


Role of scalp nerve block in improving the quality of rehabilitation in patients after meningioma resection

A randomized controlled clinical trial

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Abstract

Background: In this study, we analyzed whether scalp nerve block with ropivacaine can improve the quality of rehabilitation in patients after meningioma resection.

Methods: We included 150 patients who were undergoing craniotomy in our hospital and categorized them into 2 groups – observation group (patients received an additional regional scalp nerve block anesthesia) and control group (patients underwent intravenous general anesthesia for surgery), using the random number table method approach (75 patients in each group). The main indicator of the study was the Karnofsky Performance Scale scores of patients at 3 days postoperatively, and the secondary indicator was the anesthesia satisfaction scores of patients after awakening from anesthesia. The application value of different anesthesia modes was studied and compared in the 2 groups.

Results: Patients in the observation group showed better anesthesia effects than those in the control group, with significantly higher Karnofsky Performance Scale scores at 3 days postoperatively (75.02 vs 66.43, $P < .05$) and anesthesia satisfaction scores. Compared with patients in the control group, patients in the observation group had lower pain degrees at different times after the surgery, markedly lower dose of propofol and remifentanyl for anesthesia, and lower incidence of adverse reactions and postoperative complications. In addition, the satisfaction score of the patients and their families for the treatment was higher and the results of all the indicators were better in the observation group than in the control group, with statistically significant differences ($P < .05$).

Conclusion: Scalp nerve block with ropivacaine significantly improves the quality of short-term postoperative rehabilitation in patients undergoing elective craniotomy for meningioma resection. This is presumably related to the improvements in intraoperative hemodynamics, relief from postoperative pain, and reduction in postoperative nausea and vomiting.

Abbreviations: KPS = Karnofsky Performance Scale, rANOVA = repeated-measures analysis of variance, SPSS = Statistical Product and Service Solutions.

Keywords: craniotomy, quality of postoperative rehabilitation, regional scalp nerve block, surgery anesthesia

1. Introduction

Surgery is a common therapeutic modality for various types of clinical diseases, and the application rate of different types of clinical surgeries has increased significantly in recent years thanks to the continuous development and progress of medical

technology. However, trauma is an unavoidable problem in surgery, particularly in craniotomy, which is even more traumatic and dangerous. In addition, most patients with cranio-cerebral trauma and lesions have varying degrees of increased intracranial pressure and cerebral edema, which can further increase the difficulty of clinical surgery. Therefore, it is

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Written informed consent was obtained from all participants.

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

This study was conducted with approval from the Ethics Committee of People's Hospital of Qiannan (no. QNZY-gzswjw-23-0705). This study was conducted in accordance with the declaration of Helsinki.

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necessary to strengthen the management of anesthesia in clinical craniotomy and select the safest and most effective surgical anesthesia program for patients. This approach not only ensures the safety of the surgery but also reduces the degree of postoperative pain in patients, thereby increasing the efficiency of postoperative rehabilitation of patients.^[1] The key to neurosurgical anesthesia is to maintain hemodynamic stability during the induction and intraoperative periods, reduce complications due to postoperative pain, and guarantee the smooth and rapid postoperative awakening of the patients. In neurosurgery, head nailing, scalping, and bone sawing are considered the most stimulating procedures, which can easily cause increased blood pressure and tachycardia and elevate the risk of intracranial hemorrhage and increased intracranial pressure.^[2] This hemodynamic response is commonly mitigated by increasing the dose of general anesthetics, using antihypertensive or antiarrhythmic drugs, and performing local nerve block. Most patients with craniocerebral lesions requiring neurosurgical intervention such as a craniotomy, have varying degrees of intracranial neurological damage and intracranial hypertension. In addition, the underlying condition can be made worse by the stimulation of surgical trauma and pain, leading to hemorrhage and edema of brain tissues and even intracranial hemorrhage, which pose an immediate risk to the life and safety of the patients. Accordingly, we conducted a comprehensive evaluation of the impact of regional scalp nerve block on the administration of anesthesia for patients undergoing a craniotomy, in this study.

