

**Research Article**

# **Ultrasound-Guided Bilateral Infraorbital Nerve Block in Endoscopic Transnasal Transsphenoidal Pituitary Surgery: A Randomized Comparison of 0.2% Ropivacaine Alone Versus 0.2% Ropivacaine with Fentanyl for Intraoperative Analgesia and Postoperative Recovery**

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## **ABSTRACT**

**Background:** Endoscopic transnasal transsphenoidal (TNTS) pituitary surgery involves significant nociceptive stimulation of richly innervated nasal structures, necessitating robust multimodal analgesia. Ultrasound-guided bilateral infraorbital nerve block (IONB) is an emerging adjunct in this setting. Whether the addition of fentanyl to ropivacaine augments analgesic efficacy remains insufficiently studied.

**Objectives:** To compare intraoperative opioid consumption and postoperative analgesic outcomes between 0.2% ropivacaine alone (Group R) and 0.2% ropivacaine combined with 25 mcg fentanyl (Group F) for ultrasound-guided bilateral IONB in patients undergoing endoscopic TNTS pituitary resection.

**Methods:** In this prospective, randomized, double-blind study conducted at a tertiary neuroscience centre (January 2024–April 2025), 50 adult patients (ASA I–III) scheduled

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for elective endoscopic TNS pituitary tumor resection were allocated by computer-generated randomization to Group R (0.2% ropivacaine, n=25) or Group F (0.2% ropivacaine + 25 mcg fentanyl, n=25). Ultrasound-guided bilateral IONB was performed post-induction under standardized general anesthesia. Primary outcome was total intraoperative intravenous fentanyl consumption. Secondary outcomes included postoperative VAS pain scores, time to first rescue analgesic, and total rescue analgesic doses in 24 hours.

**Results:** Intraoperative fentanyl requirement was significantly lower in Group F ( $212 \pm 50.58$  mcg) compared to Group R ( $292 \pm 45.83$  mcg;  $p < 0.0001$ ). Group F demonstrated significantly lower postoperative VAS scores at 1, 4, 18, and 24 hours ( $p < 0.05$ ), a prolonged time to first rescue analgesic ( $285.2 \pm 14.48$  vs.  $219.72 \pm 17.38$  minutes;  $p < 0.0001$ ), and fewer rescue analgesic doses in 24 hours ( $2.8 \pm 0.577$  vs.  $4.08 \pm 0.759$ ;  $p < 0.0001$ ). No adverse events attributable to the block or fentanyl adjuvant were observed in either group.

**Conclusion:** The addition of 25 mcg fentanyl to 0.2% ropivacaine for ultrasound-guided bilateral IONB significantly reduces intraoperative opioid requirements and improves postoperative analgesia in patients undergoing endoscopic TNS pituitary surgery, without compromising safety. This combination represents an effective opioid-sparing regional analgesic strategy in neuroanaesthetic practice.

**Keywords:** *infraorbital nerve block; ropivacaine; fentanyl; pituitary surgery; transnasal transsphenoidal; neuroanaesthesia; regional analgesia; opioid-sparing*

## 1. INTRODUCTION

Pituitary tumors constitute approximately 10–15% of all intracranial neoplasms in the adult population. The endoscopic transnasal transsphenoidal (TNS) approach has become the preferred surgical technique for the majority of pituitary adenomas, offering superior visualization, reduced morbidity, and a lower complication profile compared to the historical transcranial approach. First described fully by Jankowski et al. in 1992, the technique has been progressively refined over three decades and is now the standard of care for accessible pituitary lesions.

Despite its minimally invasive nature, TNS surgery is associated with significant nociceptive stimulation arising from submucosal nasal dissection, sphenoid bone resection, and nasal packing. These stimuli produce pronounced intraoperative haemodynamic fluctuations and substantial postoperative pain and discomfort. Conventionally, haemodynamic stability has been maintained through high-dose systemic opioid administration under general anaesthesia. However, high-dose opioids carry well-recognised risks including delayed emergence, respiratory depression, postoperative nausea and vomiting (PONV), and opioid-induced hyperalgesia—all of

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which are particularly undesirable in neurosurgical patients where prompt neurological assessment is critical.

