Gabapentin Premedication Decreases the Hemodynamic Response to Skull Pin Insertion in Patients Undergoing Craniotomy

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Background: In patients undergoing craniotomy, skull pin insertion produces significant increases in heart rate (HR) and blood pressure. We investigated whether premedication with gabapentin would prevent or attenuate this increase.

Methods: Forty-seven ASA I and II patients, 18 to 60 years, undergoing elective craniotomy for intracranial tumor surgery were recruited prospectively and randomly divided into 3 groups; L (oral placebo plus 2% lidocaine infiltration at pin sites; n = 12), G (oral gabapentin 900 mg plus normal saline infiltration; n = 21) and GL (oral gabapentin 900 mg plus 2% lidocaine infiltration; n = 14). The oral medications were administered 2 hours before induction of anesthesia. Measurements were made at preinduction baseline, before skull pin insertion and at every 1 minute from pin insertion till end of 10 minutes.

Results: Forty-three patients completed the study (L, n = 11; G, n = 20; GL, n = 12). Premedication with gabapentin significantly attenuated the rise in systolic (SBP) and mean arterial pressure (MAP) after pin insertion when compared with placebo (for SBP, $P < 0.001$ at 1 and 2 min and < 0.05 at 3 to 5 min between L and G; $P < 0.001$ at 1 to 4 min and < 0.05 at 5 min between L and GL; for MAP, $P < 0.05$ at 1 min, < 0.001 at 2 min and < 0.05 at 3 to 4 min between L and G; $P < 0.001$ at 1 to 2 min and < 0.05 at 3 to 5 min between L and GL). HR responses were also attenuated in patients premedicated with gabapentin; however, the responses were more variable in group G ($P = 0.03$ between L and G at 4 min after pin insertion) as compared with group GL ($P < 0.05$ at 1 min, < 0.001 at 2 min and < 0.05 at 3 to 10 min between L and GL).

Conclusion: In conclusion, 900 mg of gabapentin, administered orally 2 hours before induction of anesthesia along with lidocaine scalp infiltration abolished the hemodynamic response after skull pin insertion. Premedication with gabapentin alone significantly attenuated the SBP and MAP; however, HR responses were more variable. A larger trial is required to corroborate the findings of the study before clinical recommendations would be warranted.

Key Words: gabapentin, craniotomy, skull pin, hemodynamics

(*J Neurosurg Anesthesiol* 2011;23:110–117)

In patients undergoing craniotomy for neurosurgery, application of the Mayfield skull pin head-holder clamp to fix the head produces a brief but intense, noxious stimulus. This may result in precipitous increases in heart rate (HR), blood pressure (BP) and the intracranial pressure (ICP).[1] Increases in ICP can affect cerebral perfusion pressure (CPP) resulting in increased intracranial blood flow, cerebral edema, and rupture of intracranial aneurysms.[1] The various methods used to attenuate the hemodynamic response to insertion of skull pins include use of α_2 agonists such as dexmedetomidine,[2] and clonidine,[3,4] local anesthetic infiltration at pin sites,[5–7] scalp blocks,[7] opioids,[8–12] β blockers,[12] subanesthetic dose of ketamine,[13] and deepening of general anesthesia.[14]

Gabapentin, a newer antiepileptic drug, is commonly used in the perioperative period to reduce opioid requirements and to decrease postoperative pain.[15] 800 mg of gabapentin, administered orally 1 hour before the surgery, has been found to be effective in reducing the noxious stimuli to laryngoscopy and intubation, thereby attenuating the hemodynamic response.[16] With this background, the researchers hypothesized that 900 mg of gabapentin, administered orally 2 hours before the induction of anesthesia would attenuate the hemodynamic response to the application of skull pin head-holder in patients undergoing craniotomy.

METHODS

After approval from the hospital ethics committee, and after obtaining consent, 47 consecutive ASA I and II patients of either sex between 18 and 60 years, undergoing planned elective craniotomy for intracranial tumor

Received for publication November 29, 2009; accepted February 22, 2010.

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surgery in the supine position were recruited prospectively into the study and randomly divided into three groups. Only the first case in any theatre was included so as to accurately time the administration of study drugs.

