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Original Research Article

A Comparison of Effect of Oral Premedication with Clonidine and Metoprolol on Intraoperative Haemodynamics and Surgical Condition during Functional Endoscopic Sinus Surgery

Devendran P[1], L. Uma Pradeepa[2], Kiruthika Rathinasabapathy[3], K Uma[4]

[1]Senior Resident, Department of Anesthesia, Siddipet Govt Medical College, and Hospital, Siddipet, Telangana State.
[2]Assistant Professor, Department of Anesthesia, Osmania Medical College, Hyderabad, Telangana State.
[3]Senior Resident, Department of Anesthesia, Kakatiya Medical College and MGM Hospital, Warangal, Telangana State.
[4]Professor, Department of Anesthesia, Osmania Medical College, Hyderabad, Telangana State.

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Corresponding Author: Dr. Devendran P
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Abstract:

Background: Achieving an optimal surgical field in functional endoscopic sinus surgery (FESS) is crucial, as even minor bleeding can significantly impair an already limited visual perspective. Therefore, if controlled hypotension can be safely facilitated through a relatively straightforward method without compromising patient safety, it has the potential to significantly enhance the surgical field. The present study was conducted to assess the impact of oral clonidine and oral metoprolol as premedication in reducing blood loss and enhancing the surgical field during FESS.

Methods: The patients were selected form those undergoing functional Endoscopic sinus surgery (FESS) based on the inclusion and exclusion criteria. All the patients were instructed to remain nil per oral, 8 hours for solids and 2 hours for clear liquids. In group I, patients received oral Tab. clonidine 300 µg, and in group II Tab. metoprolol 50 mg orally 2 hours before induction of anesthesia with sips of water. Intraoperative PR, SBP, DBP, and SPO_2 were recorded at 0, 2, 5, 10, 15, 30, 45, and 60 minutes from the start of surgery.

Results: A total of 80 cases divided equally between two groups. Although the clonidine group exhibited a greater mean heart rate decrease than the Metoprolol group, statistical significance was only observed at 30 minutes ($p=0.08$). A significant drop in systolic and diastolic blood pressure was noted in the Clonidine group at 15 minutes compared to Metoprolol ($p < 0.05$). Differences in mean arterial pressure (MAP) were significant at 30, 45, and 60 minutes, favoring Clonidine.

Conclusion: Both clonidine and metoprolol demonstrated effectiveness and safety in establishing a stable hemodynamic profile and reducing intraoperative bleeding when administered orally as premedication to patients undergoing functional endoscopic sinus surgery. However, when comparing the two drugs, clonidine exhibited superior performance in terms of reducing blood loss and enhancing the overall quality of the surgical field compared to metoprolol.

Keywords: Functional Endoscopic sinus surgery, Clonidine, Metoprolol, Premedication, Surgical field.

Introduction

Functional endoscopic sinus surgery (FESS) represents a significant advancement in managing chronic rhinosinusitis and other sinonasal diseases. [1] Despite its benefits, certain limitations, particularly blood loss, can impede optimal visualization of intranasal anatomy during the procedure. Complications in any surgical intervention are more likely when local anatomy and vital structures have limited visibility, potentially leading to tissue damage and affecting postoperative outcomes. [2] Various factors contribute to the surgical field, including the patient's physical condition, concurrent diseases like bleeding disorders, and the pre-existing state of the vascular network. [3] Local interventions, such as the use of topical and injected vasoconstrictors, and induced hypotension, come with their own set of side effects. [4] However, achieving controlled hypotension without compromising patient safety can significantly enhance the surgical field. Numerous pharmacological and non-pharmacological techniques exist for intraoperative bleeding control.

Non-pharmacological methods for deliberate hypotension involve patient positioning and intermittent positive pressure ventilation (IPPV) to manage venous return. Pharmacological interventions include volatile anesthetics, direct-acting vasodilators, beta-blockers, ganglion-blocking drugs, alpha-blockers, combined alpha and beta-blockers, calcium channel blockers, propofol, magnesium sulfate, prostaglandins, alpha2 agonists, and tranexamic acid. [5] This study aims to compare hemodynamic changes and surgical conditions during FESS after oral premedication with clonidine or metoprolol. The goal is to assess the impact of oral clonidine and oral metoprolol as premedication in reducing blood loss and enhancing the surgical field during FESS.

Material and Methods

This cross-sectional study was done in the Department of Anesthesiology, Government ENT Hospitals, Koti, Hyderabad under Osmania General Hospital, Hyderabad. Institutional Ethical approval was obtained for the study. Written consent was obtained from all the participants of the study after explaining the nature of the study in the vernacular language.