Multimodal analgesic strategies incorporating regional nerve blocks have emerged as effective alternatives in neuroanaesthetic practice. The infraorbital nerve, a terminal branch of the second division of the trigeminal nerve, provides sensory innervation to the lateral nasal wall, nasal floor, nasal septum, upper lip, lower eyelid, and adjacent cheek—anatomical territories directly manipulated during TNTS surgery. Bilateral IONB thus offers a physiologically rational analgesic target for these procedures. The advent of ultrasound guidance has enhanced the precision, safety, and efficacy of this block by enabling real-time visualisation of the infraorbital foramen and adjacent neurovascular structures.

Ropivacaine, a long-acting S(-)-enantiomer amide local anaesthetic, is widely favoured for peripheral nerve blocks owing to its favourable cardiotoxicity and neurotoxicity profile relative to bupivacaine. Fentanyl, a potent synthetic opioid, has been investigated as an adjuvant to local anaesthetics in peripheral nerve blocks, with proposed mechanisms including direct peripheral opioid receptor activation, potentiation of local anaesthetic action, and systemic absorption with central analgesic effects.

While several studies have evaluated bilateral IONB for nasal and transsphenoidal procedures, comparative evidence on the efficacy of fentanyl as an adjuvant to ropivacaine specifically in TNTS pituitary surgery remains sparse. This prospective, randomised, double-blind study was therefore designed to compare 0.2% ropivacaine alone versus 0.2% ropivacaine combined with 25 mcg fentanyl for ultrasound-guided bilateral IONB in patients undergoing endoscopic TNTS resection of pituitary tumours, with particular focus on intraoperative opioid sparing and postoperative analgesic quality.

### **1.1 Hypothesis**

We hypothesised that the addition of 25 mcg fentanyl as an adjuvant to 0.2% ropivacaine for ultrasound-guided bilateral infraorbital nerve block would improve the quality and extend the duration of the block, thereby reducing intraoperative systemic opioid requirements and enhancing postoperative analgesia, compared to 0.2% ropivacaine alone, in adult patients undergoing endoscopic transnasal transsphenoidal resection of pituitary tumours—without increasing the incidence of adverse effects.

### **1.2 Aim and Objectives**

**Aim:** To compare intraoperative analgesia—in terms of total intraoperative opioid consumption—and postoperative recovery profile—in terms of duration and quality of analgesia in the first 24 hours postoperatively—between 0.2% ropivacaine alone and 0.2% ropivacaine combined with 25 mcg fentanyl, when used for ultrasound-guided bilateral infraorbital nerve block in patients undergoing endoscopic transnasal transsphenoidal resection of pituitary tumours.

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**Primary Objective:** To quantify and compare the total intravenous fentanyl administered intraoperatively for haemodynamic rescue (heart rate or MAP >20% above baseline) during endoscopic TNS pituitary surgery between Group R and Group F.

**Secondary Objectives:**

- (i) To compare the time to first postoperative rescue analgesic requirement and the total number of rescue analgesic doses within the first 24 hours postoperatively between the two groups.
- (ii) To determine the quality of postoperative analgesia in each group using the Visual Analogue Scale (VAS) from recovery until the time of first rescue analgesic requirement.
- (iii) To assess intraoperative and postoperative haemodynamic stability (heart rate and mean arterial pressure) and overall safety profile of the two interventions.

### **1.3 Novel Contribution**

To our knowledge, this is the first prospective, randomised, double-blind study to evaluate fentanyl as an adjuvant to ropivacaine specifically in ultrasound-guided bilateral infraorbital nerve block for adult patients undergoing endoscopic transnasal transsphenoidal pituitary surgery. While prior studies have examined infraorbital nerve block in paediatric cleft lip repair and in nasal surgery, comparative evidence for adjuvant-augmented IONB in this neurosurgical population is absent from the literature. Additionally, the use of ultrasound guidance—rather than classical landmark or intraoral techniques—for bilateral IONB in TNS pituitary surgery has not been previously reported in a controlled trial. The present study therefore addresses a dual gap: the evolving role of regional anaesthesia in neurosurgery, particularly the use of fentanyl as an adjuvant in transnasal transsphenoidal (TNS) surgery, and the clinical applicability of ultrasound-guided infraorbital nerve block (IONB) as a component of multimodal neurosurgical anaesthesia in adult patients.

