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OUTCOMES OF NON OPIOID VERSUS OPIOID BASED GENERAL ANESTHESIA IN ENDOSCOPIC SINUS SURGERIES

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ABSTRACT

Background : Functional endoscopic sinus surgery is a standard procedure for the treatment of chronic sinusitis. This procedure is associated with mild to moderate postoperative pain, which is related to both surgical and nasal packing . Routine analgesic treatment is usually based on non-opioid analgesics with rescue opioids. However, there is no consensus concerning the optimal analgesic regimen after endoscopic nasal surgery and an opioid-oriented treatment is still often used. So the aim of this study was to compare Opioid Free versus Opioid Based General Anesthesia outcomes in Functional Endoscopic Sinus Surgeries.

Patients and methods: Patients were divided into 2 equal groups :

Group 1: Opioid free group: (Group OFA) 22 participants received , **Group 2:** Opioid based group: (Group OBA) 22 participants. All participants were subjected to medical history, 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 post-operative.

Conclusion :

Of a 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 with good postoperative analgesia and other postrecovery criteria.

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

INTRODUCTION

Functional endoscopic sinus surgery (FESS) is a highly sophisticated type of surgery, which has revolutionized the surgical management of acute and chronic sinus pathologies when conservative management has failed. During FESS under general anesthesia (GA), bleeding impairs the visibility of surgical field and increases the operation risk and time. Intraoperative bleeding may be reduced most effectively by induced systemic hypotension. There are several important advantages of using intentional hypotensive anesthetic technique during the functional endoscopic sinus surgeries such as reduction in blood loss hence reduction in blood transfusion rate, improvement in the surgical field, and reduction of the duration of surgery. In hypotensive anesthesia, the patient's baseline mean arterial pressure (MAP) is reduced by 30% or MAP was kept at 60-70 mm Hg [(1)].

Opioids are the most commonly used analgesics peri-operatively and it is considered one of the main pillars of anesthesia. The use of synthetic (fentanyl and remifentanil) or natural (morphine) opioids during the peri-operative 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 post-operative analgesia. Consequently, improves patients comfort and satisfaction **[(2)].**

However, opioids administration is not devoid of adverse effects that limit their effectiveness in peri-operative care, the most relevant adverse effects include respiratory depression, gastrointestinal alterations, hyper algesia, 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)].

With the increasing literature supporting restraint in opioid prescription practices following FESS surgery. 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

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cardiac and non-cardiac surgery. Additionally, the use of lidocaine has been associated with a decrease in arrhythmias and a non-constant improvement in post-operative cognitive functions. Also magnesium were shown to have analgesic effects and opioid-sparing effects, both drugs provide effective post-operative analgesia as well as a reduction in opioid consumption [(5)].

So, 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&II patients undergoing elective bilateral FESS during the period from February 2021 to August 2021.

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

Inclusion criteria: Age from 21- 60 yrs, 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 is less than 2 hours

Exclusion criteria: 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 the24 h before induction of anesthesia.

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 15mg/kg immediately preoperative then IV bolus of magnesium sulfate 50 mg/kg in a total of 100ml saline over 10 min followed by infusion of 10 mg/kg/h till the end of surgery and lidocaine infusion 2 mg/kg/h with maximum of 200 mg/h 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 1µg / kg/ hr till the end of surgery.

All participants were subjected to:

- Pre-operative 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, establishing suitable IV line and routine monitoring of 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 5min. Anesthesia was induced by IV Propofol 2mg /kg and Rocuronium 1mg / 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 0.2mg/kg IV every 30 min.

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

Post-operatively, 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 more than 3, IM administration of 75mg diclofenac sodium was given. The time of first rescue analgesic requirement and the total amount of diclofenac sodium given to each patient during first 12 h of the post-operative period was detected and recorded.

Any adverse effects in the first 12 h post-operatively were recorded and treated, including nausea and/or vomiting which recorded and treated by Ondansetron 8mg 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.

Statistical analysis

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) **(**Statistical Package for the Social Sciences) software for analysis.

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According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean ± SD, the following tests were used to test differences for significance; .difference and association of qualitative variable by Chi square test (X^2). Differences between quantitative independent groups by t test. P value was set at <0.05 for significant results and <0.001 for high significant result.

RESULTS

This prospective randomized comparative study was carried out on 44 adult ASA I and II patients of both sex requiring elective FESS and they were admitted to Zagazig University Hospitals during the period from February 2021 to August 2021. Patients were randomly allocated into 2 equal groups (OBA and OFA 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/m²)	27.29±2.33	26.84±2.25	0.515¥
ASA status			
ASA I N (%)	17 (77.3%)	16 (72.7%)	0.72∞
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; number (percentage). ∞ p for Chi square test ¥P for independent sample t test P > 0.05 is significant.

Table (1) showed 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 (2): Comparison between the studied groups regarding heart rate at different times pre, intra and postoperatively:

Variables	Opioid free anesthesia Group (N=22)	Opioid based anesthesia Group (N=22)	P¥
HR base	86.04±8.43	91.09±10.86	0.093
HR 5m	88.13±6.31	99.36±10.14	**<0.001****
HR 10m	89.31±6.03	105.0±10.23	**<0.001****
HR 15m	88.04±6.98	99.40±12.74	0.001**
HR 30m	89.77±7.78	95.90±10.19	0.030*
HR 40m	91.13±8.0	97.66±9.85	0.012*
HR 60m	90.45±8.08	101.40±10.96	**<0.001****
HR end	90.90±8.54	106.13±11.01	**<0.001****
HR post1	87.04±9.21	97.27±11.20	0.002*
HR post2	85.36±7.36	94.50±11.92	0.004*

HR: Heart Rate m: minute post1: the first hour postoperatively Post2: two hours postoperatively

Table (2) showed 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 significant lower in the OFA group.

