Research Article

The Effect of Pyridoxine on Prostaglandin Plasma Level in Patients with Primary Dysmenorrhea

Efek Pemberian Piridoksin terhadap Kadar Prostaglandin Plasma pada Pasien Dismenore Primer

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Abstract

Objective: To determine the effect of vitamin B6 (pyridoxine) to the levels of prostaglandins and intensity of pain in primary dysmenorrhea.

Methods: The levels of prostaglandin (PGF2α) in plasma measured by ELISA and pain intensity by verbal rating scales conducted on 35 women with primary dysmenorrhea (n=35) supplemented with vitamin B6 100mg for four days and controls with placebo (n=35).

Results: Prostaglandin levels decreased significantly after vitamin B6 supplementation (2212.9±1374.2 vs 1490.3±1119.0; p<0.05) followed by a significant reduction in pain intensity (4.29±0.7 vs 1.71±0.5; p<0.05) in the test group compared to control.

Conclusion: Due to vitamin B6 effects on decreasing prostaglandin levels and pain of primary dysmenorrhea, so that B6 vitamin can become the treatment for the primary dysmenorrhea.

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Keywords: primary dysmenorrhea, prostaglandin, pyridoxine

Abstrak

***Tujuan**: Untuk mengetahui pengaruh pemberian vitamin B6 (piridoksin) terhadap kadar prostaglandin dan intensitas nyeri pada dismenore primer.*

***Metode**: Pemeriksaan kadar prostaglandin (PGF2α) dengan ELISA dan pengukuran intensitas nyeri dengan verbal rating scales dilakukan pada 35 orang (n=35) wanita dengan dismenore primer yang mendapatkan vitamin B6 100mg selama 4 hari dan kontrol yang mendapatkan plasebo (n=35).*

***Hasil**: Kadar prostaglandin menurun bermakna setelah pemberian vitamin B6 (2212,9±1374,2 vs 1490,3±1119,0; p<0,05) disertai dengan penurunan intensitas nyeri yang bermakna (4,29±0,7 vs 1,71±0,5; p<0,05) pada kelompok uji dibandingkan kontrol.*

***Kesimpulan**: Vitamin B6 menurunkan kadar prostaglandin dan nyeri sehingga vitamin B6 dapat dipertimbangkan menjadi salah satu pengobatan dismenore primer.*

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***Kata kunci**: dismenore primer, piridoksin, prostaglandin*

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INTRODUCTION

Dysmenorrhea, abdomined pain during menstruation usually cramps and centred at the lower abdomen, is a common gynecologic disorder in reproductive-aged women. Various studies in different populations reported dysmenorrhoea prevalence range between 20%-94%[1-3]. Primary dysmenorrhea is painful spasm pain in the lower abdomen that occurs before and/or during menstruation without macroscopic pelvic pathology. The onset of pri-mary dysmenorrhea usually occurs in adolescents, on or shortly after menarche (6-24 months)[4,5].

Prostaglandins (PGF2α and PGE2) are involved in the pathogenesis of primary dysmenorrhea pain particularly PGF2α[6]. Elevated levels of PGE2 and PGF2α observed in primary dysmenorrhea which stimulates the myometrium resulting in increased contraction and uterine dysrhythmias leading to decreased blood flow to the uterus and ischemia[5-8].

Early management of primary dysmenorrhea is a non-steroidal anti-inflammatory pain medication (GAINS) that inhibits prostaglandin[9]. However, these drugs have side effects such as dyspepsia syndrome and peptic ulcer[5]. Dietary supplements such as vitamins (E, B1, B3, B6) is an alternative treatment for dysmenorrhea although it is not as widely studied[10]. Pyridoxine (vitamin B6) is a water-soluble vitamin and part of the B complex vitamin. Vitamin B6 can stimulate cell membranes in transferring magnesium and increase intracellu-

lar magnesium that plays a role in muscle relaxation. In addition, decreased levels of vitamin B6 in the blood resulted in the liver not being able to conjugate estrogen so that estrogen levels increased associated with complaints of menstrual pain[5,10,11]. This study aimed to determine the effect of vitamin B6 (pyridoxine) the levels of prostaglandins and pain in primary dysmenorrhea.

METHODS

This randomised pretest-posttest control group study was conducted on a student of the Faculty of Medicine, Universitas Hasanuddin Makassar with primary dysmenorrhea and met the study criteria from September to November 2016. All of the women who enrolled were fully informed about the study and gave their consent before enrollment. The study was approved by the Health Research Ethics Committee of Faculty of Medicine, University of Hasanuddin. Students received vitamin B6 (100 mg/day for four days) and placebo (control). Plasma prostaglandin level was measured by ELISA technique whereas the intensity of pain with Visual Analog Scale (VAS). An unpaired t-test was used to compare the effect of vitamin B6 and placebo in prostaglandin levels and menstrual pain. A p value of less than 0.05 was taken to be statistically significant. Results presented in mean ± SD.