## **2. MATERIALS AND METHODS**

### **2.1 Study Design and Setting**

This was a prospective, randomised, double-blind, parallel-group interventional study conducted at the Institute of Neurosciences, Medanta – The Medicity, Gurgaon (a 1600-bed tertiary care teaching hospital), from January 2024 to April 2025. The study was approved by the Medanta Institutional Ethics Committee (IEC Reference No. 1610/2023 DNB; approval date 12 December 2023) and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrolment.

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## **2.2 Participants**

Eligible patients were adults aged  $\geq 18$  years with clinical and radiological features consistent with pituitary space-occupying lesion, scheduled for elective endoscopic TNS resection under general anaesthesia, with ASA physical status I, II, or III. Exclusion criteria comprised: age  $< 18$  years, known hypersensitivity to ropivacaine or fentanyl, refusal of consent, ASA grade IV–V, and intraoperative change of surgical plan due to complications. A sample size of 25 patients per group was calculated based on an anticipated mean difference in intraoperative fentanyl consumption of 7.9 mcg ( $m_1 = 14.2$ ;  $m_2 = 22.1$ ; CV = 50%), with  $\alpha = 0.05$  (two-tailed) and 80% power ( $Z\beta = 0.84$ ).

## **2.3 Randomisation and Blinding**

Eligible patients were allocated by computer-generated block randomisation to Group R (0.2% ropivacaine) or Group F (0.2% ropivacaine + 25 mcg fentanyl). Allocation concealment was maintained using sequentially numbered, sealed opaque envelopes. The study drug was prepared by an anaesthesia resident not involved in patient care; the attending consultant performing the block and the outcome assessor recording intraoperative and postoperative parameters were both blinded to group allocation, as were the nursing staff and neurointensivist supervising postoperative care.

## **2.4 Anaesthetic Protocol**

A standardised general anaesthetic technique was used for all participants. After preoxygenation with 100% O<sub>2</sub> for 3 minutes, patients were premedicated with intravenous (IV) lidocaine 1.5 mg/kg and IV fentanyl 2 mcg/kg, followed by induction with IV propofol 2 mg/kg and muscle relaxation with IV rocuronium 0.6 mg/kg. The trachea was intubated, throat packs applied, and eyes protected. Anaesthesia was maintained with sevoflurane in an air-oxygen (50:50) mixture with IV vecuronium 0.1 mcg/kg/hr. End-tidal CO<sub>2</sub> was targeted at 32–35 mmHg. Anaesthetic depth was monitored with Bispectral Index (BIS), targeting BIS 40–60. Radial arterial line and urinary catheter were inserted post-induction. Nasal decongestion used standardised cottonoids soaked in adrenaline (1:200,000), 2% lidocaine (5 ml), and saline (4 ml) in all patients.

## **2.5 Study Drug Preparation and Block Technique**

Group R received 1.5 ml of 0.2% ropivacaine per side. Group F received a mixture of 1.0 ml 0.2% ropivacaine and 25 mcg fentanyl drawn via tuberculin syringe, constituting a total volume of 1.5 ml per side. Ultrasound-guided bilateral IONB was performed post-induction using a high-resolution 12.5 MHz linear probe (Venue Go system). The infraorbital foramen was identified as a disruption in the hyperechoic bony line on transverse scanning from medial to lateral. Colour Doppler confirmed the infraorbital artery, and a 23-gauge needle advanced in-plane from the caudal probe edge under real-time visualisation. Following negative aspiration, 1.5 ml of study solution was deposited bilaterally after povidone-iodine skin preparation. Surgery commenced 15 minutes post-block.

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## **2.6 Intraoperative Monitoring and Rescue Protocol**

Haemodynamic variables (heart rate [HR], mean arterial pressure [MAP], SpO<sub>2</sub>, EtCO<sub>2</sub>, and mean alveolar concentration [MAC]) were recorded at: T0 (baseline, pre-induction), T1 (5 minutes post-block), T2 (cottonoid insertion), T3 (endoscope insertion), T4 (mucosal resection), T5 (sphenoid bone resection), T6 (sellar ridge dissection and tumour excision), and T7 (endoscope withdrawal). HR >20% above baseline was treated as tachycardia; MAP >20% above baseline as hypertension (treated with IV esmolol); MAP <20% below baseline as hypotension (treated with IV ephedrine). Total IV fentanyl administered intraoperatively for haemodynamic rescue constituted the primary outcome. All patients received IV paracetamol 15 mg/kg and IV ondansetron 0.1 mg/kg before emergence. Neuromuscular block was reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg.

