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Original article

The Effect of Oral Clonidine Premedication on the blood Loss and the Quality of Surgical Field during Endoscopic Sinus Surgery

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Abstract:

Aim of the study: This study aims to assess the effect of oral clonidine premedication on blood loss and the surgical field quality during endoscopic sinus surgery in individuals with bilateral sinonasal polyposis. **Patients and methods:** At the Beni- Suef University Hospital, a randomised, controlled, double-blind clinical experiment was done. Approval from research ethics committee of faculty of medicine of Beni-Suef University and an informed consent from patients diagnosed as sinonasal polyposis was obtained, in the duration from June 2019 to February 2020. Forty patients were randomly assigned to equal groups; group 1 (20 patients) received oral clonidine 200 micrograms (the recommended dose) 1 to 1.5 hours before the time of operation and group 2 (20 patients) did not receive clonidine. Surgeries in both groups were done using hypotensive anesthesia in the form of deep general anesthesia and heavy analgesia under general anesthesia. An uncinectomy,

middle meatal antrostomy, anterior ethmoidectomy, posterior ethmoidectomy, and, if necessary, sphenoidectomy were performed as part of endoscopic sinus surgery (ESS). **Results:** The blood loss in the jar and the total blood loss in group 2 are statistically significant higher than group 1 (P-value<0.05). That there was a statistically significant difference between the two groups regarding the mean Boezart scale and its categories (P-value<0.05). There was a statistically significant increase of the intraoperative time in group 2 than group 1 (P-value<0.05). **In conclusion**, the pre-medication with clonidine improves hemodynamic status, surgical field, decrease the blood loss inside the jars and the total blood loss and subsequently decrease the intraoperative time.

1. Introduction

Despite a variety of techniques for enhancing the operative field, functional endoscopic sinus surgery (FESS) bleeding is still a difficulty for both surgeons and anesthesiologists **(1).**

Even though significant blood loss occurs infrequently during FESS, maintaining an ideal surgical field is essential for the surgeon since even a tiny quantity of blood can impair the endoscopic image, extend the surgical procedure, and even cause surgery to be unsuccessful **(2).**

The operative field in sinus surgery has been suggested to be improved by a number of methods. Among the most popular techniques are induced hypotension, topical vasoconstrictors, and bipolar diathermy. Diathermy may cause localized tissue injury and subsequent bleeding as a result of these **(1).**

Hemodynamic instability may develop with topical vasoconstrictors, particularly in individuals with a history of hypertension or ischemic heart disease. Patients are exposed to more anaesthetic medicines and, as a result, their adverse effects when hypotension is artificially induced using narcotics or volatile substances. Furthermore, none of these methods have consistently given the surgeon a preferred blood-free environment **(3).**

Due to its calming and analgesic properties as well as its positive effects on patients' hemodynamic profiles, clonidine has become a common adjuvant medication in anaesthesia **(4).** Through its hypotensive properties, it has been utilized to lessen intraoperative bleeding during significant abdominal and orthopaedic procedures **(5).** In animal studies, it has been hypothesised that clonidine, an alpha2-agonist, reduces nasal mucus blood flow via constricting peripheral blood vessels **(5).**

Therefore, clonidine may improve the surgical field in FESS and lessen bleeding related to paranasal sinus endoscopy and other procedures performed in similarly vascular-rich settings **(6).**

2. Aim of the Work

The purpose of this study is to assess how oral clonidine premedication affects blood loss and the surgical field during endoscopic sinus surgery on patients with bilateral sinonasal polyposis.

3. Patients and Methods

Study Design

The Beni- Suef University Hospital served as the site of this clinical investigation that was randomized, controlled, and double-blind. In the period from June 2019 to February 2020, approval from the local ethics council and informed permission from patients with bilateral sinonasal polyposis were acquired.

Population/ Sample size

Study was conducted on 40 patients suffering from sinonasal polyposis. The sample size was calculated by G. Power 3.1 and the T test was used to calculate the sample size. At an effect size 1.2, allocation ration one to one, alpha error 0.05 and power 95%, the sample size was 40 patients with 20 in each group.

