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The effect of craniotomy location on postoperative pain and nausea

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Abstract
Purpose. At least one retrospective study has suggested that the need for postoperative control of pain and nausea depends on the location of the cranial surgery. This prospective study was performed to examine the hypothesis that patients who have had infratentorial craniotomy experience more severe pain and more frequent nausea than those with supratentorial procedures.
Methods. We compared postoperative outcomes in 28 patients with infratentorial craniotomy, 53 with supratentorial craniotomy, and 47 with complex spinal cord surgery (the control group). Anesthesia was standardized for all three groups and the concentration of isoflurane was titrated to keep mean arterial pressure within 30% of preoperative values. Severity of pain and frequency of nausea and vomiting were recorded for 24 h after surgery. Pain was assessed with a verbal pain score scale of 0–10, with 10 being the worst pain imaginable. Data were collected for 24 h postoperatively.
Results. Because nausea and pain diminish drastically 2 h after surgery, pairwise differences were assessed at each point within the first 2 h. Within 30 min of extubation, median pain scores in the supratentorial and spine groups rose to 2 and in the infratentorial group to 5. The statistical differences between groups were not significant ($P > 0.06$) by logistic regression. Also, the incidence of nausea was not significantly different (57% supratentorial, 57% spine, 67% infratentorial; $P = 0.62$) by Dunn's procedure.
Conclusion. There were no significant differences in the severity of pain or the frequency of nausea based on the craniotomy site.

Key words Neurosurgical anesthesia · Craniotomy · Pain · Nausea

Introduction

In recent decades, pain and nausea after surgery have been investigated extensively, and major advances have been made in the management of these symptoms. Nevertheless, pain and nausea are the most common distressing symptoms after anesthesia for surgery for intracranial lesions [1]. After craniotomy, postoperative pain and nausea may worsen arterial hypertension, intracranial hypertension, and respiratory function. Pain itself may also be a cause of postoperative nausea [2]. The proximity of cranial nerve pathways and of the chemoreceptor trigger zone to the surgical field may increase the risk of pain and nausea after posterior fossa surgery. Quiney et al. [3] demonstrated that most patients undergoing craniotomy experience postoperative pain, with severity ranging from mild to severe.

In a retrospective analysis of patients undergoing elective craniotomy, Fabling et al. [4] found that the incidence of postoperative nausea and vomiting was greater in patients who had infratentorial craniotomy compared with those with supratentorial craniotomy. Such a finding is clinically important because it would help predict the need for control of pain and nausea postoperatively in these patients. However, that study had two limitations. First, the study was retrospective. Second, the large number of variables it examined increased the possibility that chance differences would be considered significant. To determine the effect of surgical location on postoperative pain and nausea, we prospectively examined the hypothesis that the severity of pain and the incidence of nausea are higher after infratentorial when compared with supratentorial craniotomy. We also compared craniotomy patients with a group of patients undergoing complex spinal operations to serve as controls.

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Subjects and methods

The institutional review board approved this study, and written informed consent was granted by all participants. We studied 128 patients scheduled for elective craniotomy or spinal surgery. This group consisted of 81 patients scheduled for elective craniotomy (study group) and 47 who were to have elective spine surgery (control group). We tried to match the operative duration of the spine group to that of the craniotomy group by selecting procedures expected to last more than 3 h. As a result, only patients undergoing complex spine instrumentation were enrolled in this study. Also, only patients having resection of intracranial tumors were studied, excluding patients who were to have brain biopsy alone. The anesthetic technique was standardized. The technique consisted of thiopental 2–3 mg·kg^{-1} and sufentanil 1–2 μg·kg^{-1} for induction, followed by sufentanil infused at a rate of 0.2–0.5 μg·kg^{-1}·h^{-1}, nondepolarizing neuromuscular blockade, nitrous oxide (60% inspired), and isoflurane (<0.5% end-tidal), titrated to keep the mean arterial pressure within 30% of the preoperative value. At the time of dural closure for craniotomy patients, and at the time of spinal muscle closure for the controls, sufentanil infusion was discontinued. Isoflurane and nitrous oxide were discontinued during skin closure and after application of head dressing, respectively. Neuromuscular block was reversed with neostigmine and glycopyrrolate. Before the patient emerged from anesthesia, the location of the patient's brain lesion was classified as supratentorial (n = 53) or infratentorial (n = 28). Local anesthesia was not used to infiltrate the skin or the scalp.

