Original article

Bupivacaine scalp nerve block: hemodynamic response during craniotomy, intraoperative and post-operative analgesia

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Background: Noxious stimuli during craniotomy may induce hypertension and tachycardia, giving rise to morbidity in patients with intracranial hypertension. Craniotomy is followed by moderate level of postoperative pain.

Objective: Evaluate the effectiveness of scalp block on hemodynamic response to noxious stimuli, intraoperative fentanyl requirement and post-operative analgesia.

Methods: Sixty patients undergoing elective craniotomy were randomly assigned to receive a scalp block with either 0.5% bupivacaine or 0.25% bupivacaine and 1:200,000 adrenaline (group A and B) or normal saline with 1:200,000 adrenaline (group C). Fentanyl 0.5 mcg/kg was administered for hemodynamic control. Intraoperative mean arterial blood pressure (MAP), heart rate (HR), fentanyl doses, and post-operative pain scores were recorded. Post-operative analgesia was provided by patient-controlled analgesia (PCA) morphine for 24 hours.

Results: MAP was greater in group C than group A during pinning and incision ($p < 0.05$), and was greater in group C than group B during pinning, incision and craniotomy ($p < 0.05$). HR differences were not statistically significant between all groups ($p > 0.05$). Intraoperative fentanyl requirement was significantly greater in group C compared with group A and B ($p < 0.05$). Pain score, time to the first morphine administration and total morphine consumption were not significantly different between all groups.

Conclusion: Pre-incision scalp blocks using either 0.25% or 0.5% bupivacaine with 1:200,000 adrenaline were effective to prevent rising of MAP, but not HR in response to cranial pinning and skin incision, causing less intraoperative fentanyl requirement. However, they did not reduce post-craniotomy pain and morphine consumption.

Keywords: Bupivacaine, craniotomy, intra-operative analgesia, post-operative analgesia scalp, nerve block

Different stimuli during craniotomy include insertion of cranial pins, skin incision, craniotomy, periosteal dural contact, brain manipulation and dural, bone and skin closing. They cause different levels of nociception. These noxious events can result in sudden increases in blood pressure and heart rate. Hypertension may further increase intracranial

pressure in patients with impaired autoregulation [1]. It may cause rupture of an intracranial aneurysm [2] and post-operative intracranial hematoma [3]. Methods to blunt these noxious stimuli may be by administration of systemic opioids, deepening the level of anesthesia, or scalp nerve blocks (SNB) using scalp infiltration by local anesthetics. Given high dose opioids, and anesthetic agents may result in prolonged emergence and hypotension during periods of low levels of stimuli. Many studies have showed that both SNB and scalp infiltration by local anesthetics can blunt those hemodynamic responses during craniotomy [4-7].

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Although 45% of post-craniotomy patients reported no pain in the immediate postoperative period [8], 60-80% of patients reported moderate to severe pain [9, 10]. This undertreated pain during intracranial operation is due to fear of causing respiratory depression and masking changes in conscious due to surgical complications by sedative effects of opioids. Regional anesthesia such as wound infiltration or SNB might be a better choice for pain relief. Scalp infiltration by local anesthetics was previously shown to be beneficial for post-operative analgesia in the early post-operative period [11-13]. Three studies of SNB after skin closure resulted in lower pain score and less analgesic requirement [14-16].

In this study, we designed a prospective double-blind randomized approach to assess the efficacy of pre-incision scalp block using 0.25% and 0.5% bupivacaine with 1:200,000 adrenaline to blunt the hemodynamic response to noxious stimuli and to provide post-operative analgesia by a preemptive mechanism.

Materials and methods

After institutional ethics committee approval and informed patient consent, 60 ASA I and II patients aged 16 to 65 years undergoing elective supratentorial craniotomy were included in the study. We excluded patients who could not assess pain, those with documented allergy to local anesthetics, those with hypertension, history of opioid dependence, coagulopathy, scalp infection, and previous craniotomy.

Pre-operatively, all patients were given explanations of the visual analogue scale (VAS) scores for pain assessment and how to use the patient controlled analgesia (PCA) machine for post-operative analgesia. Standard monitors (electrocardiogram, non-invasive blood pressure, and pulse oximetry) were attached. Baseline blood pressure and heart rate were recorded. The anesthesia protocol was standardized for all patients. No premedication was given. Anesthetic induction was performed with fentanyl 3 mcg/kg, thiopentone 3-5 mg/kg, and pancuronium 0.1 mg/kg. After intubation, anesthesia was maintained with 60% nitrous oxide in oxygen and isoflurane up to an end-tidal concentration of 1.2%. A 20-gauge catheter was placed in the radial artery of every patient and connected to a transducer placed at midaxillary level. The scalp block was performed by one anesthesiologist who was blinded to the agents. The dose of bupivacaine was calculated not to exceed

3 mg/kg of the patient's body weight to avoid systemic toxicity.

