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Effectiveness of Ketoprofen Suppositories in Reducing the Risk of Preterm Labor at a Teaching Hospital in Malang

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Partus prematurus imminens (PPI) was a condition that threatened preterm labor, marked by labor signs before term (20 to <37 weeks) and birth weight under 2500 grams. Management included rest, hydration, and pharmacological measures. One approach used to delay labor was tocolytic therapy, such as ketoprofen suppositories, to inhibit uterine contractions. This study aimed to analyze the difference in uterine contractions before and after the administration of ketoprofen suppositories in women at risk of preterm labor. This study used a quasi-experimental design with a pre-test and post-test without a control group. The sample included 30 pregnant women with PPI who met the inclusion criteria. Consecutive sampling was used. The intervention administered was ketoprofen suppository therapy, 200 mg (2 tablets) given rectally. Data were collected using an observation sheet and analyzed using the Wilcoxon signed-rank test. The results showed that the mean uterine contraction score before therapy was 2,17, which decreased to 1,20 after therapy. There was a statistically significant difference in uterine contractions before and after the intervention. The Wilcoxon signed-rank test resulted in a p-value of 0,001 ($p \leq 0,05$). The findings indicated a significant difference in uterine contractions before and after the administration of ketoprofen suppositories in pregnant women at risk of preterm labor. Ketoprofen suppository therapy was effective in reducing uterine contractions in pregnant women at risk of preterm labor, with routine fetal monitoring ensuring the safety of the intervention.

Keywords: uterine contractions, imminent preterm labor, ketoprofen suppository, tocolytic

INTRODUCTION

Preterm labor has been one of the leading causes of neonatal mortality and can result in various serious health complications, both short-term and long-term, due to the immaturity of vital organs such as the lungs and central nervous system (WHO, 2021). In 2015, approximately 15 million babies worldwide were born prematurely, with over one million of them dying due to complications related to preterm birth. More than 60% of these preterm births occurred in Africa and South Asia. The incidence of preterm birth in Indonesia remained high, with an estimated 675.700 cases annually. Indonesia ranked fifth globally in terms of the highest number of preterm births (WHO, 2018).

Premature delivery significantly contributed to morbidity and mortality rates and affected the long-term health of a child due to the immaturity of organ systems resulting from delivery before 37 weeks of gestation (Casanova et al., 2019). Prematurity, along with low birth weight (LBW), ranked third (19%) as a cause of neonatal mortality in Indonesia, following intrapartum events (28,3%) and respiratory and cardiovascular disorders (21,3%) (Lontaan et al., 2025).

One of the indicators of successful healthcare services in a country could be seen through the Maternal Mortality Rate (MMR) and Infant Mortality Rate (IMR). In Indonesia, 19% of infant deaths were caused by preterm labor (Raihana et al., 2023). Data from the East Java Provincial Health Office in 2021 showed 20.627 cases of preterm birth (3.7%) out of 563.716 live birth. In 2022, the Malang District Health Office reported 1.317 low birth weight (LBW) infants out of 36.009 total live births, although LBW did not fully represent the number of preterm births.

. A preliminary study conducted at RSUD Kanjuruhan, Malang District, from January to August 2024 found 75 cases of partus prematurus imminens (PPI) and 14 cases of preterm delivery (5,51%) out of 254 total spontaneous or cesarean section deliveries in the Delivery Room. These preterm births contributed to the increased neonatal mortality rate due to low birth weight.

One of the causes of labor was the prostaglandin theory. The concentration of prostaglandins increased from the 15th week of pregnancy and was released by the decidua. Prostaglandins were considered triggers for the onset of labor. This was also supported by the presence of high levels of prostaglandins in both the amniotic fluid and peripheral circulation of pregnant women before or during labor (K, 2019). Ketoprofen is a non-steroidal anti-inflammatory drug (NSAID) used to reduce inflammation and pain. It works by inhibiting the cyclooxygenase (COX) enzyme, which is involved in the production of prostaglandins. As prostaglandin levels decrease, symptoms such as pain and swelling also diminish. Ketoprofen was found to be 800–1500 times more potent than ibuprofen, phenylbutazone, and aspirin. Rectal administration of ketoprofen was as effective as intravenous administration in pain

management. Its use was significantly more effective than placebo, as 73–93% of ketoprofen was directly absorbed after rectal administration (Maddeppungeng & Rahman, 2021; X et al., 2022).

