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Psychoeducation Dhikr Influence on Oxytocin and Interleukin-8 Levels on Pregnant Women

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Abstract: Emotional instability often occurs in mothers during pregnancy and puts the mother in a vulnerable condition, and is a stress transition, increasing pro-inflammatory cytokines that can trigger preterm labor. The pregnancy period is a condition to be closer to God and make life more meaningful by using religious beliefs as a strong coping mechanism. This study aims to prove that routine midwifery care and psychoeducation dhikr is more decreasing oxytocin and Interleukin-8 levels in pregnant women. The research aims to prove that routine midwifery care and dhikr psychoeducation lowers oxytocin levels and interleukin-8 levels more than routine midwifery care alone. The Quasi-experimental research design with pre-test post-test control group design was applied. Seventy-five pregnant women starting the third trimester of pregnancy completed the entire study series. The psychoeducation dhikr intervention is added to routine midwifery care—a statistical test using the Mann-Whitney test. The mean difference of oxytocin levels in the intervention group (30.18) was lower than the control group (46.03), $p = 0.02$. The mean difference of Interleukin-8 level in the intervention group (39.84) was higher than in the control group (36.11), $p\text{-value} = 0.458$. Routine midwifery care plus Psychoeducation dhikr is thought to reduce oxytocin levels and lower Interleukin-8 levels in pregnant women, but there is no difference between routine midwifery care. This study provides evidence that psychoeducation dhikr added to routine midwifery care reduces oxytocin levels and lowers interleukin-8 levels more than routine midwifery care itself. Thus, the intervention involves spiritually controlling oxytocin and IL-8 in pregnancy so that it has the potential to prevent preterm labor.

Keywords: psychoeducation, *dzikr*, oxytocin, IL-8, pregnancy.

心理教育 齊克爾 對孕婦催產素和白細胞介素 8 水平的影響

摘要: 情緒不穩定經常發生在懷孕期間的母親身上, 使母親處於脆弱狀態, 是一種壓力過渡, 可以增加促炎細胞因子, 從而引發早產。懷孕期間是一個條件, 通過使用宗教信仰作為一種強大的應對機制, 可以更接近上帝並使生活更有意義。本研究旨在證明常規助產士護理加心理教育日克爾更能降低孕婦的催產素和白細胞介素 -8 水平。準實驗研究設計與前測後測控制組設計。共有 75 名妊娠晚期開始的孕婦完成了整個研究系列。思維心理教育干預被添加到常規助產士護理中。使用 曼惠特尼 檢驗進行統計檢驗。干預組的平均催產素水平 (32.22) 低於對照組 (43.93), 磷 = 0.02。干預組白細胞介素 8 水平平均值 (38.86) 高於對照組 (37.12), 磷值 = 0.730。常規助產護理加心理教育被認為可以降低孕婦的催產素水平和 IL-8 水平, 但與常規助產護理相比沒有差異。

关键词: 心理教育, 齊克爾, 催產素, 伊爾-8, 懷孕。

1. Introduction

Pregnancy is a transitional period that can cause stress, where oxytocin may be associated with anxiety or depression in pregnancy. Oxytocin (OT) has a modifying effect on anxiety, prenatal depression, and early pregnancy stress [1], increasing of plasma oxytocin levels in pregnant women may indicate a risk of mental health symptoms during the prenatal period [2], OT may play a role in the etiology of depressive symptoms [3].

During pregnancy, there is also dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis [4], which is a classic neuroendocrine stress response system; and stimulates the release of cytokines as inflammatory mediators [5].

Focusing on the immune challenge model (since infection is a major cause of preterm labor in women), the resulting study has found that the response of oxytocin neurons to IL-1b is strongly suppressed in late pregnancy, in addition to reproductive (i.e., uterine contractions and suction) and osmotic stimulation, oxytocin neurons also respond to stress stimulation [1]. The review resulted that patients with depression had increased levels of pro-inflammatory cytokines, such as interleukin-1 (IL-1), IL-2, IL-6, IL-8, IL-12, interferon- γ (IFN γ and tumor necrosis factor- α). (TNF α) [6].