## **2.7 Postoperative Assessment**

Patients were monitored in the Neurointensive Care Unit by nursing staff and neurointensivists blinded to group allocation. Pain was assessed using a 0–10 visual analogue scale (VAS; 0–3 no pain, 4–5 mild, 6–7 moderate, 8–10 severe) at 0 hours, hourly until 4 hours, two-hourly until 8 hours, then at 12, 18, and 24 hours postoperatively. When VAS exceeded 3, IV paracetamol 15 mg/kg was administered as rescue analgesia. Time to first rescue analgesic request (duration of analgesia) and total number of rescue analgesic doses within 24 hours were recorded.

## **2.8 Statistical Analysis**

Data were compiled in Microsoft Excel and analysed using SPSS version 24.0. Continuous data are presented as mean  $\pm$  standard deviation; categorical data as absolute numbers and percentages. Between-group comparisons of continuous variables were performed using the independent Student's t-test; categorical variables were compared using the Chi-square test. A p-value <0.05 was considered statistically significant.

# **3. RESULTS**

## **3.1 Demographic and Baseline Characteristics**

Fifty patients were enrolled and randomised, with 25 in each group. Baseline characteristics were comparable between the two groups with no statistically significant differences (Table 1). Mean age was  $32.80 \pm 9.44$  years in Group R and  $35.36 \pm 12.61$  years in Group F ( $p = 0.420$ ). Gender distribution (Group R: 19 males, 6 females; Group F: 15 males, 10 females;  $p = 0.225$ ), mean weight ( $71.32 \pm 9.19$  kg vs.  $67.20 \pm 7.83$  kg;  $p = 0.094$ ), and ASA grade distribution (14 grade I and 11 grade II in each group;  $p = 1.000$ ) were all comparable. Duration of surgery was also similar between the groups ( $168.2 \pm 9.56$  vs.  $168.8 \pm 9.49$  minutes;  $p = 0.825$ ).



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**Table 1. Baseline Demographic and Clinical Characteristics**

| Parameter                                | Group R (Ropivacaine)<br>n = 25 | Group F (Ropivacaine +<br>Fentanyl)<br>n = 25 | p-value |
|------------------------------------------|---------------------------------|-----------------------------------------------|---------|
| Age (years), mean $\pm$ SD               | 32.80 $\pm$ 9.44                | 35.36 $\pm$ 12.61                             | 0.420   |
| Gender (M/F)                             | 19 / 6                          | 15 / 10                                       | 0.225   |
| Weight (kg), mean $\pm$ SD               | 71.32 $\pm$ 9.19                | 67.20 $\pm$ 7.83                              | 0.094   |
| ASA I / II                               | 14 / 11                         | 14 / 11                                       | 1.000   |
| Duration of surgery (min), mean $\pm$ SD | 168.2 $\pm$ 9.56                | 168.8 $\pm$ 9.49                              | 0.825   |
|                                          |                                 |                                               |         |

### 3.2 Primary Outcome: Intraoperative Fentanyl Consumption

Total intraoperative IV fentanyl consumption was significantly lower in Group F (212  $\pm$  50.58 mcg) compared to Group R (292  $\pm$  45.83 mcg;  $p < 0.0001$ ), representing a reduction of approximately 27.4% (Table 2). This demonstrates a clinically and statistically significant opioid-sparing effect conferred by the addition of fentanyl to the infraorbital nerve block.

**Table 2. Intraoperative Fentanyl Consumption and Postoperative Analgesic Outcomes**

| Outcome Measure                        | Group R<br>(mean $\pm$ SD) | Group F<br>(mean $\pm$ SD) | p-value    |
|----------------------------------------|----------------------------|----------------------------|------------|
| Total intraoperative IV fentanyl (mcg) | 292 $\pm$ 45.83            | 212 $\pm$ 50.58            | $< 0.0001$ |
| Time to first rescue analgesic (min)   | 219.72 $\pm$ 17.38         | 285.2 $\pm$ 14.48          | $< 0.0001$ |
| Total rescue analgesic doses in 24 hrs | 4.08 $\pm$ 0.759           | 2.8 $\pm$ 0.577            | $< 0.0001$ |
|                                        |                            |                            |            |

