

Comparison of the Effects of Clonidine Added to 0.25% Bupivacaine versus Bupivacaine Alone in Scalp Block for Supratentorial Craniotomies: A Prospective Randomized Clinical Trial

¹Dr. Riddhi Pinalkumar Gandhi, Senior Resident, Department of Anaesthesiology, B.J. Medical College, Ahmedabad, India

²Dr. Bijal M. Shah, Associate Professor, Department of Anaesthesiology, The Gujarat Cancer and Research Institute, B.J. Medical College, Ahmedabad, India

³Dr. Neeta Gosai, Professor and Head of Department of Anaesthesiology, The Gujarat Cancer and Research Institute, B.J. Medical College, Ahmedabad, India

Corresponding Author: Dr. Riddhi Pinalkumar Gandhi, Senior Resident, Department of Anaesthesiology, B.J. Medical College, Ahmedabad, India

How to citation this article: Dr. Riddhi Pinalkumar Gandhi, Dr. Bijal M. Shah, Dr. Neeta Gosai, “Comparison of the Effects of Clonidine Added to 0.25% Bupivacaine versus Bupivacaine Alone in Scalp Block for Supratentorial Craniotomies: A Prospective Randomized Clinical Trial”, IJMACR– October– 2026, Volume – 9, Issue – 5, P. No. 201 – 207.

Open Access Article: © 2026 Dr. Riddhi Pinalkumar Gandhi, et al. This is an open access journal and article distributed under the terms of the creative common’s attribution license (<http://creativecommons.org/licenses/by/4.0>). Which allows others to remix, tweak, and build upon the work non - commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: Application of cranial pins and craniotomy incision produce intense noxious stimuli that can precipitate hemodynamic instability and elevate intracranial pressure. Scalp block with local anaesthetic attenuates this response, but the analgesic effect of bupivacaine alone is relatively short-lived. Clonidine, an α_2 -adrenergic agonist, has been shown to prolong peripheral nerve block and improve haemodynamic stability when used as an adjuvant. This study compared the perioperative haemodynamic effects and postoperative analgesic efficacy of clonidine added to

0.25% bupivacaine versus 0.25% bupivacaine alone in scalp block for supratentorial craniotomy.

Methods: In this prospective randomized clinical trial conducted at the Department of Anaesthesia, Gujarat Cancer and Research Institute, Ahmedabad (2023–2025), 60 ASA grade I–II adult patients (18–65 years) undergoing elective supratentorial craniotomy were randomly allocated to two groups of 30. Group A received scalp block with 0.25% bupivacaine (20 mL) plus clonidine 2 μ g/kg; Group B received 0.25% bupivacaine (20 mL) alone. Heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were recorded from

pin insertion, intra op and postoperative period, also postoperative pain was assessed using the Visual Analogue Scale (VAS) for four hours. Data were analysed using Student's t-test, with $p < 0.05$ considered significant.

Results: Baseline demographic and haemodynamic parameters were comparable between groups ($p > 0.05$). From pin insertion onward, HR, SBP, DBP, and MAP were significantly lower and more stable in Group A than in Group B at nearly all intraoperative and postoperative time points ($p < 0.05$, with several comparisons reaching $p < 0.001$). Postoperative VAS scores were significantly lower in Group A than Group B at every measured interval in the first four postoperative hours (e.g., 1st hour: 0.37 ± 0.49 vs 2.13 ± 0.34 ; $p = 0.0012$). No adverse events (bradycardia, hypotension, nausea/vomiting, respiratory depression, or arrhythmia) were recorded in either group.

Conclusion: Addition of clonidine as an adjuvant to 0.25% bupivacaine in scalp block provides superior perioperative haemodynamic stability and more prolonged, effective postoperative analgesia compared with bupivacaine alone in patients undergoing supratentorial craniotomy, without an increase in adverse effects.

Keywords: Scalp Block, Clonidine, Bupivacaine, Craniotomy, Haemodynamic Response, Postoperative Analgesia

Background

Immobilization of the head is required during neurosurgical procedures, and application of the Mayfield skull-pin clamp produces an intense noxious stimulus with a profound sympathetic stimulating effect. In patients with impaired cerebral autoregulation, the resulting surge in systemic blood pressure can produce

an abrupt rise in intracranial pressure, precipitating intracranial hypertension. Postoperative pain after craniotomy similarly produces detrimental effects on outcome, prolongs hospital stay, and increases morbidity^{1,2}.