In the third trimester of pregnancy, levels of pro-inflammatory cytokines increase and function to fight infection and heal wounds. High levels of pro-inflammatory cytokines are the body's response in preparing for labor and as a protector in helping to prevent infection [7]. The study results indicate that physical and psychological stress that increases inflammation, such as sleep disturbances, postpartum pain, and psychological trauma, is a stressor that causes pro-inflammatory cytokine levels to increase [8].

Increased proinflammatory cytokines trigger uteroplacental insufficiency and lead to preterm labor [9]. Increased oxytocin secretion during late pregnancy is likely to stimulate premature uterine contractions and increase the risk of preterm labor [10], a single direct cause of 35% of neonatal deaths and long-term complications [11, 12].

Interventions in psychological illness are effective if physical well-being can be improved by reducing stress or improving coping. Religious beliefs in pregnancy are a strong coping mechanism [13] to carry out pain management independently on cancer patients' religious activities [14]. Meanwhile, the program for providing maternal health services, in general, is still related to physical health, treatment, infant care, and family.

One of the spiritual interventions is *dhikr*, which is interpreted by remembering, mentioning, understanding as verbal speech, body movements, or vibrations of the heart according to what religion teaches to get closer to God, and knows no time limit [15]. Several studies on *dhikr* have been carried out,

with midwifery care plus psychoeducation. *Dhikr* reduces stress and depressive syndrome in the first pregnant woman, further lowering cortisol levels and increasing IgG levels in primiparous mothers. Relax training with *dhikr* can reduce pregnancy anxiety for first pregnant women [16]; *dhikr* is significantly correlated with subjective well-being [15].

Some of the weaknesses of previous studies are that they have not evaluated the impact of using a religious approach on oxytocin and IL-8 levels as markers of risk of preterm labor. This study aims to prove that routine midwifery care (RMC) plus psychoeducation *dhikr* (PD) has more effect on oxytocin levels and IL-8 levels of pregnant women compared to RMC alone. The hypothesis is that routine midwifery care plus psychoeducation *dhikr* (PD) reduces oxytocin levels and IL-8 levels more than routine midwifery care itself.

2. Materials and Methods

Data collection was carried out from July to September 2019. This research has been experimental research with a randomized two-group pre-test post-test quasi-experimental design. The intervention was the RMC plus PD, while the control group got the RMC only. The authors decided to recruit 82 pregnant women, and then 75 pregnant women signed the informed consent. Then random allocation to either the intervention or the control groups was carried out based on the area of the Community Health Centers to avoid conflict, and there were 38 pregnant women in the intervention group and 40 in the control group. Sample size by comparing the two means of the independent group.

Pregnant women were included if they were on 20 weeks gestation, normal pregnancy, willing to be a subject in research, could read and write in Indonesian, memorize or be able to read some of *al-Qu'ran's* letters (*Al-Fatihah*, *Al-Falaaq*, *An-Nass*, *Al-Ikhlās*, *Al-Insyirah*). The authors exclude the pregnant women are a single parent.

Interventions had been given two times on the third trimester of pregnancy, for 45-60 minutes of each intervention, using modules in the same sequence of activities, beginning with deep breathing relaxation activities, followed by reading some of *al-Qu'ran's* letters, *Sholawat Prophet Muhammad SAW*, some *Asmaul Husna*, *toyyibah* sentence, *Istighfar*, *Tauhid* sentence and mention Allah's name and end with a deep breath. The materials used in the study include the psychoeducation *Dhikr* (PD) module [17]. The intervention was carried out by researchers assisted by six midwives with the same perception and training.

The oxytocin and IL-8 levels were taken from the subject's blood and measured in the third trimester of pregnancy, tested using the Enzyme-Linked Immuno Sorbant Assay (ELISA) method at the GAKY Laboratory Diponegoro University. Data were analyzed in SPSS, analysis of the oxytocin and IL-8 level

variables in the intervention group and control group used Mann Whitney U-Test at the significance level of $P < 0.05$.

Ethical permission was obtained from Research Ethics Committee at Politeknik Kesehatan Kemenkes Surakarta, with number no.LB.02.02/1.3/1683/2019. All respondents signed Informed Consent in Bahasa.

3. Results and Discussion

Research data collection and intervention were first carried out after the research ethics letter was issued. Subjects were selected using criteria. This was done to control variations in the characteristics of the subject.

