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Effect of Bilateral Superficial Cervical Plexus Block (BSCP) on Interleukin-6 Levels in Ishmolobectomy Patients

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ABSTRACT

Background: Bilateral superficial cervical plexus block (BSCP) can be used as preoperative analgesia or to manage postoperative pain in surgery cases. Interleukin-6 (IL-6) is the most relevant marker of tissue damage during surgical procedures and is an important and accurate biomarker of pain. This study aims to determine the effects of bilateral superficial cervical plexus block (BSCP) on IL-6 levels in patients undergoing ishmolobectomy.

Methodology: The research employed a quasi-experimental design. Samples were divided into two groups: an intervention group (levobupivacaine 0.25%) and a control group (NaCl 0.9%).

Results: Patients receiving BSCP with levobupivacaine 0.25% showed a decrease in the average IL-6 levels, which were lower than those of patients receiving NaCl 0.9%. Levobupivacaine 0.25% significantly affected IL-6 levels at 6 and 12 hours post-ishmolobectomy ($p < 0.05$).

Conclusion: BSCP with levobupivacaine 0.25% in ishmolobectomy patients has a positive effect on pain management by reducing IL-6 levels, thereby accelerating recovery. There is a need for extended follow-up to assess long-term effects.

Keywords: BSCP, levobupivacaine, IL-6, ishmolobectomy

INTRODUCTION

The process of pain occurs through several stages, namely transduction, transmission, modulation and perception. Stimulation of nociceptors will initiate the process of pain stages. Pain is also one of the cardinal signs of inflammation. There are many mediators that play a role in the process of pain, such as histamine, prostaglandins, bradykinin, substance P, and interleukin (IL)-6 (Wicaksono et al., 2017; Tantri et al., 2023). IL-6 is the most relevant marker of tissue damage during surgical procedures and is an important and accurate biomarker of pain (Tantri et al., 2023).

Based on immunology, IL-6 is a pro-inflammatory cytokine that has a role in pain modulation. Janus-activated kinase/signal transducer activator of transcription (JAK/STAT) is the most studied pathway activated in response to signal transduction cytokine receptors. This pathway can stimulate nociceptive receptors and amplify pain stimulation. Surgical procedures cause an increase in IL-6 within the first 3 hours and variations in surgical procedures and postoperative management may influence differences in the magnitude of IL-6 increase (Indra et al., 2023).

IL-6 is the most relevant marker of tissue damage during surgical procedures and is an important and accurate biomarker of pain (Tantri et al., 2023). Most patients undergoing thyroid surgery have thyroid cancer, symptomatic thyroid goiter, or failed medical management of hyperthyroidism (Abdelmalak and Doyle, 2014). After thyroid surgery, most patients experience mild-moderate postoperative discomfort due to several mechanisms, such as cervicotomy, orotracheal intubation, and cervical hyperextension positioning can cause postoperative discomfort, neck pain, and shoulder pain (Yoo et al., 2014).

Peripheral nerve block is a simple, safe and effective method of postoperative analgesia. Bilateral superficial cervical plexus block (BSCP) can be used as preoperative analgesia or to manage postoperative pain in isthmolobectomy surgery cases because it can block nerve branches originating from the superficial cervical plexus. The anesthetic agent often used for regional blocks is levobupivacaine 0.25% (Bajwa and Kaur, 2013; Sharma et al., 2018; Folino and Mahboobi, 2020; Harmon and Huecker, 2023). There is significant debate regarding the application of BSCP in thyroid surgery as postoperative analgesia. Some study showed that SCPB reduced intraoperative and postoperative analgesic requirements, whereas other studies showed that SCPB had no significant effect in thyroid surgery. In this study, IL-6 was used to assess the analgesic use of levobupivacaine 0.25% with BSCP technique in thyroid surgery patients.

MATERIALS AND METHODS

The type of research conducted was prospective double blind. The research design used quasi-experimentation with simple random sampling design, in which the research sample was taken by simple randomization of research subjects who were included in the inclusion criteria.

The sampling technique in this study is using consecutive sampling technique, which is looking for subjects who meet the inclusion criteria, then recruited until the required number of samples is met. Subjects will be selected consecutively from patients aged 18-60 years who will undergo isthmolobectomy surgery at Bahteramas Hospital, South Sulawesi who are given levobupivacaine 0.25% with bilateral superficial cervical plexus block technique and calculated the difference in pre and postoperative IL-6 serum levels. The collected data will be processed descriptively and analytically.

RESULTS AND DISCUSSION

The total sample in this study was 36 samples consisting of 18 samples in the intervention group and 18 samples in the control group (Table 1). In the characteristics of the study samples, it was found that both the control group using NaCl 0.9% and the intervention group using levobupivacaine 0.25% were more female (83.33-86.67%) than male (16.67%-27.78%).

