Original Article

Ropivacaine instillation through subgaleal drain: A novel approach for acute post-craniotomy pain

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ABSTRACT

Background and Aims: Post-craniotomy pain has often been overlooked and undertreated. Various classes of analgesic drugs have been used, not without limitations. Therefore, we planned to study the novel technique of wound instillation of ropivacaine through the surgical drain in patients undergoing supratentorial craniotomy to study its effect on post-craniotomy pain, analgesic requirement in the post-operative period along with the recovery profile of the patient and the side effects. **Methods:** This prospective, randomised, placebo-controlled, double-blinded study enroled 50 patients of either gender, scheduled to undergo elective craniotomy, under general anaesthesia. They were randomly divided into two groups and received either 12 ml of 0.25% ropivacaine (group R) or 12 ml of normal saline (group NS), through the subgaleal drain, after the closure of the dura. Pain scores were assessed at 1, 2, 4, 8 and 24 hours post-operatively. Student's t-test was used for comparison of continuous variables and the Chi-square test or Fisher's exact test was used for comparing the nominal categorical data. **Results:** The visual analogue scale score was higher in group NS than in group R, and the difference was statistically significant ($P = 0.012$, 0.016, and 0.005 at 0, 1, and 2 post-operative hours, respectively). The difference in the mean emergence time in the two groups was 1.12 minutes ($P = 0.024$). **Conclusion:** Single-time wound instillation of ropivacaine (12 ml of 0.25%) through surgical (subgaleal) drain during wound closure is an effective and simple technique for reducing post-operative pain and analgesic consumption and early emergence in neurosurgical patients undergoing supratentorial craniotomy.

Key words: Craniotomy, drug instillation, pain, ropivacaine

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INTRODUCTION

A majority of patients experience moderate-to-severe pain after craniotomy, which, if untreated, may provoke abrupt changes in sympathetic activity and haemodynamic parameters, causing complications such as raised intracranial pressure, cerebral haemorrhage, brain herniation and even chronic headache. Therefore, adequate pain relief is an important aspect of neuroanaesthesia.[1,2]

Opioids have remained the cornerstone drugs for post-operative pain management. Numerous other drugs such as gabapentin, clonidine, dexmedetomidine, tramadol, cyclooxygenase-2 inhibitors, and dexamethasone have also been studied for the same with variable success rates. Each of these drugs has its own side effects, which may not be acceptable in neurosurgical patients.[3]

Wound instillation of local anaesthetic drugs, as a modality for post-operative pain management, has proved quite useful in surgeries such as laparoscopy, mastectomy, hysterectomy, and caesarean section. Various local anaesthetic (LA) drugs such as

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bupivacaine, levobupivacaine, and ropivacaine have been studied for this technique.[4,5]

Ropivacaine is long-acting, exhibits differential blockade predominantly on sensory nerve fibres, and has a better safety profile. It has been successfully and safely used in neurosurgical patients for local infiltration at pin sites, the incision site, and scalp block but has not been instilled via surgical drains.[6]

Hence, we planned to study the role of wound instillation of ropivacaine through subgaleal drains in patients undergoing supratentorial craniotomy. The primary objectives were to assess post-operative pain and analgesic requirements over 24 hours, and the secondary objectives were to assess the recovery profile of the patient and to look for side effects if any.

METHODS

This prospective, randomised, placebo-controlled, double-blinded study was conducted at a tertiary-level teaching hospital after obtaining institutional ethics committee clearance (no. IEC/Th/18/Anst03, dated 20/01/2018). Our estimated sample size was based on the visual analogue scale (VAS) score among groups. Based on a previous study, the sample size was calculated to be 21 patients per group with an effect size of 1.0, with a power of 90%, and an α error of 0.05 to detect the significant difference of one in VAS score between the two groups.[5] To increase the power of the study and to compensate for any possible dropouts, we included 25 patients in each group.