Various anaesthetic and pharmacological techniques have been used to attenuate the haemodynamic response to skull-pin placement and incision, of which scalp block with local anaesthetic is among the most widely used. Blocking the six principal sensory nerves of the scalp — the supraorbital, supratrochlear, auriculotemporal, zygomaticotemporal, and greater and lesser occipital nerves — prevents the haemodynamic response to pin application and incisional pain, and reduces the postoperative inflammatory response.^{3,4} Local anaesthetic infiltration is an accepted practice, but its analgesic effect with bupivacaine alone is relatively short-lived⁵.

Clonidine, an α_2 -adrenergic agonist, has hypotensive and analgesic actions and has been shown to potentiate and prolong the duration of intrathecal, epidural, and various peripheral nerve blocks, including brachial plexus and peribulbar blocks.^{6,7} The systemic hypotensive effect of clonidine may additionally benefit neuroanaesthesia practice, and the pre-emptive analgesia provided by scalp block may reduce postoperative morbidity. Wajekar et al. reported improved analgesia with clonidine added to bupivacaine for scalp block in supratentorial craniotomy.⁸ Other studies have similarly evaluated clonidine and related α_2 -agonists in scalp block.⁹⁻¹²

This study was designed to evaluate the efficacy and adequacy of adding clonidine to 0.25% bupivacaine, compared with plain 0.25% bupivacaine, in scalp block for perioperative haemodynamic control and

postoperative analgesia in patients undergoing supratentorial craniotomy. The specific objectives were to evaluate the haemodynamic response to pin insertion and incision, to evaluate perioperative haemodynamic changes and complications, and to evaluate postoperative analgesia.

Methods

Study design and setting

This was a prospective, randomized control trial conducted in the Department of Anaesthesia, The Gujarat Cancer and Research Institute (GCRI), Ahmedabad, India, between 2023 and 2025, following institutional ethics board approval and written informed consent from all participants.

Participants

Sixty patients of ASA physical status I or II, aged 18–65 years, of either sex, scheduled for elective supratentorial craniotomy were enrolled.

Inclusion criteria: patients scheduled for supratentorial craniotomy; Glasgow Coma Scale 15/15; age 18–65 years; ASA I or II.

Exclusion criteria: uncontrolled hypertension, bradycardia, Ischaemic cardiac disease, Cardiac arrhythmia, or pulmonary, hepatic, or renal dysfunction; known allergy to clonidine; preoperative use of alpha-blockers; pregnancy; refusal of consent; emergency surgery; and prior history of Craniotomy.

Randomization and group allocation

Patients were randomly allocated with chit method to two groups of 30 each.

Group A received scalp block with 0.25% bupivacaine plus clonidine 2 µg/kg (total volume 20 mL).

Group B received scalp block with 0.25% bupivacaine alone (20 mL).

Anaesthetic protocol

All patients underwent a standard preanaesthetic evaluation and routine investigations. Patients were familiarized preoperatively with the Visual Analogue Scale (VAS; 0 = no pain, 10 = worst imaginable pain) for postoperative pain assessment.

Standard monitoring (pulse oximetry, electrocardiography, non-invasive blood pressure, end-tidal CO₂) was applied, and intravenous access secured. All patients were premedicated with intravenous glycopyrrolate 0.004 mg/kg and antibiotic prophylaxis. General anaesthesia was induced with fentanyl 2 µg/kg, propofol 2 mg/kg, and vecuronium 0.1 mg/kg to facilitate oral endotracheal intubation, and maintained with propofol infusion (75–100 µg/kg/h), oxygen–nitrous oxide (50:50), and vecuronium 0.01 mg/kg, with volume-controlled ventilation (tidal volume 6 mL/kg, respiratory rate 12/min).

Scalp block technique

Ten minutes before cranial pin insertion, the anaesthesiologist performed bilateral blockade of the supraorbital and supratrochlear nerves (2 mL each), zygomaticotemporal nerves (2 mL), auriculotemporal nerves (3 mL), postauricular branches of the greater auricular nerve (2 mL), and the greater and lesser occipital nerves (2 mL), using the technique described by Pinosky et al., for a total injectate volume of 20 mL.[13]. Surgeons additionally infiltrated adrenaline (1:200,000) locally at the incision site to reduce scalp bleeding.