Table 1. Research Objects Overview

Characteristics	NaCl 0.9%	Levobupivacaine 0.25%
	N=18 n (%)	N=18 n (%)
Gender		
Male	5 (27.78%)	3 (16.67%)
Female	13 (86.67%)	15 (83.33%)
Age (years)		
18–30	5 (27.78%)	6 (33.33%)
31–60	13 (86.67%)	12 (66.67%)

This is according to research that currently, one in 55 United States women and one in 149 United States men are expected to be diagnosed with thyroid cancer during their lifetime (Kitahara and Schneider, 2022). This is supported by other studies that mention thyroid cancer represents 1% to 4% of all malignancies and is the fifth most common cancer in women in the United States (Siegel et al., 2015). It has a prevalence in women of about 3:1 (Franceschi et al., 1993). Other studies suggest that thyroid cancer affects both sexes equally but may be detected more often in women than men. This difference may be explained by access to medical care (LeClair et al., 2021). In addition, there are studies that show male gender is reported as an independent risk factor although not all (Yang et al., 2013; Oyer et al., 2012).

The age characteristics of the samples in both the control group using NaCl 0.9% and the intervention group using levobupivacaine 0.25% were more patients aged 31-60 years (66.67%-86.67%). This is in accordance with research that 45 years old, female gender, and family history of thyroid cancer are factors predisposing to the development of thyroid cancer (Hay et al., 1993; Hay et al., 2002; Matsuzu et al., 2014; Haugen et al., 2015).

Thyroid cancer has been shown to have a higher incidence in 45 years old and in some staging systems, 45 years of age is used as the boundary between low risk and high risk for developing thyroid cancer (Hay et al., 2002; Haugen et al., 2015). Ganly et al (2015) analyzed a cohort of 3,664 patients affected by differentiated thyroid cancer treated at Memorial Sloan Kettering Cancer Center over 25 years [1985-2010] to determine the significance of age at diagnosis. The study concluded that there is no specific age limit that can determine cancer risk stratification for papillary thyroid carcinoma (PTC) patients. However, mortality from PTC increases progressively with age (Ganly et al., 2015).

Table 2. IL-6 Research Descriptive Data

N	Minimum	Maximum	Mean	Std. Deviation
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Pre-Intervention	18	.90	4.66	1.8683	1.11311
6 Hours Intervention	18	.90	8.10	2.9294	2.11830
12 Hours Intervention	18	.50	4.30	1.7667	1.21068
Age Intervention	18	23	65	40.61	13.652
ASA Intervention	18	1	2	1.44	.511
Pre-Control	18	.90	5.79	2.5217	1.59495
6 Hours Control	18	3.27	8.90	6.8428	1.60150
12 Hours Control	18	1.45	7.60	4.4900	1.40364
Age Control	18	18	61	38.44	11.937
ASA Control	18	1	2	1.39	.502

BSCPb with levobupivacaine 0.25% contributes to a reduction in IL-6 levels which is associated with a reduction in pain intensity and inflammatory response. The anesthetic agent often used for regional blocks is levobupivacaine 0.25% (Bajwa and Kaur, 2013; Sharma et al., 2018; Folino and Mahboobi, 2020; Harmon and Huecker, 2023). From the data in Table 2, it shows that patients given BSCPb with levobupivacaine 0.25% had lower IL-6 levels than patients given NaCl 0.9% either 6 hours after ishmolobectomy or 12 hours after ishmolobectomy. IL-6 is the most relevant marker of tissue damage during surgical procedures and is an important and accurate biomarker of pain (Tantri et al., 2023). This is in accordance with the research of Haddadi et al (2020) who said that IL-6 can be used as a biomarker to predict postoperative pain relief and disability improvement.

The paired sample t test is used to determine whether there is a difference in the average of two paired samples. The paired sample t test in this study was used to answer "Is there a difference in IL-6 serum levels in ishmolobectomy patients who were given levobupivacaine 0.25% analgesic with Bilateral Superficial Cervical Plexus Block (BSCPb) technique compared to NaCl 0.9% at Bahteramas General Hospital, South Sulawesi?". To answer this question, paired sample t test was conducted on the data of pre ishmolobectomy, 6 hours, and 12 hours after ishmolobectomy with BSCPb using levobupivacaine 0.25%. Then the data of pre ishmolobectomy, 6 hours, and 12 hours after ishmolobectomy with BSCPb using NaCl 0.9%.

