RESEARCH

The Relationship Between Interleukin-1β Levels and Visual Analog Scale Value in Preeclampsia Patients Who Received Perioperative C-Sectional Parecoxib With Spinal Anesthesia

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ABSTRACT

Background: Interleukin1β (IL-1β) increases during inflammation and functions as a mediator that terminates endothelial dysfunction and regulates cellular apoptosis in preeclampsia. Parecoxib is a potential agent because of its superiority as an analgesic and anti-inflammatory that can work peripherally and centrally, with minimal side effects on the mother and baby.

Objective: This study aimed to determine the relationship between IL-1β levels and visual analog scale (VAS) scores in preeclampsia patients who received parecoxib perioperatively for cesarean section with spinal anesthesia.

Methods: Non-experimental cross-sectional research on preeclampsia patients who received perioperative parecoxib and underwent cesarean section with spinal anesthesia as many as 18 people at Arifin Ahmad Hospital, Riau Province, and Bina Kasih Hospital, Pekanbaru. Samples were taken by Consecutive Sampling.

Result: There was a moderate negative correlation between IL-1β and VAS ($p < 0.05$; correlation coefficient -0.487).

Conclusion: In preeclampsia patients who received parecoxib following a 24-hour spinal anesthetic cesarean surgery, there is a correlation between IL-1β levels and VAS scores.

Keywords: cytokines; interleukin-1beta; parecoxib; preeclampsia; visual analogue scale

INTRODUCTION

One of the main causes of maternal and perinatal morbidity and mortality throughout the world is preeclampsia.[1,2] According to national health surveys, preeclampsia occurs in 25% of all pregnancies in Indonesia, with the highest cases occurring in women over the age of 35 years.[3,4] At Arifin Ahmad Regional Hospital, a Type B Hospital in Pekanbaru, Riau Province, 155 cases of preeclampsia were recorded in 2018 according to local data.[5] In addition, there were 102 cases at Bina Kasih Hospital, which is one of the Type C hospitals in the city of Pekanbaru.

Interleukin 1β (IL-1β) is thought to play an important role in the pathogenesis of preeclampsia. IL-1β is the first interleukin secreted which acts as a mediator that causes endothelial dysfunction and regulates cellular apoptosis.[6,7] Together with tumor necrosis factor α (TNF-α), IL-1β would increase the production of thrombin, platelet-activating factor, and vascular cell adhesion molecule (VCAM)-1, increase endothelial cell permeability, and increase coagulation which would trigger an inflammatory response.[8] Various studies have found increased levels of IL-1β in the maternal periphery and also found increased placental expression of IL-1β in patients with preeclampsia.[9,10]

Parecoxib is a COX-2 inhibitor that can cross the blood-brain barrier, so it can provide anti-neuroinflammatory effects by inhibiting prostaglandin synthesis in the central and peripheral areas.[11,12] Other advantages include the absence of side effects in the form of platelet inhibition, and gastrointestinal disorders, and it does not cause side effects in neonates.[13,14] Some of the advantages of the parecoxib drug are that it is very suitable for the analgesic characteristics needed in labor with preeclampsia, namely that this drug is effective as a potent perioperative analgesic, and limits excessive systemic inflammatory activity both centrally and peripherally, and does not have negative side effects on neonates.

A study on the effects of administering parecoxib as a perioperative analgesic has been carried out in several educational centers in Indonesia. For example, a study in Makassar regarding the preventive effect of multimodal analgesia in the form of administering epidural anesthesia bupivacaine 0.125% and parecoxib 40 mg in medical laparotomy operations showed a decrease in post-operative levels of IL-1β, IL-6, and C-reactive protein (CRP) in the sample group compared to controls.[15,16] Another study conducted in Bandung regarding the effect of administering a combination of bupivacaine and parecoxib in open reduction internal fixation (ORIF) surgery under epidural anesthesia showed a significant reduction in IL-1β and IL-6 levels 2 hours after surgery in the sample group.[17]

This study aims to determine the relationship between IL-1β levels and VAS scores in preeclampsia patients who received parecoxib perioperatively for cesarean section with spinal anesthesia.

METHOD

Research subjects were patients with preeclampsia who received perioperative parecoxib and underwent cesarean section with spinal anesthesia at Arifin Ahmad Regional Hospital, Riau Province, and Bina Kasih Hospital, Pekanbaru, who met the

inclusion criteria, namely Willing to sign informed consent, Singleton pregnancy, Age 18 – 45 years, and ASA II and ASA III physical status. Meanwhile, the exclusion criteria were patients with eclampsia, HELLP Syndrome, massive bleeding during surgery, undergoing surgery again at that time, and not having fever and leukocytosis (leukocytes >14,000/µL).

Researchers determined the standard deviation of the minimum difference in means that is considered meaningful ($X_1 - X_2$) to be 2.02 and for the S value it was found to be 2.33 according to the standard deviation value from the literature.[17] Based on this formula, the minimum sample size was 18 people and was taken by Consecutive Sampling.

Handling perioperative pain complaints for all patients involved in this studywould be the responsibility of the researcher as an anesthesia specialist for up to 48 hours after surgery. Patients who met the inclusion and exclusion criteria underwent spinal anesthesia by inserting 10 mg bupivacaine and 25 µg fentanyl into the subarachnoid space. Patients in this study received perioperative analgesics in the form of parecoxib 40 mg bolus IV 4 times. If the patient experiences very severe pain after surgery, researchers would provide additional analgesics in the form of other non-steroidal anti-inflammatory drugs (NSAIDs) such as ketorolac.