Inclusion Criteria

1. ASA grades I and II
2. 18 to 40 years of age; both male and female
3. Who gave informed written consent
4. Patients scheduled to undergo FEES
5. Non-hypertensive

Exclusion Criteria

1. Pregnant, Lactating, and menstruating females.
2. Baseline heart rate less than 60 beats per minute.
3. Patient with a history of Hypotension and Hypertension.
4. History of Ischemic heart disease, and cardiac failure.
5. Coagulation disorder, anemia.
6. History of kidney and liver dysfunction and asthma.

All the patients were thoroughly examined on the day before surgery and on the day of surgery, the pre-operative assessment sheet was checked. The height, weight, and body mass index of the patient were measured. A detailed general and systemic examination was done. Preoperative investigations like Complete blood picture, random blood sugar, Blood grouping and typing, electrocardiogram, chest x-ray, Renal and Liver function tests, bleeding time, clotting time, blood urea, Serum creatinine, and viral markers are done for all the patients. All the patients were instructed to remain nil per oral, 8 hours for solids and 2 hours for clear liquids. In group I, patients received oral Tab. clonidine 300 µg, and in group II Tab. metoprolol 50 mg orally 2 hours before induction of anesthesia with sips of water.

Methodology: Every effort was made to standardize the anesthetic technique; general anesthesia was used in all the patients. The patients were brought to the operation theatre and standard ASA monitoring was instituted (HR, SBP, DBP, MAP, ECG) and baseline parameters were recorded. Peripheral venous access was established, and IVF was started.

Premedication: All the patients were given inj. Ondansetron 0.1 mg/kg IV, inj. Midazolam 20 µg/kg IV, inj. Fentanyl 2 µg/kg IV before induction. All the patients were pre-oxygenated with 100% oxygen for 3 minutes. Induction was done with inj. Propofol 2 mg/kg. After confirming ventilation, the patient was given an inj. atracurium 0.5 mg/kg IV and direct laryngoscopy was performed. All patients were intubated with an appropriate-size cuffed endotracheal tube. Intraoperatively anesthesia was maintained with a mixture of nitrous oxide (50%) in oxygen (50%) and sevoflurane 1% and inj. Atracurium 0.1 mg/kg + IPPV. All the patients received IVF ringer lactate solution at 10 ml/kg/hour during the first hour of anesthesia. Intraoperative PR, SBP, DBP, and SPO_2 were recorded at 0, 2, 5, 10, 15, 30, 45, and 60 minutes from the start of surgery. Intraoperatively, the surgeon assessed the Quality of the surgical field and graded it according to the average category scale (ACS) proposed by Fromm et al. [6] and Boezaart et al. [7]

At the end of the surgery, administration of the anesthetic agent was discontinued, and reversal of neuromuscular blockade was done using Inj. Glycopyrrolate (20µg/kg) IV + Inj. neostigmine (0.07mg/kg) IV. Endotracheal extubation was done after the return of adequate muscle tone, power, and protective reflex (cough) and with the normal breathing pattern of the patient. Total blood loss during surgery was calculated from the fluid volume of the suction bottle. The volume of irrigating fluid was excluded from the total volume of fluid collected in the suction bottle. A fully soaked cotton strip was estimated to contain 10 ml of blood and a partially soaked one to contain 5 ml of blood. Total Duration of surgery was recorded. Patients were observed for 2 hours for SpO_2, pulse rate, blood pressure, and adverse effects if any were recorded. During the intraoperative period and postoperative period rescue drugs for hypotension and bradycardia like inj. Atropine and vasopressors were kept ready. In our study, hypotension and bradycardia were not seen. Hypotension defined as a 30% decrease in systolic blood pressure as compared with baseline control value was noted. Bradycardia was considered when the heart rate was less than 60 beats/minute.

Results

A total of 80 cases divided equally between two groups were included in the study.

Age: The average age of patients in Group 1 was 31.03 years, while the average age of patients in Group 2 was 28.7 years. The p-value of 0.1398 indicates that there is no statistically significant difference in the average age between the two groups.

Weight: The average weight of patients in Group 1 was 59.725 kg, while the average weight of patients in Group 2 was 59.15 kg. The p-value of 0.73 indicates that there is no statistically significant difference in the average weight between the two groups.