### 3.3 Intraoperative Haemodynamic Parameters

Both groups maintained stable oxygenation ( $\text{SpO}_2 \geq 99.24\%$  throughout) and comparable  $\text{EtCO}_2$  and MAC values at all time points (all  $p > 0.05$ ). Statistically significant differences in HR were observed at T2 (84.8  $\pm$  10.04 vs. 78.96  $\pm$  8.51 bpm), T3 (83.6  $\pm$  8.74 vs. 77.4  $\pm$  8.99), T4 (83.04  $\pm$  10.28 vs. 75.72  $\pm$  9.25), T6 (81.6  $\pm$  9.45 vs. 66.8  $\pm$  5.29), and T7 (79.8  $\pm$  8.43 vs. 69.8  $\pm$  4.13), with Group F showing higher HR values; however, all values remained within the normal clinical range. Mean arterial pressure was significantly lower in Group F at T3–T6, reflecting superior attenuation of nociceptive haemodynamic responses.

**Table 3. Intraoperative Heart Rate (bpm) at Key Time Intervals**

| Time Point | Group R (bpm) | Group F (bpm) | p-value |
|------------|---------------|---------------|---------|
|------------|---------------|---------------|---------|

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|                           |              |               |         |
|---------------------------|--------------|---------------|---------|
| T0 (Baseline)             | 90.2 ± 16.71 | 86.92 ± 18.32 | 0.512   |
| T1 (Post-block)           | 82.2 ± 11.30 | 87.32 ± 9.82  | 0.094   |
| T2 (Cottonoid insertion)  | 78.96 ± 8.51 | 84.8 ± 10.05  | 0.031*  |
| T3 (Endoscope insertion)  | 77.4 ± 8.99  | 83.6 ± 8.74   | 0.017*  |
| T4 (Mucosal resection)    | 75.72 ± 9.25 | 83.04 ± 10.28 | 0.011*  |
| T5 (Sphenoid resection)   | 75.68 ± 8.74 | 80.24 ± 9.29  | 0.080   |
| T6 (Tumour excision)      | 66.8 ± 5.29  | 81.6 ± 9.45   | 0.0001* |
| T7 (Endoscope withdrawal) | 69.8 ± 4.13  | 79.8 ± 8.43   | 0.0001* |

\*  $p < 0.05$  (statistically significant). All values within normal clinical range.

### 3.4 Postoperative Pain Scores (VAS)

Postoperative VAS scores were significantly lower in Group F at 1 hour ( $0.16 \pm 0.374$  vs.  $1.76 \pm 0.97$ ;  $p < 0.0001$ ), 4 hours ( $1.16 \pm 0.943$  vs.  $2.66 \pm 1.165$ ;  $p < 0.0001$ ), 18 hours ( $2.08 \pm 1.075$  vs.  $3.36 \pm 0.812$ ;  $p < 0.0001$ ), and 24 hours ( $1.28 \pm 1.068$  vs.  $3.16 \pm 0.614$ ;  $p < 0.0001$ ). Early postoperative scores were comparable between groups. Group F consistently maintained pain scores in the 'no pain' to 'mild pain' category (VAS 0–3) throughout the 24-hour observation period (Table 4).

**Table 4. Postoperative VAS Pain Scores**

| Time Point | Group R (VAS)    | Group F (VAS)    | p-value      |
|------------|------------------|------------------|--------------|
| 0 hours    | $0.48 \pm 0.714$ | $0.16 \pm 0.374$ | 0.053        |
| 1 hour     | $1.76 \pm 0.97$  | $0.16 \pm 0.374$ | $< 0.0001^*$ |
| 2 hours    | $1.72 \pm 1.10$  | $1.64 \pm 1.35$  | 0.819        |
| 3 hours    | $2.12 \pm 1.364$ | $1.84 \pm 0.943$ | 0.403        |
| 4 hours    | $2.66 \pm 0.943$ | $1.16 \pm 1.165$ | $< 0.0001^*$ |
| 6 hours    | $2.08 \pm 0.812$ | $2.04 \pm 1.485$ | 0.906        |
| 8 hours    | $2.12 \pm 0.971$ | $2.56 \pm 1.193$ | 0.159        |
| 12 hours   | $2.56 \pm 0.768$ | $2.44 \pm 0.917$ | 0.618        |
| 18 hours   | $3.36 \pm 0.812$ | $2.08 \pm 1.075$ | $< 0.0001^*$ |
| 24 hours   | $3.16 \pm 0.614$ | $1.28 \pm 1.068$ | $< 0.0001^*$ |

