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RESEARCH ARTICLE

Scalp Nerve Block in Combination to General Anesthesia Lower the Increase of Inflammatory Markers Compared to General Anesthesia alone in Craniotomy Surgeries

I Gusti Agung Gede Utara Hartawan, Tjokorda Gde Agung Senapathi*, I Gusti Ngurah Mahaalit Aribawa, Pontisomaya Parami, Christopher Ryalino, Adinda Putra Pradhana

***Corresponding Author: Tjokorda Gde Agung Senapathi**

Abstract

Background: Regional anesthesia reduces the inflammatory response and surgery-related immunosuppressive response. The scalp nerve block technique is a relatively simple and safe technique. The goal of this study was to compare the inflammatory response between a combination of general anesthesia and scalp nerve block compared with general anesthesia in craniotomy surgery. Methods: This was a double-blind, randomized controlled trial with pre and post-test study in 50 subjects carried out at Sanglah General Hospital (Bali, Indonesia). Group A treated with scalp nerve block using 0.25% levobupivacaine solution, and group B treated with scalp nerve block using 0.9% NaCl solution. Blood tests were carried out before and after the surgery to measure platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), and C-reactive protein (CRP) as inflammatory markers. Results: The mean difference of PLR, NLR, and CRP between the two groups were significantly different ($p < 0.001$) at 72 hours after the surgery. The tests found no significant difference at before and right after the surgery ($p > 0.05$). Conclusion: The application of scalp nerve block in combination to general anesthesia lower the increase of PLR, NLR, and CRP compared to general anesthesia alone in craniotomy surgeries.

Keywords: *PLR, NLR, CRP, Inflammation, Regional anesthesia.*

Introduction

Brain tumors are abnormal growths of cells in or around the brain [1]. Brain tumors can affect anyone with different symptoms. Brain tumor treatment is based on the type, size, and location of the tumor. Surgery is a rocedure that provides effective results against brain tumor [2]. According to the Central Brain Tumor Registry of the United States (CBTRUS), in 2010-2014, the incidence of tumors in the central nervous system was 22.64/100,000 per year with a mortality rate of 4.33/100,000 [3].

Its incidence in adults was 29.41/100,000. The most common types of tumors were meningiomas (36.3%), pituitary tumors (16.2%) and glioblastoma (14.9 %) [4]. The goal of anesthesia in brain tumor surgery is to prevent secondary brain injury that can be caused by increased intracranial pressure, hypotension or hypertension [5-7]. Low-level inflammation in brain tumor surgery is associated with better survival rates [8-10].

Regional anesthesia reduces the inflammatory response and surgery-related immunosuppressive response. The use of scalp nerve block in craniotomy is associated with the effect of modulation on the local and systemic inflammatory response. The neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and C-reactive protein (CRP) are inflammatory and immunosuppressed biomarkers. Scalp nerve block decreases NLR and PLR in glioblastoma patients who underwent craniotomy [11].

The scalp nerve block technique is a relatively simple and safe technique, but its use has not been done routinely all over the world. The purpose of this study was to compare the inflammatory response between a combination of general anesthetics-scalp nerve block compared with general anesthesia in craniotomy surgery.

Patients and Methods

This was a double-blind, randomized controlled trial with pre and post-test. This research was carried out in Sanglah General Hospital (Bali, Indonesia) in 2019. Inclusion criteria include patients undergoing craniotomy surgery with general anesthesia aged 18-65 years. Exclusion criteria include ASA ≥3, allergy history to bupivacaine, international normalized ratio (INR) level of >1.5, history of immune system diseases, history of malignancy, and body mass index (BMI) ≤18.5 kg/m^2 or ≥30 kg/m [2].

We used a standard sample size formula for this study and found that a minimum sample size of 22 subjects per study group. The randomization technique was carried out by permuted block randomization. The subjects in this study were divided into two groups based on the treatment received by the subjects. Group A treated with scalp nerve block using 0.25 % levobupivacaine solution with a total volume of 21 ml, and group B treated with scalp nerve block using 0.9 % NaCl solution.

Before a scalp nerve block is performed, one anesthetist opened and read the labeled envelope, and prepared a solution according to the instructions in the envelope into a prepared syringe. The anesthetist performed the scalp nerve block without knowing the contents of the solution in the syringe prepared by the researcher.

