Effects of red ginger capsule supplement in reducing PGF2α concentrations and pain intensity in primary dysmenorrhea

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Abstract. Primary dysmenorrhea is a gynecological disorder which most commonly occurs like a pain in the initial menstruation. One of the attempts to handle dysmenorrhea is by using non-pharmacological method such as herbal therapy which uses red ginger. The research was at Akbid and Akper Harapan Mama, Deli Serdang Regency, with pre-experimental design and one group pretest-posttest. The samples were 32 female students as the respondents, taken by using non-probability or consecutive sampling technique. PGF2α content measurement by ELISA, the intensity of pain by Visual Analogue Scale and analyzed by using Wilcoxon test. PGF2α content before giving red ginger capsule supplement median was 156.50 pg/ml (min-max: 57-1037 pg/ml), after giving it was 101 (min-max: 22-785), pain intensity before giving it in the mean score of 2 was 15 respondents (47%), after giving it in the mean score of 0 was 14 respondents (44%). The result of statistic test on PGF2α content before and after giving it was p-value = 0.001, and pain intensity before and after giving it was p < 0.001 which indicated that there was a significant decrease in PGF2α and pain intensity after giving it. Red ginger capsule supplement could decrease PGF2α content during primary dysmenorrhea.

1. Introduction
Primary dysmenorrhea is a gynecological disorder of females which most commonly occurs like a pain in the initial menstruation.[1] Primary dysmenorrhea in Australia 16%-91% occurs in active reproductive women [2], Italy 84% [3], Iran 89.1% [4], Georgia 56.6%. Adolescents are absent due to primary dysmenorrhea [5] and at State Senior High School 10 Medan the incidence of primary dysmenorrhoea 81.30%. In the preliminary survey at the Midwifery Academy and Nursing Academy, Harapan Mama found 77% of female students experienced primary dysmenorrhea. Pharmacologic handling of dysmenorrhea can cause side effects. Nonpharmacological handlers such as taking vitamin E [7], Zinc [8], physiotherapy [9], acupressure [10], and exercise.[11] Several studies have reported that the effect of red ginger decreases the intensity of pain in primary dysmenorrhea significantly.[12,13,14] The content of red ginger contains a lot of starch and essential oil suitable for use as a drug.[15] Ginger contains an active ingredient of gingerol which inhibits the synthesis of PGF2α in Cox-2 and 6-gingerol stronger affinity in inhibiting COX-2 ligand.[16,17] The content of ginger extract can inhibit the activation of NF-kB as an inflammatory gene activator so that no COX-2 transcription occurs.[18- 21] PGF2α is produced during luteolysis and necrosis of...
endometrial cells in the menstrual cycle, acting as myometrial constrictors and uterine blood vessels.[22] The purpose of this study was to determine the effect of red ginger extract supplementation on levels of PGF2α and pain intensity in primary dysmenorrhea.

2. Methods

The design of this study is a pre-experimental one-group pretest-posttest. The respondents of this research were 32 Akbid and Akper Harapan Mama students Deliserdang, age between 17-22 years, experienced menstrual pain since menstruation, never give birth, menstrual cycle between 21-35 days, ultrasound results no pelvic abnormalities, no history of allergy in red ginger.

Giving red ginger capsule supplement from North Sumatra. Already identified plants (Herbarium Medanense Sumatera Utara University). Ginger cleaned, sliced 3-4 cm, dried at 50°C, mashed to an extract through a maceration process and made in capsule packs with 50 mg extract content per capsule by pharmacy staff Sumatera Utara University. Provision of red ginger extract supplements three times a day one capsule for three days (first day, second and third) menstruation.

To see PGF2α concentrations and pain intensity is out coming of this research. Measurement of PGF2α second days and measurement of pain intensity for three consecutive days and take the average scale. Measurements were made before and after red ginger capsule supplement, and the results were compared to the same person. Measurement of PGF2α content using ELISA method. Menstrual blood is accommodated one cc on day 2 of menstruation and centrifuged one act (1x1000g) at 4°C, take the supernatant and check PGF2 concentrations using the Elabsience® kit. Pain intensity was measured during primary dysmenorrhea on the first, second and third day by assessing the mean scales using Visual Analog Scale.