Gender: The distribution of gender was similar between the two groups. In Group 1, 22 patients were male, and 18 patients were female. In Group 2, 25 patients were male, and 15 patients were female. The p-value of 0.46 indicates that there is no statistically significant difference in the distribution of gender between the two groups. Overall, the results suggest that the two groups of patients were well-matched in terms of age, weight, and gender.

Table 1: Distribution of different parameters in two groups of patients

Variable	Group 1	Group 2	p-value
Age in years			
Mean	31.03	28.7	0.1398
SD	7.46	6.44	
Weight in Kgs			
Mean	59.725	59.15	0.73
SD	6.990791	7.590649	
Gender			
Male	22	25	0.46
Female	18	15	

Figure 1 shows the change in heart rate at 0, 2, 5, 10, 15, 30, 45, and 60 minutes after administration of Clonidine and metoprolol in the respective groups. The Independent t-test is applied to find differences between groups. There is a higher decrease in mean heart rate in the clonidine group when compared to the Metoprolol group which is not statistically significant ($p>0.05$) except at 30 minutes where it is statistically significant between groups ($p=0.08$).

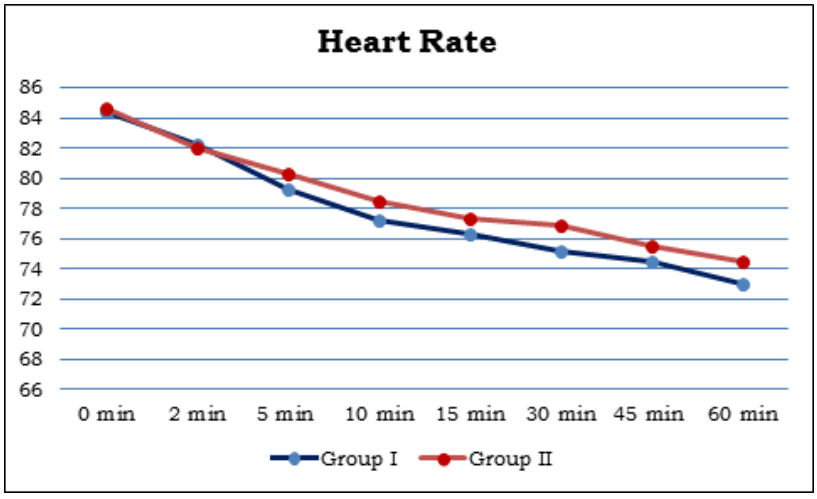

Figure 1: showing the measurement of heart rate at various intervals in both groups

Figure 2 shows the systolic blood pressure (SBP) of patients in Groups I and II at different time intervals after receiving clonidine and metoprolol, respectively.

Group I (Clonidine): The average SBP at baseline was 121.4 mmHg. After 2 minutes, the average SBP decreased to 117.8 mmHg. At 5 minutes, the average SBP further decreased to 115.7 mmHg. This trend continued, with the average SBP decreasing to 113.1 mmHg at 10 minutes, 110.3 mmHg at 15 minutes, and 109.3 mmHg at 30 minutes. The average SBP was lowest at 45 minutes (103.4 mmHg), and then it started to increase slightly, reaching 107 mmHg at 60 minutes.

Group II (Metoprolol): The average SBP at baseline was 122 mmHg. After 2 minutes, the average SBP decreased to 120 mmHg. However, the decrease in SBP was smaller than in Group I. At 5

minutes, the average SBP was 116 mmHg. At 10 minutes, the average SBP was 113 mmHg. At 15 minutes, the average SBP was 115 mmHg. At 30 minutes, the average SBP was 114 mmHg. At 45 minutes, the average SBP was 111 mmHg. At 60 minutes, the average SBP was 107 mmHg. Overall, the results suggest that both clonidine and metoprolol are effective in lowering SBP. There is a more drop in systolic blood pressure in the Clonidine group at 15 minutes when compared to the Metoprolol group which is statistically significant ($p < 0.05$). Therefore, clonidine appears to have a more rapid and pronounced effect on SBP reduction. This is likely because clonidine is a central alpha-2 agonist, while metoprolol is a beta-blocker.