Both anesthetists did not get involved in the subsequent data collection and evaluation. Blood tests were carried out at before, after, and 72-hours after the surgery to measure PLR, NLR, and CRP as inflammatory markers.

Data analysis in this study consisted of descriptive analysis, normality test, homogeneity test, and average comparison analysis. The normality test used in this study is the Shapiro Wilk normality. We used the Levene's test as the homogeneity test for this study. The independent t-test was used if the data is normally distributed in both groups, otherwise, the Mann-Whitney test was used. We used SPSS 20.0 (IBM Corp. Released in 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.) for the entire statistical analysis. A p-value of >0.05 was considered significant.

Results

Descriptive statistical analyses on the characteristics of the subjects included age, sex, BMI, ASA physical status, duration of surgery, and total intraoperative opioids. A description of the characteristics of the study subjects by the treatment group is presented in Table 1. We then tested the subjects for PLR, NLR, and quantitative CRP levels at preoperative, postoperative, and 72-hours postoperative periods (Table 2).

Table 1: Characteristics of the study subjects

Variables	Groups		p
	A (n=25)	B (n=25)	
Age (years), median(IQR)	43 (16)	51 (17)	0.016[a]
Sex			
Male, n(%)	9 (36)	8 (32)	0.765
Female, n(%)	16 (64)	17 (68)	
BMI, kg/m^2	22.89 (4.94)	21.88 (2.84)	0.214[a]
ASA physical status			
II, n(%)	7 (28)	5 (20)	0.508
III, n(%)	18 (72)	20 (80)	
Surgery duration (minutes), median (IQR)	155 (75)	180 (78)	0.546[a]

[a]Mann-Whitney U-test; **IQR**: interquartile range; **BMI**: body mass index;
ASA: American Society of Anesthesiologists

The difference in PLR, NLR, and CRP between the combination of general anesthesia and scalp nerve block compared to general anesthesia only in patients underwent craniotomy are displayed in table 3. The change of PLR, NLR, and CRP in both groups were tested by repeated measures of two-way ANOVA, where we can see that the results are significant at 72-hours post craniotomy (p <0.001).

Table 2: Mean PLR, NLR, and CRP levels in each group

Variables	Groups	
	A (n=25)	B (n=25)
PLR, mean±SD		
- preoperative	192.89 ± 69.39	193.97 ± 94.55
- postoperative	270.55 ± 94.01	337.61 ± 138.11
- 72-hours postoperative	187.12 ± 54.89	309.86 ± 125.52
NLR, mean±SD		
- preoperative	3.77 ± 1.99	3.30 ± 1.62
- postoperative	16.55 ± 8.04	24.48 ± 12.77
- 72-hours postoperative	7.59 ± 4.09	20.13 ± 7.86
CRP, mean±SD		
- preoperative	2.01 ± 1.82	1.89 ± 2.10
- postoperative	2.78 ± 2.49	3.26 ± 3.05
- 72-hours postoperative	28.11 ± 12.20	65.78 ± 26.36

PLR: platelet-to-lymphocyte ratio; **NLR**: neutrophil-to-lymphocyte ratio;
CRP: C-reactive protein; **SD**: standard deviation

Table 3: Mean difference of PLR, NLR, and CRP between the two groups

Dependent variables	Independent variables	β	CI95%	p
PLR				
- preoperative	Mean difference	1.367	-49.799 – 52.534	0.957[a]
- postoperative	Mean difference	-72.102	-144.928 – 0.725	0.052[a]
- 72-hours postoperative	Mean difference	-120.469	-180.252 – -60.685	<0.001[a]
NLR				
- preoperative	Mean difference	0.717	-0.386 – 1.820	0.197[a]
- postoperative	Mean difference	-8.064	-14.651 – -1.477	0.018[a]
- 72-hours postoperative	Mean difference	-12.956	-16.810 – -9.102	<0.001[a]
CRP				
- preoperative	Mean difference	0.669	-0.458 – 1.796	0.239[a]
- postoperative	Mean difference	0.226	-1.396 – 1.848	0.780[a]
- 72-hours postoperative	Mean difference	-37.737	-50.419 – -25.054	<0.001[a]

[a]Two-way ANOVA test; PLR: platelet-to-lymphocyte ratio; **NLR**: neutrophil-to-lymphocyte ratio;
CRP: C-reactive protein; **CI**: confidence interval

Discussion

The concept of a peripheral nerve block of the scalp was first introduced by Harvey Cushing and George Crile in the 1900s.[12] In 1910, Heinrich Braun performed the addition of epinephrine adjuvant under local anesthesia before the incision of craniotomy surgery [13]. While the term scalp nerve block was first used by Girvin in 1986 [14].

