Original Article

Quality of recovery (QoR-15) following opioid-free versus opioid anaesthesia for elective endoscopic nasal surgeries: A randomised, open-label comparative trial

Yashika Pandey, Manisha Sapate, Harsha H. Narkhede, Poonam Mane
Department of Anaesthesia, PCMC's PGI and YCM Hospital, Pimpri, Pune, Maharashtra, India

Address for correspondence:
Dr. Harsha H. Narkhede, Department of Anaesthesia, PCMC's PGI and YCM Hospital, Pimpri, Pune – 411 018, Maharashtra, India.
E-mail: hhnarkhede@gmail.com

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ABSTRACT

Background and Aims: Newer modalities like opioid-free analgesia overcome the opioid-related side effect profile and are equally efficacious. This study aims to compare the clinical outcomes between opioid-free anaesthesia (OFA) and opioid-based anaesthesia (OA) in elective nasal endoscopic surgeries. **Methods:** A randomised, open-label trial was conducted to evaluate the quality of recovery (QoR). The study included 64 patients with American Society of Anesthesiologists physical status I and II, of either gender, aged between 18 and 60 years, scheduled for elective endoscopic nasal surgery at a tertiary care centre. The patients were randomised into two groups: Group OA (patients receiving opioid anaesthesia) and Group OFA (patients receiving opioid-free anaesthesia). The primary outcome was the effects of OFA versus OA on the QoR-15 in patients undergoing endoscopic nasal surgeries under general anaesthesia. Secondary outcomes included intraoperative haemodynamics, respiratory depression, nausea/vomiting, pruritus, postoperative analgesia, and length of stay in the post-anaesthesia care unit. An independent sample *t*-test and Chi-squared test were employed for between-group comparisons. **Results:** Patients undergoing OFA showed higher postoperative QoR-15 scores compared to the opioid group. Intraoperatively, the OFA group demonstrated a better haemodynamic profile at 15, 30, 60, 90, and 120 min, with lower mean arterial pressure values compared to the opioid group. Notably, the OFA group experienced reduced nausea/vomiting and pruritus. Postoperative analgesia requirements and length of stay in recovery were also lower in the OFA group. **Conclusion:** OFA in elective nasal endoscopic surgeries results in higher QoR-15 scores, better postoperative analgesia and fewer adverse effects associated with opioids.

Keywords: Analgesia, endoscopic nasal surgery, haemodynamics, opioids, opioid-free anaesthesia, postoperative analgesia, quality of recovery

INTRODUCTION

Opioid analgesic drugs have long been the most commonly used perioperative analgesics.[1] Their efficacy in providing analgesia has made them indispensable in surgical procedures, where they suppress the sympathetic response and offer effective pain relief.[2]

High doses of opioids used in ambulatory surgery can lead to several adverse effects, reducing their perioperative effectiveness. The most notable complications include respiratory depression, gastrointestinal disturbances, increased pain sensitivity (hyperalgesia), altered inflammatory response and immune system modulation.[3] These

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complications can extend recovery time and contribute to the development of acute tolerance, leading to a growing interest in opioid-free anaesthesia (OFA).[4] OFA combines non-opioid analgesics, regional anaesthesia techniques and adjunct medications to ensure effective pain management while reducing opioid-related risks. Several studies suggest that OFA enhances perioperative outcomes by improving haemodynamic stability, reducing postoperative nausea and vomiting (PONV) and shortening hospital stays.[5] However, limited research compares OFA and opioid-based anaesthesia (OA) in elective endoscopic nasal surgeries, particularly concerning the 15-item quality of recovery (QoR-15) questionnaire, a validated patient-centred measure of postoperative well-being.