All participants were pre-tested by measuring oxytocin and IL-8, then intervention and post-test were performed. All participants filled out a characteristic questionnaire consist of age, parity, and premature labor and delivery. The participants' demographic characteristics, the oxytocin, and IL-8 levels are homogeneous in both groups. The normality test results using the Shapiro-Wilk test showed that the pre-test and post-test oxytocin levels in both groups and the pre-test IL-8 level data in the control group were not normally distributed ($p < 0.05$), and the data were transformed. The normality test results of the data after the transformation showed that the data distribution was not normal (Table 1).

The results showed that RMC plus PD decreased oxytocin levels in pregnant women more than RMC alone. The mean \pm SD oxytocin levels before intervention were 214.01 ± 213.22 for the RMC plus PD group and 257.7 ± 181.76 for the RMC. Mann Whitney U t-test showed a difference between the two groups' oxytocin levels at the baseline ($p = 0.028$). The mean \pm SD oxytocin levels after the intervention were 221.06 ± 177.32 for the RMC plus PD group and 186.65 ± 165.21 for the RMC. Mann Whitney U t-test showed no difference between the two groups' oxytocin levels at the baseline ($p = 0.092$). The mean difference of oxytocin levels in mothers was 30.18 for the RMC plus PD group and 46.03 for the RMC. Based on the Mann-Whitney U t-test, a statistically significant of the oxytocin levels of the mothers between groups was $p = 0.002$. The oxytocin levels between groups were also compared and shown in Table 2.

Oxytocin, a peptide hormone comprising nine amino acids, is synthesized in neurons of the supraoptic nucleus and paraventricular nucleus of the hypothalamus after specific stimulation of the brain [18]. Oxytocin synthesized by magnocellular neurons in the supraoptic and paraventricular nuclei plays an important role in mammalian birth [19].

Oxytocin is needed during labor and delivery to facilitate labor [18], [20], but not during pregnancy. High levels of oxytocin in pregnancy have a risk of preterm delivery. High levels of oxytocin cause smooth muscle contractions, which stimulate uterine

contractions in pregnancy, which triggers preterm labor.

Dzikir is a ritual performed by Moslems in which they chant the names of God repeatedly to stimulate happiness [15], thus triggering a comfortable and relaxed condition. Meanwhile, oxytocin will be released in the brain in a relaxed state, or a type of emotional stimulation and brain mood that contributes to relaxation, trust, psychological stability, and reduced stress responses, including anxiety [18].

This may be because high oxytocin is one of the protective results of a high-stress response. Therefore, high stress on prenatal anxiety and depression was seen in the high oxytocin group. In addition, it may be because pregnant women are more sensitive to stress due to the protective effect of oxytocin. Interestingly, this is similar to the resilience-modifying effect between early pregnancy stress and prenatal anxiety and depression in our previous study, the association between pregnancy stress and prenatal anxiety or depression, was stronger in the highest resilience group [1].

Although both groups experienced decreased mean oxytocin levels, the average oxytocin levels in the RMC plus PD group were less than the RMC group alone. This is under the results of previous research that relaxation training with dhikr in pregnant women has been shown to reduce anxiety and help individuals form perceptions about the belief that any stressor will be handled well with God help, interventions based on religious beliefs that one has can help improve a person's mental health [21] manifested by increased levels of oxytocin [3].

The addition of PD to RMC is important to consider as an alternative to mothers during pregnancy so that it causes a relaxed condition. The results of this study add to the fact that additional dhikr psychoeducation in midwifery care has been shown to reduce oxytocin levels which have an impact on preventing preterm labor.

Another study result shows that both groups experienced a decrease in the mean levels of IL-8 and the results of the analysis showed that there was no difference in the mean difference in IL-8 levels before and after the intervention between the RMC plus PD group compared and the RMC only group (Table 1).

The mean \pm SD IL-8 levels before intervention were 7.65 ± 5.08 for the RMC plus PD group and 5.83 ± 2.61 for the RMC. Mann Whitney U t-test showed no difference between the two groups' IL-8 levels at the baseline ($p = 0.228$). The mean \pm SD IL-8 levels after the intervention were 5.33 ± 3.43 for the RMC plus PD group and 5.13 ± 3.76 for the RMC. The Mann Whitney U t-test showed no difference between the two groups' IL-8 levels at the baseline ($p = 0.528$).