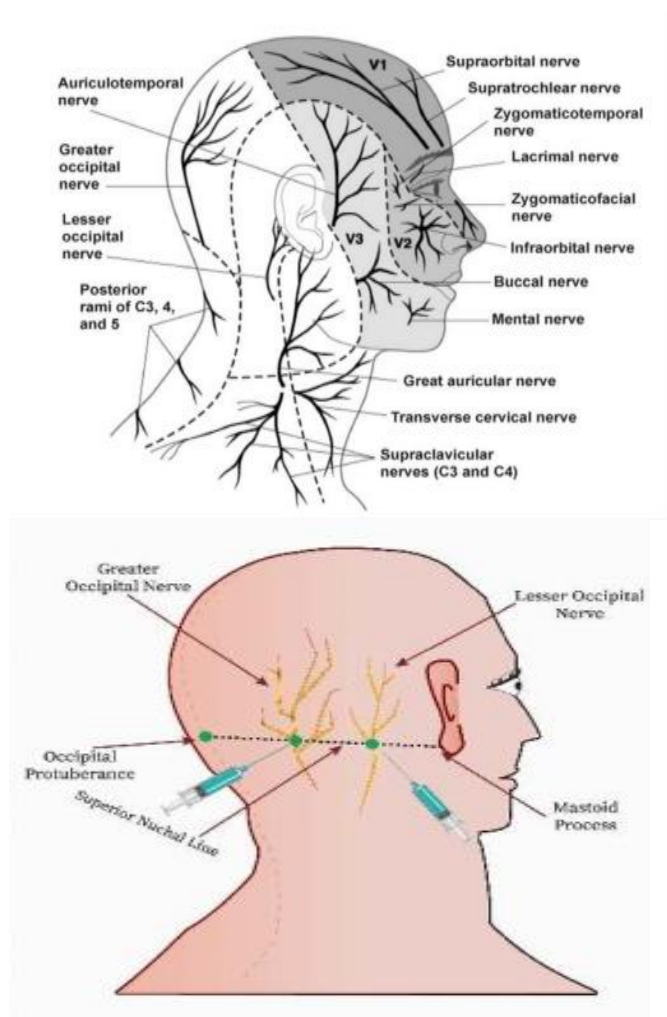
Outcome measures

The primary endpoint was comparison of intraoperative haemodynamics (HR, SBP, DBP, MAP) between groups, recorded every 5 minutes from pin insertion to dura opening and intraoperatively, with particular attention to the response to pin insertion and incision.

Secondary endpoints were postoperative haemodynamics (hourly for 4 hours), duration and quality of postoperative analgesia (VAS, verbal rating score, and rescue analgesic requirement — intravenous paracetamol 1 g when VRS > 3), and intraoperative haemodynamic complications (tachycardia, bradycardia, hypotension, hypertension).

Statistical analysis

Data were tabulated as mean $\pm$ standard deviation and analysed using Student's t-test. Microsoft Word and Excel were used to generate tables and graphs, and statistical computation was performed using socialsciencestatistics.com. A p-value < 0.05 was considered statistically significant.



Results

Sixty patients were enrolled and analysed (30 per group). Demographic characteristics — age, weight, and height — were comparable between the two groups (Table 1).

Table 1: Demographic characteristics

Variable	Group A (mean $\pm$ SD)	Group B (mean $\pm$ SD)	P value
Age (years)	38.8 $\pm$ 8.38	38.7 $\pm$ 5.58	0.898*
Weight (kg)	58.2 $\pm$ 6.2	58.5 $\pm$ 6.17	NS
Height (cm)	154.03 $\pm$ 5.88	154.9 $\pm$ 7.02	0.606

