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Comparison Study between Opioid Free and Opioid Based General Anesthesia in Functional Endoscopic Sinus Surgeries

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ABSTRACT

Background: Functional endoscopic sinus surgery is a standard procedure for the treatment of chronic sinusitis. This surgery is usually conducted under general anesthesia and it is better to be performed under controlled hypotensive technique to improve surgical field and to decrease the operation time. Routine analgesic treatment is usually based on non-opioid analgesics with rescue opioids. **Objective:** The aim of this study was to compare opioid free versus opioid based general anesthesia in functional endoscopic sinus surgeries regarding hypotension, surgical field, operation time and postoperative pain. **Patients and methods:** Patients were divided into 2 equal groups: Group 1: Opioid free group: (Group OFA) 22 participants, Group 2: Opioid based group: (Group OBA) 22 participants. All participants were subjected to medical history taking, complete clinical examination and premedication and routine laboratory investigations. **Results:** There was no statistical significant difference between the studied groups regarding the mean arterial pressure, oxygen saturation and need for analgesia. Duration of stay in post anesthesia care unit was significantly shorter in OFA group than OBA group. OBA Group was significantly associated with higher VAS score at 6-, 10- and 12-hours postoperatively. **Conclusion:** OFA provided satisfactory intraoperative analgesia and control of surgery-induced pressor reflexes. Also, the perioperative safety and efficacy of the opioid-free anesthesia techniques provided for functional endoscopic sinus surgeries had good postoperative analgesia and other postrecovery criteria. There is a need for wider-scale comparative studies with large number of patients with long period in multi-center studies to confirm our finding.

Keywords: Endoscopic, Opioid Based Anesthesia, Opioid Free Anesthesia, Sinus surgery.

INTRODUCTION

Endoscopic sinus surgery is the most commonly performed otolaryngological procedures. Moreover, functional endoscopic sinus surgery (FESS) could be considered the gold standard surgical treatment of chronic rhinosinusitis (CRS). This surgery is usually conducted under general anesthesia and it is better to be performed under controlled hypotensive technique where mean arterial pressure (MAP) is between 55 and 65 mmHg to improve surgical field and to decrease the operation time. Mild to moderate postoperative pain is commonly encountered with these types of surgeries owing to both nasal packing and surgical trauma itself [(1)].

Opioids are the most commonly used analgesics perioperatively and it is considered one of the main pillars of anesthesia. The use of synthetic (fentanyl and remifentanil) or natural (morphine) opioids during the perioperative period provides an important component of balanced anesthesia. Timely administered opioid during surgery is well known to reduce the dose of general anesthetic needed, enable faster recovery and provide good postoperative analgesia. Consequently, improves patients comfort and satisfaction [(2)]. However, opioids administration is not devoid of adverse effects that limit their effectiveness in perioperative care, the most relevant adverse effects include respiratory depression, gastrointestinal alterations, hyperalgesia, inflammation and immunologic modulation which raise questions about the routine systemic administration of opioids during general anesthesia and the development of recent non-opioid strategies [(3)]. Literature supporting restraint in opioid prescription practices following FESS surgery are increasing. Opioid free anesthesia (OFA) which has been applied mainly in bariatric surgery has begun to receive more attention as an alternative anesthetic strategy [(4)].

Several OFA protocols have been published. The most commonly used non-opioid agents are lidocaine, dexamethasone and magnesium sulfate. Lidocaine has demonstrated analgesic and opioid-sparing effects in cardiac and non-cardiac surgery. Additionally, the use of lidocaine has been associated with a decrease in arrhythmias and a non-constant improvement in postoperative cognitive functions. Also magnesium were shown to have analgesic effects and opioid-sparing effects, both drugs provide effective postoperative analgesia as well as a reduction in opioid consumption [(5)].

The aim of this study was to reduce complications of opioid in patients undergoing endoscopic sinus surgeries.

PATIENTS AND METHODS

This prospective randomized comparative clinical study was conducted at Zagazig University Hospitals, on 44 ASA I and II patients undergoing elective bilateral FESS during the period from January 2021 to July 2021.

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Ethical approval:

Written informed consent was obtained from all participants or their legal guardains and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (Institutional review board ZU-IRB # 6650/10-1-2021). The work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Patients from 21- 60 years, both sex, BMI <35 Kg /m^2, physical status: ASA I and II patients, elective bilateral functional endoscopic sinus surgery and duration of the operation less than 2 hours were included in this study.