Exclusion criteria included patients undergoing craniotomy for emergency surgery, raised ICP, obese patients (body mass index $> 30\,kg/m^2$ for males and $28\,kg/m^2$ for females), patients having systemic comorbidities (cardiac, renal, hepatic, and endocrinal), hypertensive patients (including those detected after admission), patients undergoing intracranial aneurysm clipping (as most of them are on antihypertensive drugs and/or nimodipine), patients with known or suspected pregnancy, patients on multiple antiepileptic drug therapy including gabapentin for seizure prophylaxis (patients receiving only phenytoin as monotherapy were considered for inclusion) and patients in whom the Mayfield clamp was applied more than once. Patients undergoing tumor decompression in positions other than supine were also excluded as the hemodynamic responses are altered.

In group L (Placebo plus scalp infiltration with lidocaine; n = 12), patients were administered placebo (Vitamin B complex capsule) orally, 2 hours before induction of anesthesia followed by scalp infiltration with 2 mL of 2% lidocaine at each of the 3 pin sites (total volume 6 mL), 1 minute before application of skull pins. Group G patients (Gabapentin plus scalp infiltration with normal saline; n = 21) received gabapentin 900 mg orally, 2 hours before induction of anesthesia followed by infiltration of normal saline (total volume 6 mL) at the pin sites, 1 minute before skull pin insertion. In group GL (Gabapentin scalp infiltration with lidocaine; n = 14), patients were given gabapentin 900 mg orally, 2 hours before anesthesia induction followed by scalp infiltration with 2 mL of 2% lidocaine at the 3 pin sites (total volume 6 mL), 1 minute before the skull pins were applied.

Randomization was done by means of a color card scheme and the orders for premedication, that is, vitamin B complex capsule (Group L) or gabapentin (Groups G and GL) were written by an anesthesia resident carrying out the preoperative visit after consulting the color card. Intraoperatively, scalp infiltration was performed by the same resident who carried out the preoperative visit. The resident then took no further part in the study. The color card code was to be broken for initiating treatment in the event of adverse outcome in any of the study patients.

Upon arrival in the operating room, monitoring was established with 3 lead electrocardiogram and pulse oximetry. The radial artery was cannulated percutaneously with a 20 G BD Insyte-W Teflon catheter (Becton Dickinson Inc., Sandy, UT) for invasive blood pressure monitoring, after local skin infiltration with 2% lidocaine. Before induction of anesthesia, the modified Wilson sedation scale[17] (Table 1), was used to assess the sedation level of the patients. Anesthesia was induced in all cases with intravenous fentanyl (4 μg/kg) and propofol (titrated to loss of eye-lash reflex). Intravenous vecuronium bromide (0.2 mg/kg) was administered to facilitate tracheal intubation. Anesthesia was maintained with sevoflurane in a mixture of oxygen in air (1:1). Boluses of fentanyl were avoided before skull pin placement. A background infusion of 1 μg/kg/h of fentanyl and 1 μg/kg/min of vecuronium was started 10 minutes after pin insertion and head fixation (ie, after the study period) and continued till end of surgery.

Additional monitoring after induction of anesthesia included end-tidal CO_2 (E_TCO_2), the inspired (F_I) and the end-tidal (F_{ET}) concentration of sevoflurane and bispectral index (BIS) (Aspect Medical Systems Inc, Norwood, MA). A 7 French central venous catheter (BL Lifesciences Pvt. Ltd., Greater Noida, India) was inserted in the right internal jugular vein under ultrasound guidance (Site Rite 5, Bard Access System Inc., Salt Lake City, US) in all patients after induction to guide fluid therapy. Mechanical ventilation was adjusted to maintain an E_TCO_2 of 30 to 35 mm Hg.

A total volume of 500 mL of lactated Ringers' solution was infused in all patients from induction until skull pin insertion with further intraoperative maintenance fluids being guided by central venous pressures (CVP) and blood losses. 2 mL of either 2% plain lidocaine solution (without adrenaline) (Groups L and GL) or normal saline (Group G) was infiltrated at each of the 3 pin sites (total volume 6 mL) with the last pin site infiltration ending 1 minute before application of the Mayfield skull pin head-holder clamp.

The skull pins were applied in all patients approximately 45 minutes after induction of anesthesia. Measurements included HR, systolic blood pressure (SBP) and mean arterial pressure (MAP) made at the subsequent time points: before induction of anesthesia (Baseline), 1 minute after scalp infiltration but just before application of pin (Before PIN) and subsequently at every 1 minute interval after pin insertion until the end of 10 minutes (PIN 1 to PIN 10). Boluses of propofol were given intravenously in 30 mg aliquots whenever the HR was more than 120 beats/min and/or the SBP was more than 160 mm Hg in any patient within the 10 minutes after pin application. The number of patients requiring rescue therapy was recorded.