After obtaining written informed consent, 50 patients of either gender, aged 18–65 years, belonging to the American Society of Anesthesiologists (ASA) physical class I to III, scheduled to undergo elective supratentorial craniotomy under general anaesthesia, were enroled in the study. The study was conducted from January 2019 to December 2020 in accordance with the principles of the Declaration of Helsinki and was registered with the Clinical Trials Registry of India (CTRI/2020/01/022806).

The patients with Glasgow coma scale score <13, inability to communicate or comprehend, allergy to local anaesthetics, previous history of craniotomy, history of drug/alcohol abuse, and those posted for aneurysm clipping or planned for post-operative ventilator support were excluded from the study, and patients who were not extubated or reintubated within 24 hours of surgery were considered as dropouts.

Preoperative fasting of 6 hours was ensured, and no premedication was administered. Patients were explained about the study protocol and were educated regarding the VAS for measuring pain (on a scale of 0 to 10 where 0 is no pain and 10 is the worst pain experienced). In the operating room, all routine monitors were attached, and baseline parameters were recorded. A standard protocol for induction of anaesthesia was followed for all patients. The airway was secured with a cuffed endotracheal tube of appropriate size. After the surgery was commenced, the type and size of craniotomy were noted.

Anaesthesia was maintained with isoflurane (0.8–1.5 minimum alveolar concentration), in a 65% nitrous oxide in oxygen mixture, along with an injection of fentanyl (1 μg kg^{-1}) and vecuronium bromide (0.02 mg kg^{-1}) intermittently as per requirement. The duration of surgery and anaesthesia were recorded. The last dose of injection of fentanyl (1 μg kg^{-1}) along with an injection of ondansetron (4 mg) was given at the time of dural closure, and the exact time was noted.

On the basis of computer-generated randomisation numbers, the patients were then divided into group NS (n = 25) and group R (n = 25).

Once a subgaleal drain was placed and subcutaneous tissue was sutured, the patients received either 12 ml of 0.25% ropivacaine (group R) or normal saline (group NS) (12 ml) depending upon the group allocated. The volume was based on a study conducted in pilot cases, which are not included in the current study. The drug was instilled through the surgical drain which was then clamped for 15 minutes. The drugs were prepared by an anaesthesiologist, in identical syringes, who did not participate in further recording of data or patient management. The person recording the data was blinded to the assignment of groups. After the instillation of the drug, skin closure and dressing of the wound were done, and thereafter, isoflurane was stopped. Skull pins were removed, nitrous oxide was then turned off (time noted), and the patient was given 100% oxygen.

After the return of spontaneous respiration, residual neuromuscular blockade was reversed, and the first response of the patient to verbal commands was checked. The time from switching off of nitrous oxide until response to verbal commands was noted and termed as ‘emergence time’, and the trachea was extubated. The time from switching off of nitrous oxide until tracheal extubation was noted as the ‘extubation time’. At the time of extubation, vital parameters, modified Aldrete score (MAS),[7] Richmond agitation–sedation scale (RASS),[8] VAS and post-operative nausea vomiting (PONV)[9] were assessed and noted.

Once in the post-anaesthesia care unit, the vital parameters, sedation scale (RASS) and pain score were then assessed at 1, 2, 4, 8 and 24 hours post-operatively. Pain was assessed as per VAS score; if at any time VAS >3 was observed, intravenous diclofenac, 75 mg, was given as the primary analgesic. The time for the first analgesic required (in minutes) was recorded as the ‘duration of analgesia’. An injection of diclofenac was given up to a maximum of three doses, every 8 hours; for adequate post-operative analgesia, if pain was still uncontrolled, 30 mg of ketorolac was given intravenously as a rescue analgesic. The total number of doses of the analgesic consumed in 24 hours were recorded.

The total amount of blood collected from the surgical drain in 24 hours was also noted. The time from the day of surgery (day 0) to discharge from the hospital was noted as hospital stay (in days).

Statistical testing was conducted using the software Statistical Package for the Social Sciences system version 17.0. Continuous variables in the data were presented as mean ± standard deviation, and categorical variables were presented as percentage and absolute numbers. Student’s t-test was applied for comparison of normally distributed continuous variables between the groups. As appropriate, the Chi-square test or Fisher’s exact test were used for comparing the nominal categorical data. A value of $P < 0.05$ was considered statistically significant.