Ketoprofen suppositories were used as an early prevention strategy for preterm labor in the Delivery Room of the Teaching Hospital in Malang District. Ketoprofen acted by inhibiting the COX enzyme, which plays a role in the production of prostaglandins. During uterine contractions, prostaglandin levels increase, intensifying contractions, promoting cervical dilation, and triggering preterm labor. However, ketoprofen also posed potential risks to the fetus. Prolonged use of NSAIDs (over 48 hours) in the third trimester could cause premature closure of the ductus arteriosus and oligohydramnios. This theory is expected to support the present study, which aimed to evaluate the effect of ketoprofen suppositories on uterine contractions in women at risk of preterm labor.

METHODOLOGY

This study was a non-randomized clinical trial, using a quantitative approach with a quasi-experimental design, specifically the pre-test and post-test without control group. The population in this study consisted of pregnant women diagnosed with imminent preterm labor (PPI) who were admitted to the Delivery Room at RSUD Kanjuruhan, Malang District, from Januari to April 2025.

The sample size was determined using Dell's sample size formula for a single-group experiment, resulting in 30 pregnant women with PPI who met the inclusion criteria. The inclusion criteria were pregnant women with gestational age between 20 and <37 weeks, experiencing sustained uterine contractions (not Braxton Hicks) that could potentially lead to labor. The exclusion criterion in this study was respondents with an allergy to ketoprofen. The sampling technique applied in this study was consecutive sampling.

The study was conducted on 30 pregnant women who met the inclusion criteria and were treated with ketoprofen suppositories (200 mg/2 tablets per rectal) in the Delivery Room. Uterine contractions were observed before and one hour after the administration of ketoprofen suppositories (200 mg/2 tablets per rectally). Uterine contractions before and after the administration of ketoprofen suppositories will be compared and the differences will be noted. For the statistical analysis, the Wilcoxon signed rank test was used as a non-parametric comparative test for two related samples. The study was conducted after obtaining approval from the Research Ethics Committee of Kanjuruhan District Hospital, Malang Regency, under approval number 072.1/EA.KEPK/006/35.07.302.101/2025.

RESULT AND DISCUSSION

Results

Table 1. Respondent Characteristics

Characteristics	n	%
Age		
< 20 years	2	6,67%
20 - 35 years	25	83,33%
>35 years	3	10,00 %
Pregnancy Status		
Primigravida	12	40,00%
Multigravida	11	36,67%
Grandemultigravida	7	23,33%

Table 1 showed that the majority of respondents consisted of pregnant women aged between 20 and 35 years, with a total of 25 respondents (83.33%), and indicated that most of the pregnant women in this study were first-time mothers, totaling 12 respondents (40%).

Table 2. Uterine contractions before and after the administration of ketoprofen suppository therapy

Uterine Contractions	Treatment (administration ketoprofen suppository 200mg (2 tablets)/rectal)			
	Before	%	After	%
Orderly (≥ 3x/10 minutes)	5	16,67%	0	0,00%
Disordered (1 – 2x/10 minutes)	25	83,33%	6	20,00%
Very disordered (<1x/10 minutes)	0	0,00%	24	80,00%

Table 2 showed that 25 respondents (83.33%) experienced irregular uterine contractions occurring 1–2 times every 10 minutes.

Table 3. Descriptive averages before and after the administration of ketoprofen suppository therapy

	N	Mean	Std. Deviation	Min	Max	p value
Before	30	2,17	0,38	2,00	3,00	p = 0, 001
After	30	1,20	0,41	1,00	2,00	

Table 3 showed that uterine contractions were categorized based on the following criteria: a score of 1 indicated very disordered contractions (<1 contraction per 10 minutes), a score of 2 indicated disordered contractions (1–2 contractions per 10 minutes), and a score of 3 indicated orderly contractions (≥3 contractions per 10 minutes). The analysis showed that the mean uterine contractions before the administration of 200 mg (2 tablets) of ketoprofen suppositories was 2,17, while the mean uterine contractions after the administration was 1,20. The results of the Wilcoxon signed-rank test, with a p-value (Asymp. Sig. 2-tailed) of 0,001 ($p \leq 0,05$), indicated that the hypothesis was accepted. These results demonstrated a significant difference in uterine contractions in pregnant women before and after the administration of 200 mg (2 tablets) of ketoprofen suppositories.