TABLE 1. Modified Wilson Sedation Scale[17]

Score	Description
1	Oriented; eyes may be closed but can respond to "Can you tell me your name?" "Can you tell me where you are right now?"
2	Drowsy; eyes may be closed, rousable only to command: "(name), please open your eyes"
3	Rousable to mild physical stimulation (ear-lobe tug)
4	Unrousable to mild physical stimulation

TABLE 2. Demographic Data (Number of Patients or Mean ± SE)

Groups	L (Oral Placebo Plus Lidocaine Scalp Infiltration)	G (Oral Gabapentin Plus Normal Saline Scalp Infiltration)	GL (Oral Gabapentin Plus Lidocaine Scalp Infiltration)
No. patients	11	20	12
Sex (Male: Female)	7:4	9:11	8:4
Age (y)	38.6 ± 1.6	34.75 ± 0.8	33.5 ± 1.5
Weight (kg)	59.5 ± 2.5	59.2 ± 1.6	60.5 ± 2.3
Height (cm)	161.3 ± 1.6	159.7 ± 0.8	160.1 ± 1.5

P was not significant between the groups.

Phenylepherine and atropine were to be administered in the event of hypotension (SBP ≤90 mm Hg) and bradycardia (HR ≤50 beats/min) respectively at any time period after induction of anesthesia. At the end of surgery, residual neuromuscular paralysis was reversed with a mixture of intravenous 0.05 mg/kg neostigmine and 0.02 mg/kg atropine. The recovery from anesthesia was assessed 10 minutes after, and at 1 and 2 hours after arrival of the patients in the postoperative intensive care unit. A record was kept of the number of patients who could not be extubated in the theatre despite adequate reversal (judged by neuromuscular monitor).

Statistical analysis was done using the software Statistical Product for the Social Sciences (SPSS version 17.0). Demographic data, preinduction sedation score, prepin BIS, CVP, F_I and F_{ET} of sevoflurane and the pre and post pin HR, SBP, and MAP were expressed either as number of patients or mean ± standard error (SE). For intragroup comparison, one way analysis of variance (ANOVA) followed by least significant difference (LSD) for post hoc multiple comparisons were used. For intergroup comparison, the Student *t* test was used. A *P* value < 0.05 was considered to be statistically significant and $P < 0.001$ as very significant.

RESULTS

The Mayfield clamp was applied more than once in 1 patient in each of the 3 groups and not applied in 1 additional patient in group GL (surgical plan was changed). Thus, 4 patients were excluded and a total of 43 patients completed the study. The 3 groups were comparable with respect to demographic data (Table 2), although group G had more number of patients. In our institute, gabapentin is available as 300 mg tablets. Hence, the study dose was achieved by administering 3 such tablets, whereas patients receiving placebo took a single vitamin B complex capsule.

HR (Table 3)

The baseline (preinduction) HR was less in the groups premedicated with gabapentin (groups G and GL) as compared with placebo (group L), although this difference was not significant. Intragroup comparison revealed a significant rise ($P < 0.05$) in the HR in group L (Placebo plus 2% lidocaine infiltration), 1 minute after insertion of skull pin until 4 minutes with respect to baseline (preinduction) values. Compared to prepin values, only the 1 minute rise in HR was significant. In group G (Gabapentin plus normal saline), there was a significant rise in HR at 1 and 2 minutes after insertion of skull pins compared with baseline values.

Intergroup comparison of HR revealed that there was a significant difference in the HR between groups L and GL ($P = 0.02$) before pin insertion (Fig. 1). After pinning, there was a significant rise in HR in group L compared with group GL at all time-points within the 10 minutes after skull pin insertion [significant ($P < 0.05$) at 1 min and between 3 to 10 min and highly significant ($P < 0.001$) at 2 min]. However, the difference between groups L and G was only significant ($P < 0.05$)

TABLE 3. Heart Rate (Beats/min) in the 3 Groups at Various Time Points (Mean ± SE)