Table 3. IL-6 Paired Sample T Test

		Paired Differences				t	df	Significance	
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference Lower Upper			One-Sided p	Two-Sided p
Pair 1	Pre Intervention - 6 Hours Intervention	-1.06111	2.49317	.58765	-2.30093 .17871	-1.806	17	.044	.089
Pair 2	Pre Intervention - 12 Hours Intervention	.10167	1.67854	.39564	-.73305 .93639	.257	17	.400	.800

Pair 3	Pre Control - 6 Hours Control	-4.32111	1.69939	.40055	-5.16620	-3.47602	-10.788	17	<.001	<.001
Pair 4	Pre Control - 12 Hours Control	-1.96833	1.82839	.43096	-2.87757	-1.05909	-4.567	17	<.001	<.001

Based on Pair 1 (Table 3), the Sig. (2-tailed) of 0.089 > 0.05, it can be concluded that there is no significant difference between IL-6 levels pre ishmolobectomy compared to 6 hours after ishmolobectomy with BSCPb using levobupivacaine 0.25%. Based on the Pair 2 output, the Sig. (2-tailed) of 0.800 > 0.05, it can be concluded that there is no significant difference between IL6 levels pre ishmolobectomy compared to 12 hours after ishmolobectomy with BSCPb using levobupivacaine 0.25%.

Based on the output of Pair 3 obtained Sig value. (2-tailed) of 0.000 <0.05, it can be concluded that there is a difference in IL-6 levels pre ishmolobectomy compared to 6 hours after ishmolobectomy with BSCPb using NaCl 0.9%. Based on the output of Pair 4 obtained Sig value. (2-tailed) of 0.000 <0.05, it can be concluded that there is a difference in IL-6 levels pre ishmolobectomy compared to 12 hours after ishmolobectomy with BSCPb using NaCl 0.9% (Table 3).

Effect of BSCPb on IL-6

Table 4. IL-6 Paired Sample Statistics

		Mean	N	Std. Deviation	Std. Error Mean
Pair 1	Pre-Intervention	1.8683	18	1.11311	.26236
	6 Hours Intervention	2.9294	18	2.11830	.49929
Pair 2	Pre-Intervention	1.8683	18	1.11311	.26236
	12 Hours Intervention	1.7667	18	1.21068	.28536
Pair 3	Pre-Control	2.5217	18	1.59495	.37593
	6 Hours Control	6.8428	18	1.60150	.37748
Pair 4	Pre-Control	2.5217	18	1.59495	.37593
	12 Hours Control	4.4900	18	1.40364	.33084

In Table 4, the mean value of pre ishmolobectomy with BSCPb using levobupivacaine 0.25% was 1.8683 while 12 hours after the intervention amounted to 1.7667 this shows there is a decrease in the mean value of IL-6 between pre and 12 hours after the intervention. Whereas in patients with NaCl 0.9%, IL-6 levels increased from 2.5217 pre ishmolobectomy to 4.4900 12 hours after ishmolobectomy with BSCPb using NaCl 0.9%.

Table 5. IL-6 Wilcoxon Signed Ranks Test

		N	Mean Rank	Sum of Ranks
6 Hours Intervention - Pre Intervention	Negative Ranks	6 ^a	8.50	51.00
	Positive Ranks	12 ^b	10.00	120.00
	Ties	0 ^c		
	Total	18		
6 Hours Control - Pre Control	Negative Ranks	0 ^d	.00	.00
	Positive Ranks	18 ^e	9.50	171.00

	Ties	0 ^f		
	Total	18		
12 Hours Intervention – Pre Intervention	Negative Ranks	7 ^g	11.57	81.00
	Positive Ranks	11 ^h	8.18	90.00
	Ties	0 ⁱ		
	Total	18		
12 Hours Control - Pre Control	Negative Ranks	3 ^j	3.67	11.00
	Positive Ranks	15 ^k	10.67	160.00
	Ties	0 ^l		
	Total	18		

- a. 6 Hours Intervention < Pre Intervention
- b. 6 Intervention > Pre Intervention
- c. 6 Hours Intervention = Pre Intervention
- d. 6 Hours Control < Pre Control
- e. 6 Hours Control > Pre Control
- f. 6 Hours Control = Pre Control
- g. 12 Hours Intervention < Pre Intervention
- h. 12 Hours Intervention > Pre Intervention
- i. 12 Hours Intervention = Pre Intervention
- j. 12 Hours Control < Pre Control
- k. 12 Hours Control > Pre Control
- l. 12 Hours Control = Pre Control

In Table 5, there are 6 patients who experienced a decrease in IL-6 levels from pre-intervention using levobupivacaine 0.25% to 6 hours after intervention with a mean rank or average decrease in IL-6 levels of 8.50. Whereas in control patients who used NaCl 0.9%, the results were 0 in N value, mean rank, and sum rank which showed no decrease in IL-6 levels pre ishmolobectomy and 6 hours after ishmolobectomy. After 12 hours of ishmolobectomy, there were 7 patients who experienced a decrease in IL-6 levels from pre-intervention using levobupivacaine 0.25% with a mean rank or average decrease of 11.57, while for control patients who used NaCl 0.9% there were 3 patients who experienced a decrease in IL-6 levels from pre-ishmolobectomy with a mean rank or average decrease in IL-6 levels of 3.67.