Patients were divided into three groups, group A received the scalp block with 0.5% bupivacaine and 1:200,000 adrenaline, group B received the scalp block with 0.25% bupivacaine and 1:200,000 adrenaline, and group C received the scalp block using normal saline with 1:200,000 adrenaline.

The following nerves were blocked bilaterally using a 24G needle, supratrochlear, supraorbital, zygomaticotemporal, auriculotemporal, great auricular, lesser occipital and greater occipital. Each nerve used 1.5-2.0 mL of agents. Careful aspiration was made before injection of local anesthetics to avoid intravascular injection.

Cranial pins in the Mayfield head holder were placed eight minutes after scalp block. Systolic, diastolic and mean arterial blood pressure (MAP) and heart rate (HR) were recorded at the following times: induction, intubation, three minutes after intubation, during scalp blocks, before head pinning, during head pinning, one minute and three minutes after head pinning, at skin incision, three minutes after skin incision, working with bone, dural opening, every 30 minutes after dural opening, dural, bone and skin closing. If blood pressure increased by more than 15 mmHg, or heart rate increased by more than 10 beats/minute, the isoflurane concentration was increased to maximal end-tidal concentration of 1.2%. If the blood pressure and heart rate remained greater as described, additional 0.5 mcg/kg of fentanyl was given.

At the end of the procedure, neuromuscular blockade was reversed with neostigmine 0.05 mg/kg and atropine 0.02 mg/kg. Extubation was done when the patients were able to obey simple commands. Post-operative analgesia was assessed using VAS scores (0 = no pain at all and 10 = the worst possible pain) at time intervals of 30 minutes and 1, 1.5, 2.0, 6.0, 12.0 and 24.0 hours post-operatively.

Others parameters recorded were sedation and nausea vomiting scores and antiemetics given to the patients. Sedation was assessed using a four-point scale: 1 = awake and communicative, 2 = asleep, responds to normal speech, 3 = asleep, responds to pain, 4 = deeply sedated. Nausea vomiting was assessed using four points scale: 0 = no nausea and vomiting, 1 = mild nausea, 2 = severe nausea with retching, 3 = vomiting. Morphine 0.05 mg/kg was given as a loading dose when VAS pain scores were 3 or more than 3. Then, post-operative analgesia was

continued with PCA morphine. The PCA device was set up to deliver morphine 1 mg bolus with eight-minute lock out interval, 30 mg of morphine for four hours limit, and no background infusion. Glasgow coma scale (GCS) scores and respiratory rate were scored hourly by a nurse in the neurosurgical intensive care unit (NICU). Time from extubation to the first analgesic given and total morphine consumption in 24 hours post-operatively was recorded.

The sample size was calculated to detect a significant difference in MAP during skin incision. A pilot study was done to compare MAP during skin incision after 0.5% bupivacaine with 1:200,000 adrenaline (MAP=85.0±4.2 mmHg) and normal saline with 1:200,000 adrenaline (90.0±5.2 mmHg) for scalp block. To detect a difference of MAP between the groups, with 90% power at an α -value of 0.05 and β -value of 0.01, a sample size of 20 per group was required.

Demographic data, sedation scores, nausea vomiting scores, and antiemetics requirement were compared using χ^2 test. Intraoperative blood pressure and heart rate, additional fentanyl requirement, VAS scores, time to first morphine administration, total morphine consumption were compared using one-way ANOVA. Data analysis was performed using SPSS (version 11.5).

Results

Sixty patients were enrolled in the study, 20 in each group. One patient in group B experienced post-

operative intracranial hematoma and was excluded from the study.

Demographic data is shown in **Table 1**. There were no statistically significant differences in the demographic data with respect to age, sex, body weight, type, and duration of surgery.

Figure 1 (A, B) shows average mean arterial pressure (MAP) (mmHg) and mean heart rate (HRT) (beat/minute) for three groups: Group A = 0.5% bupivacaine with 1:200,000 adrenaline, Group B = 0.25% bupivacaine with 1:200,000 adrenaline, Group C = normal saline with 1:200,000 adrenaline. Intra-operative MAP levels were statistically significantly higher in group C, compared to group A, during pin insertion and skin incision. They were statistically significantly higher in group C, compared to group B, during pin insertion, skin incision and bone manipulation. Heart rate was not significantly different between groups at any time.