Time Points	Groups: Group L (N = 11)	Group G (N = 20)	Group GL (N = 12)	*P* Value Between L and G	*P* Value Between L and GL	*P* Value Between G and GL
Before Induction (Baseline)	76.2 ± 4.5	69.7 ± 1.1	68 ± 2.3	0.2	0.1	0.5
Before PIN	81.9 ± 3.4	73.4 ± 4.1	68.5 ± 3.8	0.11	0.02#	0.4
PIN 1	94.6 ± 6.3	80.1 ± 4.4	69.3 ± 4.1	0.07	0.003#	0.08
PIN 2	93 ± 4.2	82.5 ± 3.8	69.2 ± 4.2	0.08	0.0007##	0.03§
PIN 3	90.2 ± 4.5	78.7 ± 3.6	68.1 ± 3.9	0.06	0.0014#	0.06
PIN 4	90.4 ± 4.4	77.7 ± 3.6	68.1 ± 3.9	0.03*	0.0011#	0.08
PIN 5	84.6 ± 4.4	77.1 ± 3.4	67.8 ± 3.9	0.2	0.01#	0.08
PIN 6	83.4 ± 4.5	74.7 ± 3.7	67.7 ± 4.3	0.1	0.02#	0.2
PIN 7	80.5 ± 4.7	74 ± 3.6	65.8 ± 4.2	0.3	0.03#	0.1
PIN 8	80.1 ± 4.3	73.9 ± 3.7	65.7 ± 4.1	0.3	0.02#	0.1
PIN 9	79.8 ± 4.2	73.5 ± 3.7	65.7 ± 3.8	0.3	0.02#	0.2
PIN 10	79.5 ± 4.1	71.4 ± 3.6	63 ± 3.5	0.1	0.006#	0.1

*$P < 0.05$ between groups L and G; #$P < 0.05$ and ##$P < 0.001$ between groups L and GL; §$P < 0.05$ between groups G and GL. PIN 1 is 1 minute and PIN 10 is 10 minutes after skull pin insertion.

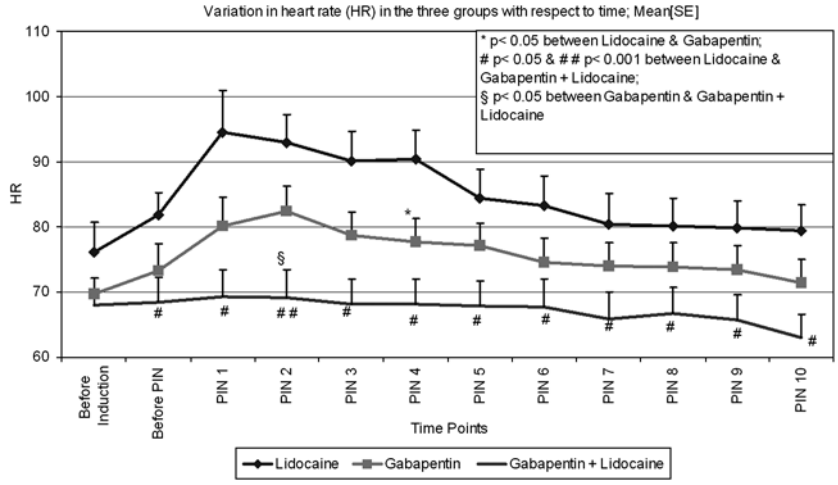

FIGURE 1. Variation in heart rate (HR) in the 3 groups with respect to time. Values are expressed as mean ± standard error (Mean ± SE). * is $P < 0.05$ between groups L and G, # is $P < 0.05$ and ## is $P < 0.001$ between groups L and GL and § is $P < 0.05$ between groups G and GL. PIN 1 is 1 minute and PIN 10 is 10 minutes after pin insertion. Values were recorded before induction and pinning and at every 1-minute interval after pin insertion till end of 10 minutes. Intergroup comparisons were carried out with the Student *t* test.

at 4 minutes after pin insertion. The difference between groups G and GL was significant ($P < 0.05$) at 2 minutes after pin insertion.

SBP and MAP (Tables 4, 5)

Intragroup comparison showed a significant rise in SBP in group L at 1 ($P < 0.001$), 2 ($P < 0.001$) and 3 minutes ($P < 0.05$) after insertion of pins compared with baseline and prepin values. A significant difference in SBP was also observed at various time points after pinning in group L (1 and 2 min vs. 4 to 10 min; 3 min vs. 5 to 10 min; 4 min vs. 6 to 10 min and 5 min vs. 7 to 10 min). In group G, compared with baseline values, there was a significant fall in SBP just before pin insertion and at 6 to 10 minutes after pinning. There was a significant rise in SBP in group G at 1, 2, and 3 minutes after pin insertion compared with prepin values; however, no significant difference was observed between preinduction baseline values and at 1 to 3 minutes after pinning.