After full emergence from general anesthesia, all patients were asked about nausea or pain. Pain was assessed by a verbal pain score (0–10, with 10 being the worst pain imaginable). Vital signs and oxygenation (pulse oximetry) were recorded every 15 min for 1 h, then every hour for 4 h, and again at 24 h. Pain and nausea were assessed every 15 min for 2 h. Pain was treated with intravenous morphine sulfate, and nausea was treated with droperidol. Intravenous morphine 2 mg to 4 mg was given as needed for pain 24 h after surgery; 0.625 mg of droperidol was administered intravenously for nausea as needed in the postoperative period. No prophylactic intraoperative antiemetics were administered. We relied on narcotic-nitrous oxide-based anesthetic for intraoperative and initial postoperative pain relief.

For statistical analysis, the association between pain score and type of surgery was first assessed with a repeated-measures analysis of variance, using time after extubation. Pairwise differences between median pain scores in the supratentorial, infratentorial, and spine groups were assessed at each point within the first 2 h after operation, using the nonparametric Kruskal-Wallis and Dunn pairwise comparison tests. Logistic regression was used to compare groups on frequency of nausea and vomiting. A Bonferroni correction for multiple comparisons was applied at each time point so that P values <0.017 (or 0.05/3) were deemed statistically significant. No additional adjustment to the significance criteria was made for comparing groups at multiple time points.

Results

Except for a higher percentage of female patients in the craniotomy group, there were no substantive differences in demographic, operative, or anesthetic characteristics between groups (Tables 1 and 2). In the repeated-measure analysis of variance of the pain score, there was no significant interaction between surgery groups and time and no differences among surgery groups collapsing over time. Furthermore, no statistically significant differences were found in median pain scores at any point in time among the spine surgery, supratentorial, and infratentorial groups (Table 3). Although the median pain score in the infratentorial group rose to 5 by 30 min, and the median scores in the other groups remained at about 2 (Table 3), these differences did not reach P = 0.017, the alpha level determined by the Bonferroni correction (Table 3).

When the supratentorial, infratentorial, and spine groups were compared, with logistic regression, for incidence of nausea at each time point, no significant differences were found (Table 4). Also, there were no differences at any time between tumor and spine patients with respect to nausea (Table 4). Differences between these two groups in the amount of morphine and droperidol that was administered intravenously to treat pain and nausea during the first 24 h postoperatively did not reach statistical significance.

Discussion

This prospective clinical investigation found no statistically significant differences in postoperative pain scores or nausea among patients undergoing infratentorial craniotomy, supratentorial craniotomy, and spine surgery when not infiltrated with local anesthetic intraoperatively. However, median pain scores in the infratentorial craniotomy group did rise substantially higher than scores in the two other groups at 30 and 45 min, suggesting that the infratentorial group may, in fact, experience more pain. However, our sample size was too small to determine whether the effect was statistically significant.

Table 1. Characteristics of patients undergoing infratentorial, supratentorial, and spine surgery

	Supratentorial (n = 53)	Infratentorial (n = 28)	Spine (n = 47)	P[a]
Age, mean (years) ± SD	50 ± 15	50 ± 15	52 ± 13	0.419
No. of women (%)	35 (66)	12 (43)	14 (30)	0.002
Height, mean (cm) ± SD	169 ± 10	169 ± 10	175 ± 10	0.002
Weight, mean (kg) ± SD	75 ± 17	75 ± 17	83 ± 16	0.009
No. with ASA III (%)	53 (100)	18 (64)	5 (11)	<0.001
No. with hypertension (%)	15 (28)	5 (18)	16 (34)	0.26
No. with heart disease (%)	4 (8)	2 (7)	8 (17)	0.08
No. with epilepsy (%)	1 (2)	1 (4)	0	0.30
No. right handed (%)	53 (100)	18 (64)	45 (96)	0.21