Patients with history of allergic reaction to any drug used in this study, or bleeding disorders, aspirin ingestion in the preceding week before surgery. Pre-existing neurological diseases, unstable hemodynamics, pregnant patients, patient currently taking opioid for chronic pain and patients with history of nausea and/or vomiting during the 24 h before induction of anesthesia were excluded from this study.

The patients were randomly allocated into 2 equal groups by using computerized randomization table:

Group 1: Opioid free group: (Group OFA) 22 participants received IV paracetamol 15 mg/kg immediately preoperatively then IV bolus of magnesium sulfate 50 mg/kg in a total of 100 ml saline over 10 minutes followed by infusion of 10 mg/kg/hour till the end of surgery and lidocaine infusion 2 mg/kg/ hour with maximum of 200 mg/ hour starting at induction of general anesthesia until the end of the surgery.

Group 2: Opioid based group: (Group OBA) 22 participants received fentanyl (2 μg/kg) over 10 minutes before induction of anesthesia followed by continuous infusion of 1 μg/kg/hour till the end of surgery.

All participants were subjected to:

- Preoperative visit for patient selection (inclusion/exclusion criteria), medical history, complete clinical examination and premedication.
- Routine laboratory investigations including: CBC, CRP, INR, PT, PTT, LFT, RFT and ECG.
- Uniform general anesthesia.

Procedure:

In pre-anesthetic room, suitable IV line was established and heart rate (HR), blood pressure (BP) (systolic, diastolic and mean) and oxygen saturation (SpO_2) were measured and recorded as a base line parameters.

All enrolled patients were under general anesthesia after pre-oxygenation with 100% oxygen for 5 minutes. Anesthesia was induced by IV propofol 2 mg /kg and rocuronium 1 mg/kg was given to facilitate tracheal intubation. For all patients, anesthesia was maintained by volume-controlled ventilation, isoflurane 1.15% in 100% oxygen. Neuromuscular blockade was maintained with rocuronium 0.2 mg/kg IV every 30 minutes.

At the end of surgery, isoflurane discontinued and muscle relaxant was reversed by slowly IV neostigmine (0.05 mg/kg) and atropine sulphate (0.02 mg/kg) followed by extubation after taking good regular tidal volume then the patients were transferred to the post-anesthesia care unit (PACU).

Hemodynamic parameters (HR, systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP)) were measured and recorded before induction of anesthesia as a baseline, after intubation, during anesthesia at 3 minutes intervals for the first 15 minutes and once the target of heart rate and blood pressure was achieved the recording were continued at 5 minutes interval till the end of surgery.

Postoperatively, pain was evaluated by visual analogue scale (VAS) where 0=no pain and 10=severe pain at the following time points: at 30 minutes after admitted to the PACU and then every 4 hours for 12 hours. If the VAS score was more than 3, IM administration of 75 mg diclofenac sodium (Voltaren) was given. The time of first rescue analgesic requirement and the total amount of diclofenac sodium given to each patient during first 12 hours of the postoperative period was detected and recorded. Any adverse effects in the first 12 hours postoperatively were recorded and treated, including nausea and/or vomiting which was recorded and treated by ondansetron 8 mg slowly IV.

The length of stay in the post anesthesia care unit (PACU), which is defined by the time spent by the patient in PACU from the moment of PACU admission till the ward discharge decision by the anesthetist, was recorded.

Statistical analysis

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures were coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) software for analysis. According to the type of data; qualitative were represented as number and percentage and quantitative were represented by mean ± SD. Difference and association of qualitative variable was tested by Chi square test (X^2). Differences between quantitative independent groups were tested by independent t test. P value was set at <0.05 for significant results and <0.001 for high significant results.

RESULTS

Table (1) shows that there was no significant differences between the 2 groups regarding patients' demographic and clinical characteristics (Age, sex, BMI, and ASA status) as well as the duration of surgery did not differ significantly between the 2 groups.