Discussion

Labor was the process of the movement of the fetus, placenta, and membranes from the uterus through the birth canal. This process began with the opening and dilation of the cervix caused by uterine contractions with regular frequency, duration, and strength. Labor was considered normal if it occurred at full term (after 37 weeks) without complications (Yuriati & Khoiriyah, 2021). One of the threats during pregnancy was Imminent Premature Labor (IPL), which referred to the onset of labor signs at a gestational age that was not yet term (20 weeks to < 37 weeks) and a birth weight of less than 2500 grams. The ongoing labor process showed clinical signs such as contractions occurring about 4 times every 20 minutes or 8 times in one hour, along with progressive changes in the cervix, including dilation of more than 1 cm, softening of about 75-80%, and cervical thinning. Imminent premature labor could lead to premature birth if not addressed promptly (Kirana et al., 2020)

Research showed that the majority of pregnant respondents in this study were aged 20–35 years, with 25 respondents (83.33%), which was considered the most optimal and productive reproductive age. The age of 20–30 years was regarded as the ideal age for a woman to become pregnant. Pregnancy at an age over 35 years or under 20 years could pose risks for the expectant mother. Women who became pregnant before the age of 20 faced higher risks because the function of their reproductive organs was not yet fully mature and therefore could not work properly. High-risk pregnancies also occurred in women over the age of 30. The risks experienced by women aged under 20 years and over 30 years included preeclampsia, eclampsia, abortion, low birth weight, and prematurity (Dumilah, 2019).

Most pregnant women who experienced imminent preterm labor were those undergoing their first pregnancy (primigravida). Primigravidas had a higher risk of anxiety, lack of awareness of pregnancy danger signs, and delays in seeking medical help. Primigravida and multigravida pregnancies were considered lower-risk compared to grand multipara pregnancies. Parity referred to the number of children

born to a mother, whether alive or deceased. Parity was classified into three categories: primigravida, multigravida, and grandemultigravida. Primigravida referred to a mother who was pregnant for the first time and lacked experience, while grandemultigravida referred to a mother who had been pregnant more than three times, with the uterus becoming weaker, thus increasing the risk of pregnancy complications. Multigravida parity was considered the safest in pregnancy (Arifah & Mudlikah, 2024).

As many as 29 out of 30 respondents experienced a decrease in uterine contractions (his) after the administration of 200 mg (2 tablets) of ketoprofen suppositories. The mean uterine contractions before the administration of 200 mg (2 tablets) of ketoprofen suppositories were higher compared to after the administration, with a decrease in the mean value of 0,97. This average difference of 0,97 supported the finding that the administration of 200 mg (2 tablets) of ketoprofen suppositories had a significant clinical impact on reducing uterine contraction activity. The results of the data analysis using the Wilcoxon signed-rank test yielded a p-value of 0,001 ($p \leq 0,05$), indicating a significant difference in uterine contractions before and after the administration of ketoprofen suppositories.

One way to inhibit the signs of premature labor was by pharmacologically suppressing uterine contractions using tocolytics, which aimed to prolong pregnancy and delay delivery. Tocolytic agents were administered to stop uterine contractions during the acute phase. Tocolytics were pharmacological agents and therapies used to prevent premature birth, relax the uterine endometrium, and inhibit uterine contractions, thereby extending the duration of pregnancy and reducing neonatal complications. Tocolytics acted through various mechanisms to reduce the availability of intracellular calcium ions, thereby inhibiting the actin-myosin interaction (Karmelita, 2020). The administration of tocolytics will inhibit myometrial contractions and can delay labor for 24-48 hours. This effect has been observed in both in vitro and in vivo administration, including beta-adrenergic agonists, Ca-Channel antagonists, oxytocin antagonists, NSAIDs and magnesium sulfate. This medication can inhibit uterine contractions, thereby prolonging pregnancy and reducing short-term complications in neonates, among which the most common are Respiratory Distress Syndrome (RDS), Necrotizing Enterocolitis (NEC), bronchopulmonary dysplasia, sepsis, patent ductus arteriosus and intra/periventricular hemorrhage. Meanwhile, in the long term, it can lead to neurological disorders such as cerebral palsy, retinopathy, mental retardation, neurobehavioral dysfunction, and poor school performance (Irwan et al., 2022).