ASA, American Society of Anesthesiologists
[a] Two-sided t-tests were used to compare means; likelihood ratio χ^2 test was used to compare proportions; significance was set at 0.017

Table 2. Characteristics of the operative procedure

	Spine			Tumor			
	No.	Mean	SD	No.	Mean	SD	P
Duration (min)							
Induction to dressing	46	4.96	2.39	81	5.70	1.86	0.05
Opioid off to dressing	46	49.98	25.14	81	66.12	33.01	0.002[a]
Isoflurane off to dressing	46	9.72	11.39	81	10.25	13.69	0.82
N_2O off to extubation	46	5.83	4.51	81	6.22	5.05	0.66
Isoflurane off to extubation	46	19.36	10.99	81	21.34	13.90	0.40
Anesthetics							
Isoflurane MAC (h)	46	1.58	0.96	81	1.90	0.79	0.04
Total sufentanil dose ($\mu g \cdot kg^{-1}$)	46	2.08	0.86	81	2.30	0.86	0.17
Thiopental dose ($mg \cdot kg^{-1}$)	40	3.44	1.51	79	3.90	1.27	0.08
P_{ET}Iso (when discontinued, mmHg)	42	0.22	0.11	78	0.25	0.10	0.12
P_{ET}Iso (when N_2O discontinued, mmHg)	38	0.06	0.09	69	0.08	0.08	0.26
Miscellaneous							
$P_{ET_{CO_2}}$ (at dural closure, mmHg)	45	25.76	2.93	65	22.30	3.48	<0.001[a]
Temperature (at skin closure, °C)	46	35.53	0.68	82	35.89	0.90	0.01[a]

MAC, minimum alveolar concentration; $P_{ET_{CO_2}}$, extrapolated end-tidal carbon dioxide tension; P_{ET}Iso, end-tidal concentration of isoflurane
[a] Two-sided t-test unless noted otherwise; significant at 0.01 criterion

Patients undergoing craniotomy have traditionally been thought to experience minimal pain in the postoperative period. In addition, the clinician's desire to conduct a neurologic examination and preserve pupillary signs may lead to underappreciation of postoperative pain in patients undergoing craniotomy. Experimental studies on humans undergoing intracranial surgery [5] have found various structures that are pain-sensitive, including all extracranial structures, the great venous sinuses, and the dural, meningeal, and cerebral arteries. These structures are innervated by cranial nerves V, IX, and X, and the upper three cervical nerves. Stimulating pain-sensitive structures on or above the superior surface of the tentorium cerebelli causes pain in the anterior part of the head, whereas stimulating structures on or below the inferior surface of the tentorium produces pain in the inferior aspect [6]. Furthermore, pain from the supratentorial structures is mediated by the trigeminal nerve, whereas pain from the infratentorial structures is transmitted by afferent fibers in cranial nerves V, IX, and X, and the upper three cervical nerves. Cranial bones are not pain-sensitive, but the scalp and its arterial supply are [6].

The fact that the cranial nerves involved in sensory innervation of the head and neck originate in the infratentorial compartment might be thought to contribute to higher pain scores after infratentorial craniotomy. Consistent with this notion are the observations of De Benedittis et al. [7], who demonstrated that patients undergoing surgery by the subtemporal and suboccipital routes have the highest incidence of postoperative pain. We did not study this group of patients separately.