Table (1): Comparison between the studied groups regarding patients' demographic and clinical characteristics

Parameter	Opioid free anesthesia Group (N=22)	Opioid based anesthesia Group (N=22)	P
Age (year)	44.59±9.73	42.40±10.61	0.481
Sex			
Male n (%)	12 (54.5%)	14 (63.6%)	0.54
Female n (%)	10 (45.5%)	8 (36.4%)	
BMI (kg/m^2)	27.29±2.33	26.84±2.25	0.515
ASA status			
ASA I N (%)	17 (77.3%)	16 (72.7%)	0.728
ASA II N (%)	5 (22.7%)	6 (27.3%)	
Duration of surgery (minute)	81.36±12.45	84.09±11.71	0.459

N = Total number of patients in each group, BMI = Body mass index, ASA = American Society of Anesthesiologists Data were expressed as mean ± SD or number (percentage).

Figure (1) shows that there was no statistical significant difference between the studied groups regarding the baseline heart rate (before induction of anesthesia) while, the intra- and postoperative heart rate mean values were statistically significantly lower in the OFA group.

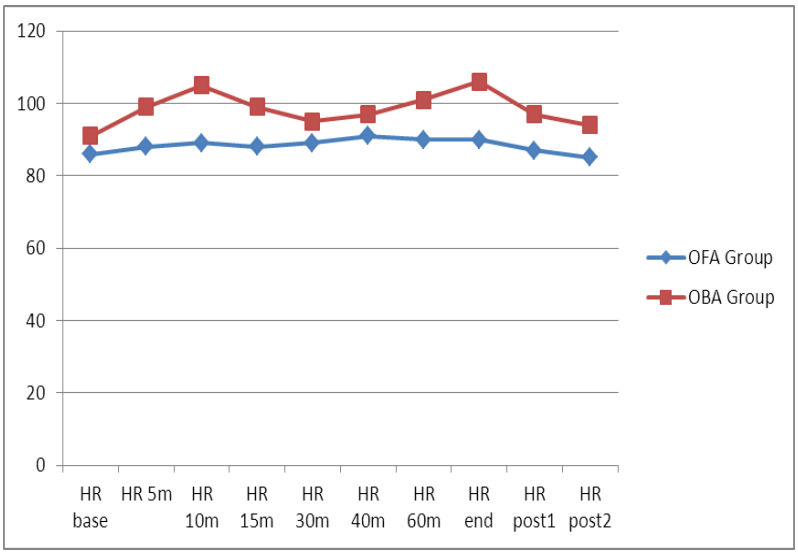

Fig. (1): Comparison between the studied groups regarding heart rate at different times pre-, intra- and postoperatively

Figure (2) shows that there was no significant difference between the studied groups regarding the mean arterial pressure except at 60 minute and 2 hours postoperatively as OFA group was significantly higher.

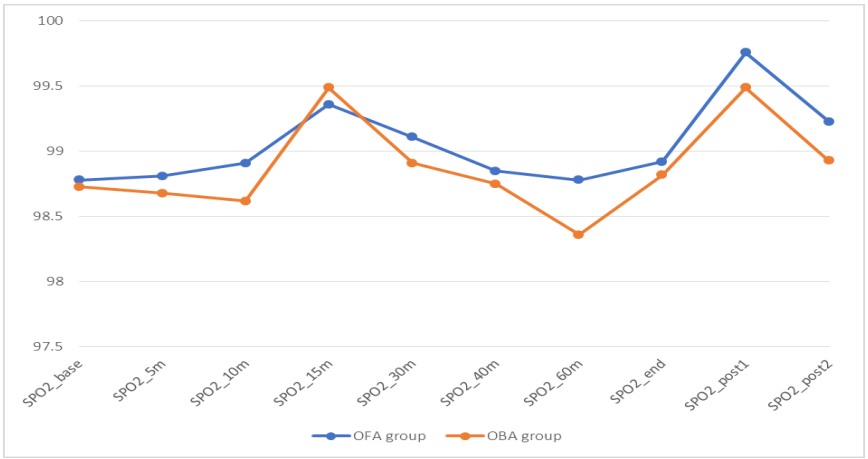

Fig. (2): Comparison between the studied groups regarding mean arterial blood pressure at different times pre-, intra- and postoperatively

Figure (3) shows that there was no statistical significant difference between the studied groups regarding the oxygen saturation at different times either pre-, intra- or postoperatively.

