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CLINICAL TRIAL REPORT

Effects of Infraorbital Nerve Block with Dexmedetomidine-Added Bupivacaine on Intraoperative Opioid Consumption and Postoperative Analgesia During Endoscopic Transsphenoidal Surgery: A Prospective, Randomized, Double-Blind Controlled Trial

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Purpose: In endoscopic transsphenoidal surgery (ETSS) for pituitary adenoma, perioperative discomfort often requires opioid use under general anesthesia. Infraorbital nerve block (IONB), which targets nasal structures involved in ETSS-related pain, may improve analgesia. Combining dexmedetomidine with bupivacaine for IONB may further reduce intraoperative opioid requirements and improve recovery.

Patients and Methods: In this prospective, randomized, double-blind study, total of 63 patients was randomized and undergoing ETSS received bilateral ultrasound-guided IONB and were assigned to dexmedetomidine + bupivacaine (2 mL of 0.5% bupivacaine with 5 μg dexmedetomidine per side), bupivacaine alone (2 mL of 0.5% per side), or control (2 mL of normal saline per side). 47 patients were included in the final analysis. The study aimed to evaluate the effects of IONB with dexmedetomidine-added bupivacaine on intra/postoperative analgesic requirements and postoperative pain scores. The study was registered on ClinicalTrials.gov (ID: NCT04785222) on 3 March 2021.

Results: The dexmedetomidine + bupivacaine group required significantly less intraoperative fentanyl (1.80 ± 0.67 mcg/kg) than the bupivacaine (2.26 ± 0.78 mcg/kg) and control (2.83 ± 1.87 mcg/kg) groups ($p < 0.001$). Adjusted analysis showed a mean difference reduction of 1.12 mcg/kg in fentanyl use in the dexmedetomidine added group ($p = 0.037$). Regarding postoperative analgesic requirements, the time to first rescue fentanyl dose was significantly longer in the dexmedetomidine-added group (+33.9 minutes; $p < 0.001$), while the requirements for other postoperative analgesics were lower. Postoperative pain scores from the immediate postoperative up to 48 hours, and adverse events showed no significant differences. Hemodynamic parameters, hypotension and bradycardia, were comparable among groups.

Conclusion: IONB with dexmedetomidine-added bupivacaine reduces intraoperative fentanyl use and prolong time for rescue opioid requirements during ETSS without increasing hemodynamic risk. Although postoperative pain scores were comparable among all groups, the intraoperative opioid-sparing effect support its role in multimodal analgesia for neurosurgical anesthesia.

Keywords: analgesia, local anesthesia, neurosurgical procedures, opioid-related disorders, postoperative analgesic

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Introduction

Endoscopic transsphenoidal surgery (ETSS) is a minimally invasive approach, offering reduced brain and tissue trauma compared to traditional craniotomy or microscopic techniques.[1,2] Key goals of ETSS include hormonal optimization, clear surgical exposure, rapid control of cavernous sinus bleeding, hemodynamic stability, and fast emergence from anesthesia.[3–5] However, significant perioperative discomfort, during surgical manipulation of the nasal cavity and septum can generate significant nociceptive input, often necessitating intraoperative opioid administration.[4,6] General anesthesia with endotracheal intubation and intraoperative opioid administration remains the standard anesthetic approach for managing intraoperative nociceptive stimuli during ETSS. Previous studies have suggested that regional techniques, including infraorbital nerve block (IONB), may reduce pain related to the nasal surgical approach, particularly in transsphenoidal pituitary surgery and other nasal procedures.[7–10] In neurosurgical anesthesia, minimizing opioid use is particularly important to facilitate rapid postoperative neurological assessment and to reduce opioid-related adverse effects such as nausea and vomiting, which may increase intracranial pressure. Therefore, adjunctive strategies that provide effective analgesia while reducing opioid requirements are highly desirable.

