

Comparison of Post-Caesarean Section Wound Healing Methods Based on Reeda Scale and Platelet Lymphocyte Ratio

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ABSTRACT

To evaluate post-caesarean section wound healing on patient given standard analgesia compared with Transversus Abdominis plane Block (TAP Block) and wound site infiltration based on REEDA scale and platelet Lymphocyte Ratio 72 hours post-caesarean section. A randomized clinical controlled trial study was conducted on 30 post-caesarean section women under spinal anesthesia. Participants were randomly divided into the groups: Standard Analgesia groups (SA), TAP Block groups (TAP), and Wound Site Infiltration groups (Infiltration). Each group received standard analgesia (ketorolac and tramadol) and adjuvant analgesia Ropivacain 0.2% on transversus abdominis space (TAP block group) and wound site infiltration in infiltration group. Wound healing was evaluated based on REEDA Scale and Platelet Lymphocyte Ratio (PLR) 72 hours post-operation. There were significant differences on REEDA scale and PLR value between the three groups 72 hours post-caesarean section ($P < 0.001$). TAP groups had the lowest REEDA Scale (0.2 ± 0.422) and PLR value (134.2 ± 18.57) Transversus abdominis plane block showed the best healing process compared to standard analgesia only and wound site infiltration.

Keywords: Caesarean, Platelet Lymphocyte Ratio, REEDA scale, TAP block, wound healing

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INTRODUCTION

Caesarean section (c-section) is the most common surgical procedure in obstetrics and its prevalence has increased in the recent years (de la Cruz et al., 2015). C-section causes a moderate to severe post-surgery pain. Pain after C-section surgery makes some patients afraid to make mobilization and it has effect on their wound healing and causes patient a longer stay in hospital (Villar et al., 2006, 2007). Some of the methods to reduce pain after c-section surgery have attracted attention from many medical scientists for research. In the majority of methods for pain management after c-section opioid is often used. It reduces the pain, infection, and also accelerates the wound healing process (Schug and Chandrasena, 2015; Kranke et al., 2016). However, opioid has some disadvantages; small doses induce nausea, vomiting, and sedation whilst in large doses it has the effect of hypotension and respiratory depression (Khalife et al., 2020).

The commonly used local anesthetic methods are transversus abdominis plane (TAP) block and wound infiltration. These methods are subdermal and effectively reduce pain sensation (Jadon et al., 2018; Theodoraki et al., 2019). TAP block and wound site infiltration methods are effective to provide an excellent analgesic in a variety of procedures surgery with minimal side effect (Tawfik et al., 2017). The wound infiltration technique reduces pain intensity by inhibiting the transmission of pain impulse, thereby reducing glucocorticoid hormone secretion and accelerating wound healing. It reduces the pain during the first 24 hours post-surgery, the dose of opioid and the release of catecholamines, cortisol, and glucagon reduces the stress response of surgery. The TAP block controls the pain up to 48 hours after surgery and helps the healing process by cutting the stress response that arises as a

result of pain after c-section (Brogi et al., 2016; Tawfik et al., 2017). Nonetheless, no study has been conducted on the effect of TAP block analgesia and wound site infiltration on the wound healing process compared with standard analgesia. Thus, the objective of this study was to compare the effect of standard analgesia, Transversus Abdominis plane Block (TAP Block) and wound site infiltration analgesia on post-caesarean wound healing.

METHODS

This single-blind experimental randomized clinical trial (RCT) was conducted in Dr. Soetomo Academic Medical Centre Hospital, from January 2020 until March 2020. Ethical committee approval was obtained from the Ethics Committee of Clinical Investigations of Dr. Soetomo Academic Medical Centre Hospital (Decision no: 1792/KEPK/1/2020). A written and signed informed consent was obtained from the patients who participated in this study. The participants of this study were 30 pregnant women, randomly divided into three groups: Standard Analgesia groups (SA), TAP Block groups (TAP), and Wound Site Infiltration groups (Infiltration). The inclusion criteria were patients aged 20-40 years old who underwent caesarean-section (c-section) in the ASA I-II risk group, had body mass index (BMI) < 40 and had undergone pfannenstiel incision. Participants were excluded from the study if they had an allergy to local anesthesia/ analgesia agent, if intra uterine fetal death was detected before c-section, if the following diagnoses were present - diabetes, eclampsia, any gestational diseases such as HELLP syndrome and coagulopathies, if they had mental illness, if there was an infection in the region where the block or infiltration would be performed, or if they refused to participate in the study.

Drop out from the study would be obtained if there was a change in technique from spinal anesthesia to general anesthesia, if the operation procedures took more than three hours, and if massive bleeding (> 3000 ml) was detected.

All patients received standard analgesia (ketorolac 30 mg TID bolus intravenously and tramadol 75 mg TID drip in 100 ml NaCl 0, 9% within three days; ondansetron 8 mg bolus intravenously TID within a day). SA groups received standard analgesia only, TAP block group received standard analgesia and TAP block analgesia, infiltration group received standard analgesia and wound site infiltration analgesia. The TAP block using Ropivacain 2% was performed by the anesthesiologist using USG guiding after operation. Wound site infiltration was performed by obstetrician before skin closure.

