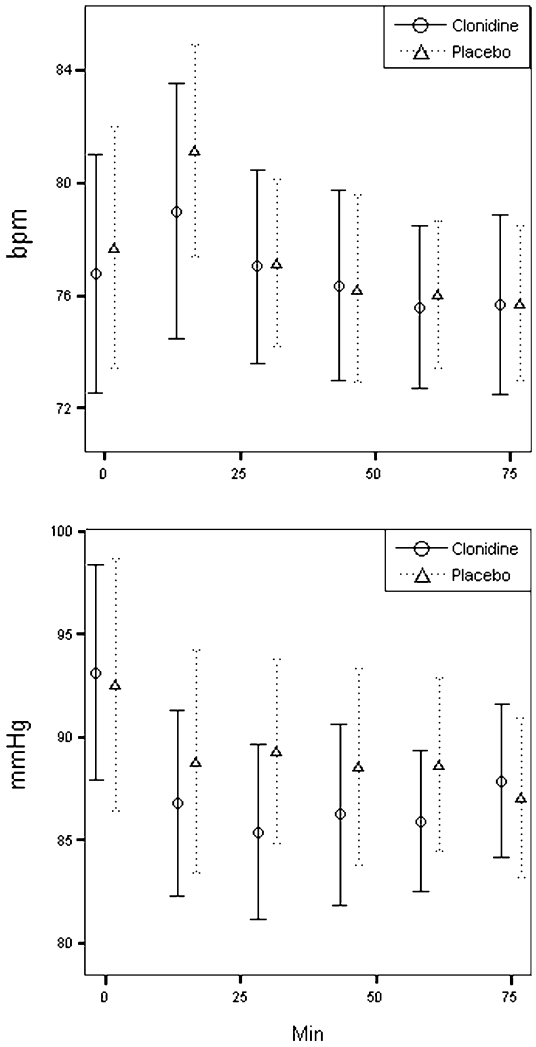

Fig. 1 Trends in heart rate (*above*) and mean arterial pressure (MAP) (*below*) in clonidine (*circles*) and placebo (*triangles*) groups. Data are presented as means (standard error); $p > 0.05$ with general linear model repeated measurement of analysis of variance (GLM ANOVA). *bpm* beats per min

lower than that in the placebo group (2 (1–3) vs. 2.5 (2–4), $p < 0.0001$). The data showed that in 9.4% of the patients given clonidine, no suctioning was required during the surgery, whereas all of the patients in the placebo group had bleeding scores more than 1 and thus required suctioning (Table 1). Accordingly, the surgeon was more satisfied with the surgical field in the clonidine group than with that in the placebo group (median score, 4 (3–5) vs. 3 (1–5), $p < 0.001$). There were no significant differences between the two groups regarding the demographic data and coagulation profiles of the patients (Table 1). Figure 1 shows similar trends in mean arterial pressure (MAP) and heart rate in the two groups ($p > 0.05$).

The results of this study verify the efficacy of premedication with oral clonidine in reducing the amount of blood loss in FESS; this occurred independently of hemodynamic variables. This finding may support the hypothesis of reduced nasal mucous blood flow due to the peripheral vasoconstrictive effects of clonidine proposed in an earlier animal study [9]. The major advantage of clonidine over other vasoconstrictors is its known stable hemodynamic profile, whereas most other vasoconstrictors such as phenylephrine and epinephrine used in nasal surgery induce blood pressure elevation.

In this study, besides estimating the amount of blood loss, we used a validated scale to evaluate the quality of the surgical field as well as the satisfaction of the surgical team. The latter measurement modalities even more accurately reflect the efficacy of hemostatic interventions, seeing that the direct objective of the anesthesia in FESS is to make a clean surgical field rather than reduce the blood loss. Recently, a multicenter standardized reliability analysis has verified the inter- and intraobserver reliability of the Boezaart scale [11].

Hypotension and bradycardia are the major possible adverse effects of clonidine that may be encountered more frequently with the intraoperative intravenous use of clonidine [12]. In the present study, patients receiving beta blockers, calcium channel blockers, or digoxin were not included. However, the requirement for fluid challenge was comparable in the two study groups and no case of significant bradycardia was observed; this feature supports the safety of premedication with oral clonidine in otherwise healthy candidates for sinus surgery.

One limitation of this study was that we could not address the severity of the sinus disease in our patients because our surgical team does not routinely use relevant validated scales such as the Kennedy staging system. However, all patients in this survey were first-time candidates for two-sided FESS due to chronic sinusitis.

In conclusion, regarding the efficacy and safe therapeutic profile of clonidine, we recommend its use in otherwise healthy candidates for sinus surgery.

Conflict of interest None.

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