2. Materials and methods

2.1. General information

We included 150 patients admitted to our hospital for craniotomy from August 2019 to August 2021. These patients were allocated into the observation (75 patients) and control (75 patients) groups using the random number table method. The comparison of the clinical baseline data of the patients showed that the difference between the 2 groups was not statistically significant ($P > .05$), indicating the existence of clinical comparability.

The inclusion criteria were: Patients who met the criteria for craniotomy through clinically relevant examinations; Patients with complete clinical data; Patients with normal communication ability and intellectual functioning; and Patients and family members who had a detailed understanding of the present study and voluntarily signed an informed consent form.

The exclusion criteria were: Patients with congenital mental retardation and verbal communication disorders; Patients with severe infectious diseases; Patients with serious mental diseases who cannot cooperate with nursing treatment; Patients with contraindications to surgery; Patients with coagulation disorders; and Patients and family members who could not actively cooperate with the whole treatment process.

2.2. Treatment methods

After patients in both the groups entered the operating room, they were placed in the supine position, followed by continuous monitoring of their electrocardiogram, blood pressure, and oxygen saturation. After the lower-extremity venous access was established, the patients underwent local anesthesia and radial artery puncture. Next, an indwelling catheter was inserted, and vital indicators including blood pressure, respiration, and pulse were monitored. Anesthesia was induced with dexmedetomidine (0.4 $\mu\text{g}/\text{kg}/\text{h}$), etomidate (0.3 mg/kg), cis-atracurium (0.2 mg/kg), and sufentanil (0.4 $\mu\text{g}/\text{kg}$), and then endotracheal intubation, breathing control, and general anesthesia were performed. In the control group,

the patients received intravenous general anesthesia, which was maintained through intravenous infusion with propofol (4–8 mg/kg/h) and remifentanyl (6–10 $\mu\text{g}/\text{kg}/\text{h}$). The depth of anesthesia was regulated through inhalation of 0.5% to 1% sevoflurane based on the circulatory fluctuations of the patients. Cis-atracurium besylate was intermittently injected to maintain the requisite muscle relaxation without nerve block anesthesia. The patients in the observation group additionally received regional scalp nerve block. The nerve block locations, such as supraorbital nerve, supratrochlear nerve, auriculotemporal nerve, greater occipital nerve, and lesser occipital nerve, were determined according to the surgical site of patients. The greater and lesser occipital nerves innervate the occipital skin and are usually anatomically located 4 and 7 cm adjacent to the superior nuchal line and external occipital protuberance, respectively. The greater occipital nerve is often accompanied by the greater occipital artery. The greater and lesser occipital nerves were blocked through ultrasound-guided linear injection of the local anesthetic in the middle third of the superior nuchal line. The auriculotemporal nerve originates from the mandibular nerve. The needle was inserted 1.5 cm in front of the tragus using ultrasound guidance to avoid puncturing the superficial temporal artery. The supraorbital and supratrochlear nerves are branches of the ophthalmic nerves, which innervate sensation in the forehead and anterior scalp. The supraorbital nerve exits through the supraorbital notch to the subcutis and is distributed to the frontal skin. The needle was inserted toward the tip of the supraorbital notch, located with ultrasound guidance, while the orbital margin was held down with one hand to protect the eyeball. Then, the supraorbital nerve was blocked by injecting local anesthetics, and the supratrochlear nerve was blocked by inserting the needle 1 to 1.5 cm next to the supraorbital notch. The dose of 0.5% ropivacaine was 2 mL for supratrochlear or supraorbital nerve block and 3 to 5 mL for auriculotemporal, greater occipital, and lesser occipital nerve block. The operator was a senior anesthesiologist who was skilled in scalp nerve block. After 5 minutes, patients were re-needed to assess their level of blockage; if it did not meet the standard, corrective action was taken promptly to ensure full blockage before surgery.