Inclusion criteria

Patients with bilateral sinonasal polyposis not responding to medical treatment who came to Ear, Nose & Throat clinic of Beni- Suef University Hospital were included in the study.

Exclusion criteria

The research excluded individuals with ischemic heart disease, blood disorders, liver or renal failure, known clonidine allergies, and those taking anticoagulants, beta blockers, calcium channel blockers, or digoxin.

Preoperative assessment

Preoperatively all patients were subjected to all careful history taking, routine Otorhinolaryngological examination, endoscopic nasal examination, C.T. scan of the nose and paranasal sinuses, routine laboratory investigations including coagulation profile, blood sugar, complete blood count, renal and liver function tests.

Technique

Patients were randomly divided into two equal groups A and B (20 patients in each group). Group 1 (Intervention Group): 20 patients received oral clonidine 200 micrograms (the recommended dose) 1 to 1.5 hours before the time of operation. Group 2 (Control Group): 20 patients did not receive clonidine.

Surgeries in both groups were done using hypotensive anesthesia in the form of deep general anesthesia and heavy analgesia. The same anesthetic and the same surgeon have performed all surgeries in both groups. Based on the study protocol, the surgeries were performed under general anesthesia.

Endoscopic sinus surgery included an uncinectomy, middle meatal antrostomy, anterior ethmoidectomy, posterior ethmoidectomy, and, if required, sphenoidectomy (ESS). Technically speaking, the micro debrider was not used; instead, cutting forceps and grasping tools were used. For 48 hours, Merocel was placed on all patients.

Data collection methods and tools

•beginning of operation blood loss utilizing:

-After using less saline for cleaning, blood gathered in the graded suction chamber.

-Measurement of nasal packs weight and converting the blood weight into milliliters, according to Al Kadri, who reported that: (wet item gram weight - dry item gram weight) = (milliliters of blood within the item) **(7).** Net Blood Loss (ml) = [blood accumulated in the suction chamber (ml) – (the amount of saline used for washing (ml)+ The amount of saline in nasal packs)] + Blood amount in the packs (ml). Electronic scale for calculating the weight of nasal packs **(7).**

•Regarding nasal polypi, they have been removed by Blakesley forceps (Surgeon tried to avoid suction of any nasal polypi in the suction apparatus).

•Using a Boezaart grading system with 1–5 points, the surgical field's quality was evaluated prior to operation **(8).** Bleeding emerges more quickly than the suction can stop it; the surgical field is significantly endangered, and surgery is typically not an option.

• Intraoperative time was measured in both groups.

Postoperative care and follow up:

•Postoperatively, all patients were received parental antibiotic for 7 days (ceftriaxone 1 gram intramuscular once daily), local nasal steroids spray (once at night), antihistaminic (once at night), and analgesics on demand.

•Postoperative follow-up was performed weekly for one month.

•In the post-anesthesia care unit and the ward, the frequency of potential therapeutic side

effects such nausea and vomiting was assessed.

•There were no postoperative complications such as bleeding or orbital complications.

•Patients stayed in the hospital until the nasal packing removed after 48 hours.

Statistical analysis

SPSS v. 25 (Statistical Package for Social Science) for Windows was used to analyse the data. The mean and standard deviation of the quantitative variables served as their descriptions (SD). The qualitative factors were described using numbers (No.) and percentages. The Kolmogorov-Smirnov test was used to examine the data for normalcy. The Mann-Whitney test was used to compare groups with respect to non-normally distributed variables, while the T-test was employed to compare two groups with respect to regularly distributed scale variables. To compare groups with reference to the categorical variables, the chi-square test was utilised. The results' significance was determined using a P-value, which was divided into two categories: non-significant when P-value 0.05 and significant when P-value 0.05.

Ethical consideration

Nobody was obliged to participate in the study, and all information was kept private and anonymous. The patients' written informed permission was acquired before they agreed to participate in the trial. The Beni-Suef University faculty of medicine's ethics committee reviewed and approved the study protocol number FMBSUREC/07072019/ Arafat.

4. Results:

The mean age of group 1 was 28.2±10.9 and group 2 was 33.5±10.5 years. Table (1) showed that there was no statistically significant difference between the two groups regarding the age, sex distribution, systolic, diastolic blood pressure and heart rate (P-value>0.05).