This study aimed to compare QoR-15 scores between OFA and OA in patients undergoing elective nasal endoscopic surgeries. The primary objective of the study was to assess the effects of OFA versus OA on the QoR-15 in patients undergoing endoscopic nasal surgeries under general anaesthesia. The secondary objectives were to compare intraoperative haemodynamics, postoperative complications (respiratory depression, nausea, vomiting and pruritus), functional activity and sedation level, postoperative analgesic requirement over 24 h and length of stay in postoperative recovery unit. We hypothesised that patients receiving OFA would have significantly higher QoR-15 scores, indicating better recovery. In addition, OFA was expected to provide superior intraoperative haemodynamic stability, lower PONV incidence, reduced analgesia requirements and shorter recovery room stays compared to OA.

METHODS

This was a randomised, open-label trial conducted from August 2023 to July 2024, following approval from the Institutional Ethics Committee of the Postgraduate Institute, YCM Hospital, Pimpri (vide approval number ECR/1236/Inst/MH/2019, dated June 6, 2023). The study was registered with the Clinical Trials Registry-India (CTRI/2023/07/055387, accessible at https://ctri.nic.in/Clinicaltrials/advsearch.php). Written informed consent was obtained from all participants for both study participation and the use of their data for research and educational purposes. The study adhered to the ethical principles outlined in the World Medical Association Declaration of Helsinki (2013) and followed the Good Clinical Practice guidelines in medical research involving human subjects.

The eligibility criteria included 70 patients with American Society of Anesthesiologists physical status I and II, of either gender, aged between 18 and 60 years, scheduled for elective endoscopic nasal surgeries under general anaesthesia. Patients with known hypersensitivity to local anaesthetics, alcohol or drug abuse, clinically significant neurological, psychiatric, cardiovascular, renal or hepatic diseases, and those who received opioid analgesic medication within 24 h before surgery were excluded from the study. The primary outcome was to compare the quality of postoperative recovery, as measured by the QoR-15 score, between the OFA and OA groups in patients undergoing elective endoscopic nasal surgeries under general anaesthesia. Secondary outcomes included comparing intraoperative haemodynamic parameters, side effects like respiratory depression, nausea, vomiting and pruritus, functional activity, sedation level, postoperative analgesia time, total dose consumed in 24 h and length of stay in the post-anaesthesia care unit.

Written informed consent was obtained from all eligible patients before their participation. A pre-validated QoR-15 questionnaire was used to evaluate the postoperative quality of recovery, and patients were asked to complete the questionnaire in the pre-anaesthetic area on the day of surgery. The QoR-15 scale, developed and validated by Stark PA *et al.* at Alfred Hospital and Monash University, is a reliable and psychometrically tested tool for assessing postoperative recovery.[6] All patients were preloaded with 10–15 mL/kg of Ringer's lactate solution and premedicated with 0.004 mg/kg glycopyrrolate, 0.1 mg/kg ondansetron, and 0.03 mg midazolam intravenously (IV) for each group.

Patients were randomised into two groups using simple random sampling for further premedication 10 min before anaesthesia induction. In Group OA (opioid analgesia), patients were premedicated with IV fentanyl 1 μg/kg and dexamethasone 8 mg, followed by maintenance with a continuous IV infusion of fentanyl at 0.2–0.7 μg/kg/h, which was discontinued 10 min before the end of surgery. Group OFA patients received a multimodal premedication regimen, including IV lignocaine (preservative free) 1.5 mg/kg, paracetamol 15 mg/kg, dexamethasone 8 mg, magnesium sulphate 20 mg/kg and dexmedetomidine 1 μg/kg, administered over 10 minutes. Maintenance in the OFA group was achieved using a IV infusion of dexmedetomidine at 0.2–0.7 μg/kg/h, which was stopped 10 min before the end of surgery.