3. Results

Characteristics of respondents are at most age 20 years (28%), Body Mass Index 20 and 22 kg/m² each 7 people (22%), menarche age 12 years 9 people (28%), menstrual cycle 28 days 17 people (53%), menstrual period 7 days 21 people (66%) and treatment of dysmenorrhea by resting 21 people (66%).

Table 1. PGF2α concentrations before supplementation of red ginger extract.

| PGF2α concentration (pg/ml) | Amount | Percentage (%) |
|-----------------------------|--------|----------------|
| 57                          | 1      | 3.1            |
| 71                          | 2      | 6.3            |
| 86                          | 1      | 3.1            |
| 94                          | 1      | 3.1            |
| 95                          | 1      | 3.1            |
| 105                         | 1      | 3.1            |
| 114                         | 2      | 6.3            |
| 115                         | 1      | 3.1            |
| 116                         | 2      | 6.3            |
| 122                         | 1      | 3.1            |
| 128                         | 1      | 3.1            |
| 152                         | 2      | 6.3            |
| 161                         | 1      | 3.1            |
| 196                         | 1      | 3.1            |
| 213                         | 1      | 3.1            |
| 329                         | 1      | 3.1            |
| 340                         | 1      | 3.1            |
| 398                         | 1      | 3.1            |
| 425                         | 1      | 3.1            |
| 434                         | 2      | 6.3            |
| 670                         | 2      | 6.3            |
| 684                         | 1      | 3.1            |
| 713                         | 2      | 6.3            |
| 1037                        | 2      | 6.3            |
| **Total**                   | **32** | **100**        |
Median of PGF2α concentration respondents before administration of red ginger extract supplement that is 156.50 pg / ml (min-max: 57-1037 pg / ml).

Table 2. PGF2α concentration after supplementation with red ginger extract.

| PGF2α concentration (pg/ml) | Amount | Percentage (%) |
|-----------------------------|--------|----------------|
| 22                          | 1      | 3.1            |
| 43                          | 1      | 3.1            |
| 67                          | 1      | 3.1            |
| 68                          | 2      | 6.3            |
| 69                          | 1      | 3.1            |
| 75                          | 2      | 6.3            |
| 79                          | 1      | 3.1            |
| 81                          | 1      | 3.1            |
| 93                          | 2      | 6.3            |
| 97                          | 2      | 6.3            |
| 100                         | 1      | 3.1            |
| 101                         | 2      | 6.3            |
| 107                         | 2      | 6.3            |
| 114                         | 1      | 3.1            |
| 132                         | 1      | 3.1            |
| 136                         | 1      | 3.1            |
| 151                         | 1      | 3.1            |
| 453                         | 1      | 3.1            |
| 492                         | 1      | 3.1            |
| 502                         | 1      | 3.1            |
| 511                         | 1      | 3.1            |
| 572                         | 2      | 6.3            |
| 649                         | 2      | 6.3            |
| 785                         | 1      | 3.1            |
| **Total**                   | **32** | **100**        |

Based on table 2 that the median concentration of PGF2α respondents after supplementation of red ginger extract was 101 (min-max: 22-785 pg/ml).

Table 3. The intensity of pain before supplementation of red ginger extract.

| Scale | Amount | Percentage (%) |
|-------|--------|----------------|
| 0     | 0      | 0              |
| 1     | 11     | 34             |
| 2     | 15     | 47             |
| 3     | 6      | 19             |
| **Total** | **32** | **100** |

Based on table 3 of pain intensity before supplementation of red ginger extract at most on 2 (15%), 15% (47%), followed by a scale of 1 (11%) and the remaining 3 (6%), median 2 min-max 1-3.

Table 4. The intensity of pain after supplementation of red ginger extract.

| Scale | Amount | Percentage (%) |
|-------|--------|----------------|
| 0     | 14     | 44             |
| 1     | 12     | 38             |
| 2     | 4      | 12             |
| 3     | 2      | 6              |
| **Total** | **32** | **100** |
Based on table 4 after supplementation of extract at most average scale 0 as many as 14 people (44%). Followed by average scale 1 as many as 12 people (38%), average scale 2 as many as 4 people (12%) and continued with an average scale of 3 as many as 2 people (6%), median 1 min-max 0-3.