\*  $p < 0.05$  (statistically significant)

### 3.5 Postoperative Rescue Analgesia

Time to first rescue analgesic was significantly prolonged in Group F ( $285.2 \pm 14.48$  minutes) compared to Group R ( $219.72 \pm 17.38$  minutes;  $p < 0.0001$ ), indicating approximately 65 minutes of additional analgesic coverage. The mean total number of rescue analgesic doses required within 24 hours was significantly lower in Group F ( $2.8 \pm 0.577$  vs.  $4.08 \pm 0.759$ ;  $p < 0.0001$ ).



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### **3.6 Postoperative Haemodynamics**

Postoperative HR and SpO<sub>2</sub> were comparable between the groups at all time points. However, MAP was significantly lower in Group F at multiple postoperative time intervals including 0 hours (68.08 ± 3.58 vs. 71.96 ± 6.93 mmHg; p = 0.016), 3 hours (70.04 ± 5.15 vs. 74.24 ± 8.42; p = 0.039), 6 hours (69.68 ± 4.15 vs. 74.0 ± 7.95; p = 0.020), 18 hours (68.56 ± 4.41 vs. 75.72 ± 8.31; p < 0.0001), and 24 hours (68.88 ± 4.05 vs. 77.04 ± 10.29; p = 0.001), reflecting superior postoperative pain suppression and reduced sympathetic activation in Group F.

### **3.7 Safety Profile**

No adverse events attributable to the infraorbital nerve block or to the fentanyl adjuvant were documented in either group. There were no episodes of intravascular injection, haematoma, orbital injury, or significant respiratory depression. All patients met standard extubation criteria and had comparable modified Aldrete scores at 5 and 10 minutes post-extubation.

## **4. DISCUSSION**

This study demonstrates that the addition of 25 mcg fentanyl to 0.2% ropivacaine for ultrasound-guided bilateral IONB significantly reduces intraoperative opioid consumption and enhances the quality and duration of postoperative analgesia in patients undergoing endoscopic TNS pituitary surgery. These findings are clinically meaningful in the context of neuroanaesthesia, where minimising systemic opioid exposure while ensuring haemodynamic stability and facilitating early neurological assessment are paramount objectives.

The primary finding of a 27.4% reduction in intraoperative fentanyl consumption in Group F aligns with prior evidence supporting opioid-sparing effects of peripheral nerve blocks in nasal and transsphenoidal surgery. Rajan et al. demonstrated that infraorbital nerve block significantly reduced both intraoperative fentanyl and sevoflurane consumption in infants undergoing cheiloplasty, and also shortened extubation time and reduced postoperative delirium. Choi et al. similarly reported significantly lower intraoperative remifentanyl requirements and reduced postoperative tramadol need following bilateral infraorbital and infratrochlear nerve block in septorhinoplasty patients. The present study extends this opioid-sparing evidence base to adult patients undergoing TNS pituitary surgery with fentanyl-augmented IONB.

The mechanisms underlying fentanyl's analgesic augmentation in peripheral nerve blocks are multifactorial. Peripheral opioid receptors on sensory afferents and dorsal root ganglia can be directly activated by exogenously administered opioids. Additionally, fentanyl may potentiate the action of local anaesthetics and reduce peripheral pain signal transmission. Systemic absorption contributes a central analgesic component, which may explain the prolonged effect observed in Group F at 18 and 24 hours

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postoperatively, extending well beyond the expected duration of a local anaesthetic-only block.

The intraoperative haemodynamic findings deserve careful interpretation. While Group F demonstrated higher HR at certain time points, all values remained within the clinically acceptable range; this is attributable to compensatory tachycardia secondary to more pronounced MAP reduction from superior nociceptive suppression. The significantly lower MAP in Group F at T3–T6 is concordant with findings by Chadha et al., who demonstrated that bilateral maxillary nerve blocks markedly attenuated hypertensive responses during nasal infiltration and speculum application in TNTS surgery. Similarly, Makhija et al. reported that bilateral infratrochlear and infraorbital nerve blocks provided superior intraoperative haemodynamic stability compared to general anaesthesia alone in nasal surgeries.