Following premedication, anaesthesia induction was carried out using IV propofol 2 mg/kg, and tracheal intubation was facilitated with IV succinylcholine 1.5 mg/kg. Anaesthesia was maintained with a combination of oxygen, nitrous oxide and sevoflurane, along with intermittent doses of atracurium as a muscle relaxant. The surgical procedure lasted between 60 and 120 min. Throughout the surgery, vital parameters, including haemodynamics, peripheral capillary oxygen saturation (SpO_2), and end-tidal carbon dioxide, were closely monitored. Any intraoperative complications, including bradycardia, hypotension or arrhythmias, were identified and managed accordingly. At the conclusion of the procedure, the anaesthetic agents were discontinued, and residual neuromuscular blockade was reversed using IV neostigmine 0.05 mg/kg and glycopyrrolate 0.008 mg/kg. Patients were then allowed to regain spontaneous breathing before tracheal extubation.

Following their transfer to the recovery room, patients were checked for pain using an 11-point Numeric Rating Scale (NRS) of 0–10], where 0 represented 'no pain' and 10 represented 'severe pain'. If the patient's NRS score was greater than 4, a rescue dosage of IV paracetamol 1 g was administered, ensuring a minimum interval of 4 h after surgery for patients in the OFA group who had received paracetamol intraoperatively. The duration until the first rescue analgesia and the total number of analgesic doses were noted according to Chhabra *et al.*'s[7] study. Postoperative adverse effects such as metallic taste, nausea, vomiting, dizziness, hypotension, visual disturbances and convulsion-like movements were documented. An investigator evaluated functional recovery using the QoR-15 questionnaire at 24 h post-surgery. This validated tool consists of 15 items, each scored on an 11-point numerical scale, with total scores ranging from 15 to 150. Functional activity scores were assessed based on the degree of pain-related limitation, with A indicating unlimited activity, B representing mild to moderate activity limitation due to pain and C denoting severe activity limitation caused by pain. Sedation levels were evaluated using a numerical scale, where 0 indicated the patient was awake, 1 corresponded to mild sedation (easily rousable), 2 represented moderate sedation (rousable but unable to keep eyes open for more than 10 sec) and 3 signified severe sedation (difficult or unable to rouse).

MedCalc Statistical Software version 19.2.6 (MedCalc Software bv, Ostend, Belgium) was used for calculating the sample size. To achieve 80% power with a type 1 error of 0.05, 32 patients per group were required. The calculation was based on the formula: $n = \{(Z_{\alpha/2} + Z_{\beta})/d\}^2 \times 2\sigma^2$, where $Z_{\alpha/2} = 1.96$, $Z_{\beta} = 0.84$, $\sigma^2 = 222.01$ and $d = 10.44$, derived from a reference article.[7] Considering a 10% non-response and dropout rate, the final sample size was 35 per group.

Statistical analysis was done using the Statistical Package for Social Sciences for Windows, version 26.0 (International Business Machines, Armonk, NY, USA). The data was presented using descriptive statistics and frequency distribution. The normality of data was tested using the Kolmogorov–Smirnov test, and data was found to be normally distributed; hence, further analysis was done using parametric tests of significance. Within-group comparisons at various durations were performed using repeated measures analysis of variance for QoR-15 scores, NRS pain scores and sedation levels. Between-group comparisons were conducted using an independent sample *t*-test for age, operative time, preoperative and postoperative QoR-15 scores, NRS pain scores, time until postoperative mobilisation, ICU stay duration and rescue analgesia time. The Chi-squared test was employed to analyse the differences in proportions of respiratory depression, nausea and vomiting, pruritus and sedation levels between the two groups. A significance level of 5% was set, with *P* values below 0.05 considered statistically significant.