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Table (3): Comparison between the studied groups regarding mean arterial blood pressure at different times pre, intra and postoperatively

Parameter	Opioid free anesthesia Group (N=22)	Opioid based anesthesia Group (N=22)	P¥
MAP base	62.54±5.0	62.04±4.72	0.735
MAP 5m	62.27±4.35	61.63±4.11	0.621
MAP 10m	63.13±4.83	60.90±3.74	0.095
MAP 15m	62.54±5.55	61.04±4.09	0.314
MAP 30m	62.63±5.26	60.45±3.48	0.112
MAP 40m	62.63±4.95	61.45±4.04	0.391
MAP 60m	64.68±5.89	60.81±3.83	0.014*
MAP end	60.50±4.13	61.04±4.09	0.663
MAP post1	63.45±6.23	60.45±3.48	0.055
MAPpost2	64.18±7.08	59.95±4.85	0.026*

post1: the first hour postoperatively Post2: two hours postoperatively M: minute.

Table (3) showed 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.

Table (4) 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/ M	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	**>0.999¥**
		%	0.0%	0.0%	
	Yes (75 mg)	N	22	22	
		%	100.0%	100.0%	

PACU: Post-Anesthesia Care Unit

Table (4) showed that the 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 no significant difference between the studied groups regarding need for analgesia. All patients needed analgesia within each group received diclofenac sodium (voltarine) 75 mg IM.

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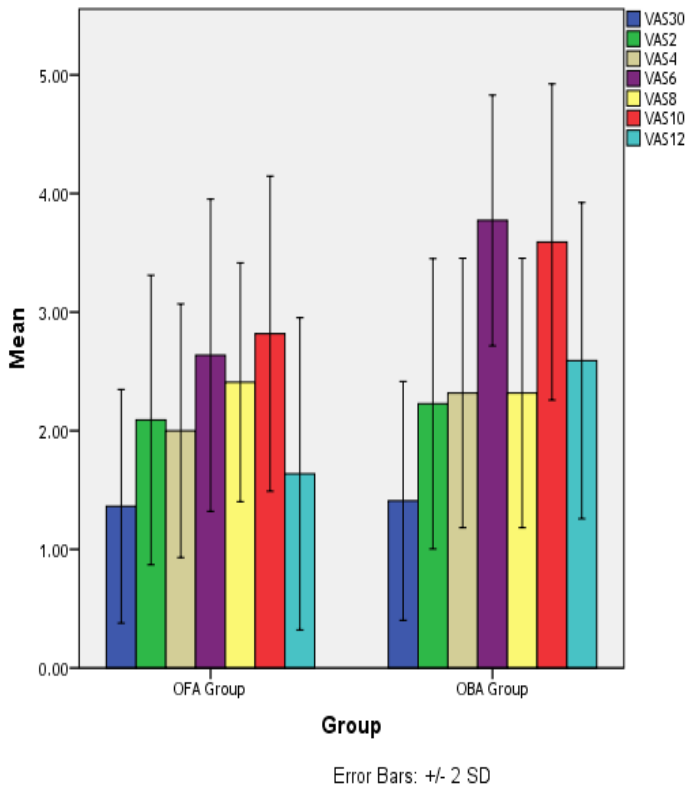

Figure (1): Comparison between the studied groups regarding VAS score over time (OFA: Opioid free anesthesia group, OBA: opioid free group anesthesia, VAS: visual analogue score, m: minute).

Figure (1) showed that OBA Group was significantly associated with higher VAS score at 6-, 10- and 12-hours post-operative.

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, 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)].

This prospective randomized comparative study was carried out on 44 adult ASA I and II patients of both sex requiring elective FESS and they were admitted to Zagazig University Hospitals during the period from February 2021 to August 2021. Patients were randomly allocated into 2 equal groups (OBA and OFA groups).

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. Which 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 ($P > 0.05$)

Abdelrahman & 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 significant lower in the OFA group.

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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 & 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 h postoperatively. While MAP showed non-significant statistical differences at the 3rd, 4th, 5th and 6th postoperative hours.

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 anesthesia. All patients needed analgesia within each group received diclofenac sodium (voltarine) 75 mg IM.

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)

The current study showed that OBA Group was significantly associated with higher VAS score at 6-, 10- and 12-hours post-operative.

Abdelrahman & 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 min, 2 and 4 h postoperative) with P values 0.001, 0.001, 0.0012 and 0.0065 respectively, but at 6 h postoperative there was no statistical difference between both groups as P value was 0.45.

Conclusion: OFA provided satisfactory intraoperative analgesia and control of surgery-induced pressor reflexes. Also, the perioperative safety and efficacy of the opioid-free anaesthesia techniques provided for Functional Endoscopic Sinus Surgeries with good postoperative analgesia and other postrecovery criteri

Recommendation : there is a need for wider-scale comparative studies with large number of patients with long period of follow up in multi-center studies to confirm our finding.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request

Conflicting Interest (If present, give more details): No Conflict of Interest

No financial disclosure

-Acknowledgements

Not applicable

Declarations

-Ethics approval and consent to participate

Written informed consent was obtained from all patients and the study was approved by the research ethical committee of Faculty of Medicine, Zagazig University (International review board **ZU-IRB #6650/10-1-2021**). The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

-Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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