The research sample was in the form of the patient's venous blood which would be taken 4 times at an interval of 12 hours, starting immediately before surgery until 36 hours after surgery according to the research flow chart. Then the blood samples were prepared at the Biomolecular Laboratory of the Faculty of Medicine, Riau University before being sent to the Biomolecular Laboratory of the Faculty of Medicine, Andalas University for examination of IL-1β levels. IL-1β levels were examined in samples I, II, III, and IV. In addition to biomolecular examination, post-operative pain complaints would be assessed and recorded in the form of a VAS scale which is carried out several times, namely: Immediately after surgery, 12 hours after the 1st administration, 24 hours after the 1st administration, 36 hours after the 1st administration. The results of the biomolecular examination in the form of IL-1β levels and VAS values recorded would become research data that would be analyzed using statistical applications.

This research was approved by the Research Ethics Committee of the Faculty of Medicine, Andalas University 683/UN.16.2/KEP-FK/2022.

RESULT

A study was conducted on 18 samples of preeclampsia patients who received parecoxib perioperatively for cesarean section with spinal anesthesia. The characteristics of the respondents, which consist of patient age, education level, and occupation, can be seen in Table 1. Based on Table 1, it is found that the majority of respondents were 26-35 years old with a total of 12 respondents (66.67%). This age division was divided according to the Ministry of Health of the Republic of Indonesia in 2009. Based on education, the highest level of education was found to be middle school (SMA) with a total of 9 people (50%). Based on occupation, the average number of people not working (housewives) is 17 people (94.44%).

Table 1. Respondent characteristics

No	Description	By administering parecoxib n (%)
1	Age (Indonesian Ministry of Health, 2009)	
	Late teens (17-25)	2 (11.11%)
	Early maturity (26-35)	12(66.67%)
	Late adulthood (36-45)	4 (22.22%)
2	Education (Law No.20, 2003)	
	Elementary (Primary and Middle School)	8 (44.44%)
	Intermediate (high school)	9 (50%)
	Higher (Diploma and Bachelor)	1 (5.56%)
3	Occupation	
	Work	1 (5.56%)
	Not Working (Housewife)	17 (94.44%)

The correlation test used is Pearson. The results of the correlation between IL-1β levels and VAS carried out serially, namely at the time before surgery (pre-operation), 12 hours, 24 hours, and 36 hours, showed that pre-operative IL-1β did not have a statistically significant correlation with Pre-operative VAS ($p > 0.05$) (Table 2). Likewise, IL-1β 12 hours and 36 hours did not have a statistically significant correlation with VAS ($p > 0.05$). Meanwhile, at 24 hours, IL-1β had a statistically significant correlation with VAS ($p<0.05$). It should be concluded that there was a moderate negative correlation between IL-1β and VAS ($p <0.05$; correlation coefficient -0.487) which means that the lower the IL-1β value, the higher the VAS value.

Table 2. Relationship between IL-1β levels and VAS scores

Variable		p value	Correlation coefficient
Pre-operative IL-1β	Pre-operative VAS	0.138	0.364
IL-1β 12 Hours	12 Hour VAS	0.805	0.063
IL-1β 24 Hours	24 Hour VAS	0.04	-0.487
IL-1β 36 Hours	36 Hours VAS	0.057	0.456

DISCUSSION

Based on research conducted, the average age of patients experiencing preeclampsia is still in the productive age range of 20-40 years. The same results were also obtained from research conducted in Bali by Vincent et al where the most common age for preeclampsia was between 20-35 years of age.[18] The same results were also obtained from research conducted in Surabaya by Adeline, Laksana, and Atika where patients who experienced preeclampsia were found in the age group 17-34 years. These results are not in line with the Indonesian National Health Survey which stated that the prevalence of preeclampsia reached 25% of all pregnancies in Indonesia with the highest presentation occurring in pregnancies over the age of 35 years.[3,4] This is probably due to the mother's age, in general, most people experience pregnancy and childbirth in their productive age, so the incidence of preeclampsia also occurs in their productive age.

VAS is an instrument for identifying and measuring postoperative pain, which helps in improving patient pain management. At this study, IL-1β and VAS levels were measured on 18 respondents at preoperative collection and assessment times, 12 hours, 24 hours to 36 hours. The results showed that there was a relationship between IL-1β levels and VAS after 24-hour collection and assessment, where the lower the IL-1β value, the higher the VAS value. Tissue damage due to caesarean section would also cause the release of various cytokines, one of which is IL-1β which is considered the main cytokine that plays a role in modulating inflammatory mechanisms related to disorders, especially in the first 24-72 hours after surgery. Acute tissue injury would result in increased synthesis and extravasation of humoral proinflammatory cytokines, such as IL-1β and IL-6. These cytokines play an important role in the irritative component of inflammatory pain.[19]

Studies show that increased levels of IL-1β result in allodynia and the development of persistent pain, so perioperative analgesia is important in reducing levels of proinflammatory cytokines.[20] Perioperative pain that occurs is unavoidable and is closely related to inflammation.[21] Pain and the immune system could influence one another. Each other, so it is difficult to determine whether nociceptor blockade could reduce the production of pro-inflammatory cytokines or vice versa, by decreasing the formation of pro-inflammatory cytokines it would result in a decrease in the scale of pain.[22]

CONCLUSION

In summary, our data show that preeclamptic patients who received parecoxib after 24 hours of cesarean section under spinal anesthesia had decreased IL-1β levels and decreased VAS scores. Pain can be an indicator of increased inflammation or inflammatory factors in sectio caesarea patients with spinal anesthesia. The weakness of this research is that it has a small sample size so a larger sample size is needed.

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