Table 6. IL-6 Wilcoxon Signed Ranks Test Statistics

Test Statistics ^a				
	6 Hours Intervention - Pre Intervention	6 Hours Control - Pre Control	12 Hours Intervention - Pre Intervention	12 Hours Control - Pre Control
Z	-1.502 ^b	-3.724 ^b	-.196 ^b	-3.245 ^b
Asymp. Sig. (2-tailed)	.133	<.001	.845	.001

*Sig < 0.05

- a. Wilcoxon Signed Ranks Test
- b. Based on negative ranks.

In Table 6, control patients who used NaCl 0.9% obtained a significance value <0.05 so it can be concluded that there is a significant increase in IL-6 levels between pre, 6 hours after and 12 hours after ishmolobectomy. From the results in Table 6, this is in accordance with the study conducted by Tantri et al (2022) to determine the effect of modified thoracolumbar interfacial plane block (TLIP) on postoperative pain and serum IL-6 levels showed that IL-6 were lower in the modified TLIP group 12 hours postoperatively.

Table 7. IL-6 Mann-Whitney Test After 6 Hours

		Ranks		
	Time	N	Mean Rank	Sum of Ranks
IL-6	6 Hours Intervention	18	11.06	199.00
	6 Hours Control	18	25.94	467.00
	Total	36		
		Test Statistics ^a		
			IL-6	
Mann-Whitney U			28.000	
Wilcoxon W			199.000	
Z			-4.244	
Asymp. Sig. (2-tailed)			<.001	
Exact Sig. [2*(1-tailed Sig.)]			<.001 ^b	

a. Grouping Variable: Time
b. Not corrected for ties.

Tabel 8. IL-6 Mann-Whitney Test After 12 Hours

		Ranks		
	Time	N	Mean Rank	Sum of Ranks
IL-6	12 Hours Intervention	18	10.86	195.50
	12 Hours Control	18	26.14	470.50
	Total	36		
		Test Statistics ^a		
			IL-6	
Mann-Whitney U			24.500	
Wilcoxon W			195.500	
Z			-4.355	
Asymp. Sig. (2-tailed)			<.001	
Exact Sig. [2*(1-tailed Sig.)]			<.001 ^b	

a. Grouping Variable: Time
b. Not corrected for ties.

Based on Table 7 and Table 8, it is known that the value of Asymp. Sig. < 0.05 (2-tailed) of 0.000 < 0.05 so that it can be said that there is a difference in IL-6 levels 6 hours and 12 hours after ishmolobectomy between BSCPb patients who use levobupivacaine 0.25% as an intervention group with NaCl 0.9% as a control group. Because there is a significant difference, it can be said that there is an effect of using levobupivacaine 0.25% on IL-6 levels at 6 and 12 hours after ishmolobectomy. This is in accordance with the study there was a significant difference between serum IL-6 levels, VAS (Visual Analog Scale), and ODI (Oswestry Disability Index) before and after surgery. The results showed that improvement in patient symptoms based on VAS and ODI correlated with serum IL-6 levels (p<0.05). Serum IL-6 levels were also lower in patients with low preoperative VAS and ODI scores. In addition, patients with low postoperative pain severity and disability had low IL levels (Haddadi et al., 2020). IL-6 can be affected by inflammatory reactions and anti-inflammatory responses to surgery as well as pain. Although the IL-6 concentration in the modified TLIP group was high preoperatively, it became lower after 12 hours of surgery; this may be due to the better analgesic effect (Tantri et al., 2022).

CONCLUSION

The study subjects who underwent ishmolobectomy were more female than male and the most age range was 31-60 years old. Bilateral superficial cervical plexus block (BSCPb) is an anesthetic technique that is beneficial in pain management including in patients undergoing ishmolobectomy.

Patients who were given BSCPb with levobupivacaine 0.25% had a decrease in the mean value of IL-6 and obtained lower IL-6 levels than patients who were given NaCl 0.9% either 6 hours or 12 hours after ishmolobectomy while patients who used NaCl 0.9% did not experience a decrease in IL-6 levels before and after ishmolobectomy. Because there is a significant difference, it can be said that there is an effect of using levobupivacaine 0.25% on IL-6 levels at 6 and 12 hours after ishmolobectomy.

The application of BSCPb with levobupivacaine 0.25% in ishmelebectomy patients can have a positive effect in pain management by reducing IL-6 levels which is expected to accelerate the recovery process. However, it is likely that effectiveness and outcomes may vary between individuals. Further research is needed by further exploring the underlying mechanisms and conducting studies with larger sample sizes to confirm the results of the study. In addition, a longer follow-up period is needed to evaluate the long-term effects of BSCPb.

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