2.3. Observation indicators

The primary indicator statistically analyzed was the Karnofsky Performance Scale (KPS) scores of the patients at 3 days postoperatively. The secondary indicators included satisfaction scores after awakening from anesthesia, which were obtained using the Iowa Satisfaction with Anesthesia Scale. The degree of pain felt by the patients at 12, 24, and 48 hours postoperatively, was evaluated using the Visual Analog Scale, with a total score of 10 (a higher score indicated more severe pain). Meanwhile, the dose of propofol and remifentanyl administered, the adverse reactions, and the postoperative complications were recorded in detail. Questionnaires were used to assess the degree of satisfaction of the patients with the treatment: the maximum score was 10 points, and a higher final score represented a higher degree of satisfaction.

2.4. Statistical analysis

IBM SPSS (Statistical Product and Service Solutions) 20.0 software (SPSS Inc., Chicago) was used for data processing. The measurement data are presented as mean + standard deviation ($\bar{x} \pm s$) and the count data as (n (%)) and were compared using the *t* test and the chi-squared test, respectively. The difference in the data comparison between the groups was significant at $P < .05$, suggesting statistical significance.

3. Results

No significant difference was observed in the basic demographics of the patients between the 2 groups (Table 1). The 2 groups were not significantly different in terms of the basic demographics, including age, gender, height, weight, body mass index, American Society of Anesthesiologists grading ($P > .05$) (Table 2).

3.1. Scalp nerve block significantly increased the KPS scores of patients at 3 days postoperatively

The repeated-measures analysis of variance (rANOVA) statistical method was used to analyze the KPS scores of the patients in the 2 groups before surgery, 3 days after surgery, and before discharge. The results showed no significant difference in the preoperative KPS scores of the patients between the 2 groups. The KPS scores at 3 days postoperatively were lower than those before surgery. The KPS scores were significantly higher in the observation group than in the control group. The KPS scores were insignificantly higher before discharge than before surgery (Table 2). These findings suggested that scalp nerve block with ropivacaine before the use of the head holder significantly increased the quality of rehabilitation in patients undergoing meningioma resection at 3 days postoperatively, but that this improvement disappeared before discharge.

3.2. Pain scores for both groups

The final scoring results showed that patients in the observation group had better anesthetic analgesia than those in the control group, accompanied by lower pain degrees at different stages of the postoperative period. The results of all indicators in the observation group were markedly superior to those in the control group, and the difference between the data of the 2 groups was statistically significant ($P < .05$) (Table 3).

3.3. Comparisons of indicators between the 2 groups

The dose of propofol and remifentanyl used for anesthesia was lower in the observation group than in the control group. Additionally, adverse reactions during anesthesia were fewer and the final complication rate was substantially lower in the observation group than in the control group. Compared with the control group, the patients and their families in the observation group had higher satisfaction scores with the treatment effect. The difference in indicators between the 2 groups was statistically significant ($P < .05$) (Table 4).

3.4. Comparison of intraoperative hemodynamics between the 2 groups

In order to clarify the mechanism of ropivacaine scalp nerve block in improving short-term postoperative rehabilitation

Table 1

Basic demographic data of patients in both groups.

Index	Observation group	Control group	t/ χ^2	P
M/F (n)	38/37	45/30	8.407	.929
Age (yr)	65 (60–73)	67 (61–72)	5.649	.364
BMI (kg/m ²)	22 (21–24)	23 (20–25)	2.663	.103
ASA II/III (n)	45/30	46/29	4.689	.288
Operation time (min)	212.5 + 12.3	202.1 + 10.2	32.741	.744
Duration of anesthesia (min)	234.8 + 15.9	236.3 + 13.2	21.843	.904
Duration of intensive care (min)	632.7 + 25.6	418.5 + 21.3 ^a	45.641	.012
Postoperative outcome	Good	Good	–	–

ASA = American Society of Anesthesiologists, BMI = body mass index.