The infraorbital nerve, a sensory branch of the maxillary division of the trigeminal nerve, innervates the anterior nasal cavity, lateral nasal wall, and nasal septum—structures involved in the surgical access pathway of ETSS.[6,11,12] Although IONB does not cover deeper structures such as the sphenoid sinus or sellar region, it effectively targets the somatic component of pain arising from the nasal approach, which represents a significant source of perioperative discomfort. Ultrasound-guided techniques may further improve the safety and accuracy of the block.[12–14]

Furthermore, dexmedetomidine has been increasingly used as an adjuvant to local anesthetics due to its ability to prolong analgesia and enhance block quality. Compared with other adjuvants, dexmedetomidine has demonstrated efficacy in prolonging regional anesthesia duration in head and neck procedures, although it may be associated with hemodynamic effects such as hypotension and bradycardiabradycardia.[15,16]

Despite the routine use of opioid-based analgesia in ETSS, reliance on systemic opioids may be associated with delayed emergence, which can adversely affect intracranial dynamics. Although IONB has been proposed to reduce nociceptive input from the nasal surgical approach, its role as an opioid-sparing strategy in ETSS remains incompletely defined. Furthermore, the potential additive effect of dexmedetomidine in enhancing the efficacy and duration of this block has not been well established. Therefore, this study aimed to evaluate whether the addition of dexmedetomidine to bupivacaine in IONB could reduce intraoperative opioid requirements and improve perioperative analgesic outcomes in patients undergoing ETSS.

Materials and Methods

This study was a prospective, randomized, double-blinded, controlled trial. 63 adult patients diagnosed with pituitary tumors and scheduled for tumor resection via the endoscopic transsphenoidal approach under general anesthesia with endotracheal intubation at Maharaj Nakorn Chiang Mai Hospital, Faculty of Medicine, Chiang Mai University, Thailand, were enrolled. Patients were excluded if they had known allergies to dexmedetomidine or bupivacaine, if the surgical approach was altered due to cavernous sinus perforation, or if intraoperative navigation systems such as the Mayfield head frame were used to localize the tumor. The study protocol was registered in the Research Operation System and on ClinicalTrials.gov (ID: NCT04785222) on 3 March 2021. Ethical approval was obtained from the Ethics Committee of the Faculty of Medicine, Chiang Mai University (Study code: ANE-2564-08007) on 24 June 2021. Written informed consent was obtained from all participants. This study was conducted in accordance with the Declaration of Helsinki.

After obtaining informed consent, randomization was performed using a computer-generated sequence, with allocation codes sealed in opaque envelopes to ensure concealment: group 1 (dexmedetomidine + bupivacaine), group 2 (bupivacaine alone), and group 3 (control). The allocation sequence was concealed, and both participants and investigators remained blinded to group assignments. The envelope was opened immediately prior to induction of anesthesia. Study medications were prepared by an anesthetic nurse not involved in patient care, using identical 3-mL syringes containing equal volumes of visually indistinguishable solutions to maintain blinding. The infraorbital nerve block was performed by a single experienced anesthesiologist to ensure consistency and minimize procedural risk. Postoperative

pain was assessed over 48 hours in the neuro-intensive care unit using a standardized numerical rating scale by trained nursing staff blinded to group allocation. Intravenous tramadol was administered when the pain score exceeded 4.

Anesthetic Procedure

Upon arrival at the operating theater, patients were monitored for standard vital signs. Anesthesia was induced with intravenous propofol (2–4 mg/kg) and fentanyl 1 mcg/kg, followed by face mask ventilation. Cis-atracurium (0.15 mg/kg) was then administered, and endotracheal intubation was performed with the tube secured at the left corner of the mouth. No additional intraoperative analgesics other than fentanyl were administered. Bilateral infraorbital nerve block was performed under ultrasound guidance with the patient in the supine position and head in a neutral alignment. A 27-gauge needle was introduced from the lateral aspect toward the midline using an in-plane approach to target the infraorbital foramen, and 2 mL of local anesthetic solution was injected slowly on each side.

Group 1 (dexmedetomidine + bupivacaine): Received 2 mL of 0.5% plain bupivacaine mixed with dexmedetomidine 5 mcg per side.

Group 2 (bupivacaine): Received 2 mL of 0.5% plain bupivacaine per side.

Group 3 (control): Received 2 mL of normal saline per side.

There is no established standard dose of dexmedetomidine for infraorbital nerve block. A low fixed dose of 5 μg per side was selected to balance analgesic efficacy with hemodynamic safety, particularly in the context of neurosurgical anesthesia. Dexmedetomidine was selected over epinephrine or clonidine for its superior α2 -selectivity and intrinsic analgesic properties. Unlike vasoconstrictors, it enhances sensory block duration through both peripheral and central mechanisms, offering more potent and predictable opioid-sparing effects.