Table 5. PGF2α concentrations before and after supplementation of red ginger extract.

| PGF2α concentrations (pg/ml) | N     | Median (min-max) pg/ml | P Value |
|------------------------------|-------|------------------------|---------|
| Before supplementation extract of red ginger extract | 32    | 156.50 (57-1037)       | 0.001   |
| After supplementation extract of red ginger extract   | 32    | 101 (22-785)           |         |

Based on table 5 median PGF2α concentrations before supplementation of red ginger extract 156.50 pg/ml min-max 57-1037 pg/ml to median 101 pg/ml min-max 22-785 pg/ml after supplementation of red ginger extract (p = 0.001). There was a decrease in PGF2α concentrations after significant red ginger extract supplementation.

Table 6. The intensity of pain before and after supplementation of red ginger extract.

| Average scales of pain intensity | N | Median (min-max) pg/ml | P Value |
|----------------------------------|---|------------------------|---------|
| Before supplementation extract of red ginger extract | 32 | 2 (1-3) | 0.000 |
| After supplementation extract of red ginger extract | 32 | 1 (0-3) |         |

Based on table 6, the intensity of pain before supplementation of red ginger extract with the median average scale of pain intensity two min-max (1-3) became median one min-max (0-3) after supplementation of red ginger extract p = 0.000. There was a decrease in the intensity of pain after supplementation of red ginger extract significantly.

4. Discussion
Concentrations of PGF2α respondents before supplementation of median red ginger extract 156.50 pg/ml (min-max: 57-1037 pg/ml), and after supplementation of median red ginger extract 101 (min-max: 22-785 pg/ml). The intensity of the respondent’s pain before supplementation of the red ginger extract was at most an average of 2 (15%) and after supplementation of the ginger extract was the average of 0 (14%). Measurement of PGF2α levels of peripheral plasma and endometrial tissue in women is not dysmenorrhea between 20-33 pg/ml whereas in women who are dysmenorrhea 32-105 pg/ml, and higher on the first days may reach 4-fold, i.e. 300-2800 pg/ml.[23] According to research based on the results of this study before giving ginger extract PGF2α minimum 55 pg/ml and maximum 1037 pg/ml in the range that caused dysmenorrhea, whereas after red ginger capsule supplement of at least 22 pg/ml and a maximum of 785 pg/ml in the coverage did not cause dysmenorrhea.

The intensity of respondent’s pain before red ginger capsule supplement at most at the average scale two as many as 15 people (47%), median two min-max 1-3. This resulted in the non-pharmacological response of respondents is only in non-pharmacologically the most with only rest alone was able to reduce the pain experienced by respondents. The intensity of the respondent’s pain after red ginger capsule supplement at most of the average scale of 0 as many as 14 people (44%) median 1 min-max 0-3 because of the respondent no longer experience pain.

There was a decrease in PGF2α levels before and after red ginger capsule supplement median PGF2α levels higher before the red ginger capsule supplement 156.50 pg/ml min-max 57-1037 pg/ml, while median PGF2 levels after consumption of red ginger extract supplements that is 101 pg/ml min-
max 22-785 pg/ml. This proves that the ginger that has been processed into 50 mg extract per capsule still containing steroids and triterpenoids that serve as an anti-inflammatory that is the content of phenols, gingerol that can inhibit the enzyme COX-2, inhibit PGF2α synthesis as the cause of primary dysmenorrhea. The content of red ginger extract contains anti-inflammatory such as 6-gingerol which can decrease inflammatory mediators such as inflammatory cytokines and chemokines that can activate NF-kB so that no COX-2 biosynthesis.[24]

The results showed that the intensity of pain before supplementation of the median red ginger extract of the average scale two min-max 1-3 while the intensity of pain after red ginger capsule supplement had median 1 min-max 0-3. The statistical test results p < 0.001 then there is a significant decrease in pain intensity based on the average scale before and after red ginger capsule supplement. It is due to the chemical content of red ginger extract supplement containing natural phenolic ingredients such as saponins, flavonoids, steroids, and triterpenoids will be converted into oleoresin with the active ingredient of gingerol as an anti-inflammatory inhibit the activation of NF-kB and COX-2 enzymes that decrease PGF2α biosynthesis in the endometrium.