Table 3. Median pain scores within 2 h after operation in patients with infratentorial craniotomy, supratentorial craniotomy, and spinal surgery

	Infratentorial		Supratentorial		Spinal		
Time	No.	Median (IQ range)	No.	Median (IQ range)	No.	Median (IQ range)	P^a
Entire 2 h	25	3.8 (1.2–6.2)	53	1.7 (0.6–4.3)	47	2.0 (0.0–5.2)	0.27
Extubation	7	0 (0–3)	32	0 (0–2.5)	25	0 (0–2)	0.98
15 min	21	4 (0–6)	43	0 (0–5)	40	0 (0–4)	0.14
30 min	22	5 (1–8)	51	2 (0–5)	43	2 (0–6)	0.09
45 min	23	5 (2–7)	52	2 (0–5)	42	2.5 (0–5)	0.06
60 min	25	5 (0–7)	47	2 (0–5)	43	2 (0–5)	0.24
120 min	25	4 (1–5)	48	2 (1–5)	40	3 (0–5)	0.62

IQ, interquartile
[a] Dunn's procedure; significance assumed at $P = 0.017$

Table 4. Incidence of nausea in first 2 h postoperatively

	Control		Supratentorial		Infratentorial		
Time	No.	(%)	No.	(%)	No.	(%)	P^a
Extubation to 2 h	27/47	(57)	30/53	(57)	18/27	(67)	0.62
Extubation	8/39	(21)	7/45	(16)	4/22	(18)	0.84
15 min	13/47	(28)	18/53	(34)	5/27	(19)	0.33
30 min	14/47	(30)	18/50	(36)	12/26	(46)	0.38
45 min	10/44	(23)	14/51	(27)	11/27	(41)	0.27
60 min	9/44	(20)	14/49	(29)	7/27	(26)	0.66
120 min	9/42	(21)	11/47	(23)	8/27	(30)	0.74

[a] Logistic regression: no overall or pairwise differences were significant

Although nausea and vomiting may have evolved as protective reflexes, they are undesirable side effects after surgery because they can lead to significant morbidity, such as increased intracranial pressure, loss of fluids and electrolytes, alkalosis, and worsening of respiratory function. The extent of surgical manipulation involved in craniotomy and the proximity of the vomiting center may predispose craniotomy patients to nausea and vomiting [8]. The vomiting center is located in the dorsal part of the reticular formation in the medulla, close to the tractus solitarius at the level of the dorsal motor nucleus of the tenth cranial nerve. The nuclei associated with vasomotor activity, salivation, respiration, and bulbar control are also close by. Emesis is a complex reflex pathway controlled by the brainstem and involving humoral factors, afferent fibers, and complex excitation and inhibition of both the somatic and the visceral musculature.

Physiologic evidence suggests that vomiting might be associated with infratentorial craniotomy. For example, the chemoreceptor trigger zone, which is one of the routes leading to emesis, is located in the infratentorial compartment and might, therefore, be expected to be inadvertently stimulated or damaged during infratentorial craniotomy [9]. However, we found no differences in the incidence of postoperative nausea after supratentorial craniotomy compared with infratentorial craniotomy. Our results agree with those of Quiney et al. [3], who, in their prospective study, reported no difference in emetic symptoms of patients undergoing craniotomy at various sites. By contrast, in a retrospective analysis by Fabling et al. [4] of patients undergoing elective craniotomy, the incidence of postoperative nausea and vomiting was greater in patients who had infratentorial craniotomy than in those with supratentorial craniotomy. However, because the Fabling group's study examined a very large number of variables, chance differences may have been considered significant. Opioids and nitrous oxide may be associated with a higher incidence of postoperative nausea and vomiting. Our reliance on a primarily narcotic nitrous oxide-based anesthetic may be expected to enhance subtle effects of cranial surgery on nausea and vomiting. In spite of this, we found no differences in the incidence of postoperative nausea after craniotomy compared with complex spine surgery.

In conclusion, our prospective clinical investigation failed to confirm a previous observation that infratentorial craniotomy is associated with a higher early requirement for immediate postoperative pain control than supratentorial or spine procedures when local anesthetic infiltration is not used. In addition, we found

no differences in the incidence of postoperative nausea between groups.

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