The mean difference of IL-8 levels mothers was 39.84 for the RMC plus PD group and 36.11 for the RMC. Based on the Mann-Whitney U t-test, there was

no statistical difference in the IL-8 levels of the mothers between groups was ($p = 0.458$). The IL-8 levels between groups were also compared and shown in Table 2.

The results indicate that physical and psychological stress increase inflammation, pregnant women are susceptible to changes in pro-inflammatory cytokines, which are significantly increased during the third trimester of pregnancy.

Pro-inflammatory cytokines have been found to interact with many pathophysiological domains that characterize depression, including neurotransmitter metabolism, neuroendocrine function, synaptic plasticity, and behavior. Stress can trigger an inflammatory response and is an early symptom of the disease [22].

Stress during pregnancy will cause the activation of the nervous system, thereby stimulating the release of catecholamines, neurotransmitters, and neuropeptides, activation of the endocrine system, which will trigger the release of Corticotrophin Releasing Hormone (CRH), cortisol, and other hormones and stimulate the release of cytokines as inflammatory mediators [23].

Table 1 Participants' demographic characteristics, the oxytocin, and IL-8 levels

Variables		RMC + PD (n = 38)		RMC (37)	
		n (%)	n (%)	n (%)	n (%)
Age	Mean	27.37	26.16		
	+SD	5.21	4.72		
Normality test	P value	0.178	0.047		
Parity					
Primigravida		27(28.9)	18(48.6)		
Multigravida		11(71.1)	19(51.4)		
Previous labor					
Abortus		1(2.6)	2(5.4)		
Spontaneous		31(81.6)	32(86.5)		
Assisted Delivery		4(10.5)	3(8.1)		
Sectio Caesarean		2(5.3)	0(0)		
Oxytocin levels					
Normality test	p value	0.000	0.000	0.000	0.000
	Mean	214.01	221.06	257.75	186.65
	+SD	213.2	177.3	181.7	165.2
IL-8 levels					
Normality test	p-value	0.000	0.286	0.000	0.000
	Mean	7.65	5.32	5.82	5.13
	+SD	5.08	3.43	2.61	3.76

In preterm labor [9], stress and depression stimulate the HPA axis, increasing cortisol secretion and the risk of preterm delivery [24]. In the third trimester of pregnancy, levels of pro-inflammatory cytokines increase, and they function to fight infection and heal wounds. High pro-inflammatory cytokines are the

body's response in preparing for labor and as a protector in helping to prevent infection [7]

Table 2 Differences in oxytocin and IL-8 levels in the intervention and control groups

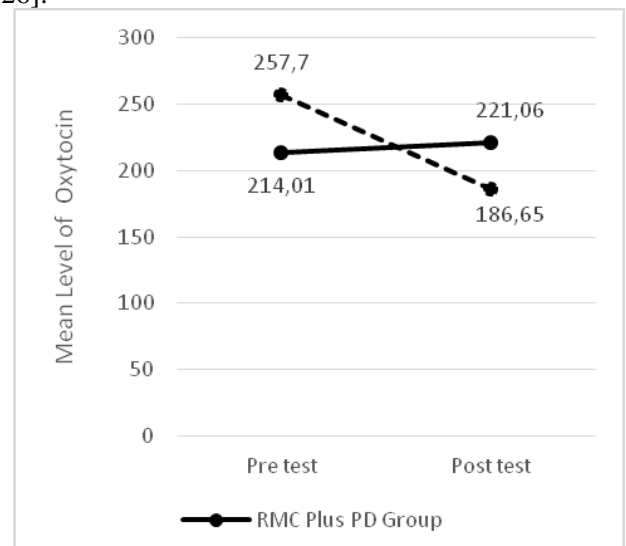
Variables	Stage of study	Mean + SD		p-value
		RMC + PD	RMC	
Oxytocin levels	Pre-test	214.01 + 213.22	257.7 + 181.76	0.028*
	Post-test	221.06 + 177.32	186.65 + 165.21	0.092*
	p value	0.01**	0.016**	
	Mean Δ	30.18	46.03	0.002*
IL-8 levels	Pre-test	7.65 + 5.08	5.83 + 2.61	0.228*
	Post-test	5.33 + 3.43	5.13 + 3.76	0.528*
	p value	0.002**	0.65**	
	Mean Δ	39.84	36.11	0.458*

* Mann-Whitney U test

** Wilcoxon test

The results of this study showed that both groups had decreased levels of IL-8. In general, IL-8 levels decrease in pregnancy, and there is suppression of the immune system to receive and maintain the products of conception so that rejection does not occur until late gestation, and therefore pregnant women are at risk for exposure to infection [25].