During abdominal fat pad harvesting, anesthesia was maintained with volatile anesthetics in an air-oxygen mixture to achieve a minimum alveolar concentration (MAC) of 1.2–1.5, to ensure an adequate depth of anesthesia. Therefore, hemodynamic changes meeting the above criteria were considered more likely to reflect inadequate analgesia (nociceptive stimulation) rather than insufficient anesthetic depth. Cis-atracurium was continuously infused at 1–2 mcg/kg/min and discontinued after the fat pad was secured.

In all groups, an additional 25 mcg of fentanyl was administered if the heart rate increased by ≥20 beats per minute and/or if blood pressure increased by ≥20% from the preoperative baseline. Neuromuscular blockade was reversed at the end of surgery, and extubating was performed with the patient in a slightly head-up position. Patients were then transferred to the neuro-intensive care unit (neuro-ICU). Postoperative pain was assessed in the neuro-ICU during the first 48 hours using a standardized pain assessment form developed for nursing staff. If the pain score (by numerical rating scale) exceeded 4, intravenous tramadol 50 mg was administered.

Endpoints

The endpoints of this study included both intraoperative and postoperative outcomes. Intraoperative outcomes comprised total intraoperative fentanyl consumption (μg), defined as the total dose of fentanyl administered during endoscopic transsphenoidal surgery. Intravenous fentanyl (25 μg) was administered when either the heart rate increased by ≥20 beats per minute from baseline and/or blood pressure increased by ≥20% from baseline. The time to first rescue dose of intravenous fentanyl was defined as the time interval from completion of the infraorbital nerve block (after induction of anesthesia) to the administration of the first additional dose of fentanyl.

Postoperative outcomes included pain scores assessed over 48 hours after surgery using a numerical rating scale. Postoperative analgesic requirements were evaluated by total tramadol consumption in the neuro-intensive care unit (neuro-ICU) and the time to first tramadol administration, defined as the time from completion of surgery to the first dose of tramadol. Additional analgesic use, including paracetamol and ibuprofen, was also recorded. Adverse events related to the intervention, including bradycardia and hypotension, were monitored and documented. Hypotension was defined as a decrease in mean arterial pressure of more than 20% from baseline or systolic blood pressure <90 mmHg. Bradycardia was defined as a heart rate <50 beats per minute.

Statistical Analysis

Statistical analyses were performed using STATA version 16.1. Sample size estimation was based on pilot data indicating mean fentanyl use of 200 ± 25 mcg without IONB and 162.5 ± 12.5 mcg with IONB. Using one-way ANOVA for three groups, 18 patients per group were required to detect a significant difference. To compensate for an anticipated 15% dropout, 63 patients were enrolled.

Following randomization, 16 patients were excluded due to withdrawal of consent (n = 6), change in surgical procedure (n = 4), or intraoperative requirement for a navigation system (n = 6), all of which were considered protocol deviations. Therefore, a per-protocol analysis was conducted on the remaining 47 patients (Figure 1).