RESULTS

The two groups, of 25 patients each, were comparable with respect to demographic data, ASA grading, diagnosis of the patients, duration of surgery, blood loss during surgery and size of the incision [Figure 1, Table 1].

The mean value of the duration of analgesia (in minutes) was 108.20 ± 102.80 in the NS group and 480.00 ± 276.80 in the R group, which was significant statistically ($P < 0.001$). The VAS score was higher in group NS than in group R, and the difference was statistically significant ($P = 0.012$, 0.016, and 0.005 at 0, 1, and 2 post-operative hours, respectively) [Figure 2].

More number of analgesic doses were consumed in the NS group as compared to group R. The mean number of injections of diclofenac (75 mg each) consumed in 24 hours was 2.48 ± 0.59 and 1.12 ± 0.44 per patient in group NS and group R, respectively ($P = 0.012$); the number of patients needing rescue analgesia was more in the NS group (one patient (4%)) than in the R group (0%), but no statistical difference was found ($P = 1.00$). The mean duration of hospital stay was 11.16 ± 6.66 days in the NS group and 11.24 ± 4.36 days in group R ($P = 0.960$). The amount of fluid collected in the drain was comparable in both groups ($P = 0.755$) [Table 2].

The changes in heart rate at all the time points in group R (1, 2, 4, 8 and 24 hours) were statistically significant as compared to group NS ($P < 0.05$), except at 0 hours [Figure 3]. The changes were also seen in systolic, diastolic and mean blood pressure but were not statistically significant ($P > 0.05$) [Figure 4]. The MAS, RASS score and incidence of PONV were comparable in the two groups. The mean emergence time in group NS and group R was 6.20 ± 1.90 and 5.08 ± 1.48 min and the mean extubation time was 6.43 ± 1.85 and 5.41 ± 1.57 min, respectively, and these were statistically significant ($P = 0.024$ and $P = 0.040$, respectively) [Table 2].

Table 1: Demographic and surgical profile of patients

Variable	Group R (*n*=25)	Group NS (*n*=25)	*P*
Age in years	43.76±14.13	42.24±14.91	0.713
Height in cm	166.48±8.01	165.68±6.09	0.693
Weight in kg	60.32±9.46	60.32±11.96	1.000
Gender (M:F)	13:12	12:13	0.777
ASA (Class I/II/III)	3/17/5	9/14/2	0.101
Diagnosis			
Meningioma	13	12	0.777
Glioma	7	6	0.747
Orbital mass	1	1	1.000
Colloidal cyst	3	2	1.000
Other tumour	1	4	0.349
Duration of surgery (min)	312.80±86.01	299.20±81.17	0.568
Total injection fentanyl consumption (μg)	195.40±27.15	207.20±26.70	0.128
Blood loss (ml)	654.00±484.75	528.00±353.87	0.299
Size of incision (cm)	21.44±4.55	20.00±2.55	0.174

(R: Ropivacaine, NS: Normal saline, M: male, F: female, ASA: American Society of Anesthesiologists, *n*: number)