Table 2

Comparison of KPS scores between the 2 groups (n = 75, $\bar{x} \pm s$).

Point-in-time	Control group (n = 75)	Observation group (n = 75)	t	P
Before the surgery	77.17 ± 6.08	76.29 ± 6.19	0.879	.381
Three days after the surgery	68.21 ± 8.76*	73.69 ± 8.73	-3.837	<.001
Before discharge	84.99 ± 6.48* [†]	84.64 ± 7.55* [†]	0.302	.763

KPS = Karnofsky Performance Scale.

*Compared with preoperative, $P < .05$.

[†]Compared with 3 days after operation, $P < .05$.

Table 3

Comparison of the effect of analgesic in patients between the 2 groups (n = 75, $\bar{x} \pm s$).

Point-in-time	Control group (n = 75)	Observation group (n = 75)	t	P
2 h	2.05 ± 0.57	1.27 ± 0.50	8.995	<.001
12 h	2.27 ± 0.55	1.43 ± 0.52	9.542	<.001
24 h	2.47 ± 0.58*	1.63 ± 0.49* [†]	9.632	<.001
48 h	2.69 ± 0.72* [†]	2.75 ± 0.66* [†]	-0.474	.636

*Compared with 2 h, $P < .05$.

[†]Compared with 12 h, $P < .05$.

[‡]Compared with 24 h, $P < .05$.

quality in patients with selective craniotomy meningioma resection, hemodynamic changes at different time points were measured in 2 groups. The results of repeated ANOVA analysis showed that there was no significant difference in mean arterial pressure and heart rate between the 2 groups of patients before extubation ($P > .05$), and there was a significant difference after extubation ($P < .05$), see Table 5. This indicates that the overall levels of mean arterial pressure and heart rate in the control group are more stable than those in the observation group.

4. Discussion

Numerous studies conducted in recent years have reported that the incidence and extent of postoperative pain after craniotomy are often underestimated.^[3] In addition, conventional postoperative analgesic methods cannot be directly applied to patients undergoing craniotomy due to the specificity of neurosurgical diseases and the need for neurosurgeons to assess the condition of the patients. It is estimated that approximately 55% to 87% of the patients undergoing a craniotomy experience moderate to severe postoperative pain.^[4,5] Postoperative pain excites the sympathetic nervous system, resulting in nervousness and anxiety, and elevates the blood pressure and cardiac load, besides increasing the cerebral oxygen consumption, intracranial pressure, the risk of intracranial hemorrhage, and the rate of unplanned reoperation, thereby lengthening the time to discharge, which is detrimental to the rehabilitation of patients after a craniotomy. Acute postoperative pain can induce stress responses to cause changes in neuro-endocrine function in the body of patients and excessive secretion of serum cortisol. When the pain is more intense, it will cause high heart rate, aggravate myocardial ischemia and hypoxia, easily cause adverse cardiovascular events, and increase the risk of postoperative adverse events.^[6] In addition, inadequately treated acute postoperative pain augments the risk of developing chronic postoperative pain.

Postoperative analgesia for patients undergoing craniotomy is still inadequate. The incidence of postoperative pain is still relatively high due to the lack of awareness of the postoperative pain in craniotomy, as well as the concerns about the adverse effects of postoperative analgesic medications, such as opioids that may cause excessive sedation and inhibit respiration to induce carbon-dioxide accumulation, thereby contributing to elevated intracranial pressure and pupil constriction, which

affect the assessment of the condition.^[7] In addition, neurosurgical complications, such as postoperative hemorrhage, elevated intracranial pressure, cerebral infarction, epilepsy, hypertension, air embolism, cranial nerve injury, and cerebral edema, increase the complexity of postoperative analgesia in patients undergoing craniotomy, rendering both neurosurgeons and anesthesiologists to hold a conservative and cautious attitude toward postoperative analgesia in patients undergoing craniotomy.^[8]