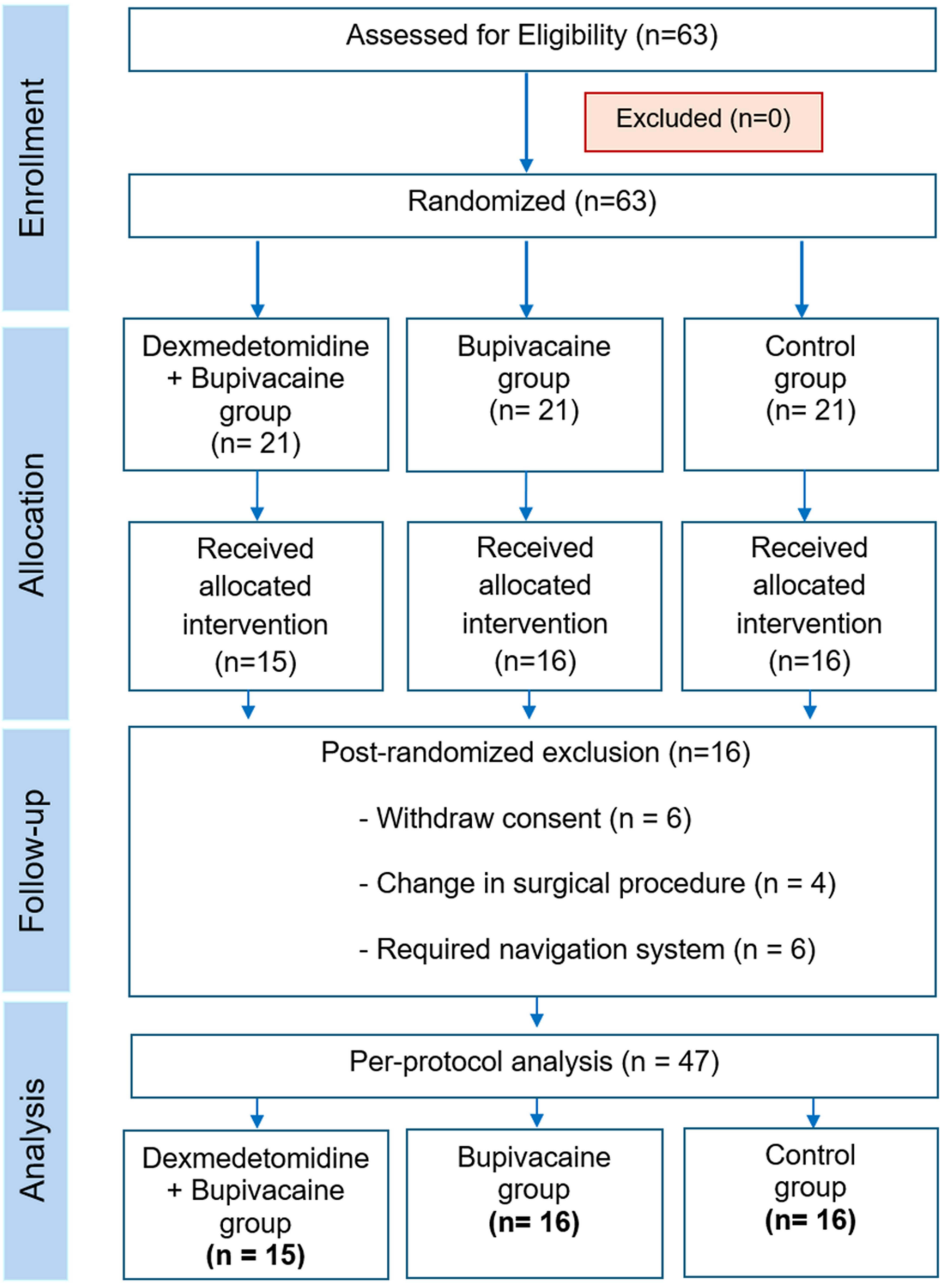

Figure 1 CONSORT flow diagram of patient enrollment, randomization, allocation, follow-up, and analysis. Bold text indicates the number of patients included in the final per-protocol analysis. Sixty-three patients were randomized equally into three groups. After randomization, 6 participants in the dexmedetomidine + bupivacaine group, 5 in the bupivacaine group, and 5 in the control group discontinued the intervention and were excluded. The remaining patients (n = 15, 16, and 16, respectively) were included in the final per-protocol analysis.

Categorical variables were compared using Fisher's exact test, and continuous variables were analyzed using one-way ANOVA or the Kruskal–Wallis test, depending on data distribution. Differences in fentanyl and tramadol dosages were analyzed using Gaussian regression, adjusting for operative time due to baseline differences. Postoperative pain scores were compared across groups using a mixed-effects model for repeated measures. A p-value of < 0.05 was considered statistically significant.

Additional

The AI tool "ChatGPT Go" was used for English grammar correction. All authors have reviewed, edited, and approved the full manuscript after AI-assisted correction. They take full responsibility for its content.

Results

A total of 47 cases were enrolled to this study. The patients were randomly into three groups. 15 (32.0%) cases received dexmedetomidine + bupivacaine, 16 (34.0%) cases received only bupivacaine, and the remaining cases (34.0%) received normal saline.

Demographic data are shown in Table 1. One statistically significant difference of operative time was indicated between groups ($p < 0.001$). This result occurred by chance due to the randomization sequence. The adjusted analysis accounting for operative duration was performed to minimize its confounding effect on fentanyl consumption.

Form Table 2, patients who received dexmedetomidine + bupivacaine had significantly lower intraoperative fentanyl requirements compared to those receiving bupivacaine alone and the control group, with a statistically significant difference ($p < 0.001$). However, although the dexmedetomidine + bupivacaine group demonstrated the longest time to first fentanyl administration, the difference did not reach statistical significance when compared with the bupivacaine-only and control groups ($p = 0.274$).