Ketoprofen worked primarily by inhibiting the cyclooxygenase (COX-1) enzyme, which was responsible for the synthesis of prostaglandins with physiological functions, and the cyclooxygenase (COX-2) enzyme, which was responsible for the synthesis of pro-inflammatory prostaglandins at sites of inflammation. COX-1 and COX-2 were also present in the central nervous system. Ketoprofen was rapidly and efficiently distributed into the central nervous system, crossing the blood-brain barrier within 15

minutes due to its high liposolubility. Its antipyretic effect was likely associated with the inhibition of prostaglandin synthesis in the hypothalamus (Kuczyńska & Nieradko-Iwanicka, 2021).

Ketoprofen was widely used in the management of inflammatory and musculoskeletal conditions such as rheumatoid arthritis, juvenile idiopathic arthritis, ankylosing spondylitis, as well as for pain and fever (Kuczynska & Nieradko-Iwanicka, 2022). Ketoprofen was available in the form of tablets, capsules, suppositories, enteric-coated tablets, extended-release tablets, and topical gel. When administered orally, ketoprofen was rapidly absorbed, reaching peak concentration at 0,52 hours, and had a short elimination half-life (T1/2) of 1,54 hours. Ketoprofen was well absorbed when given intramuscularly or rectally, but was poorly absorbed when applied topically. Administration of topical medication around the anus or rectally was considered more advantageous because it avoided gastrointestinal irritation side effects, bypassed the first-pass effect, and helped relieve internal sphincter contractions as well as reduce pain (Yurmansyah, 2018)

The results of this study were also consistent with the research by Wurnayingsih (2019), which explained that NSAIDs acted by inhibiting the enzyme prostaglandin G/H synthase, known as cyclooxygenase. These enzymes converted arachidonic acid into the unstable intermediates prostaglandin G2 and prostaglandin H2, leading to the production of thromboxane A2 and various other prostaglandins that contributed to pain. In obstetrics and gynecology, NSAIDs had long been used to control acute and chronic postoperative pain, menstrual pain, pain associated with medical abortion, menorrhagia, contraceptive devices, to assist in fertility treatments, and were administered as tocolytics in preterm labor. Increased prostaglandins during labor led to heightened uterine contractility, and prostaglandin synthesis inhibitors could delay the onset of labor.

NSAIDs had a mechanism of action that could suppress uterine contraction activity, but their use also had the potential to cause effects impacting fetal well-being. NSAIDs used in the short term during the second trimester were effective for treating pain caused by tissue degeneration and fibroblasts, but when used for a prolonged period (more than 48 hours) during the third trimester, they could cause constriction of the ductus arteriosus and oligohydramnios. In general, NSAIDs could be administered for a short duration (less than 48 hours) without the need for monitoring blood flow in the fetal ductus arteriosus and amniotic fluid volume (Yulianto Sarim & Suryono, 2020).

This study had several limitations. First, it did not include a control group, which limited the ability to compare outcomes. Second, the sample size was relatively small and drawn from a single hospital, thereby reducing the generalizability of the findings. Third, the follow-up period was short, so only immediate maternal outcomes were assessed without evaluating long-term or neonatal outcomes. Finally, the potential for observer bias could not be completely excluded.

CONCLUSION

The administration of ketoprofen suppositories rectally has been proven effective in reducing the frequency of uterine contractions in pregnant women at risk of preterm labor (partus prematurus imminens). The use of NSAID group drug therapy for more than 48 hours provides clinical benefits in delaying childbirth, but prolonged use beyond this period has the potential to affect fetal well-being, related to the risk of early closure of the ductus arteriosus and the occurrence of oligohydramnios. Healthcare facilities considered the use of ketoprofen suppositories as one of the tocolytic therapy options for pregnant women at risk of imminent preterm labor, conducting regular fetal well-being monitoring during the therapy to ensure the comprehensive safety of the intervention on the fetal condition. Future researchers were recommended to conduct randomized controlled trials with longer follow-up periods and to include neonatal outcomes.

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