Levobupivacaine is a local anesthetic agent that works through the mechanism of nerve conduction blocks by preventing action potentials in the axons. Direct interaction with specific receptors on the Na^+ channel, thus inhibiting the entry of Na^+ ions. The anesthetic drug molecules must pass through the cell membrane via passive non-ionic diffusion of the molecule and then bound to the Na^+ channel. Repeated stimulation causes additional bonding to the Na^+ channel. Increased concentration causes the transmission of autonomic, somatosensory, and somatomotor impulses to stop, resulting in the blockage of the autonomic, sensory and motor nervous systems in the area innervated by the nerves affected by the blockade.

Elimination of local anesthesia is followed by a spontaneous and complete return of nerve conduction without structural damage to nerve fibers as a result of the effects of local anesthetic drugs [15]. In regional anesthesia, there may be an anti-inflammatory effect due to the blockade of C-fibers nerve thereby reducing the production of cytokines and blocking the activity of sympathetic nerve fibers [16].

Postoperative pain caused mainly by tissue inflammation and activation of C-fibers can be inhibited by reducing cytokine production thereby limiting the inflammatory response after surgery and the severity of postoperative pain [17,18].

This study produced no complications from the scalp nerve block. Side effects from the administration of levobupivacaine 0.25 % solution were also not found in this study. Postoperatively the patients in both groups had no complaints of nausea and vomiting. In this study, we administered the scalp nerve block with 0.25 % levobupivacaine. The scalp nerve block was done by blocking the supraorbital nerve, supratrochlear nerve, auriculotemporal nerve, zygomaticotemporal nerve, major occipital nerve, minor occipital nerve, and major auricular nerve.

The results showed that scalp nerve block could reduce the increase in postoperative PLR. This is proven by the results of the study found that postoperative PLR in group A was 72.1 lower than group B, and in the 72-hour postoperative period, the PLR in group A was 120.5 lower than group B. In the study conducted by Zheng et al. between patients who received scalp nerve block and without scalp nerve block, the reported third-day postoperative PLR was 169 (117.4-253.4) while in the group without scalp nerve block was 244.8 (185.8-322.6) ($p < 0.05$).

From this study, we also found that scalp nerve block can reduce the increase in postoperative NLR. The postoperative NLR showed that group A was 8.06 lower than group B, and in the 72-hour postoperative period where NLR in group A was 12.96 lower than group B. Another study reported that the third-day postoperative NLR was 7.55 (2.87-13.79) compared to 11.85 (8.84-15.62) in the group that did not receive scalp nerve block ($p < 0.05$) [11]. This is due to the ability of the scalp nerve block to produce an adequate block of surgical stimulation which is reflected in blood pressure and a stable intraoperative pulse rate. The anti-inflammatory mechanism in this study could also be caused by the absorption of local anesthetics given in systemic scalp nerve block action. In addition there are possible anti-inflammatory effects of peripheral nerve block due to C-fiber nerve blockade and reduction of nociceptive input due to surgical trauma [11,19,20].

This study showed that scalp nerve block could reduce the increase in postoperative quantitative CRP. This is evidenced by the CRP in the 72-hour postoperative in group A was 37.74 lower than group B ($p < 0.001$). This, however, was not shown in the immediate post-operative period. In the immediate postoperative period, quantitative CRP had not yet increased in either group.

One study reported that CRP has not increased immediately after surgery compared to the preoperative period.[21] The highest increase occurred on days 2 and 3 postoperatively. In a research conducted by Yang *et al.* [22] in craniotomy surgery for brain aneurysms showed that in the third-day postoperative period, the quantitative CRP was lower in the group receiving the scalp nerve block. The result was, however, not statistically significant.

Conclusion

The scalp nerve block is effective in preventing the increase in PLR, NLR, and quantitative CRP in craniotomy surgeries.

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