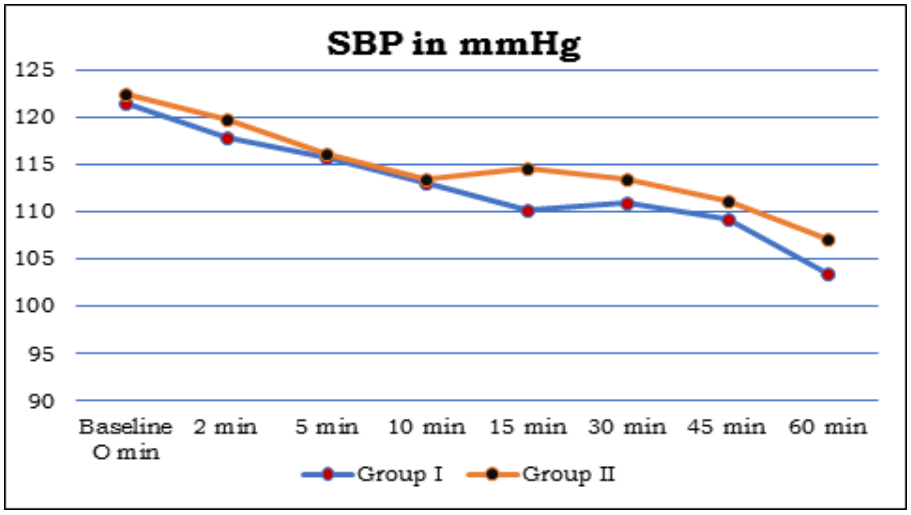

Figure 2: Showing the SBP changes in both groups at different intervals

Figure 2 shows the diastolic blood pressure (DBP) of patients in Groups I (clonidine) and II (metoprolol) at different time intervals after receiving treatment. **Group I (Clonidine):** The average DBP at baseline was 81.48 mmHg. After 2 minutes, the average DBP decreased to 77.8 mmHg. At 5 minutes, the average DBP further decreased to 75.75 mmHg. This trend continued, with the average DBP decreasing to 73.1 mmHg at 10 minutes and 70.25 mmHg at 15 minutes. At 30 minutes, the average DBP was 68.9 mmHg. At 45 minutes, the average DBP was 67.2 mmHg. At 60 minutes, the average DBP was 61.35 mmHg. **Group II (Metoprolol): t**he average DBP at baseline was 82.4 mmHg. After 2 minutes, the average DBP decreased to 79.75 mmHg. At 5 minutes, the average DBP was 76.15 mmHg. At 10 minutes, the average DBP was 73.45 mmHg. At 15 minutes, the average DBP was 74.55 mmHg. At 30 minutes, the average DBP was 71.55 mmHg. At 45 minutes, the average DBP was 69.25 mmHg. At 60 minutes, the average DBP was 65.25 mmHg.

Overall, the results suggest that both clonidine and metoprolol are effective in lowering DBP. However, clonidine appears to have a more rapid and pronounced effect on DBP reduction. This is likely due to the fact that clonidine is a central alpha-2 agonist, while metoprolol is a beta-blocker. Central alpha-2 agonists act in the brain to reduce sympathetic nerve activity, which leads to a decrease in heart rate and peripheral vascular resistance. Beta-blockers act on the heart to reduce heart rate and contractility.