The study data collected were in a demographic information form, REEDA scale and PLR value at 72 hours after caesarean section. The REEDA scale is a tool for measuring the healing process of an incision. It has five components, including redness, edema, ecchymosis,

discharge, and approximation of the two edges of the wound, each receiving a score between 0 and 3. Thus, the total score would range from 0 to 15, with lower scores representing better wound healing (10). REEDA is a standard scale with confirmed reliability and validity [11]. PLR obtained from serum blood samples at 72 hours post-surgery was used to evaluate wound healing.

Statistical analysis

The study data were analyzed using Kruskal-Wallis, and Mann-Whitney test. SPSS statistical software was used to analyse the data and $p < 0.05$ was considered to be statistically significant.

RESULTS

Characteristics of the study participants are shown in Table 1. The study result showed no significant differences among the three groups on demographic features such as age, BMI, parity, gestational age, operation time and indication, maternal comorbidities and fetal outcome.

Table 1. The demographic features of study participants

Variables	TAP group (n=10)	Infiltration group (n=10)	SA group (n=10)	P
Age (years)				0.571
20-30	2	1	1	
31-35	7	5	7	
>35	1	4	2	
BMI				0.749
<30	9	8	9	
>30	1	2	1	
Parity				0.315
Primi	2	0	2	
Multips	8	10	8	
Gestational age				0.875
<37 weeks	5	6	5	
≥ 37 weeks	5	4	5	
Operation time				0.383
Elective	3	1	1	
Emergency	7	9	9	
Indication of section				0.383
Maternal indication	5	6	2	
Fetal indication	5	4	8	
comorbidities				0.061
Hyperthyroid	2	1	0	
Pregnancy induced hypertension	4	4	4	
Obesity	1	2	1	
No comorbidity	3	3	5	
birth weight (g)				0.865
<2500	4	5	5	
2500 - <4000	6	5	4	
≥ 4000	0	0	1	
AS <7 (p=0,748)	1	2	1	0.748

AS: Apgar Score at minute 5

Table 2. REEDA scale score at 72 hours after c-section of groups

Variables		TAP group (n=10)	Infiltration group (n=10)	SA group (n=10)	P*
REEDA Scale Score ^(a)	0	8	0	0	< 0.001
	1-5	2	10	5	
	>5	0	0	5	
Mean of total REEDA scale score		0.2 ± 0.422	2.5 ± 0.527	5.5 ± 0.527	< 0.001
REEDA Scale Criteria^(b)					P**
Redness		0	0.1 ± 0.316	1	<0.001
Edema		0	0.1 ± 0.316	0.8 ± 0.422	< 0.001
Ecchymosis		0	0.9 ± 0.316	1	< 0.001
Discharge		0.2 ± 0.422	0.9 ± 0.316	1.8 ± 0.632	<0.001
Approximation		0	0.5 ± 0.527	0.9 ± 0.316	<0.001

(a) Data are presented in frequency table; (b) Data presented in Mean ±SD

*Kruskal Wallis test significant if p<0.05, **Mann Whitney test significant if p < 0.05

Table 3. Comparison of REEDA scale variables score between TAP and infiltration groups at 72 hours after c-section.

REEDA scale	TAP group	Infiltration group	P*
Redness	0	0.1 ± 0.316	0,317
Edema	0	0.1 ± 0.316	0.317
Ecchymosis	0	0.9 ± 0.316	<0.001
Discharge	0.2 ± 0.422	0.9 ± 0.316	0.002
Approximation	0	0.5 ± 0.527	0.012
Mean of total REEDA scale	0.2 ± 0.422	2.5 ± 0.527	<0.001

*Mann Whitney test, significant if p < 0.05; Data presented in Mean ±SD

The study result showed there were significant different on REEDA scale score among the three groups at 72 hours after c-section (Table 2). Most of the TAP group participants had the lowest REEDA score (80% of the participants). The TAP group revealed the lowest mean of REEDA scale score also. Discharge criteria only had score 0.2 ± 0.422. SA group showed the highest REEDA scale score. Table 3 shows that there is significant difference in ecchymosis-discharge-approximation variables, and the mean of total REEDA scale between TAP group and infiltration group (p<0.05). TAP group had lower mean of total REEDA scale score than infiltration group. Cohen's analysis was used to determine the effect size and effectiveness between TAP and infiltration method. It showed that, TAP group reduced the discharge production 1.88 times compared to infiltration group. However, there were no significant differences in redness and edema variables between the two groups.

Figure 1 shows PLR value among the three groups. It recorded significantly different mean of PLR value among the three groups (p<0.05). The TAP group had lowest PLR value among the group. All of the participants in the TAP group had PLR <160 and mean of PLR value 134.2±18.57. However, all patients in the infiltration group and the SA group had a higher PLR value.