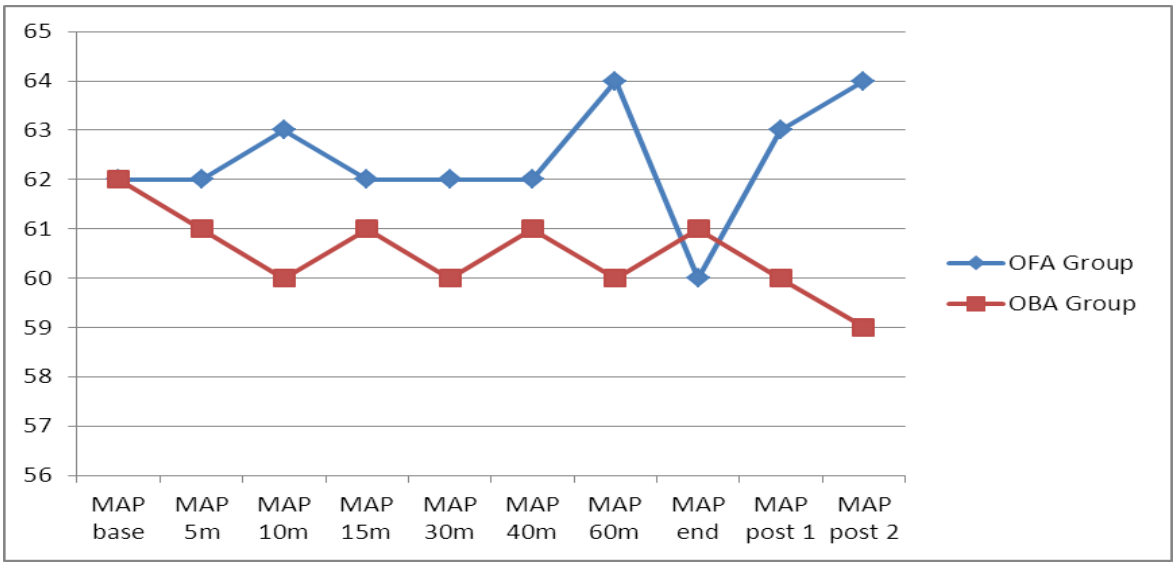

Fig. (3): SpO_2 distribution at different times between groups

Table (2) shows that there was significant difference between the studied groups regarding Boezaart scale. Larger percentage of patients within opioid based anesthesia group had scale II, III and IV.

Table (2): Comparison between the studied groups regarding Boexzaart scale

Parameter			Group		P
			Opioid free anesthesia Group(N=22)	Opioid based anesthesia Group (N=22)	
Boezaart scale	**ZERO**	N	9	1	**<0.001****
		%	40.9%	4.5%	
	I	N	9	2	
		%	40.9%	9.1%	
	II	N	4	6	
		%	18.2%	27.3%	
	III	N	0	8	
		%	0.0%	36.4%	
	IV	N	0	5	
		%	0.0%	22.7%	

**: Statistically highly significant

Table (3) shows that the duration of stay in post anesthesia care unit (PACU) was significantly shorter among OFA group than OBA group. There was no significant difference between the studied groups regarding postoperative nausea and vomiting and need for analgesia.

Table (3): Comparison between the studied groups regarding post-duration of anesthesia care unit, complications and need for analgesia

		Opioid free anesthesia Group (N=22)	Opioid based anesthesia Group (N=22)		P
PACU (minutes)		76.59±16.57	157.72±27.76		<0.001**
Complications: Absent Nausea and vomiting		21 (95.4) 1 (4.6)	20 (90.9) 2 (9.1)		0.999
Analgesia need	**No**	N	0	0	1
		%	0.0%	0.0%	
	Yes	N	22	22	
		%	100.0%	100.0%	

PACU: Post-Anesthesia Care Unit

Figure (4) shows that OBA group was significantly associated with higher VAS score at 6, 10- and 12-hours postoperatively.