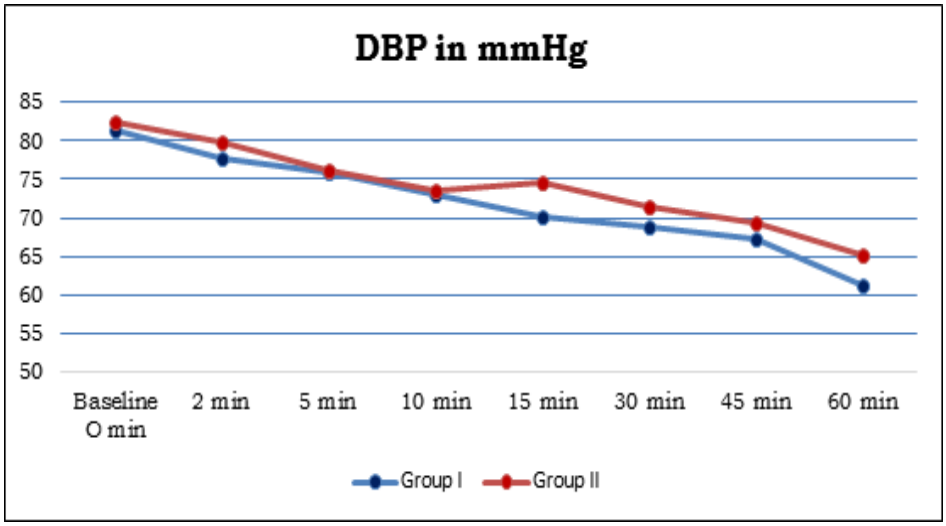

Figure 3: Showing the DBP changes in both groups at different intervals

Table 2: Showing the Mean Arterial Pressure at different intervals

MAP mmHg at minutes	Group I		Group II		P value
	Mean	SD	Mean	SD	
Baseline	94.79	4.54	95.73	3.478	0.3
2 min	91.13	4.42	93.07	4.312	0.0504
5 min	89.07	4.445	89.48	3.9	0.66
10 min	86.42	3.536	86.78	3.372	0.64
15 min	83.62	3.951	83.88	4.219	0.78
30 min	82.92	5.163	85.53	4.303	0.016*
45 min	81.22	4.283	83.23	4.568	0.046*
60 min	75.37	4.529	79.23	8.779	0.016*

* Significant

Table 2 shows the change in Mean Arterial Pressure at 0, 2, 5, 10, 15, 30, 45, and 60 minutes after administration of Clonidine and metoprolol in the respective groups. An Independent t-test is applied to find differences between groups. There is a significant difference in MAP in the clonidine group when compared to the Metoprolol group at 30, 45, and 60 minutes with MAP in the Clonidine group higher than the Metoprolol group.

Table 3: SpO_2 of the clonidine and Metoprolol group at different phases of surgery

SpO_2 at different intervals	Group I		Group II		P value
	Mean	SD	Mean	SD	
Baseline	99.27	0.751	99.1	0.841	0.33
2 min	99.40	0.496	99.35	0.483	0.65
5 min	100.0	0.000	99.98	0.158	0.32
10 min	99.98	0.158	100.0	0.000	0.32
15 min	99.98	0.158	99.95	0.221	0.56
30 min	99.98	0.158	99.95	0.221	0.56
45 min	99.98	0.158	99.95	0.221	0.56
60 min	99.95	0.221	99.98	0.158	0.56

Note: SD – Standard deviation, Group 1 – Clonidine, Group 2 – Metoprolol

Table 8 shows the change in SpO_2 at 0, 2, 5, 10, 15, 30, 45, and 60 minutes after administration of Clonidine and metoprolol in the respective groups. The Independent t-test is applied to find differences between groups. There is no statistical difference in SpO_2 between the clonidine group and the Metoprolol group. Comparison of each factor at 0, 2, 5, 10, 15, 30, 45, and 60 minutes and the change over time in two groups are compared by Multivariate analysis done using Repeated measures ANOVA. There is no significant difference in change of heart rate between groups (p=0.155). Systolic blood pressure was lower in the Clonidine group over time when compared to the Metoprolol group and the change is statistically more in the Clonidine group (p=0.021). For Mean Arterial Pressure, there is a significant difference in change of MAP over time, with the Clonidine group

showing a steady decrease in MAP when compared to the Metoprolol group (p=0.001). The change in SpO_2 among the two groups is not statistically significant (p=0.228)

Table 4: Comparison of Degree of bleeding among the two treatment groups

Treatment groups	Bleeding Groups		Total
	II	III	
Group I (Clonidine)	34	6	40
Group II (Metoprolol)	10	30	40
Total	44	36	80

There is a significant difference in the grade of bleeding and medication used. (Chi-square = 29.09 and p <0.001). For those patients who were given metoprolol the grade of bleeding is significantly higher than those patients who were given Clonidine.

Discussion

Numerous approaches have been developed to minimize bleeding during surgical procedures. The fundamental technique for mitigating bleeding from the nasal mucous membrane involves the constriction of capillaries in the targeted area. Consequently, our investigation compared the efficacy of two medications: Group I received Tab. clonidine 300 µg, and Group II received Tab. metoprolol 50 mg orally two hours before anesthesia induction. In the Clonidine group, the average age of participants was 31 years, whereas it was 28.7 years in the Metoprolol group. The mean weight of individuals in the Clonidine group was 59.7 kgs, whereas it was 59 kgs in the Metoprolol group. Additionally, 55% of participants in the Clonidine group were male, while the Metoprolol group had a male composition of 62.5%.