Postoperative VAS scores and rescue analgesic consumption further support the superiority of the fentanyl combination. The significantly lower VAS at 1, 4, 18, and 24 hours in Group F and the approximately 65-minute extension in time to first rescue analgesic are consistent with the findings of Mane et al., who reported prolonged analgesia with fentanyl-supplemented bupivacaine in bilateral IONB for cleft lip repair. Jonnavithula et al. demonstrated that bilateral intraoral IONB with bupivacaine prolonged the mean time to first analgesic demand to 21 hours in TNTS pituitary surgery compared to 3.4 hours in controls; our findings corroborate this benefit and add the incremental value of fentanyl as an adjuvant.

The favourable postoperative haemodynamic profile—specifically the lower MAP in Group F at multiple time points—merits clinical attention. Elevated postoperative MAP in neurosurgical patients is frequently a surrogate of undertreated pain-induced sympathetic activation and carries risk of hypertensive cerebrovascular complications and postoperative haematoma. The superior haemodynamic stability in Group F thus carries implications beyond analgesic comfort, potentially reducing perioperative cerebrovascular risk.

The ultrasound-guided approach to IONB employed in this study offers distinct advantages over the classical landmark-based technique. Real-time visualisation of the infraorbital foramen, nerve, and adjacent infraorbital vessels minimises the risk of intravascular injection and ensures precise drug deposition. Cao et al. and Abdellatif et al. have demonstrated improved efficacy and safety of ultrasound-guided IONB versus landmark techniques, supporting the methodological approach adopted in the present study.

The absence of adverse events in either group—including no intravascular injections, haematomas, or respiratory complications—confirms the safety of this technique in the neurosurgical population. The low volume (1.5 ml per side) and concentration (0.2%) of ropivacaine minimises systemic toxicity risk, and the small dose of peripheral fentanyl (25 mcg total) avoids clinically significant systemic opioid effects.

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Several limitations of this study warrant acknowledgement:

1. **Limited sample size:** The sample size of 25 per group, while adequately powered for the primary endpoint, limits the ability to perform meaningful subgroup analyses and may affect the statistical power of secondary outcome comparisons.
2. **Single-centre design:** As a single-institution study, external generalisability may be limited, particularly to centres without ultrasound infrastructure or high-volume neurosurgical experience.
3. **Short postoperative follow-up:** Postoperative pain evaluation was restricted to the first 24 hours, precluding assessment of delayed analgesic requirements, late complications, or longer-term recovery differences between the two groups.
4. **Subjective pain assessment:** Postoperative pain was evaluated using the Visual Analogue Scale, which is inherently subjective and may vary based on individual pain thresholds, psychological factors, and cultural differences in pain expression.
5. **Operator dependency:** Ultrasound-guided infraorbital nerve block is an operator-dependent procedure, introducing potential for inter-observer variability. This was mitigated by restricting all block performances to a single trained anaesthesiologist throughout the study period.

## 5. CONCLUSION

The addition of 25 mcg fentanyl to 0.2% ropivacaine for ultrasound-guided bilateral infraorbital nerve block significantly augments intraoperative analgesic efficacy, reduces systemic opioid requirements, and improves postoperative pain control in patients undergoing endoscopic transnasal transsphenoidal pituitary resection. The combination provides superior haemodynamic stability both intraoperatively and postoperatively without any associated adverse effects. These findings support the incorporation of fentanyl-augmented ultrasound-guided bilateral IONB as a component of multimodal analgesic protocols in neuroanaesthetic management of TNS pituitary surgery. Larger multicentre randomised trials with extended follow-up are warranted to further establish optimal adjuvant dosing strategies and long-term outcomes.

## DECLARATIONS

**Ethics Approval:** Approved by the Medanta Institutional Ethics Committee (IEC Ref: 1610/2023 DNB; December 12, 2023). All procedures conformed to the Declaration of Helsinki.