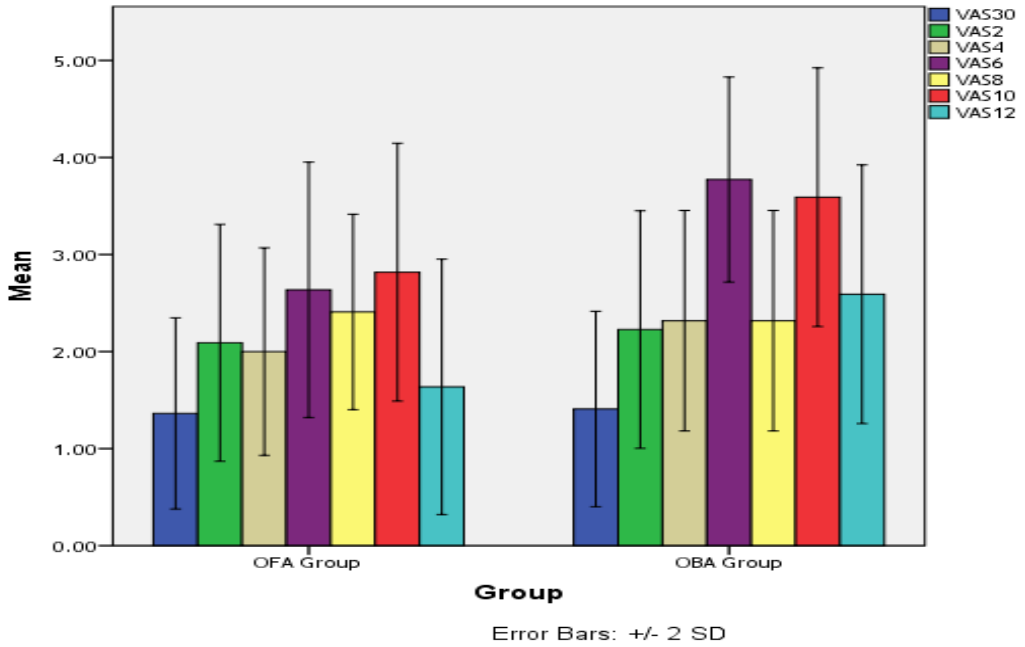

Fig. (4): Comparison between the studied groups regarding VAS score over time (OFA: Opioid free anesthesia group, OBA: Opioid based group anesthesia, VAS: visual analogue score).

DISCUSSION

The intraoperative administration of opioids was considered the cornerstone of anesthesia. Synthetic opioids were given to stabilize the hemodynamics during anesthesia. They can inhibit the sympathetic nervous system without causing cardiovascular depression and histamine release. Despite their benefits, opioids are experiencing more and more adverse side effects, which can cause significant morbidity and mortality, as respiratory depression, nausea/vomiting, constipation, tolerance and hyperalgesia [6].

Opioid-free multimodal anesthesia has become an alternative to postoperative pain relief. The use of multimodal non-opioid analgesics during the perioperative period can preventively block receptors in complex pain pathways. It has been shown that preoperative use of Cox inhibitors, GABA agonist and paracetamol can reduce postoperative opioid consumption. Sodium channel block, G protein–related receptor block, N-methyl-D-aspartate (NMDA) receptor antagonist, central alpha-2 agonist and nonsteroidal anti-inflammatory drugs may lead to opioid-free anesthesia (OFA). Thoracic paravertebral block (TPVB) combined with general anesthesia (GA) can provide excellent analgesia and reduce the severity of chronic pain after mastectomy [7].

The current study showed that there were no significant differences between the 2 groups regarding patients' demographic and clinical characteristics (Age, sex, BMI, and ASA status) as well as the duration of surgery did not differ significantly between the 2 groups. This is in agreement with the study of **Aboalsoud *et al.* [6],** who found that there was no significant differences between OFA and OBA groups regarding the demographic data and patient characteristics (age, weight, height, BMI, and Operative time). **Gousheh *et al.* [8],** reported that there was no statistically significant difference between the 2 groups in terms of age, gender distribution, body mass index (BMI), and duration of surgery. **Abdelrahman and Algharabawy [9]** reported that the patients' characteristics and surgical history of the participants showed a non-significant difference between OFA and OBA groups. **Hakim *et al.*, [10]** found that there was no significant differences between the two study groups (OBA and OFA groups) as regards age, weight, height, ASA physical status.

The current study showed that there was statistically non-significant difference between the studied groups regarding the baseline heart rate (before induction of anesthesia) while, the intra- and postoperative heart rate mean values were statistically significantly lower in the OFA group **Aboalsoud *et al.* [6],** found no significant differences in the intraoperative HR, MABP and SpO_2 between OFA and OBA; however, there was significant decrease in HR, MABP and increase in SpO_2 postoperatively in the OFA group. **Abdelrahman and Algharabawy [9]** reported that the postoperative heart rate recorded immediately post-extubation and at the first 2 hours postoperatively was significantly higher in OBA group (B) than OFA group (A) with P values 0.001, 0.001 and 0.001 respectively. While heart rate showed non-significant statistical differences at the 3rd, 4th, 5th and 6th postoperative hours. **Hakim *et al.* [10]** found that

regarding the changes in the mean arterial blood pressure and HR, they were significantly lower on OFA group.