Table 1 Patient Demographics Data

Variables	Dexmedetomidine + Bupivacaine	Bupivacaine	Control
	n=15	n=16	n=16
Age (year)	47.5 ± 13.9	54.0 ± 16.2	54.0 ± 10.0
Male	5 (33.3)	7 (43.8)	8 (50.0)
BMI (kg/m2)	23.7 ± 3.9	25.3 ± 4.3	24.1 ± 3.8
DM, n (%)	2 (13.3)	5 (31.3)	1 (6.3)
AI	9 (60)	8 (50)	7 (43.8)
Prednisolone used	8 (53.3)	7 (43.8)	4 (25.0)
ASA			
-Class I	1 (6.7)	2 (12.5)	0 (0)
-Class II	12 (80)	9 (56.3)	10 (62.5)
-Class III	2 (13.3)	5 (31.3)	6 (37.5)
Tumor size			
-Microadenoma	2 (13.3)	3 (18.8)	1 (6.3)
-Macroadenoma	13 (86.7)	13 (81.30)	15 (93.8)

(*Continued*)

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Table 1 (Continued).

Variables	Dexmedetomidine + Bupivacaine	Bupivacaine	Control
Tumor functioning	3 (20)	6 (37.5)	3 (18.8)
Acromegalic appearance	2 (13.3)	4 (25)	1 (6.3)
Operation			
-ETSS	12 (80)	12 (75)	14 (87.5)
-Re-ETSS	3 (20)	4 (25)	2 (12.5)
Operative time* (min)	244.9 ± 40.2	228.1 ± 54.6	223.1 ± 114.4
Duration of extubating (min)	12.4 ± 6.9	15.6 ± 4.9	15.5 ± 7.3

Notes: X (X); number (percent %), X ± X; Mean ± Standard deviation, *Operative time was statistically significant between groups p < 0.001, Statistically significant at p<0.05.
Abbreviations: Kg, Kilogram; m, meter; min, minutes; BMI, Body Mass Index; DM, Diabetes mellitus; AI, Adrenal insufficiency; ASA class, American society of anesthesiologist classification; ETSS, endoscopic transsphenoidal surgery.

Table 2 Intra-Operative Fentanyl Administration

Variables	Dexmedetomidine + Bupivacaine	Bupivacaine	Control	p
	n=15	n=16	n=16	
Fentanyl dosage (mcg)	106.0 ± 36.2	145.9 ± 47.8	175.6 ± 101.5	<0.001
Fentanyl dosage (mcg/kg)	1.80 ± 0.67	2.26 ± 0.78	2.83 ± 1.87	<0.001
Time to first Fentanyl (minute)	128.2 ± 72.0	102.5 ± 67.0	90.3 ± 46.8	0.274

Notes: X ± X; Mean ± Standard deviation, statistically significant at p<0.05.
Abbreviations: mcg, Microgram; Kg, Kilogram.

According to the adjusted mean differences compared between the three groups presented in Table 3. (with the control group as reference), the mean total fentanyl dosage was significantly lower in the dexmedetomidine + bupivacaine group by 81.9 mcg. Similarly, the mean fentanyl dosage used per kilogram was significantly reduced by 1.12 mcg/kg in the dexmedetomidine + bupivacaine group. Additionally, the dexmedetomidine-added group demonstrated a significantly longer mean time to first fentanyl administration (+33.9 minutes) compared to bupivacaine-only and control. The bupivacaine-only group showed no significant reduction in fentanyl requirements compared to controls, although the time to first fentanyl administration was slightly prolonged.

From Figure 2, postoperative pain scores assessed at multiple time from 0, 8, 16, 24, 36, and 48 hours showed no statistically significant differences among the three groups (Table 4). Median pain scores gradually declined over time in all groups. Although the dexmedetomidine + bupivacaine group appeared to have slightly lower pain scores at later time points, particularly at 16 and 24 hours, these differences were not statistically significant. Based on the accompanying repeated measure regression coefficients (Supplementary Table 1), all three groups demonstrated significant reductions in pain scores over time ($p < 0.001$ for all groups). The estimated pain score decrease was −0.63 in the dexmedetomidine + bupivacaine group, −0.53 in the bupivacaine group, and −0.73 in the control group. However, the between-group comparison ($p = 0.248$) showed no significant difference in pain reduction trajectories, consistent with the similar downward trends observed across all groups.