DISCUSSION

The different mean of total REEDA scale Score and PLR value among the three groups, TAP group and Infiltration group had the lower REEDA Scale score compared to the SA group, and TAP group showed the lowest REEDA scale score (Alvarenga *et al.*, 2015). Comparison of all variables on REEDA scale recorded significantly difference among the three groups. SA group showed the highest score on every variable too. It means that adjuvant analgesia using TAP block and wound site infiltration post-operative had

better impact on wound healing process compared to SA only.

However, if we compare between TAP group and infiltration group, it showed significant difference n mean of total REEDA scale score and significant difference in ecchymosis-discharge-approximation variables (Yu *et al.*, 2014). Cohen's analysis indicated that TAP group reduced the discharge production 1.88 times compared to infiltration group (Theodoraki *et al.*, 2019). Optimal pain management in a woman undergoing caesarean delivery is a key priority in managing post-caesarean surgery. Suboptimal perioperative pain management is related to the decrease of chronic pain, delayed mobilization and functional recovery, maternal-fetal bonding and wound healing process (Kuehl *et al.*, 2010; Russo *et al.*, 2017). Pain will increase the degree of patient stress and anxiety in response to a broad range of painful stimuli. C fiber will release substance P and neurokinin A (pain neuropeptides), which will release proinflammatory cytokines. These pro-inflammatory cytokines play a role in augmenting pain signals and stress response. The stress response is complex and interconnected to neuroendocrine, inflammatory, and nociceptive phenomena (Nathan and Scobell, 2012).

The Sympathetic Nervous System (SNS) will be activated during stress period and it will stimulate the adrenal glands to release the stress hormones adrenaline (epinephrine) and cortisol. Increasing of cortisol levels will suppress the immune system and result in decreasing of neutrophils. This pathway will cause decreased macrophage function and decrease the ability to remove debris from the wound (McDonnell *et al.*, 2008). Over production of Cortisol stimulates the body to produce catecholamine, leading to small arterioles vasoconstriction, continued by decreasing of peripheral blood supply, the transport of oxygen and nutrient, then

impacting the body's resistance to infection. Pain also increases the release of β -endorphin that then inhibits macrophage. This condition causes the decrease of TNF α , IL-1, IL-6, IL-8, and TGF- β , which are the growth factors. The decrease of IL-1 causes a little amount of procollagenase, as of inhibition of the collagenase process. Cortisol hormones also correlate to suppression of fibroblast proliferation and matrix degradation, then it will affect the duration and strength of the wound. Thus, stress hormones will lead to the catabolism process and affect wound healing (Schug and Chandrasena, 2015; Theodoraki *et al.*, 2019).

These literatures could explain the result of our study, that better pain management in TAP group will have impact on the wound healing process. TAP block procedure is effective in providing analgesia during 48 h after caesarean section. Sixty-two randomized participants who received TAP block and no TAP block showed that there is reducing of the use of tramadol in patients given TAP block by 50% compared to patients given no block during 48 h after surgery ($P < 0.001$). Lower pain scores both on rest and activity at each time point for 24 h in study group ($P < 0.001$), showed significantly longer time of first analgesia, higher satisfaction, and fewer side effects in study group compared to control group (McDonnell *et al.*, 2008; Jadon *et al.*, 2018).

In this study, TAP block group had the lowest mean of total REEDA scale score, reflecting the better wound healing process in this group. The TAP block provided superior analgesia. Reducing both pain scores and 24-hr morphine consumption have an important role in pain management after abdominal surgery mainly when neuraxial techniques or opioids are contraindicated (Alvarenga *et al.*, 2015). Thus, the optimal pain management will prevent physical and physiological stress, then will impact on wound healing.

Comparing analgesic efficiency between wound site infiltration and ultrasound guided transversus abdominis plane block after a caesarean delivery under spinal anesthesia showed that TAP block was superior to infiltration anesthesia and it provided longer lasting and more efficient analgesia (Khalife *et al.*, 2020). This study could explain our study finding that TAP group had lower mean of total REEDA Scale score compared to Infiltration, which means that TAP group had lower pain, thus resulting in lower stress, and having better impact on wound healing.

Many observational studies showed PLR shifts correlated to the severity of systemic inflammation and could predict infections and other comorbidities. Study on head neck reconstruction demonstrated that PLR >160 were significantly associated with the rate of wound healing failure rate ($p = 0.0042$) (McDonnell *et al.*, 2008). The results of this study are in accordance with our study result, the TAP group had the lowest PLR result and the value <160 . It could be explained that TAP group had the lowest inflammation process, thus resulting in low PLR value, as compared to the SA group which had highest PLR value and highest REEDA scale score, which might be due to suboptimal pain management.

CONCLUSION

Tranversus abdominis plane block intervention had the lowest REEDA scale score and PLR value among standard analgesia only and wound site infiltration procedure, thus it showed that TAP block had the best healing process

compared to standard analgesia only and wound site infiltration.

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