Significant differences in SBP were also observed in group G at different time points after pinning (1, 2 and 3 min vs. 5 to 10 min; 4 min vs. 7 to 10 min and 5 min vs. 9 to 10 min). In group GL, compared with baseline values, there was a significant fall in SBP at 3 to 10 minutes after pinning. The prepin value was also significantly lower than the preinduction value; however, there was no difference in SBP just before and after pin insertion.

Intergroup comparisons at the same time points revealed significantly lower SBP in group G compared with group L just before pin insertion (Fig. 2). A significant rise in SBP was observed in group L compared with groups G and GL at 1 minute after pin insertion until 5 minutes [highly significant at 1 to 2 min ($P < 0.001$) and significant ($P < 0.05$) at 3 to 5 min between groups

TABLE 4. Systolic Blood Pressure (mm Hg) in the 3 Groups at Various Time Points (Mean ± SE)

	Groups					
Time Points	**Group L (N = 11)**	**Group G (N = 20)**	**Group GL (N = 12)**	***P* Value Between L and G**	***P* Value Between L and GL**	***P* Value Between G and GL**
Before Induction (Baseline)	125.9 ± 3.6	122.9 ± 2.6	127.9 ± 5.2	0.5	0.8	0.5
Before PIN	124.6 ± 2.9	113.2 ± 1.9	114.6 ± 4	0.003*	0.06	0.78
PIN 1	149.4 ± 3.8	125.1 + 3	117.9 ± 4.9	< 0.001**	< 0.001##	0.3
PIN 2	157.5 ± 4.6	126.1 ± 3.4	116.6 ± 5.2	< 0.001**	< 0.001##	0.3
PIN 3	144.7 ± 5.5	124.2 ± 3.1	111.8 ± 4.7	0.005*	0.0002##	0.06
PIN 4	135.9 ± 4.7	118.2 ± 2.9	106.9 ± 4.3	0.005*	0.0002##	0.05
PIN 5	129.1 ± 4.3	115.7 ± 3.2	108.3 ± 4.4	0.02*	0.003#	0.2
PIN 6	121.9 ± 5.7	111.7 ± 3.1	109 ± 3.9	0.1	0.08	0.6
PIN 7	116.2 ± 5.7	109.6 ± 3.1	106.4 ± 4.1	0.3	0.2	0.5
PIN 8	115.8 ± 5.8	108.4 ± 3.3	108.4 ± 3.9	0.3	0.3	0.8
PIN 9	114.9 ± 5.6	106 ± 3.4	106.3 ± 3.1	0.2	0.2	0.7
PIN 10	114.5 ± 4.8	105.1 ± 3.7	105.7 ± 2.5	0.1	0.1	0.9

*$P < 0.05$ and **$P < 0.001$ between groups L and G; #$P < 0.05$ and ##$P < 0.001$ between groups L and GL.

TABLE 5. Mean Arterial Pressure (mm Hg) in the 3 Groups at Various Time Points (Mean ± SE)

Time Points	Groups			*P* Value Between L and G	*P* Value Between L and GL	*P* Value Between G and GL
	Group L (N = 11)	Group G (N = 20)	Group GL (N = 12)			
Before Induction (Baseline)	91.4 ± 2.7	89.4 ± 2.2	90.7 ± 2.5	0.6	0.9	0.8
Before PIN	93.8 ± 3.5	82.7 ± 2.3	87.7 ± 3.8	0.02*	0.3	0.6
PIN 1	117.4 ± 5.1	96.6 ± 2.1	91.6 ± 3.9	0.002*	0.0007##	0.3
PIN 2	118.5 ± 4.6	96.7 ± 2.2	90.8 ± 4.2	0.0007**	0.0002##	0.4
PIN 3	109.9 ± 5.4	94.5 ± 2.3	85.5 ± 3.7	0.02*	0.002#	0.08
PIN 4	100.9 ± 4.6	89.6 ± 2.5	81.8 ± 3.7	0.04*	0.004#	0.14
PIN 5	94.3 ± 4.8	87.1 ± 2.6	80.8 ± 3.7	0.2	0.04#	0.2
PIN 6	90.5 ± 4.9	84.2 ± 2.4	81.2 ± 3	0.3	0.1	0.5
PIN 7	85.9 ± 5.4	82.3 ± 2.5	80.7 ± 3.4	0.5	0.4	0.6
PIN 8	86 ± 5.2	81.1 ± 2.7	81.7 ± 2.9	0.4	0.5	0.7
PIN 9	85.3 ± 4.9	79.4 ± 2.7	79.8 ± 2.7	0.3	0.4	0.8
PIN 10	83.9 ± 4.2	78.8 ± 2.8	78.7 ± 2.7	0.3	0.3	0.8