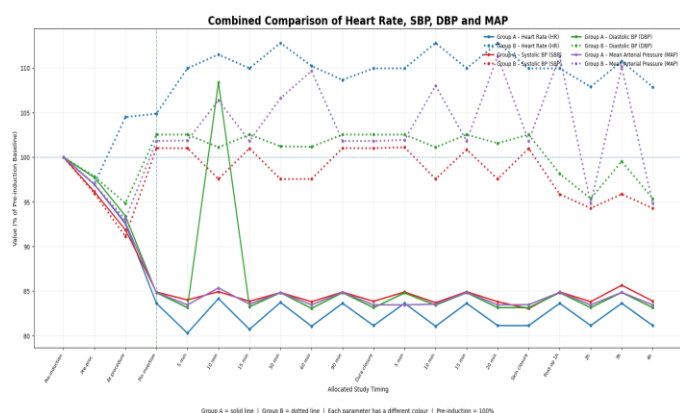
Haemodynamic response

Heart rate, SBP, DBP, and MAP were statistically similar between groups at baseline (pre-induction and pre-procedural, $p > 0.05$). From pin insertion onward, all four parameters were significantly higher in Group B than Group A at essentially every intraoperative and postoperative time point measured ($p < 0.05$; several comparisons $p < 0.001$). Representative values at key time points are summarized in Table 2.

Table 2: Heart rate, blood pressure and MAP at key time points

Time point	HR: A vs B (bpm)	SBP: A vs B (mmHg)	DBP: A vs B (mmHg)	MAP: A vs B (mmHg)
Pin insertion	66.0 vs 81.1 ($p < 0.00001$)	110.2 vs 130.5 ($p < 0.0001$)	60.9 vs 74.3 ($p < 0.0001$)	77.3 vs 93.0 ($p = 0.028$)
5 min post-pin	63.9 vs 85.1 ($p < 0.00001$)	109.1 vs 130.5 ($p = 0.0011$)	59.7 vs 74.3 ($p = 0.022$)	76.1 vs 93.1 ($p < 0.00001$)
10 min post pin	66.4 vs 86.2 ($p = 0.0002$)	110.2 vs 126.06 ($p = 0.0002$)	77.7 vs 73.3 ($p = 0.0001$)	77.7 vs 97.2 ($p = 0.0002$)
30 min (dura)	66.1 vs 87.26 ($p = 0.0002$)	110.13 vs 126.07 ($p = 0.0002$)	60.86 vs 73.4 ($p = 0.0002$)	77.2 vs 97.4 ($p = 0.0002$)

opening)		(p=0.0001)	(p=0.0001)	
Dura closure	64.1 vs 85.1 (p=0.0012)	108.9 vs 130.5 (p<0.0001)	59.7 vs 74.3 (p<0.0001)	76.0 vs 93.1 (p=0.0002)
Skin closure	64.06 vs 85.06 (p=0.0002)	107.8 vs 130.5 (p=0.0001)	59.66 vs 74.33 (p=0.0001)	76.06 vs 93.8 (p=0.0001)
Postop 1st hour	66.0 vs 85.6 (p=0.0011)	110.2 vs 123.9 (p=0.0011)	60.9 vs 71.2 (p<0.0001)	77.3 vs 101.7 (p=0.0001)
Postop 4th hour	64.1 vs 83.4 (p=0.0023)	108.9 vs 121.8 (p=0.0013)	59.7 vs 69.1 (p<0.0001)	76.0 vs 86.7 (p=0.029)



Postoperative analgesia

VAS scores were significantly lower in Group A than Group B at every postoperative interval assessed (Table 3), indicating more prolonged and effective analgesia with clonidine as an adjuvant.

Table 3: Postoperative VAS scores

Postoperative interval	Group A (mean $\pm$ SD)	Group B (mean $\pm$ SD)	p-value
Immediate recovery	0.10 $\pm$ 0.30	0.53 $\pm$ 0.90	0.0001
1st hour	0.37 $\pm$ 0.49	2.13 $\pm$ 0.34	0.0012
2nd hour	0.90 $\pm$ 0.30	2.43 $\pm$ 0.50	0.0001
3rd hour	1.83 $\pm$ 0.46	4.26 $\pm$ 0.82	0.0024
4th hour	4.40 $\pm$ 0.85	5.23 $\pm$ 1.01	0.0025

Adverse events

No episodes of nausea/vomiting, bradycardia, hypotension, dry mouth, respiratory depression, or arrhythmia were recorded in either group.