This study revealed that both groups experienced decreased levels of IL-8. The psychoeducation dhikr mediates subjects in accepting stressors through developing a source of belief based on understanding the meaning and experience of dhikr, thereby influencing the improvement of stress perception. Improved stress perception after emotional stressor reduces inflammatory reactivity and improves health [26].



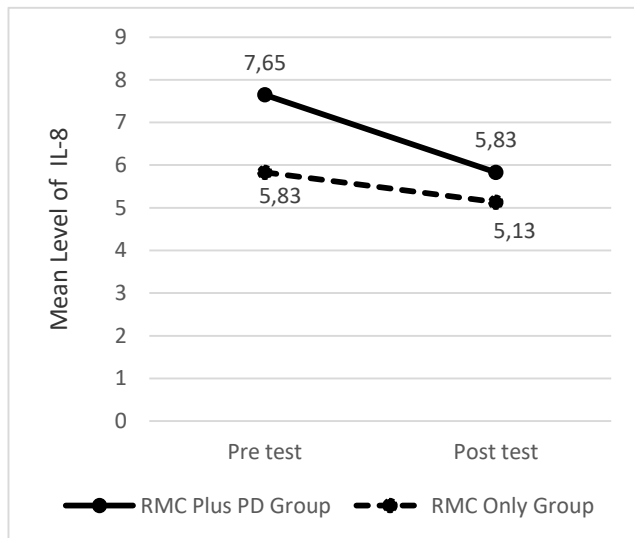


Fig. 1 Diagram of means of the oxytocin and IL-8 levels before and after intervention in both groups

Figure 1 shows a graph of Oxytocin levels in both groups tending to fall, but the average Oxytocin levels in the RMC plus PD group were lower than the average Oxytocin levels in the RMC alone. The mean level of IL-8 in both groups decreased in the mean level of IL-8, but the decrease in the mean level of IL-8 in the RMC alone group (0.7) was lower than in the RMC plus PD group (2.32).

The perinatal period is associated with many physical and psychological stressors that increase pro-inflammatory cytokines that impact inflammation [22]. However, an increase from this normal condition when followed by stress can increase the risk of depression [27]. The HPA Axis through the amygdala responds to information, thereby triggering fear and vague stimuli, causing uncertainty and anxiety, and then connecting with the hypothalamus and brainstem involved in emotional expression [28].

4. Conclusion

Based on the results of this study, it can be concluded that routine midwifery care plus psychoeducation dhikr reduces oxytocin levels in pregnant women, and there is a difference compared to routine midwifery care itself. The routine midwifery care plus psychoeducation dhikr decreased oxytocin levels in pregnant women more than routine midwifery care itself, so the results of this study add to the fact that additional psychoeducation dhikr in midwifery care has been shown to reduce oxytocin levels, thereby prevent uterine contractions during pregnancy, which have an impact on preventing preterm labor.

Both groups experienced a decrease in the mean levels of IL-8, and there was no difference in the mean difference in IL-8 levels before and after the intervention between the routine midwifery care plus Psychoeducation dhikr group compared and the routine midwifery care itself. The results indicate that physical and psychological stress increases inflammation.

Pregnant women are susceptible to changes in pro-inflammatory cytokines, which are significantly increased during the third trimester of pregnancy. Controlling pro-inflammatory cytokines in pregnancy can reduce the risk of preterm labor.

The addition of psychoeducation dhikr so that the midwifery care routine becomes holistic by optimizing the spiritual element to improve mothers' psychological and spiritual health during the perinatal period. The intervention involves spiritually proven to reduce oxytocin and IL-8 in the third trimester of pregnancy, so this has the prospective alternative to prevent preterm labor.

The limitation of this study was that the researcher could not control the spiritual activities of the respondents other than interventions that tend to affect pregnancy stress, which has the potential to bias serum oxytocin and IL-8 levels. It is necessary to develop a qualitative measurement of spiritual aspects in perinatal mothers to develop obstetric services, especially spiritual conditions, so it becomes holistic prevention of preterm birth.

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