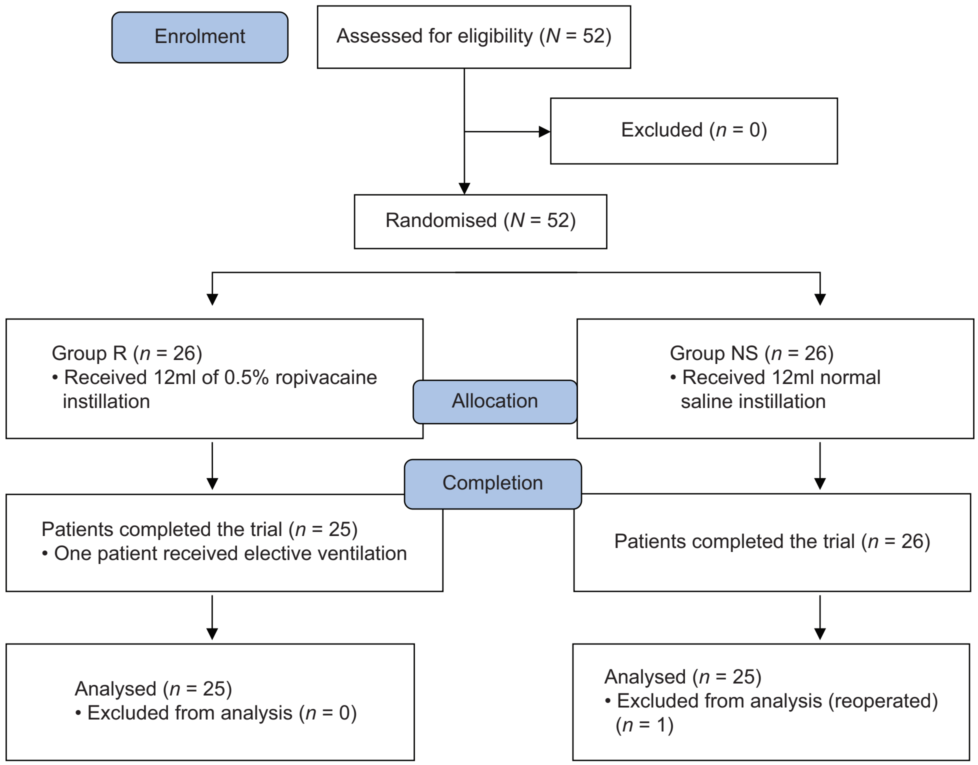

Figure 1: Consolidated standards of reporting trials (CONSORT) flow diagram

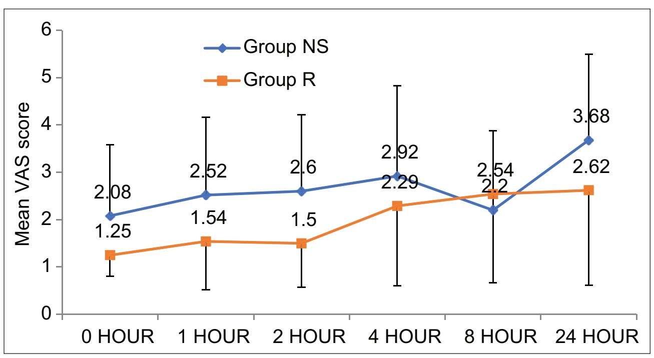

Figure 2: Post-operative pain scores (VAS). (VAS: Visual analogue score, R: ropivacaine, NS: normal saline)

There were no adverse events pertaining to our novel technique, such as delay in wound healing, wound dehiscence or wound infection.

DISCUSSION

The chief findings of our study were increased time for the first analgesic requirement and reduced analgesic requirement in the ropivacaine group. The mean value of the duration of the first analgesic requirement, in minutes, was 108.20 ± 102.80 in the NS group and 480.00 ± 276.80 in the R group, which was significant statistically ($P < 0.001$). Because ropivacaine has a long duration of action (2–6 h), this finding is expected. Moreover, it has fewer side effects and exhibits differential blockade on sensory nerve fibres compared to bupivacaine.[6] In contrast, other studies have shown single administration of LA to be effective for 12 to 14 hours.[5,10]

Table 2: Recovery and post-operative profile of patients

	Group R (*n*=25)	Group NS (*n*=25)	*P*
Emergence time (min)	5.08±1.48	6.20±1.90	0.024*
Extubation time (min)	5.41±1.57	6.43±1.85	0.040*
MAS			
0 min	6.80±1.44	6.52±1.05	0.436
5 min	8.40±1.16	8.12±0.78	0.320
10 min	9.04±0.74	8.80±0.65	0.226
RASS	(-) 1.92±1.12	(-) 1.92±1.12	0.254
PONV	1.50±0.71	1.86±0.38	0.345
Mean duration of analgesia (min)	480.00±276.80	108.20±102.80	0.001*
Mean number of injection diclofenac doses in 24 hours (per patient)	1.12±0.44	2.48±0.59	0.012*
Blood in drain (ml)	85.60±40.83	82.40±30.59	0.755
Duration of hospital stay (days)	11.24±4.36	11.16±6.66	0.960