Discussion

This randomized trial found that adding clonidine 2 μ g/kg to 0.25% bupivacaine for scalp block produced significantly better perioperative haemodynamic stability and more prolonged postoperative analgesia than bupivacaine alone in patients undergoing supratentorial craniotomy, without increasing adverse effects.

The improved haemodynamic profile in the clonidine group is consistent with two proposed mechanisms: potentiation and prolongation of the local anaesthetic block, which blunts noxious stimuli at pin insertion, incision, and closure; and a direct pharmacological effect of clonidine, which locally inhibits C-fibre conduction more than A- α fibre conduction, exerts a vasoconstrictor effect on α_2 receptors that alters local anaesthetic redistribution, and facilitates peripheral nerve block through hyperpolarization of cationic current activation.

These findings are consistent with prior work. Shrikant et al. (2014)¹⁴. Similarly found that clonidine 2 μ g/kg added to infiltrative scalp block potentiated block action, with analgesia lasting 960 ± 120 minutes. Senapathi et al. (2019)¹⁵. reported that clonidine added to levobupivacaine 0.25% for scalp block significantly reduced intraoperative fentanyl requirement, prolonged time to first patient-controlled morphine dose, and lowered postoperative morphine consumption and pain scores. Khurana et al. (2015)¹⁶ and Bithal et al.¹⁷. similarly demonstrated that pretreatment with clonidine, dexmedetomidine, or local anaesthetic infiltration blunted the tachycardic response to skull-pin insertion, while Misra et al.¹⁸. found scalp block with ropivacaine

more effective than systemic dexmedetomidine for this purpose.

The blood pressure findings parallel those of Maharani et al. (2023)¹⁹, who found that a bupivacaine–clonidine combination lowered postoperative cortisol and pain scores compared with dexamethasone, and Vidhya et al. (2020)²⁰, who reported that patients without regional scalp block had marked SBP elevation at pin application compared with those receiving scalp block.

For postoperative analgesia, the present findings are concordant with Wajekar et al. (2016)⁸, who found clonidine prolonged analgesia and reduced rescue analgesic requirement without compromising haemodynamic stability, and with a meta-analysis by Ardyan Wardhana et al. (2019)⁹ of 10 randomized trials (n = 551) showing that adjunctive analgesic techniques, including scalp block with clonidine, significantly reduced early postoperative pain and 24-hour opioid consumption.

Persistent intraoperative tachycardia and hypertension are of particular concern in neurosurgical patients because they may elevate intracranial pressure, reduce cerebral perfusion pressure, and predispose to ischaemic injury; the more stable haemodynamic profile observed with clonidine as an adjuvant is therefore of direct clinical relevance beyond its statistical significance.

Conclusion

In patients undergoing elective supratentorial craniotomy, the addition of clonidine 2 µg/kg to 0.25% bupivacaine in scalp block provided superior perioperative haemodynamic stability and more prolonged, effective postoperative analgesia compared with 0.25% bupivacaine alone, with a comparable safety profile. These findings support clonidine as a useful

adjuvant to local anaesthetic scalp block for supratentorial craniotomy.

Declarations

Ethics approval and consent to participate: Institutional ethics board approval was obtained and written informed consent was collected from all participants.

References

1. Flexman AM, Ng JL, Gelb AW. Acute and chronic pain following craniotomy. *Curr Opin Anaesthesiol.* 2010;23(5):551-557.
doi:10.1097/ACO.0b013e32833e15b9.
2. Doblar DD, Lim YC, Baykan N, Fisher W, Hadley M. Preventing the hypertensive response to skull pin insertion: a comparison of four methods. *J Neurosurg Anesthesiol.* 1994;6(4):314.
doi:10.1097/00008506-199410000-00046.
3. Osborn I, Sebeo J. “Scalp Block” During Craniotomy: A Classic Technique Revisited. *J Neurosurg Anesthesiol.* 2010;22:187-194.
4. Guilfoyle MR, Helmy A, Duane D, Hutchinson PJ. Regional scalp block for postcraniotomy analgesia: a systematic review and meta-analysis. *Anesth and Analg.* 2013;116(5):1093-1102.
doi:10.1213/ANE.0b013e3182863c22.
5. Law-Koune JD, Szekely B, Fermanian C, Peuch C, Liu N, Fischler M. Scalp infiltration with bupivacaine plus epinephrine or plain ropivacaine reduces postoperative pain after supratentorial craniotomy. *J Neurosurg Anesthesiol.* 2005;17(3):139-143.
6. Gabriel JS, Gordin V. Alpha 2 agonists in regional anesthesia and analgesia. *Curr Opin Anaesthesiol.* 2001;14:751-753.
7. Dash SK, Gosavi KS, Parikh HG, Kondilkar B. Effect of clonidine, by infiltration and by