Table (1) Baseline characteristics of the studied groups:

Baseline characteristics	Group 1 n=20 (%)	Group 2 n=20(%)	P-value
Age	28.2±10.9	33.5±10.5	0.125
Sex Males Females	 12 (60) 8 (40)	 11 (55) 9 (45)	0.796
SBP	118±13	119.3±17.4	0.790
DBP	78±9.3	76±10.8	0.534
Pulse (Beat/minute)	82±7	87±9	0.057

SBP: systolic blood pressure
DBP: diastolic blood pressure

Table (2) showed that there was a statistically significant higher systolic/diastolic blood pressure and pulse in group 2 than group 1 (P-value<0.05).

Table (2) Mean systolic blood pressure, diastolic and pulse during the operation (Measured at the start of the operation and every 20 minutes of the operation) of the studied groups:

Intra-operative	Group 1 n=20	Group 2 n=20	P-value
SBP	86.8±11.15	103±11.7	0.001*
DBP	63±7.8	77±9.2	0.001*
Pulse (Beat/minute)	67±7	78±9	0.001*

SBP: systolic blood pressure
DBP: diastolic blood pressure
*P-value is significant at <0.05

Table (3) showed that there was no statistically significant difference between both groups regarding the blood in nasal packs (P-value>0.05). The blood loss in the jar and the total blood loss in group 2 is statistically higher than group 1 (P-value<0.05).

Table (3) Comparison between both groups regarding the blood loss milli liter in nasal packs, jars and the total blood loss:

Intra-operative	Group 1 n=20 (%)	Group 2 n=20(%)	P-value
Blood loss in nasal Packs	49.5±21.6	53.5±14.7	0.497
Blood loss in nasal jar	88.3±28.5	141.3±43	0.001*
Total blood loss	137.8±45.5	194.8±49.2	0.001*

*P-value is significant at <0.05

Table (4) Boezart scale and intraoperative time in both groups:

Intra-operative	Group 1 n=20 (%)	Group 2 n=20(%)	P-value
Boezart scale	2±0.31	3±0.44	0.001*
Boezart categories II III	 18 (90) 2 (10)	 10 (50) 10 (50)	0.001*
Intra-operative time	94.8±9	106.5±10	0.001*

*P-value is significant at <0.05

Table (4) showed that there was a statistically significant difference between the two groups regarding the mean Boezart scale and its categories (P-value<0.05). There was a statistically significant increase of the intraoperative time in group 2 than group 1 (P-value<0.05).

5. Discussion:

One of the most frequent procedures carried out by otolaryngologists is ESS **(9).** Despite a variety of techniques for enhancing the operative field, functional endoscopic sinus surgery (FESS) bleeding is still a difficulty for both surgeons and anesthesiologists **(1).**

Despite the rarity of severe blood loss during FESS, it is essential for the surgeon to maintain a clear surgical field since even a tiny quantity of blood might impair the endoscopic vision, extend the surgical procedure, and potentially lead to incomplete surgery **(10).**

For surgeons and anesthesiologists, managing bleeding during and after endoscopic sinus surgery remains a difficulty. Several strategies have been proposed to enhance the operative environment during sinus surgery. Among the most popular techniques are induced hypotension, topical vasoconstrictors, and bipolar diathermy.

Diathermy may cause localised tissue injury and subsequent bleeding as a result of these **(1).**

A range of techniques, including intraoperative and postoperative blood recovery, medication, controlled hypotension, etc., as well as a mix of techniques, have been utilised in several trials to lessen blood loss during ESS. Hemodynamic instability may develop with topical vasoconstrictors, particularly in individuals with a history of hypertension or ischemic heart disease. Furthermore, none of these methods have consistently given the surgeon a preferred blood-free environment **(3).**

Due to its calming and analgesic properties as well as its beneficial effects on patients' hemodynamic profiles, clonidine has become more and more common as an adjuvant medication in anaesthesia. Through its hypotensive properties, it has been utilised to lessen intraoperative bleeding during significant abdominal and orthopaedic procedures **(11, 12).**

In animal models, clonidine, an alpha2-agonist, has been shown to slow heart rate, constrict peripheral blood vessels, and limit blood flow to the nasal mucous membranes **(13).**

Therefore, clonidine may improve the surgical field in FESS and lessen bleeding related to paranasal sinus endoscopy and other procedures performed in similarly vascular-rich settings **(7).**

This study was conducted on 40 patients randomly allocated in the two groups with respect to the matching between them regarding their age, sex and baseline blood pressure and heart rate.