The technical principle of the regional scalp nerve block is to inject 2 to 3 mL of local anesthetics to block the nociceptive afferents of the following sensory nerves: supraorbital nerve, supratrochlear nerve, zygomaticotemporal nerve, auriculotemporal nerve, great auricular nerve, lesser occipital nerve, greater occipital nerve, and the third occipital nerve. Unilateral or bilateral block or partial block of the above nerves are performed as needed for the surgery. A prior study demonstrated that a regional scalp nerve block in patients undergoing craniotomy could reduce postoperative pain scores and decrease opioid dosage. Specifically, preoperative regional scalp nerve block decreased the pain scores until about 16 hours postoperatively. Remarkable benefits were noted in anesthesia management, including reduction in hemodynamic fluctuations caused by injurious stimuli such as head nailing, scalping, and bone-flap removal, reduction in sedative medications, accelerated awakening of patients, and reduction in postoperative cognitive dysfunction.^[9]

Surgery has emerged as an indispensable and important measure in the treatment of clinical diseases. Craniotomy is a standard surgical procedure for treating craniocerebral trauma and other serious brain disorders. Nevertheless, craniotomy is highly traumatic, and most patients undergoing craniotomy have different degrees of cerebral nerve function damage, intracranial pressure increases, and cerebral edema before surgery and exhibit affected blood pressure regulation function due to the stimulation of anesthetic drugs and surgical trauma,^[10] which increases the difficulty of clinical surgery. At the same time, these factors amplify the postoperative pain level of patients after a craniotomy, whilst severe pain aggravates the postoperative stress responses in patients, leading to an increase in the incidence of postoperative complications and has a major impact on the efficacy of postoperative rehabilitation. Moreover, craniotomy is particularly difficult for elderly and pediatric patients with weakened immune systems. Therefore, good clinical anesthesia is required to ensure the efficacy and safety of craniotomy. Previously, intravenous general anesthesia

Table 4

Comparison of indicators between the 2 groups (n = 75, $\bar{x} \pm s$, %).

Group	Control group (n = 75)	Observation group (n = 75)	t/ χ^2	P
Propofol (mg)	858.74 ± 30.17	608.26 ± 28.06	7.042	<.001
Remifentanyl (μg)	2403.55 ± 273.69	1316.14 ± 193.02	28.119	<.001
Adverse reactions (%)	8 (10.7)	1 (1.3)	–	.034
Incidence of complications (%)	9 (12.0)	2 (2.7)	4.807	.028
Treatment satisfaction (%)	71 (94.7)	67 (89.3)	1.449	.229

Table 5

Comparison of intraoperative hemodynamics between the 2 groups (n = 75, $\bar{x} \pm s$).

Time	MAP (mm Hg)				HR (min)			
	Observation group	Control group	t	P	Observation group	Control group	t	P
Before intubation	81.5 ± 10.1	80.4 ± 13.4	0.864	.638	72.6 ± 10.0	74.8 ± 11.0	0.979	.123
Time of cutting	86.7 ± 12.3	81.5 ± 11.8	0.953	.745	82.8 ± 12.0	80.7 ± 10.0	0.845	.293
Time of sewing	85.4 ± 16.2	82.4 ± 15.2	0.674	.925	84.8 ± 11.0	83.5 ± 12.0	0.943	.852
After extubation	99.4 ± 12.8	80.9 ± 11.5 ^a	0.043	.023	95.8 ± 11.0	78.3 ± 12.0 ^a	0.037	.018

HR = heart rate, MAP = mean arterial pressure.

was used for craniotomy. Nonetheless, the limitations of this method of anesthesia contribute to poor surgical outcomes and elevate the probability of stress reactions and postoperative adverse reactions, thus increasing the degree of postoperative pain and affecting postoperative rehabilitation.^[11,12] As a result, improving the efficacy of anesthesia in craniotomy has become a hot topic of discussion among scholars.