- intravenous route, on scalp block for supratentorial craniotomy. S Afr J Anaesthesiol Analg. 2010;16:13-21.
8. Wajekar AS, Oak SP, Shetty AN, Jain RA. A prospective, comparative, randomised, double blind study on the efficacy of addition of clonidine to 0.25% bupivacaine in scalp block for supratentorial craniotomies. Indian J Anaesth. 2016;60(1):39-43.
 9. Wardhana A, Sudadi S. Scalp block for analgesia after craniotomy: a meta-analysis. Indian J Anaesth. 2019;63(11):886-894. doi: 10.4103/ ija.IJA_315_19.
 10. Yang Y, Ou M, Zhou H, et al. Effect of scalp nerve block with ropivacaine on postoperative pain in patients undergoing craniotomy: a randomized, double blinded study. Sci Rep. 2020;10(1):2529. doi:10.1038/s41598-020-59370-2.
 11. Sahana BN, Radhapuram SD, Samantaray A, Hemanth N, Pasupuleti H, Mangu HR. Comparison of effects of dexmedetomidine added to ropivacaine versus ropivacaine alone infiltration scalp block for attenuation of the haemodynamic response to skull pin placement in neurosurgical procedures: a double-blind, randomised clinical trial. Indian J Anaesth. 2021;65(9):782-788. doi:10.4103/ija.ija_450_21.
 12. Panchal SM, Gosavi KS, Kudre KR. Comparison of dexmedetomidine and clonidine as an adjuvant to bupivacaine in scalp block for supratentorial craniotomy surgery: a prospective, randomised Indian study. Int J Adv Res. 2023;11:1054-1062. doi:10.21474/IJAR01/17163.
 13. Bagle A, Raj A, B U RP, Kale A. Comparison of the effect of scalp block with ropivacaine vs. ropivacaine and clonidine on postoperative pain in patients undergoing craniotomy surgery under general anesthesia. Cureus. 2024;16(8):e67342. doi:10.7759/cureus.67342.
 14. Shrikant O. A prospective, comparative, randomized study to evaluate the safety and efficacy of scalp block with bupivacaine and clonidine versus bupivacaine only for supratentorial craniotomies. J Neuroanaesthesio and critic care. 2014;1:85.
 15. Senapathi, T. G. A., Syamsudin, J. B. T., Mahaalit, I. G. N., Ryalino, C., & Pradhana, A. P. (2019). The Effectivity of Clonidine Addition to Levobupivacaine 0.25% for Scalp Block in Patients Underwent Craniotomy Surgery. Journal of Global Pharma Technology, 11(8 Suppl), 224–228.
 16. Khurana, P., et al. (2015). Attenuation of Hemodynamic Response to Skull Pin Head Holder Application: Comparison between Clonidine and Dexmedetomidine. Anesthesia: Essays and Researches, 9(1), 65-70.
 17. Bithal, P., et al. (2003). Hemodynamic response to skull pins application in children. Neurology India, 51(1), 19-21.
 18. Misra, S., et al. (2020). Comparison of Dexmedetomidine Infusion versus Scalp Block with 0.5% Ropivacaine in Attenuating Hemodynamic Response to Skull Pin Insertion. Journal of Neurosurgical Anesthesiology, 32(4), 343-348.
 19. Maharani ND, Fuadi A, Halimi RA: Comparison of the effect of scalp block analgesia bupivacaine 0.25% and clonidine 2 µg/kg with bupivacaine 0.25% and dexamethasone 8 mg on cortisol levels and Numeric Rating Scale in craniotomy tumour. Med J Malaysia, 2023, 78:808-14.
 20. Vidhya, R., et al. (2020). Efficacy of scalp block in attenuating hemodynamic response during

craniotomy. Asian Journal of Neurosurgery, 15(1),
70-75.