Table 2 shows additional intraoperative fentanyl requirement. Apparently, intraoperative additional fentanyl requirements were significantly higher in group C than group A and group B (**Table 2**).

VAS score (**Table 3**), sedation score (**Table 4**), nausea vomiting score (**Table 5**), time to first morphine administration (**Table 6**), total 24 hours morphine consumption (**Table 6**) and the requirements for antiemetics (**Table 6**) were not statistically different between groups. No post-operative scalp infection or hematoma was observed in patients until they were discharged from the hospital.

Table 1. Demographic data.

	0.5% bupivacaine (n = 20)	0.25% bupivacaine (n = 19)	Normal saline (n = 20)
Age (year)*	37 ± 12	35 ± 12	31 ± 10
Sex (male/female)*	10 / 11	8 / 11	14 / 6
Weight (kg) *	59 ± 10	54 ± 9	62 ± 11
Type of surgery [#]			
- Tumor removal	9	9	10
- Epilepsy surgery	8	7	9
- AVM resection	4	3	1
Duration of surgery (minutes) *	163 ± 48	131 ± 60	150 ± 58

*Values are expressed as means ± SD. #Data are presented as total number of patients (n).

Fig. 1 Average mean arterial pressure (MAP) (mmHg) (A) and mean heart rate (HRT) (beat/minute) (B) for three groups: Group A = 0.5% bupivacaine with 1:200,000 adrenaline, Group B = 0.25% bupivacaine with 1:200,000 adrenaline, Group C = normal saline with 1:200,000 adrenaline *Significant difference between Group A and C, $p < 0.05$. #Significant difference between Group B and C, $p < 0.05$

Table 2. Additional intraoperative fentanyl requirement.

Group	Additional fentanyl requirement (mcg/kg)		
	Mean±SD	Minimum	Maximum
A	0.33±0.46*	0.0	1.5
B	0.18±0.34*	0.0	1.0
C	0.80±0.50	0.0	1.5

*p<0.05

Table 3. Visual analogue scale (VAS) pain scores.

Group	VAS scores						
	0.5 hour	1.0 hour	1.5 hours	2.0 hours	6.0 hours	12.0 hours	24.0 hours
A	4.0±3.3	4.5±3.2	4.7±3.5	4.4±3.4	4.1±3.5	2.9±2.9	2.9±2.6
B	6.3±3.7	4.2±3.3	5.0±3.3	4.2±3.5	2.2±2.1	2.0±1.7	2.5±1.6
C	5.5±3.4	5.6±2.4	5.1±2.5	4.2±2.6	2.6±2.2	2.3±2.3	2.4±2.3

Data are presented as means ± SD.

Table 4. Sedation scores.

Group	A [#]				B [#]				C [#]			
	0	1	2	3	0	1	2	3	0	1	2	3
Time												
0.5 hour	5	7	8	1	4	7	8	0	3	12	4	1
1.0 hour	6	9	4	2	3	13	3	0	4	13	3	0
1.5 hours	6	12	2	1	5	12	2	0	5	11	3	1
2.0 hours	8	12	1	0	4	13	2	0	6	10	3	1
6.0 hours	10	10	1	0	12	7	0	0	15	5	0	0
12.0 hours	15	6	0	0	13	6	0	0	16	4	0	0
24.0 hours	21	0	0	0	18	1	0	0	17	3	0	0

[#]Data are presented as total number of patients (n)

Table 5. Nausea/vomiting scores.

Group	A [#]			B [#]			C [#]		
	0	1	2	0	1	2	0	1	2
Time									
0.5 hour	18	1	2	19	0	0	18	1	1
1.0 hour	19	1	1	18	0	1	19	1	0
1.5 hours	18	1	2	17	1	1	20	0	0
2.0 hours	20	0	1	18	1	0	20	0	0
6.0 hours	14	5	2	13	4	2	19	1	0
12.0 hours	17	3	1	16	3	0	17	1	2
24.0 hours	20	1	0	16	2	1	18	1	1

[#]Data are presented as total number of patients (n)

Table 6. Time to first morphine administration, total 24-hour morphine consumption and antiemetic requirement.

Group	Time to first morphine administration (minutes)*	Total 24-hour morphine consumption (mg)*	Antiemetic requirement (times) [#]				
			0	1	2	3	4
A	246±66	13±8	11	7	3	0	0
B	207±58	13±11	11	4	2	1	1
C	242±37	15±10	12	6	1	0	1

*Values are expressed as means ± SD. [#]Data are presented as total number of patients (n).