*$P < 0.05$ and **$P < 0.001$ between groups L and G; #$P < 0.05$ and ##$P < 0.001$ between groups L and GL.

L and G; highly significant ($P < 0.001$) at 1 to 4 min and significant ($P < 0.05$) at 5 min between groups L and GL]. The difference in SBP was not significant between 6 to 10 minutes of pinning in group L compared with both groups G and GL. There was no significant difference in SBP between groups G and GL at any time point. The prepin MAP was significantly lower in group G compared with L ($P = 0.02$). Increases in MAP were significantly attenuated after pin insertion in groups G and GL compared to L ($P < 0.05$ at 1 min, < 0.001 at 2 min and < 0.05 at 3 to 4 min between L and G; $P < 0.001$ at 1 to 2 min and < 0.05 at 3 to 5 min between L and GL) (Fig. 3).

Six patients in group L and 2 patients in group G required rescue therapy with propofol after pin insertion. There was no significant difference between the groups with respect to preinduction sedation scores and the prepin F_I, F_{ET}, BIS and CVP (Table 6) and total intraoperative blood loss or fluid and transfusion requirements. One patient in group L, 2 patients in group G and 2 patients in group GL were electively ventilated because of extensive nature of the surgery; however, there was no difference between the 3 groups with respect to extubation or recovery from anesthesia.

DISCUSSION

In this study, we found that 900 mg of Gabapentin, administered orally 2 hours before induction of anesthesia along with lidocaine scalp infiltration prevented the rise in HR, SBP, and MAP after skull pin insertion in patients undergoing craniotomy when compared with oral placebo and lidocaine scalp infiltration. Premedication with gabapentin alone significantly attenuated the rise in SBP and MAP after pin insertion when compared with placebo plus lidocaine scalp infiltration; however, the HR responses were more variable. The findings of our study are similar to Fassoulaki et al,[18] who found that the BP response to laryngoscopy and intubation, but not the HR was attenuated by gabapentin.

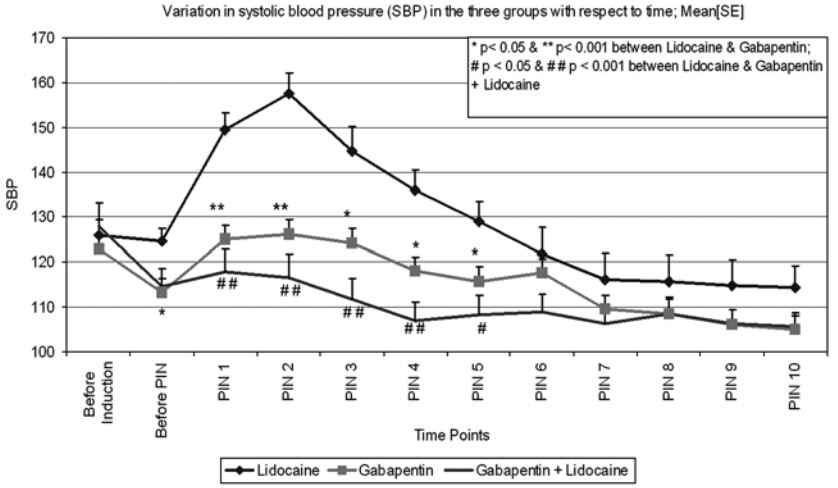

FIGURE 2. Variation in systolic blood pressure (SBP) in the 3 groups with respect to time (Mean ± SE). * is $P < 0.05$ and ** is $P < 0.001$ between groups L and G, # is $P < 0.05$ and ## is $P<0.001$ between groups L and GL.