RESULTS

This study examined prostaglandin levels and pain intensity in 35 people (n = 35) of women of reproductive age (test group) with primary dysmenorrhea who received vitamin B6 supplementation and placebo as control (n = 35). Characteristics of the study samples are shown in Table 1.

Table 1. Characteristics of Samples

Characteristics	Treatment group (n=35)	Controls (n=35)
Age (years)	18.9±0.85	18.2±0.67
Menarche (years)	12.8±0.77	12.7±0.70
BMI (kg/m^2)	20.3±2.12	20.7±1.94

Prostaglandin levels before administration were higher in the treatment group compared to placebo (2212.9±1374.2 pg/ml vs 1623.3±1111.7 pg/ml) but not significantly different (p>0.05). After administration, prostaglandin levels decreased in both groups (1490.3±1119.0 pg/ml vs 1613.9±1105.5 pg/ml). However, the differences between the two groups were not significant (p>0.05). The intensity of pain between the two groups was significantly differenced before and after administration of vitamin B6 and placebo (all p<0.05) (Table 2).

The effect of vitamin B6 and placebo on prostaglandin levels and pain intensity was also examined in this study. The results show that vitamin B6 decreased prostaglandin levels and pain intensity significantly compared to placebo (p=0.000) (Table 3).

Table 2. Effects of Vitamin E and Placebo on Prostaglandin Level and Pain

Administration	Prostaglandin level*		p	Pain score		p
	Treatment group (n=35)	Placebo (n=35)		Treatment group (n=35)	Placebo (n=35)	
before	2212.9±1374.2	1623.3±1111.7	0.053	4.29±0.7	3.80±0.8	0.011
after	1490.3±1119.0	1613.9±1105.5	0.643	1.71±0.5	3.66±0.8	0.000

** Mean ± SD pg/ml*

Table 3. Prostaglandin Level and Pain Intensity between Treatment Group and Placebo

Treatment	Prostaglandin level		*p*	Pain score		*p*
	before	after		before	after	
Vit. B6 (n=35)	2212.9±1374.2	1490.3±1119.0	0.000	4.29±0.7	1.71±0.5	0.000
Placebo (n=35)	1623.3±1111.7	1613.9±1105.5	0.295	3.8±0.8	3.6±0.8	0.257

DISCUSSION

Prostaglandins are lipid compounds from the enzymatic reaction of cyclooxygenase (COX) in arachidonic acid and specific prostanoid synthase enzymes. PGE2 and PGF2α are mainly synthesised in the reproductive system. Over expression of COX-2 in ectopic endometrial cells leads to high levels of PGE2, PGF2α and other specific prostaglandins in uterine tissues in women with menorrhagia, dysmenorrhea or endometriosis[12,13]. PGF2α primarily derived from COX-1 in the female reproductive system and plays an essential role in ovulation, luteolysis, uterine smooth muscle contraction and initiation of labour as well as pain[14].

The endometrium of the menstrual secretory phase contains an arachidonic acid compound which converted to PGF2α, PGE2, and leukotriene during menstruation. PGF2α always stimulates uterine contractions and as the major mediator for dysmenorrhea. PGF2α and PGE2 levels in the endometrium correlated with the severity of dysmenorrhea[9]. Primary dysmenorrhea is caused by spastic uterine hypercontractility. Higher levels of PGF2α and PGE2 are present in menstrual blood in women with dysmenorrhea compared to without dysmenorrhea[15]. PGF2α levels increased 4-fold in endometrium and plasma in women with dysmenorrhea compared to without dysmenorrhea[9] so that PGF2α is a smooth muscle stimulant and a strong vasoconstrictor[16]. The present study found that levels of prostaglandins in students with primary dysmenorrhea higher than control although the difference was not significant.

Primary dysmenorrhea occurs only in the ovulatory cycle in which the uterus is under the influence of progesterone while prostaglandin synthesis is associated with the ovarian function. Menstrual pain is caused by an imbalance in the control of the autonomic nervous system to the myometrium. Vitamin B6 acts as a regulator of several ion membrane transports that modulate hormonal function due to its ability to bind to the receptors of steroid hormones[17]. The nutritional status of vitamin B6 greatly influences and modulates selectively in the production of serotonin and γ-aminobutyric acid (GABA), a neurotransmitter that controls depression, perception and anxiety[18].

The prostaglandin level and pain intensity in this study decreased significantly after vitamin B6 administration despite the prostaglandin level of the test group did not differ significantly with the placebo group (control). A study by Proctor show vitamin B6 has better results in reducing menstrual pain compared to placebo[19]. Changes in the intensity of pain can be affected by hormone levels, nutritional status, stress, physiologic, exercise and diet[6].

CONCLUSION

In conclusion, vitamin B6 decrease prostaglandin and pain levels so vitamin B6 might consider as treatment for primary dysmenorrhea.

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