Discussion

Local infiltration and scalp nerve block (SNB) with local anesthetics are two regional anesthetic techniques for craniotomy. The aims of combining regional analgesia with general anesthesia are to provide intra-operative and post-operative analgesia. Head pinning, skin incision, and working with bone are periods of intense noxious stimuli resulting in hypertension and tachycardia. Methods to attenuate these hemodynamic responses are increased concentration of inhalation anesthetics, administration of narcotics, intravenous anesthetics, or antihypertensive agents and regional anesthetics. The following studies have shown that both SNB and local infiltration with local anesthetics can blunt or reduce these hemodynamic responses. Pinosky et al. [4] reported that using 0.5% bupivacaine for SNB could blunt both blood pressure and heart rate changes. Hillman et al. [5] reported that using 0.5% bupivacaine scalp infiltration significantly reduced blood pressure changes during skin incision, scalp flap reflection, and craniotomy and reduced heart rate changes during skin incision and scalp flap reflection. Hartley et al. [6] using 0.125% and 0.25% bupivacaine with 1:400,000 adrenaline for scalp infiltration in pediatric brain surgery, found that both concentrations could blunt the hemodynamic response from skin incision to dural incision. Bloomfield et al. [7] demonstrated 0.25% bupivacaine with 1:400,000 adrenaline pre-incision scalp infiltration blunt heart rate changes during dural and skin closure. They did not mention the effects of scalp infiltration on hemodynamic changes to skin incision before craniotomy. Our study demonstrated that both concentrations of bupivacaine (0.25 and 0.5%) with 1:200,000 adrenaline for SNB blunted blood pressure but not the heart rate response

to head pinning and skin incision. Only 0.25% bupivacaine blunted blood pressure response to craniotomy. The reason 0.25% bupivacaine had better intraoperative hemodynamic control was that there was one patient in the 0.5% bupivacaine group who developed intra-operative high blood pressure without preoperative history of hypertension. The effect of SNB on blood pressure response to noxious stimuli did not appear clinically significant in normotensive patients but may have a greater clinical significance in hypertensive patients. The dose of fentanyl for induction in this study was 3 mcg/kg, which could attenuate the clinical significance of SNB. MAP did not increase in all groups and were not significantly different between groups during dural, bone, and skin closure, which were the periods of increased stimulation. Group A and B experienced the analgesic effects of SNB done at the beginning while group C had the effect of additional fentanyl given during the operation. (patient in group C received higher intraoperative fentanyl) The additional fentanyl doses were significantly higher in group C (0.8 ± 0.5 mcg/kg) than group A (0.33 ± 0.46 mcg/kg) and group B (0.18 ± 0.34 mcg/kg), as shown in **Table 2**. In this study, we administered fentanyl using criteria for heart rate increase of more than 10 beats/minute and MAP increase of more than 15 mmHg. This was less than in other studies, which used 20% increase from baseline hemodynamic parameters. This is because it was our practice to give fentanyl when both parameters started rising.

Post-craniotomy pain is a topic of increased attention in neurosurgery and neuroanesthesia. In the past, it was under-treated because it was a common belief that craniotomies produced little pain and post-operative opioid therapy caused oversedation that may

interfere with frequent neurologic examinations to detect post-operative neurologic complications. However, recent studies showed that craniotomies were associated with more severe pain than recognized [9, 10] and systemic analgesics, including potent opioids, could be safely and effectively used for post-operative analgesia. Less potent analgesics including codeine, tramadol and nalbuphine were used in many studies because they may cause less respiratory depression. Codeine is demethylated in the liver to morphine, which causes the analgesic effect. Patients receiving codeine will have unpredictable serum morphine concentrations because the enzymatic process that converts codeine to morphine varies due to polymorphic inheritance [17]. Goldsack et al. [18] compared intramuscular codeine and morphine for 24 hour post-craniotomy pain. Morphine was found to be more effective as fewer doses of morphine than codeine were required. Stoneham et al. [19] found PCA morphine causing a small but non-significant reduction in pain scores more than intramuscular codeine. Both studies found that neither drugs caused respiratory depression and unwanted sedative effects. Tanskanen et al. [20] used PCA oxycodone as the rescue drug for paracetamol or ketoprofen after craniotomy. He found that the ketoprofen group required less oxycodone and had lower VAS scores than the paracetamol group. Jeffrey et al. [21] compared intramuscular 60 mg of codeine, 50 mg and 75 mg of tramadol and found the same VAS scores at 24 hours, but 75 mg tramadol caused higher scores for sedation, nausea, and vomiting. Sudheer et al. [22] studied the analgesic and respiratory effects of PCA morphine, PCA tramadol, and intramuscular codeine. Morphine produced significantly better analgesia than tramadol and codeine with less nausea and vomiting. Some patients in each group had arterial carbon dioxide tension rising more than 1 KPa. Verchere et al. [23] compared the analgesic efficacy of paracetamol alone, paracetamol with tramadol (PT), and paracetamol with nalbuphine (PN) after supratentorial craniotomy. Paracetamol alone provided inadequate analgesia, and the study for this group was stopped after the eighth patients. PT group provided the same VAS scores as the PN group, but required more doses. In addition, more cases of nausea and vomiting were observed in the PT group, but this was statistically insignificant. Most systemic medications studied for post-craniotomy pain are associated with side effects of sedation, nausea, and