(R: ropivacaine, NS: Normal saline, min: minutes, MAS: Modified Aldrete score, RASS: Richmond agitation–sedation scale, PONV: post-operative nausea vomiting, *n*: number)

We offered intravenous diclofenac, 75 mg, as the first line of analgesia, whenever VAS >3, as it is quite common and safely used in our setup. Intravenous

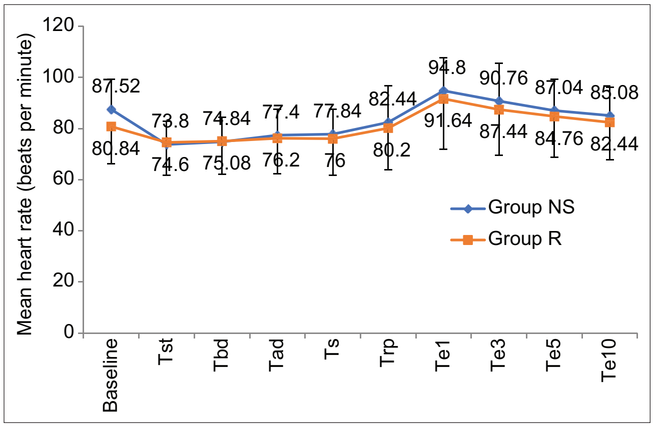

Figure 3: Variations in heart rate perioperatively. (Tst: time of subcutaneous tissue closure, Tbd: before instillation of drug/NS, Tad: after instillation of drug/NS, Ts:- time skin closure, Trp: time removal of pins, Te1: time of extubation, Te3: 3 min after extubation, Te5: 5 min after extubation, Te10: 10 min after extubation)

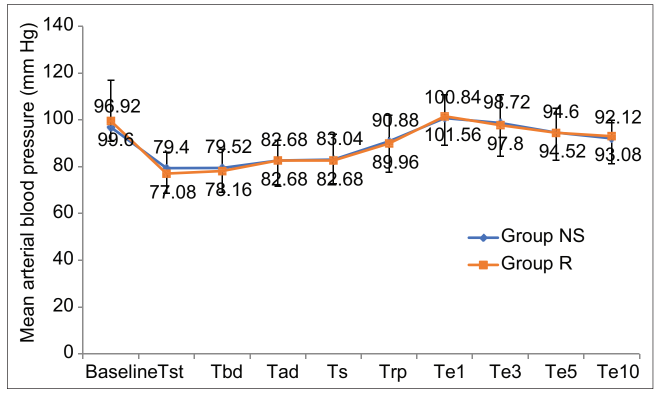

Figure 4: Variations in mean arterial blood pressure perioperatively. (Tst: time of subcutaneous tissue closure, Tbd: before instillation of drug/NS, Tad: after instillation of drug/NS, Ts: time skin closure, Trp: time removal of pins, Te1: time of extubation, Te3: 3 min after extubation, Te5: 5 min after extubation, Te10: 10 min after extubation)

ketorolac, 30 mg, which is as potent as morphine in terms of analgesia, was opted for rescue analgesia and was required only in one patient of group NS. However, the number of injection diclofenac doses consumed between the two groups varied widely. Twenty-one patients received an injection of diclofenac in the NS group in the first two hours as compared to only three such patients in the R group. This shows that the demand for analgesic was much higher in group NS. However, because almost 84% patients had taken injection diclofenac in group NS within the first two hours this led to VAS scores <4 in both the groups at 2 hours post-operatively.

The use of opioids in the post-operative period may camouflage the neurosurgical assessment; hence, multimodal analgesia using non-steroidal anti-inflammatory drugs is preferred. However, pain is still reported to be undertreated.[11] Hence, we decided to study wound instillation of ropivacaine through subgaleal surgical drains, which is a novel analgesic technique, in neurosurgical patients. We used only non-sedative analgesics as rescue analgesics, the reason being that, we wanted to be fully sure regarding the assessment of the effect of this new technique and its adverse effects. In our study, the total intraoperative fentanyl consumption was 207.20 ± 26.70 μg and 195.40 ± 27.15 μg in group NS and group R, respectively. The difference was not statistically significant (P = 0.128). Also, the last dose of injection fentanyl (1 μg kg^{-1}) was given at the time of dural closure to all of the patients, in both groups, to maintain uniformity.