Our investigation revealed a greater decrease in mean heart rate in the clonidine group compared to the Metoprolol group, although this difference was not statistically significant (p>0.05), except at 30 minutes, where a statistical significance was observed between the groups (p=0.08). A more pronounced drop in systolic blood pressure was observed in the Clonidine group at 15 minutes compared to the Metoprolol group, and this difference was statistically significant ($p < 0.05$). Similarly, there was a statistically significant decrease in diastolic blood pressure in the Clonidine group at 15 minutes compared to the Metoprolol group ($p < 0.05$). Significant differences in mean arterial pressure (MAP) were noted between the Clonidine and Metoprolol groups at 30, 45, and 60 minutes, with the MAP in the Clonidine group exceeding that of the Metoprolol group. Furthermore, a notable discrepancy was found in the grade of bleeding and the type of medication used, as indicated by a Chi-square value of 29.09 and a p-value of <0.001. Patients administered metoprolol exhibited a significantly higher grade of bleeding compared to those given Clonidine.

Gohil P et al. [8] conducted a study similar and found that both clonidine and metoprolol were effective and safe when administered orally as premedication to patients undergoing functional endoscopic sinus surgery. The findings indicated a stable hemodynamic profile and a reduction in intraoperative bleeding for both drugs. However, between the two medications, clonidine demonstrated superiority in terms of reducing blood loss and providing a high-quality surgical field compared to metoprolol. Notably, the hemodynamic effects were evident, with systolic blood pressure in group A significantly lower than in group B from 30 minutes after induction until extubation (p<0.01).

In a randomized controlled trial (RCT) conducted by Puthenveettil N et al. [9] with the same drugs, a noteworthy difference was observed between groups at pre-induction, 15, 30, 45, 60, 75, and 90 minutes ($P < 0.05$), where Group B patients exhibited a statistically lower heart rate. However, there was no significant distinction between groups at 105 and 120 minutes ($P > 0.05$). When comparing mean arterial pressure (MAP) between the groups, a significant difference emerged at 30 minutes ($P = 0.01$) and 75 minutes ($P = 0.04$), with Group B patients displaying a statistically lower MAP. In contrast, our study revealed a more pronounced decrease in mean heart rate in the clonidine group compared to the Metoprolol group. However, this difference was not statistically significant ($p > 0.05$), except at 30 minutes, where a statistically significant distinction was noted between the groups ($p = 0.08$). Notably, there was a significant difference in MAP in the clonidine group compared to the Metoprolol group at 30, 45, and 60 minutes, with the MAP in the Clonidine group surpassing that of the Metoprolol group. According to J.M. Marchal et al. [10] a notable disparity was observed in the grade of bleeding and the type of medication used, as evidenced by a Chi-square value of 29.09 and a p-value of <0.001. Specifically, patients administered metoprolol exhibited a significantly higher grade of bleeding compared to those given clonidine.

In a study conducted by A. Sadek et al. [11] it was found that the metoprolol group exhibited a significantly lower mean arterial blood pressure from 30 minutes after induction until the conclusion of the surgery ($p < 0.001$). Additionally, the heart rate was also significantly lower ($p < 0.001$) in

individuals who received metoprolol, starting from before the induction of anesthesia up to the completion of the surgery. The study concluded that metoprolol significantly enhances visual clarity and maintains hemodynamic stability during functional endoscopic sinus surgery (FESS). In our current study, when comparing heart rate among groups, a significant difference was observed between groups at pre-induction, 15, 30, 45, 60, 75, and 90 minutes ($P < 0.05$). Patients in Group 1 (clonidine) exhibited a statistically lower heart rate. However, no significant difference between groups was noted at 105 and 120 minutes ($P > 0.05$). Furthermore, there was a significant difference in mean arterial pressure (MAP) in the clonidine group compared to the metoprolol group at 0, 5, 45, and 60 minutes.

In a comparable study, Sergio Menezes et al. [12] investigated the alterations in both systolic and diastolic blood pressure at 0, 2, 5, 10, 15, 30, 45, and 60 minutes following the administration of Clonidine and metoprolol in their respective groups. The Clonidine group exhibited a more substantial decrease in mean blood pressure at 15 minutes compared to the Metoprolol group, and this difference was statistically significant ($p < 0.05$). Furthermore, there was a noteworthy discrepancy in mean arterial pressure between the clonidine and metoprolol groups at 0, 5, 45, and 60 minutes.

Conclusion

In conclusion, both clonidine and metoprolol demonstrated effectiveness and safety in establishing a stable hemodynamic profile and reducing intraoperative bleeding when administered orally as premedication to patients undergoing functional endoscopic sinus surgery. However, when comparing the two drugs, clonidine exhibited superior performance in terms of reducing blood loss and enhancing the overall quality of the surgical field compared to metoprolol. Additionally, the study found that clonidine proved to be more efficacious in attenuating hemodynamic changes during surgery when compared to metoprolol.

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