For additional postoperative analgesia, all patients received paracetamol. Only one patient in the control group received both paracetamol and ibuprofen. There was no statistically significant difference in tramadol use among the three groups (Supplementary Table 2).

Table 3 Mean Difference of Fentanyl Administration Dosage (Adjusted with Operative Time)

	Mean Difference	P	95% CI	Adjusted Mean Difference	P	95% CI
Total fentanyl dosage (mcg)						
-dexmedetomidine + bupivacaine	−68.6	0.007	−119.3, −19.9	−81.9	<0.001	−121, −42.9
-bupivacaine	−29.7	0.228	−78.6, 19.2	−32.5	0.093	−70.6, 5.62
-control	reference					
Fentanyl (mcg/kg)						
-dexmedetomidine + bupivacaine	−1.02	0.060	−2.09, 0.04	−1.12	0.037	−2.19, −0.70
-bupivacaine	−0.57	0.312	−1.68, 0.53	−0.51	0.351	−1.59, 0.56
-control	reference					
Time to first Fentanyl (minutes)						
-dexmedetomidine + bupivacaine	37.9	<0.001	30.2, 45.5	33.9	<0.001	26.1, 41.7
-bupivacaine	12.2	0.001	5.3, 19.1	9.1	0.011	2.1, 16.1
-control	reference					

Note: statistically significant at p<0.05.
Abbreviations: mcg, Microgram; Kg, Kilogram.

The adjusted analysis showed that patients receiving dexmedetomidine plus bupivacaine required significantly less total tramadol (Supplementary Table 3), with an adjusted mean difference of −10.2 mg (p = 0.004), compared to the control group. However, tramadol dosage per kilogram did not significantly differ among the groups. Notably, the time to

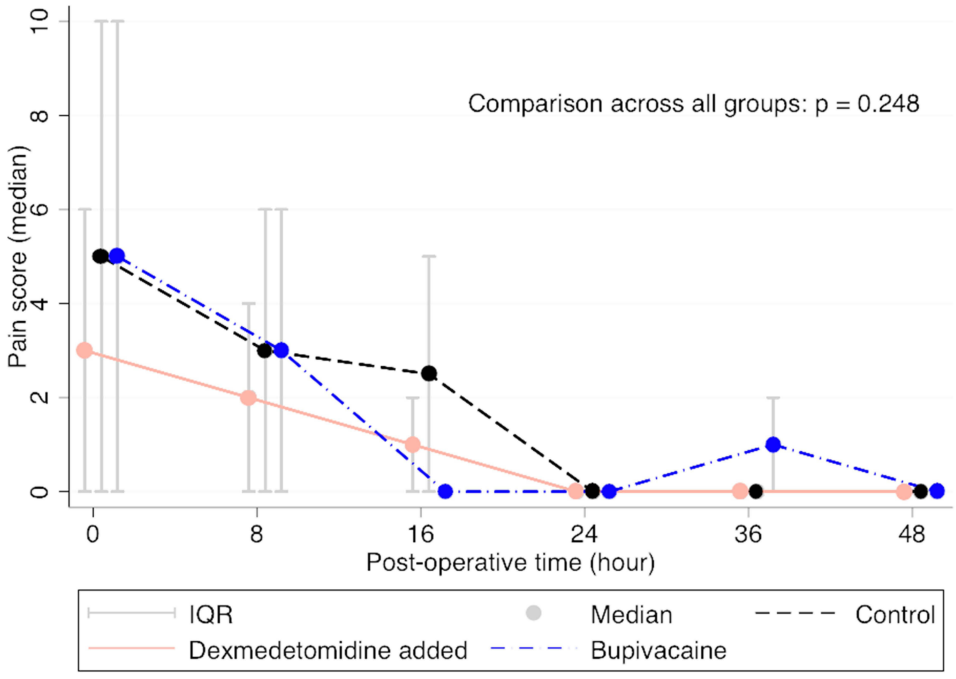

Figure 2 Median postoperative pain scores with interquartile ranges (IQR) at 0, 8, 16, 24, 36, and 48 hours after endoscopic transsphenoidal surgery. Pain score trends are shown for the dexmedetomidine + bupivacaine group, the bupivacaine group, and the control group. No statistically significant difference in overall postoperative pain was observed among the three groups (p = 0.248).