In a study on craniotomy patients, Zhou *et al.*[12] found a prolongation of time for the first analgesia in patients who had preoperative scalp infiltration with 0.5% ropivacaine (6 hours as compared to 8 hours in our study). The technique of regional anaesthesia was different in that study and they did intervention before surgery. In their control group, the patients had prolonged, 3.8 hours time, for the first analgesia as compared to 1 hour in our study. It was because they used a cut-off value of VAS >4, whereas we used VAS >3 for administering analgesia. The additional analgesic effect of pre-emptive administration of block also has to be considered. Jonnavithula *et al.*[5] also demonstrated the same results with bupivacaine infusion in modified radical mastectomy as the time of the first analgesia was more prolonged in the bupivacaine group than in the control group (4.3 ± 5.2 hours versus 14.6 ± 9.6 hours, $P < 0.05$).

Apart from good pain relief, early post-operative recovery after supratentorial craniotomy is critically important and highly desirable by surgeons and anaesthesiologists, alike.[13] With our technique, the emergence and extubation times were less in group R than in the control group, probably due to good pain relief. However, the difference in RASS and MAS was not found to be statistically significant among the two groups.

Before embarking upon this technique in neurosurgical patients, all available literature regarding the use of the LA instillation technique since 1991 was extensively reviewed. They varied in their success rates, but all of them proved it as a safe technique.[14-16] However, several precautions and safety measures were still adopted. First, the dose used, of ropivacaine, was 30 mg (12 ml of 0.25%) and was within safe limits. Second, because the scalp is a highly vascular structure, ropivacaine was consciously preferred as it is a vasoconstrictor and much safer than bupivacaine. Third, we used it in superficial tissue when the dura was closed and the bone flap was secured, thus ensuring minimal chances of it reaching the brain. Animal studies have shown that direct application of LA on the hippocampal area has sedative and anaesthetic activity.[17]

There were no adverse events pertaining to the technique such as delay in wound healing, wound dehiscence or wound infection. LA probably can decrease such events due to antimicrobial and anti-inflammatory activity although we have not analysed this effect.[18,19] None of our patients showed any adverse event related to LA toxicity. Chan *et al.*[20] studied the analgesic efficacy of continuous wound instillation with ropivacaine in hepatic surgery and found that continuous infusion is safe and did not raise blood ropivacaine to toxic levels. However, we were unable to analyse blood ropivacaine levels due to the lack of this facility in our setup.

Our study had some limitations. We compared ropivacaine instillation with that of normal saline. However, normal saline instillation can provide pain relief by washing off pain-producing substances and inflammatory markers. Furthermore, the pressure exerted by the drug/saline volume in galea on nerves can block the transmission of the pain stimulus.[5] The volume of solution instilled was empirically chosen after conducting few pilot cases, which might not be adequate for all craniotomies. Although we enroled patients undergoing supratentorial craniotomies, there was a heterogeneity of patients and the intensity of pain may not be the same in all. The myotoxicity of LA needs to be studied. However, there were no risk factors for toxicity such as higher concentrations of LA, prolonged exposure to LA and use of bupivacaine.[21,22]

CONCLUSION

Single-time wound instillation of ropivacaine (12 ml of 0.25%) through surgical (subgaleal) drains, given at the time of wound closure, is a safe, inexpensive, effective and simple technique for reducing post-operative pain and analgesic consumption in neurosurgical patients undergoing supratentorial tumour resection. It provides a stable haemodynamic profile post-operatively, with no untoward event pertaining to the drug or technique used. Hence, it may be incorporated as a part of the analgesic armamentarium in these patients. However, further studies are needed to determine the exact dose and concentration of LA.

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Conflicts of interest

There are no conflicts of interest.

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