The current study showed that there was no statistically significant difference between the studied groups regarding the mean arterial pressure except at 60 minute and 2 hours postoperatively as OFA group was significantly higher. **Abdelrahman and Algharabawy [9]** reported that the MAP showed significantly higher values in OBA group (B) than OFA group (A) immediately postextubation and at the first 2 hours postoperatively. While MAP showed non-significant statistical differences at the 3rd, 4th, 5th and 6th postoperative hours. **Ibrahim *et al.* [11]** reported that changes in MAP were significantly lower in the OFA group (13.7% versus 50%) in the OBA group), p value=0.001. In the OBA group, 16 (30.7%) patients required rescue fentanyl for a MAP elevation with a mean dose of 11.83±20.79 μg while 10 patients needed ephedrine for a drop in MAP. Only seven patients (13.7%) in the OFA group required ephedrine for a drop in the MAP.

The current study showed that there was statistically non-significant difference between the studied groups regarding the oxygen saturation at different times either pre-, intra- or postoperatively. **Abdelrahman and Algharabawy [9]** reported that the hemoglobin oxygen saturation (SpO_2) showed statistically significant lower values in the OBA group (B) than the OFA group (A) after 20 minutes, 30 minutes post-extubation and at the first and second hours postoperatively with P values 0.001, 0.001, 0.001 and 0.009 respectively. However, there was no significant differences found between both groups immediately post-extubation, 10 minutes post-extubation, third, fourth, fifth and sixth postoperative hours regarding SpO_2.

The current study showed that duration of stay in post anesthesia care unit (PACU) was significantly shorter among OFA group than OBA group. Two patients within opioid based anesthesia group versus one patient within opioid free anesthesia group had postoperative nausea and vomiting yet with statistically non-significant difference. There was non-significant difference between the studied groups regarding need for analgesia. **Hakim *et al.* [10]** found that the incidence of nausea and vomiting was statistically significant in the OBA group, whereas shivering and bradycardia showed no significant difference between the studied groups (OFA group than OBA group). **Abdelrahman and Algharabawy [9]** reported that although the number of patients required rescue analgesia during the estimated time was statistically nonsignificant (12 (80%) vs 15 (100%), but the time passed till first rescue analgesia requested was significantly longer in OFA group A than OBA group B (165.8 ± 126.6 minutes vs 23.0 ± 12.2 minutes respectively) with P value 0.001 and the total dose of rescue analgesia given to the patients were significantly higher in group B than group A with P value 0.001 during the first 6 postoperative hours. The PACU discharge readiness time (modified Aldrete score ≥ 9) was statistically longer in OFA group (A) than OBA group (B) (20.60 ± 4.64 minutes vs 14.42 ± 3.91 minutes, respectively). The duration of ICU stay was significantly shorter in OFA group A than OBA group B (2.27 ± 0.59 days and 3.40 ± 1.18 days). **Gousheh *et al.* [8],** reported that no significant difference was observed between the 2 groups in the rate of nausea after FESS surgery. Vomiting was not observed in the patients in the studied groups.

The current study showed that OBA group was significantly associated with higher VAS score at 6-, 10- and 12-hours postoperatively. **Abdelrahman and Algharabawy [9]** found that the postoperative VAS was significantly lower in OFA group (A) than OBA group (B) in the measured time points (immediate postextubation, 30 minutes, 2 and 4 hours postoperative) with P values 0.001, 0.001, 0.0012 and 0.0065 respectively, but at 6 hours postoperative there was no statistical difference between both groups. **Aboalsoud *et al.* [6],** found significant decrease in VAS at rest and on arm movement at all times in the OFA group. Patients in the OFA group were more satisfied than those in the OBA group (P < 0.001).

CONCLUSION

OFA provided satisfactory intraoperative analgesia and control of surgery-induced pressor reflexes. Also, the perioperative safety and efficacy of the opioid-free anesthesia techniques provided for functional endoscopic sinus surgeries had good postoperative analgesia and other postrecovery criteria. There is a need for wider-scale comparative studies with large number of patients with long period in multi-center studies to confirm our finding.

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