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Table 4 Median Postoperative Pain Scores with Interquartile Ranges (IQR) at 0, 8, 16, 24, 36, and 48 hours After Endoscopic Transsphenoidal Surgery

Time	Dexmedetomidine + Bupivacaine	Bupivacaine	Control	p
	n=15	n=16	n=16	
At 0 hour	5 (2,7)	3 (0,5)	5 (2,7)	0.202
At 8 hours	3 (0,5)	2 (0,4)	3 (2,5)	0.346
At 16 hours	0 (0,3)	1 (0,3)	3 (0,4)	0.533
At 24 hours	0 (0,2)	0 (0,1)	0 (0,2)	0.816
At 36 hours	1 (0,2)	0 (0,2)	0 (0,3)	0.577
At 48 hours	0 (0,1)	0 (0,3)	0 (0,0)	0.432

Notes: X (X, Y); median (p25, p75), statistically significant at p<0.05.

first tramadol administration was significantly prolonged in the dexmedetomidine plus bupivacaine group by 31.7 minutes ($p < 0.001$), whereas it was significantly shorter in the bupivacaine-only group by 45.0 minutes ($p < 0.001$) compared to the control.

In this study, no complications related to IONB occurred. Regarding drug-related adverse effects, no bradycardia was observed in any of the groups. Intraoperative hypotension was observed at similar rates across the groups—46.7% in the dexmedetomidine + bupivacaine group, 43.8% in the bupivacaine group, and 50.0% in the control group ($p = 1.000$), indicating comparable safety profiles regarding these adverse effects.

Discussion

Using a combination of bupivacaine and dexmedetomidine as a targeted refinement of IONB aimed at enhancing intraoperative analgesia significantly reduces intraoperative fentanyl requirements during ETSS. Patients in this group required substantially lower total fentanyl doses, both in absolute terms and per body weight, compared to those receiving bupivacaine alone or no block. Although unadjusted comparisons may be influenced by differences in operative time, adjusted analyses controlling for operative duration confirmed that the reduction in fentanyl use was independent of operative time, supporting a true analgesic effect of the intervention.

The time to first fentanyl administration was prolonged in the dexmedetomidine group, suggesting enhanced and longer-lasting intraoperative analgesic effects. Additionally, the time to first postoperative tramadol administration was also significantly delayed in this group, further supporting the extended duration of analgesia provided by dexmedetomidine. However, despite these intra- and postoperative benefits, pain scores remained comparable across all groups, and no significant differences were observed in the trajectories of pain reduction over time. The observed benefits of dexmedetomidine-added IONB were primarily limited to intraoperative opioid reduction and delayed rescue analgesia, without significant improvement in postoperative pain scores. This suggests that its clinical utility may be most relevant for intraoperative analgesia and early recovery rather than sustained postoperative pain control.

There have been relatively few studies evaluating the use of bilateral IONB with bupivacaine for postoperative pain control in transsphenoidal surgery. In 2005, McAdam et al reported a case of a patient receiving bilateral IONB with 0.25% bupivacaine for transsphenoidal resection experienced mild pain and no additional analgesics.[7] Similarly, Jonnavit-hula et al found that bilateral IONB in ETSS significantly prolonged the time to rescue analgesic use compared to those who did not receive the block.[8] These findings are consistent with the results of our result, supporting the efficacy of IONB in reducing pain associated with transsphenoidal procedures.

Pain in ETSS is multimodal, originating from nasal cavity and sphenoid sinus dissection, packing, and facial pain. While the infraorbital nerve primarily innervates the midface, its medial-inferior branches may contribute sensory coverage to parts of the nasal septum and vestibule, particularly the anterior-inferior regions. Thus, although IONB

may not fully anesthetize all structures involved in ETSS, it can still provide meaningful analgesia by reducing nociceptive input from the anterior-inferior nasal septum, nasal floor, and upper lip—areas that are commonly manipulated during the initial surgical approach. This partial blockade can significantly lessen the overall pain burden, even if deeper structures like the sphenoid sinus are not directly covered. By targeting these key anterior areas, IONB contributes to the attenuation of cumulative pain signals, supporting its role as part of a multimodal analgesic strategy.

Dexmedetomidine's role is a critical factor in enhancing the success of such blocks. The reduction in fentanyl consumption observed in the dexmedetomidine group is consistent with its known pharmacological effects as an α_2-adrenergic agonist. Importantly, this effect remained significant after adjustment for operative time, despite longer procedures in this group. Because of the benefit for prolongs and enhances the local anesthetic effect, making the IONB more potent and longer lasting. Even if some pain signals from the anterior ethmoidal nerve still reach the brain, the reduced input from the infraorbital nerve -innervated areas can significantly modulate the patient's overall perception of pain, thereby lowering their subjective pain scores and, consequently, their objective fentanyl requirement.