vomiting and depressed ventilation. Much research using regional anesthetic techniques have been conducted as multimodality managements for post-craniotomy pain and to decrease those systemic complications. Scalp infiltration with local anesthetics performed before incision or after scalp closing demonstrated a transient effect. Bloomfield et al. [7] infiltrated the scalp with 0.25% bupivacaine with 1:200,000 adrenaline both at pre-incision and at the end of surgery. They studied VAS scores only up to 60 minutes postoperatively and found lower pain scores in the bupivacaine group when compared to normal saline. Biswas et al. [11] reported that pre-incision scalp infiltration with 0.25% bupivacaine delayed the time for first analgesic requirement (intramuscular diclofenac) without affecting the amount of analgesic consumed. Law-Koune et al. [12] demonstrated that both 0.375% bupivacaine with 1:200,000 adrenaline and 0.75% ropivacaine scalp infiltration at the end of craniotomy decreased morphine consumption during the first two post-operative hours but not significantly up to sixteenth post-operative hour. The VAS scores were not different at any time when compared to normal saline. Grossman et al. [13] reported using combined local anesthetic scalp infiltration and intramuscular metamizol (dipyrone) 30 minutes before the end of the operation to control postoperative pain after awaking from craniotomy. In their study, 27 out of 40 patients did not require any analgesic during 12 post-operative hours. Nguyen et al. [14] performed SNB with 0.75% ropivacaine after skin closure. Average VAS scores were higher in the saline group as compared with the ropivacaine group during the first 24 hours. Neither the total dose of codeine up to 48 hours was different nor did the time before the first dose of codeine. Bala et al. [15] used 0.5% bupivacaine with 1:400,000 adrenaline for SNB after skin closing, it decreased the amount of rescue pain medication requested (intramuscular diclofenac and intravenous tramadol), increased the time for the first analgesic requirement, and lowered median VAS scores up to six post-operative hours. SNB after skin closure has also been shown to be effective in providing transitional analgesia similar to that of intravenous morphine in the immediate post-operative period following a remifentanyl-based anesthetic [16].

All studies performed SNB for postoperative analgesia after skin closure and used intramuscular analgesics for postoperative analgesia as requested

by the patients, which was not a good quantitative measurement for post-operative analgesia. Therefore, we aimed to study whether pre-incision SNB could decrease post-operative analgesic requirements, using PCA morphine as post-operative analgesia. If preincision SNB could decrease PCA morphine consumption, it should decrease systemic side effects including sedation, nausea, and vomiting. However, our study showed that pre-incision SNB with either 0.25% or 0.5% bupivacaine with 1:200,000 adrenaline was not beneficial for post-craniotomy pain. In fact, there were no differences between groups in 24-hour morphine consumption, time to first morphine requirement, VAS scores at any time, sedation scores, nausea/vomiting scores, and amounts of antiemetics requirement. This may be explained as follows. The duration of SNB may not last long enough to provide post-craniotomy pain, and pre-incision SNB does not provide preemptive analgesia. The location of craniotomy affects post-operative pain. Temporal and suboccipital craniotomy is associated with increase post-craniotomy pain [24] because of more muscle reflections. In our study, the location of craniotomy was not different between groups, so that it should not affect post-operative pain and analgesic requirement.

Conclusion

Pre-incision SNB with 0.25% bupivacaine with 1:200,000 adrenaline can decrease the hypertensive responses without affecting heart rate during pin insertion, scalp incision, and craniotomy and 0.5% bupivacaine with 1:200,000 adrenaline affected the blood pressure response to pin insertion and scalp incision. They also decreased intraoperative fentanyl requirement. However, pre-incision SNB did not provide an analgesic effect for post-craniotomy pain and did not decrease post-operative analgesic requirements. Therefore, preincision 0.25% bupivacaine with 1:200,000 adrenaline for SNB may be sufficient to blunt the hemodynamic responses to craniotomy and post-craniotomy SNB may be required to provide more effective post-craniotomy analgesia.

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