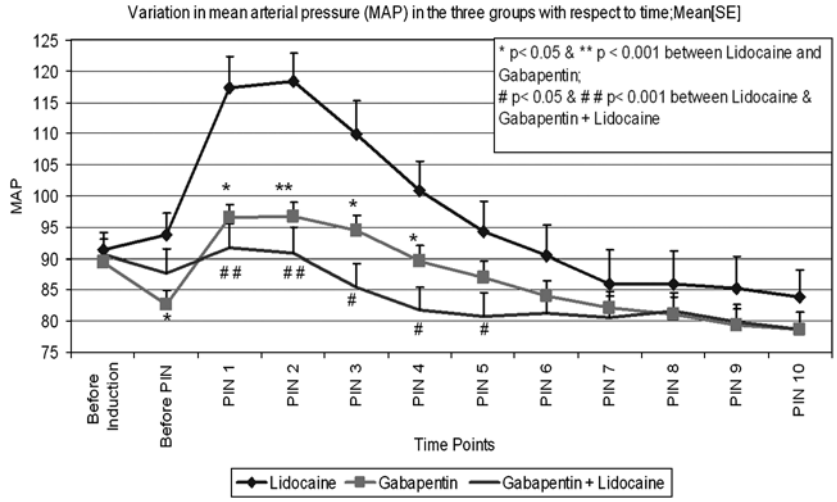

FIGURE 3. Variation in mean arterial pressure (MAP) in the 3 groups with respect to time (Mean ± SE). * is $P<0.05$ and ** is $P<0.001$ between groups L and G, # is $P<0.05$ and ## is $P<0.001$ between groups L and GL.

The Mayfield skull pin head-holder clamp is a C-shaped metal clamp with 3 sharpened metal pins arranged triangularly. The pins are inserted into the periosteum of the skull to stabilize and fix the head during craniotomy and the subsequent surgery. Tightening of the pins into the periosteum produces approximately 80 pounds of pressure.[3] Thus, this produces a reproducible source of intense stimulus each time the pins are applied resulting in brief but undesirable increases in HR, BP, and ICP.[1] In patients with borderline CPP, this may result in cerebral edema, hemorrhage, and ischemia.

Various drugs have been used as pretreatment for preventing or attenuating the hemodynamic responses to insertion of the skull pin head-holder clamp. Uyar et al,[2] studied the effect of the α_2 agonist dexmedetomidine on skull pin insertion and found that a bolus dose of 1 μg/kg given intravenously over 10 minutes before induction of anesthesia attenuated both hemodynamic and neuroendocrinal response. A similar effect has also been observed with the other α_2 agonist, clonidine.[3,4] Opioids such as fentanyl,[8–10] sufentanil,[10,11] and alfentanil,[12] have also been found to attenuate the hemodynamic response to skull pin insertion.

Gabapentin, introduced in 1993, is a second generation antiepileptic drug that has also been found useful in treating neuropathic pain.[15] Gabapentin has an opioid sparing action and is increasingly used in treating acute perioperative pain.[15] In fact, the role of gabapentin has been extended to provide preoperative anxiolysis, prevention of chronic postsurgical pain, attenuation of stress responses to noxious perioperative stimuli, prevention of postoperative delirium and nausea and vomiting.[15] However, only a few studies have examined the effects of gabapentin on the cardiovascular response to acute stress.[16,18]

Two studies have examined the effects of gabapentin on the hemodynamic response to laryngoscopy and intubation.[16,18] Although Memiş et al,[16] found a single dose of 800 mg of gabapentin, administered orally 1 hour before surgery to be effective in attenuating the hemodynamic responses to laryngoscopy and intubation, Fassoulaki et al,[18] found that 1600 mg of gabapentin, started the day before surgery, in 4 divided doses, attenuated the increases in BP owing to laryngoscopy but not the HR. The mechanism by which gabapentin attenuates the cardiovascular responses to stress is unknown. The drug may act by inhibiting voltage gated calcium channels similar to calcium channel blockers.[19]

In this study, we found that while gabapentin alone was effective in attenuating the increase in SBP and MAP after skull pin insertion when compared with placebo, the HR responses were more variable (Group G vs. GL). Although the maximal HR in group G (Gabapentin plus normal saline scalp infiltration) after pinning was 82.5 ± 3.8 beats/min, there was a significant rise in HR in this group at 1 and 2 minutes after pin insertion, compared with baseline preinduction values. Similarly, the difference in HR between groups L and G was only

TABLE 6. Preinduction Sedation Score and the Prepin F1, FET, BIS and CVP in the 3 Groups (Mean ± SE)