The goal of the current investigation was to evaluate if clonidine affected intraoperative bleeding or visualisation, as the field's quality was thought to be the most crucial element in ESS. In order to establish a homogenous population for the sake of using a consistent anaesthetic procedure, this study used tight inclusion and exclusion criteria.

Regarding the hemodynamically stability after the operation, it was found that the administration of clonidine preoperatively, significantly decreased the heart rate compared with placebo (67±7 versus 78±9 beat/ minutes for both groups respectively). This result was agreed with many trials that clonidine decreased the heart rate after induction till the end of operation **(14).**

Regarding the systolic and diastolic blood pressure, it was found that clonidine significantly decreased the systolic and diastolic blood pressure in this study as seen in many other studies as in Fehr and his colleagues' study (2003) **(15)** and Dimou et al., study (2006) **(16).**

In this study, the mean amount of collected blood during surgery was 137.8± 45.5 ml for clonidine group and 194.8±49.2 ml for control group with a significant difference between both groups.

This agrees with the results of most of the previous studies such as that of Mohseni et al., 2011 where the blood loss in the clonidine group was 214 ± 67 ml significantly lower than the placebo group it was 276 ± 78 ml **(12).**

As regard the quality of the surgery field, based on the Boezaart grading scale, the surgical field in clonidine group was better

than the other group in most of cases. There was a significant difference between both groups (P-value =0.001). The intraoperative time was ranging between 60 - 135 min in the clonidine group with mean± SD= 94.80±9 min., whereas in control group it was ranging between 80 – 140 min. with mean±SD= 106.5±10 min, and this showed significant differences between both groups. There was a statistically significant increase of the intraoperative time in control group than clonidine group.

This result further corroborated the prior animal study-proposed theory that the peripheral vasoconstrictive effects of clonidine resulted in decreased nasal mucus blood flow **(14).**

The improvement of surgical field and shorter operative time were found in Wawrzyniak et al., 2013 study, who conducted a study on 44 patients allocated randomly in 2 groups administered clonidine and midazolam, it was found that the clonidine gave significantly better quality of surgical field and shorter duration of the surgical procedure **(17).**

The better surgical field and the shorter operative time were explained by the vasoconstrictor effects of clonidine on nasal mucosa vessels allowed better visualization of the surgical field resulting in shorter duration of the procedure as well. Similar results were observed in two other clinical studies **(1,18).**

On contrary to our study there was a study conducted by Das and his colleagues (2016) **(19)** who compare dexmedetomidine and clonidine effect on producing controlled hypotensive anesthesia during FESS in adults, they found superiority of dexmedetomidine on clonidine in decreasing the dosage of nitroglycerine and the dose of fentanyl required for anesthesia, But the duration of controlled hypotension was almost similar in both the groups. This study is different from our study in comparing the effect of clonidine versus dexmedetomidine, but our study compared the clonidine effect with hypotensive anesthesia versus control (hypotensive anesthesia only) without any other medication.

6. Conclusion:

In conclusion, this randomized controlled trial shows that pre-medication with clonidine improves hemodynamic status, improve the surgical field, decrease the blood loss inside the jars and the total blood loss and subsequently decrease the intraoperative time.

Limitations of the study

The present research's drawback is that it is unicentric study with relatively low sample size.

Recommendation

There should be more research done to examine clonidine's effectiveness in various patient subgroups, including those with and without polyposis and those with bleeding issues. Also, to address the optimal dose and regimen. More trials are required to assess the efficacy of different higher doses of clonidine on blood loss, quality of surgical field, operative time and complications of clonidine, and trials are required to explore clonidine efficacy in the patients without hypotensive anesthesia.

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