RESULTS

Seventy patients were screened, and 64 were recruited for the study [Figure 1]. The age distribution between the two groups did not show any statistically significant difference ($P = 0.179$). The operative time also showed no significant variance ($P = 0.664$). Preoperative QoR-15 scores demonstrated no significant difference ($P = 0.079$) [Table 1]. However, postoperative QoR-15 scores were significantly lower in Group OA than in Group OFA ($P = 0.001$) [Table 2]. No significant difference was found in SpO_2 between the two groups at any time interval. NRS scores were significantly higher in Group OA ($P = 0.047$). Heart rate differences between the OA and OFA groups were most notable at 30 min (*t*-stat = 3.03, $P = 0.000$), 90 min ($t = -2.62$, $P = 0.010$) and 120 min ($t = -2.97$, $P < 0.001$), with Group OA showing significantly lower values at these time points compared to Group OFA. There were statistically significant differences between

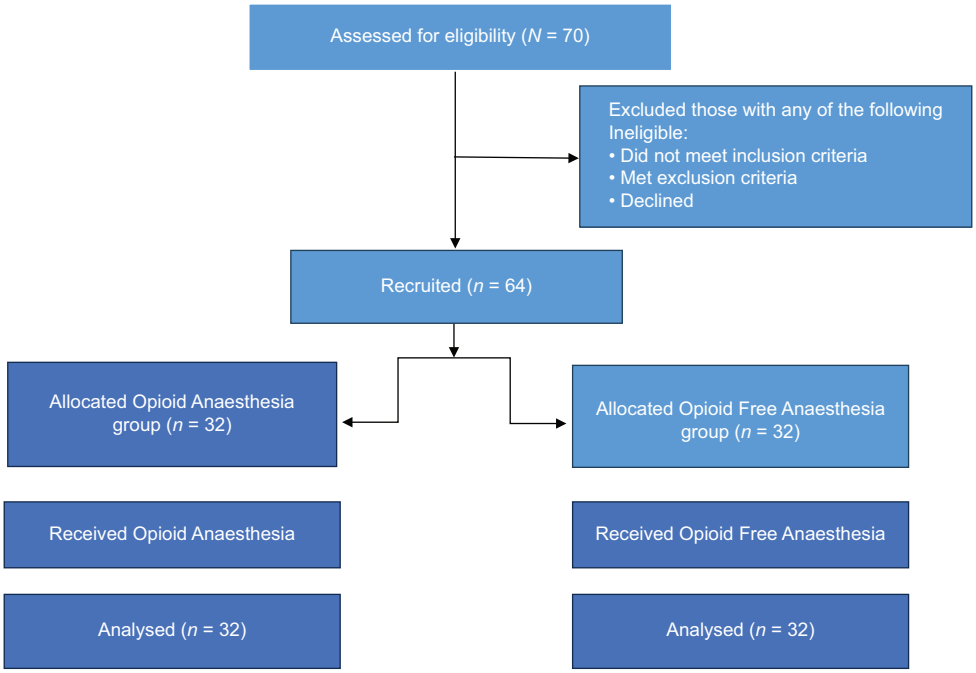

Figure 1: Participant flow diagram

Table 1: Demographic characteristics and baseline values of the study participants

Parameter	Group OA (*n*=32)	Group OFA (*n*=32)	*P*
Age (in years)	36.25 (13.22)	32.19 (10.59)	0.179
Gender, *n*			
Male	20	17	0.448
Female	12	15	
Operative time (min)	98.75 (33.6) (86.72, 110.78)	102.66 (37.99) (88.96, 116.36)	0.664
Baseline HR (0 min) (beats/min)	83.78 (13.17)	90.75 (16.70)	0.070
Baseline (0 min) SpO_2 (%)	99.75 (0.67)	99.50 (0.76)	0.170
Baseline (0 min) MAP (mmHg)	92.98 (2.45) (92.07, 93.89)	94.87 (2.65) (93.88, 95.86)	0.280
Pre-op QoR-15	100.63 (6.54) (98.27, 102.99)	102.83 (2.8) (101.81, 103.85)	0.079

Data presented as Mean (SD) (95% CI) or *n*. CI=confidence interval, HR=heart rate, OA=opioid anaesthesia, OFA=opioid-free anaesthesia, MAP=mean arterial pressure, pre-op QoR-15=preoperative quality of recovery, SD=standard deviation, SpO_2=peripheral capillary oxygen saturation, *n*=number of patients