Groups	Group L (N = 11)	Group G (N = 20)	Group GL (N = 12)
Preinduction sedation score	1.2 ± 0.1	1.4 ± 0.1	1.3 ± 0.1
F1 (percent)	1.4 ± 0.1	1.5 ± 0.1	1.4 ± 0.1
FET (percent)	1.2 ± 0.1	1.2 ± 0.04	1.1 ± 0.02
BIS	48.5 ± 1.8	44.8 ± 0.8	49.1 ± 1.3
CVP (mm Hg)	7.9 ± 0.3	8.2 ± 0.2	8.5 ± 0.2

F1 is inspired concentration of sevoflurane, FET is end-tidal concentration of sevoflurane, BIS is bispectral index and CVP is central venous pressure. *P* was not significant between the groups.

significant at 4 minutes after pin insertion. Furthermore, a significant difference was also observed between groups G and GL at 2 minutes after pin insertion. The maximal attenuation in hemodynamic response (HR, SBP and MAP) to pin insertion was observed in group GL (Gabapentin plus lidocaine scalp infiltration).

Local anesthetic agents are commonly infiltrated into the skull before application of pins to obtund the hemodynamic responses, either with other drugs,[3,8,13] or as standalone therapy.[5,6] Although the purported benefits of local anesthetic infiltration include use of small volume of the drug, rapid onset of analgesia, no additional increase in depth of anesthesia and attenuation of hemodynamic perturbations,[13] the true advantage can be obtained if the local anesthetic is infiltrated into the scalp at least 1 to 2 minutes before the insertion of the pins.[9] Second, the infiltrated dose may be inadequate and the area infiltrated may not match the exact pin site.[8] Furthermore, the advantage of infiltration is lost in case the pins are applied more than once. Finally, it increases the risk of needle-stick injury and requires cooperation on the part of the surgeon.

However, in this study, with the same depth of anesthesia, lidocaine scalp infiltration alone (Group L) proved to be ineffective in preventing or attenuating the increase in hemodynamic response after skull pin insertion. When lidocaine was infiltrated in patients premedicated with gabapentin (Group GL), the hemodynamic response to pin insertion was abolished. This suggests that while lidocaine is useful as an add-on therapy, it may be ineffective when used alone for infiltration, although sufficient time is allowed for onset of the effect of local anesthetic. More number of rescues was also required in group L compared with groups G or GL (6 patients in group L vs. 2 in group G and none in GL). The intragroup variability in HR, SBP and MAP during the study period was also more in group L compared to groups G and GL and could have resulted from rescue treatment with propofol.

Gabapentin is administered orally 1 to 2 hours before induction of anesthesia.[15] It is generally well tolerated with a favorable side-effect profile.[20] There is no comprehensive evidence that multiple doses of gabapentin provide better analgesia than single dose.[15] The recommended dose of gabapentin is 900 mg, administered 1 to 2 hours before surgery,[15] which is what was chosen for this study. Türe et al,[21] found that in patients undergoing supratentorial tumor resection, premedication with gabapentin was associated with delayed extubation and increased postoperative sedation. However, in their study, patients received 1200 mg of gabapentin in divided doses starting 1 week before surgery as compared to the single dose of 900 mg in our patients. This may have accounted for the differences in sedation and recovery in our patients.

The main limitation of our study is a small sample size. A larger trial would be required to corroborate the findings of this study. An additional limitation was the process of blinding as group allocation, premedication, and intraoperative scalp infiltration was carried out by anesthesia residents who were familiar with the randomization process. However they played no part in the recording and/or analysis of data. Although skull pin insertion produces a neuroendocrinal stress response,[2] we did not evaluate the effect of gabapentin on the level of stress hormones before and after pinning. Phenytoin itself has analgesic properties,[21] and could have interacted with gabapentin to attenuate the hemodynamic response to pinning; however, as it was not possible to exclude antiepileptic therapy preoperatively, we therefore excluded patients on multiple antiepileptic drugs and included only the patients receiving phenytoin as monotherapy.

In conclusion, 900 mg of gabapentin, administered orally 2 hours before induction of anesthesia along with lidocaine scalp infiltration abolished the hemodynamic response after skull pin insertion. Premedication with gabapentin alone significantly attenuated the SBP and MAP; however, HR responses were more variable. A larger trial is required to corroborate the findings of the study before clinical recommendations would be warranted.

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