The current study improved upon previous efforts by including a regional scalp nerve block in surgical patients under general anesthesia. Scalp nerve block can enable anesthesia drugs to quickly act on the cell membrane Na⁺ channels and produce highly inhibitory effects, which reduces the excitability and conductivity of nerve fibers, prevents stress responses due to the stimulation of the nerve center by surgical trauma, and decreases the dose of anesthesia drugs. Therefore, scalp nerve block can not only improve surgical outcomes, but also lessen postoperative pain, decrease the likelihood of adverse reactions, and improve the rehabilitation efficacy of patients. In this present study, we compared the KPS scores before the surgery, 3 days after the surgery, and before discharge between the 2 groups. The KPS scores at 3 days postoperatively were significantly higher in the observation group than in the control group ($*P < .05$), and the KPS scores before discharge were not significantly different between the 2 groups. The addition of the regional scalp nerve block during the surgery of the patients in the observation group significantly reduced the dose of anesthetic drugs used, the incidence of adverse reactions and complications, and the pain degree at different stages of the postoperative period. In addition, patients in the observation group fared better on the indicators than those in the control group, who only received intravenous general anesthesia.

5. Conclusion

Scalp nerve block elevates the quality of short-term postoperative rehabilitation and anesthesia satisfaction of patients and reduces the incidence of postoperative pain, nausea, and vomiting. However, the effect of scalp nerve block on the quality of long-term rehabilitation needs to be further studied and explored.

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References

- [1] Guan XP. Observation on the application effect of head nerve block combined with intravenous general anesthesia in craniotomy anesthesia. *Med Forum.* 2019;23:1472–3.
- [2] Zong SL, Tang S. Research progress in scalp nerve block during craniotomy. *Int J Anesthesiol Resuscitation.* 2020;41:501–5.
- [3] Wang J, Chen XL, Qin XW, et al. Application of head nerve block combined with general anesthesia in craniotomy for elderly supratentorial tumors. *Chin J Gerontol.* 2020;40:3231–4.
- [4] Li DX. Exploring the clinical application of head nerve block combined with intravenous general anesthesia in craniotomy anesthesia. *World Latest Med Inform.* 2019;19:117–8.
- [5] Zhang JX, Bai YC, Wang XH, et al. Safety and efficacy of general anesthesia combined with scalp nerve block in craniotomy. *Clin Res Pract.* 2021;6:101–103,106.
- [6] Haldar R, Kaushal A, Gupta D, Srivastava S, Singh PK. Pain following craniotomy: reassessment of the available options. *Biomed Res Int.* 2015;2015:509164.
- [7] Guilfoyle MR, Helmy A, Duane D, Hutchinson PJA. Regional scalp block for postcraniotomy analgesia: a systematic review and meta-analysis. *Anesth Analg.* 2013;116:1093–102.
- [8] Hwang JY, Bang JS, Oh CW, et al. Effect of scalp block with levobupivacaine on recovery profiles after craniotomy for aneurysm clipping: a randomized, double-blind, and controlled study. *World Neurosurg.* 2015;83:108–13.
- [9] Stieger A, Romero CS, Anderegg L, Heisenberg D, Urman RD, Luedi MM. Nerve blocks for craniotomy. *Curr Pain Headache Rep.* 2024;28:307–13.
- [10] Wang YH, Chai JR, Xu X, et al. Pharmacological characterization of dezocine, a potent analgesic acting as a kappa partial agonist and mu partial agonist. *Sci Rep.* 2018;8:14087.
- [11] Chowdhury T, Garg R, Sheshadri V, et al. Perioperative factors contributing the post-craniotomy pain: a synthesis of concepts. *Front Med (Lausanne).* 2017;4:23.
- [12] Akcil EF, Dilmen OK, Vehid H, Ibisoglu LS, Tunali Y. Which one is more effective for analgesia in infratentorial craniotomy? The scalp block or local anesthetic infiltration. *Clin Neurol Neurosurg.* 2017;154:98–103.