Table 2: Between-group comparison of the study parameters

Study parameter	Group OA (*n*=32)	Group OFA (*n*=32)	*P*
HR after 30 min (beats/min)	88.88 (3.21) (87.68, 90.08)	71.64 (3.68) (7.27, 80.01)	<0.001
HR after 60 min (beats/min)	85.91 (3.45) (84.62, 87.20)	73.42 (3,54) (72.10, 74.74)	0.041
Highest MAP (mmHg)	92.98 (2.45) (92.07, 93.89)	94.87 (2.65) (93.88, 95.86)	0.280
Lowest MAP (mmHg)	83.25 (3.67) (81.88, 84.62)	56.37 (3.72) (54.98, 57.76)	<0.001
Post-op QoR-15	94.781 (8.72) (91.64, 97.93)	100.53 (1.97) (99.82, 101.24)	0.001
NRS	3.19 (2.442) (2.31, 4.07)	2.06 (1.96) (1.35, 2.77)	0.047
Time until post-op mobilisation (h)	4.06 (1.74) (3.42, 4.70)	2.69 (1.28) (2.23, 3.16)	<0.001
Stay in PACU (h)	1.55 (0.544) (1.34, 1.76)	1.43 (0.445) (1.27, 1.59)	0.365
Rescue analgesia	6.58 (3.86) (4.24, 8.91)	14.67 (6.43) (1.30, 30.6)	0.011
Sedation level			
Sedation level 0	22	32	<0.001
Sedation level 1	10	0	
Side effects			
Nausea, vomiting	8	2	0.488
Respiratory depression	0	0	
Pruritus	2	0	

Data presented as Mean (SD) (95% CI) or *n*. CI=confidence interval, HR=heart rate, OA=opioid anaesthesia, OFA=opioid-free anaesthesia, MAP=mean arterial pressure, PACU=post-anaesthesia care unit, post-op QoR-15=postoperative quality of recovery, SD=standard deviation, SpO2=peripheral capillary oxygen saturation, *n*=number of patients

the two groups in terms of time until postoperative mobilisation ($t = 3.545, P < 0.001$) and rescue analgesia time ($t = -2.922$, $P = 0.011$) [Table 2]. However, there was no statistically significant difference between the two groups in terms of recovery stay ($t = 0.913$, $P = 0.365$) [Table 1].

At 0 and 10 min, there were no statistically significant differences in mean arterial pressure (MAP) levels between the OA and OFA groups ($P > 0.05$). However, significant differences in MAP were observed at 15 min ($P = 0.030$), 30 min ($P < 0.001$), 60 min ($P = 0.041$) and 90 min ($P < 0.001$). At 120 minutes, the OA group had higher MAP values than Group OFA; however, the difference was not statistically significant ($P = 0.061$) [Table 2].

No respiratory depression was encountered in either group during the study. In Group OA, eight cases (25%) of nausea and vomiting were reported [Table 2], while in Group OFA, two cases (6.25%) were reported. In Group OA, two cases (6.25%) of pruritus (itching) were reported, while no cases were reported in the OFA group.

The sedation levels significantly differed between the OA and OFA groups, with a higher proportion of patients in Group OFA achieving a sedation level of 0 ($P < 0.001$) [Table 2].

DISCUSSION

This study demonstrated that OFA significantly enhances postoperative recovery in patients undergoing elective endoscopic nasal surgeries compared to OA. The OFA group showed higher QoR-15 scores, indicating better recovery, along with superior haemodynamic stability, lower pain scores, reduced nausea and vomiting and quicker mobilisation. These findings highlight the benefits of a multimodal analgesic approach involving dexmedetomidine, lignocaine, magnesium sulphate and paracetamol, which reduces opioid-related side effects such as pruritus and sedation.