Additionally, this study found no significant adverse hemodynamic events (hypotension and bradycardia) from adding dexmedetomidine to bupivacaine in IONB. The relatively high incidence of intraoperative hypotension observed across all groups may reflect the effects of general anesthesia and anesthetic maintenance protocols rather than the specific impact of IONB or dexmedetomidine. This observation was consistent with a previous study by Sumalatha et al, which also found that 0.5 mcg/kg of dexmedetomidine added to 0.25% bupivacaine in IONB for children undergoing cleft lip surgery prolonged analgesic time without significant hemodynamic side effects.[17] Although the pain mechanisms in these procedures are predominantly superficial and somatic, which differ from the more complex and multimodal pain associated with adult ETSS. Therefore, hemodynamics was not disturbed as they are in adult neurosurgical populations.

By significantly lowering fentanyl usage without increasing postoperative pain or complications, this approach could enhance perioperative opioid-sparing protocols, particularly important in patients at risk for opioid-related side effects, such as respiratory depression or delayed recovery. Although postoperative pain scores remained similar among groups, the improved intraoperative analgesic profile may contribute to reduced anesthetic requirements, and potentially faster emergence and recovery profiles. These findings support the selective use of regional anesthesia techniques with dexmedetomidine to optimize multimodal analgesia in ETSS settings. As no significant differences were observed in postoperative pain scores or overall recovery outcomes, its clinical benefit appears to be primarily intraoperative, and its role in postoperative analgesia remains limited.

This study possesses several notable strengths that enhance the validity and clinical applicability of its findings. Most importantly, it was designed as a prospective, randomized, double-blind controlled trial, which minimizes bias and strengthens the reliability of the results. The primary outcome, total intraoperative fentanyl requirement, was an objective and quantifiable measure, allowing for accurate comparisons across groups. By reporting both absolute and weight-adjusted fentanyl doses, the analysis accounted for individual patient variability and improved the generalizability of the findings. The study also incorporated postoperative pain assessments at multiple time points, providing a comprehensive view of analgesic effects beyond the intraoperative period.

This study has several limitations. Notably, it was analyzed using a per-protocol approach due to post-randomization exclusions, which may introduce attrition bias and limit the preservation of randomization. The final analyzed sample size was smaller than initially calculated, which may have reduced the statistical power of the study, particularly for secondary outcomes. While the reduction in intraoperative opioid consumption may be clinically relevant in the context of neuro-anesthesia, its impact on postoperative outcomes was not demonstrated in this study. Therefore, the absence of significant differences in postoperative pain scores should be interpreted with caution. Second, the use of infraorbital nerve block with dexmedetomidine in ETSS is a novel approach, and while the results are encouraging, larger studies are needed to confirm its safety and efficacy. Third, the study primarily focused on intraoperative opioid use and reported only the absence of major hemodynamic complications such as hypotension and bradycardia. Other potential adverse effects associated with nerve blocks or dexmedetomidine were not explicitly assessed or reported. Additionally, the small sample size reflects the exploratory nature of this study, highlighting the need for larger, multicenter trials to validate these findings.

Conclusion

Bilateral infraorbital nerve block with dexmedetomidine-added bupivacaine significantly reduced intraoperative fentanyl consumption and prolonged the time to rescue analgesic administration during endoscopic transsphenoidal surgery, without compromising hemodynamic stability compared with standard care. Although postoperative pain scores did not differ among groups, the demonstrated intraoperative opioid-sparing effect may have important implications for recovery and perioperative management. These findings support the use of dexmedetomidine as an adjuvant to enhance the efficacy of infraorbital nerve block as part of a multimodal analgesic strategy in endoscopic transsphenoidal surgery.

Data Sharing Statement

The authors intend to share individual deidentified participant data. The data that will be shared include demographic characteristics, intraoperative fentanyl consumption, postoperative pain scores, and postoperative analgesic requirements. The study protocol and statistical analysis plan will also be made available upon reasonable request.

Data will be available from the corresponding author upon reasonable request, for researchers who provide a methodologically sound proposal. Data will be available beginning after publication and ending 3 years after publication.

Disclosure

The authors report no conflicts of interest in this work.

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