**Consent to Participate:** Written informed consent was obtained from all participants.

**Conflict of Interest:** The authors declare no conflicts of interest.

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Intraoperative Analgesia and Postoperative Recovery**

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## REFERENCES

1. Melmed S. Pituitary-tumor endocrinopathies. *N Engl J Med*. 2020;382:937–950.
2. Jankowski R, Auque J, Simon C, et al. Endoscopic pituitary tumor surgery. *Laryngoscope*. 1992;102:198–202.
3. Dunn LK, Nemergut EC. Anesthesia for transsphenoidal pituitary surgery. *Curr Opin Anaesthesiol*. 2013;26(5):549–554.
4. Chadha R, Padmanabhan V, Rout A, et al. Prevention of hypertension during trans-sphenoidal surgery – the effect of bilateral maxillary nerve block with local anaesthetics. *Acta Anaesthesiol Scand*. 1997;41(1 Pt 1):35–40.
5. Mane RS, Sanikop CS, Dhulkhed VK, Gupta T. Comparison of bupivacaine alone and in combination with fentanyl or pethidine for bilateral infraorbital nerve block for postoperative analgesia in paediatric patients for cleft lip repair. *J Anaesthesiol Clin Pharmacol*. 2011;27(1):23–26.
6. Jonnavithula N, Durga P, Kulkarni DK, Ramachandran G. Bilateral intra-oral, infra-orbital nerve block for postoperative analgesia following transsphenoidal pituitary surgery. *Anaesthesia*. 2007;62(6):581–585.
7. Boselli E, Bouvet L, Augris-Mathieu C, et al. Infraorbital and infratrochlear nerve blocks combined with general anaesthesia for outpatient rhinoseptoplasty: a prospective randomised, double-blind, placebo-controlled study. *Anaesth Crit Care Pain Med*. 2016;35(1):31–36.
8. Rajan S, Mathew J, Kumar L. Effect of bilateral infraorbital nerve block on intraoperative anesthetic requirements, hemodynamics, glycemic levels, and extubation in infants undergoing cheiloplasty under general anesthesia. *J Dent Anesth Pain Med*. 2021;21(2):129–137.
9. Choi H, Jung SH, Hong JM, et al. Effects of bilateral infraorbital and infratrochlear nerve block on emergence agitation after septorhinoplasty: a randomized controlled trial. *J Clin Med*. 2019;8(6):769.
10. El-Emam ES, Abd El Motlb EA. Comparative evaluation of dexamethasone and dexmedetomidine as adjuvants for bupivacaine in ultrasound-guided infraorbital nerve block for cleft lip repair. *Anesth Essays Res*. 2019;13(2):354–358.
11. Makhija P, Sahu P, Khan MV, et al. Effect of bilateral infratrochlear and infraorbital nerve block combined with general anesthesia for nasal surgeries. *Int J Pharm Clin Res*. 2024;16(2):393–399.
12. Cao Z, Zhang K, Hu L, Pan J. Application of ultrasound guidance in the oral and maxillofacial nerve block. *PeerJ*. 2021;9:e12543.

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13. Ramsali MV, Saradadevi V, Kulkarni D, et al. Bilateral infraorbital nerve block for postoperative analgesia after functional endoscopic sinus surgery. *Res Innov Anest.* 2023;8(1):6–10.
14. McAdam D, Muro K, Suresh S. The use of infraorbital nerve block for postoperative pain control after transsphenoidal hypophysectomy. *Reg Anesth Pain Med.* 2005;30(6):572–573.
15. Abdellatif AA, Elagamy AE, Elgazzar K. Ultrasound-guided infraorbital nerve block for cleft lip repair in pediatrics: a new technique for an old block. *Ain-Shams J Anesthesiol.* 2018;10:3.
16. Zhou W, Li Y, Lin N, et al. Comparison of the postoperative analgesic effects of bupivacaine and ropivacaine in infraorbital nerve block anesthesia for cheiloplasty in infants. *Int J Pediatr Otorhinolaryngol.* 2025;193:112373.
17. Desai N, Albrecht E. Local anaesthetic adjuncts for peripheral nerve blockade. *Curr Opin Anaesthesiol.* 2023;36(5):533–540.
18. Nicodemus HF, Ferrer MJ, Cristobal VC, de Castro L. Bilateral infraorbital block with 0.5% bupivacaine as post-operative analgesia following cheiloplasty in children. *Scand J Plast Reconstr Surg Hand Surg.* 1991;25(3):253–257.