Opioids are traditionally used in anaesthesia for their potent analgesic and autonomic stabilising effects. Yet their administration is not without concern and is associated with many side effects such as constipation, urinary retention, respiratory depression and PONV.[8] Growing concerns over these side effects have led to increased interest in OFA, which relies on alternative agents to modulate surgical stress and pain perception. Studies have shown that OFA effectively controls hormonal stress responses, sympathetic activity and inflammation, making it a feasible alternative, particularly in resource-limited settings where opioid availability may be restricted.

Chhabra *et al.*[7] found that while preoperative QoR-15 scores were comparable between OA and OFA groups, postoperative scores were significantly higher in the OFA group ($P < 0.001$), a finding consistent with our study. Our data also aligns with those of Ragupathy *et al.*,[9] who reported reduced analgesic consumption in OFA patients undergoing laparoscopic surgery, with none requiring opioid rescue analgesia, whereas in the OA group, additional opioid use was needed due to higher pain scores. This supports the efficacy of multimodal analgesic strategies in reducing opioid dependence and enhancing postoperative recovery.

Similarly, Choi *et al.*[10] examined the impact of OFA on postoperative quality of recovery following gynaecological laparoscopies and found lower pain scores, fewer incidences of PONV and improved recovery times in the OFA group. Feenstra *et al.*[11] conducted a meta-analysis comparing OFA and OA. They found no significant differences in postoperative pain scores or opioid consumption, but superior quality of recovery (QoR-40) and reduced PONV in the OFA group. Our study echoes these findings, with the OFA group experiencing lower pain scores, reduced PONV and shorter recovery room stays compared to fentanyl-based anaesthesia.

Our study also found greater haemodynamic stability in the OFA group, likely due to a reduced surgical stress response. Dexmedetomidine, a key component of OFA, has been shown to modulate cytokine production, exert central sympatholytic effects and mitigate stress-induced inflammation, leading to improved haemodynamic stability. Lignocaine, another component, has been reported to lower inflammatory cytokine levels and enhance postoperative pain relief. The combination of these agents appears to provide superior perioperative control compared to opioid-based regimens. Sedation levels were lower in the OFA group, with patients appearing more alert upon extubation than those in the OA group. These findings align with those of Guinot *et al.*[5], who demonstrated that OFA resulted in better postoperative alertness and reduced respiratory depression compared to OA in cardiac surgery. This study strengthens the evidence

supporting OFA as a safe and effective option for elective endoscopic nasal surgeries, aligning with the findings of Feenstra *et al*.[11] While OFA offers many benefits, concerns remain about its haemodynamic effects, particularly dexmedetomidine-induced bradycardia and hypotension.

The primary strengths of this study include its prospective design, the use of the validated QoR-15 score for comprehensive recovery assessment and a well-defined multimodal OFA protocol. However, several limitations must be acknowledged. The study was conducted at a single center and had a relatively small sample size, which limited the generalisability of the findings. The short follow-up period (24 h) precludes an assessment of the long-term benefits or potential late-onset complications associated with OFA. Future research should focus on optimising drug combinations, evaluating cost-effectiveness and developing evidence-based guidelines.

CONCLUSION

OFA in elective endoscopic nasal surgeries under general anaesthesia improved QoR-15 scores, haemodynamic stability, pain control, nausea/vomiting and early mobilisation, compared to OA.

Study data availability

De-identified data may be requested with reasonable justification from the authors (via email to the corresponding author) and will be shared after approval in accordance with the author's institution's policy.

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Conflicts of interest

There are no conflicts of interest.

ORCID

Yashika Pandey: https://orcid.org/0009-0001-6924-3428
Manisha Sapate: https://orcid.org/0000-0002-1332-4376
Harsha H. Narkhede: https://orcid.org/0000-0002-3741-9628
Poonam Mane: https://orcid.org/0009-0001-0400-4856

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