5. Conclusion

There was a decrease in PGF2α levels after red ginger capsule supplement and decreased pain intensity after significant red ginger extract supplementation. It is recommended to use red ginger extract supplement as an option in reducing pain in primary dysmenorrhea as well as informing people to use red ginger extract supplement in reducing pain in primary dysmenorrhea.

References
[1] Dawood M Y, et al. 1981 Primary dysmenorrhea - pathophysiology and management (University of Illionis Collage of Medicine: Departement of Obstetrics & Gynecology) JIMA 13
[2] Ju, Jones and Mishra 2013 The prevalence and risk factors of dysmenorrhea Available from: http://epirev.oxfordjournals.org/Australia
[3] Grandi G, et al. 2012 Prevalence of menstrual pain in young women: What is dysmenorrhea J. Pain Res. 5 169-74
[4] Habibi, et al. 2015 Prevalence of primary dysmenorrhea and factors associated with its intensity among undergraduate students Am. Soc. Pain Manag. Nursing
[5] Gagua, Besarion and Gagua 2013 Pain and quality of life of adolescents with primary dysmenorrhea in tbilisi, Georgia, 2008 Revista Colombiana de Obstetricia y Ginecologia 64(2)
[6] Sophia, et al. 2013 Faktor-faktor yang berhubungan dengan dismenore pada siswi SMK negeri 10 Medan tahun 2013 (Universitas Sumatera Utara: Departemen Epidemiologi)
[7] Nayeban, et al. 2014 A comparison of the effects of vitamin E and vitamin B1 on the severity and duration of pain in primary dysmenorrhea J. Midwifery Reprod. Health
[8] George E 2006 Zinc treatment prevents dysmenorrhea Med. Hypotheses Elsevier 69 297-301
[9] Gerson, et al. 2014 Physiotherapy in primary dysmenorrhea: literature review Rev. Dor. 15(4) Available from: http://dx.doi.org/10.5935/1806-0013.20140063
[10] Jiang 2013 Systematic review of randomized clinical trials of acupressure therapy for primary dysmenorrhea Hindawi Publish. Corp. Evidence-Based Complementary Altern. Med. 2013
[11] Sirait, et al. 2014 Faktor-faktor yang berhubungan dengan kejadian dismenore pada siswi SMA negeri 2 Medan tahun 2014 (Universitas Sumatera Utara: Departemen Epidemiologi)
[12] Rahnama 2012 Effect of zingiber officinale r. rhizomes (ginger) on pain relief in primary dysmenorrhea: a placebo randomized trial J. Complementary Altern. Med.
[13] Toyskeran J E 2013 The effect of ginger for relieving of primary dysmenorrhoa (Department Of Midwifery, Toyskeran Branch, Islamic Azad University)
[14] Arfiana 2014 Pengaruh minuman jahe merah (zingiber officinale roscoe) terhadap intensitas nyeri haid pada mahasiswa D-IV kebidanan stikes ngudi waluyo [Skripsi] (Program Studi D-IV Kebidanan Stikes Ngudi Waluyo)

[15] Hernani C W 2011 Kandungan bahan aktif jahe dan pemanfaatannya dalam bidang kesehatan (Bogor: Balai Besar Penelitian dan Pengembangan Pascapanen Pertanian)

[16] Breeman, et al. 2012 Cyclooxygenase-2 inhibitors in ginger (zingiber officinale) Fitoterapia

[17] Tjedraputra, et al. 2001 Effect of ginger constituents and synthetic analogues on cyclooxygenase-2 enzyme in intact cells Bioorg. Chem. 29 156–63

[18] Li, et al. 2013 Attenuation of proinflammatory responses by S-[6]-gingerol via inhibition of ROS/NF-Kappa B/COX2 activation in HuH7 cells [Open access article] (Australia: The Creative Commons Attribution License)

[19] Li, et al. 2010 Ethanolic extract of gingiber officinale suppresses hepatic NF kappa B in proceeding of the ozbio conference (Melbourne, VIC, Australia)

[20] Roufogalis 2014 Review article: Zingiber officinale (ginger) a future outlook on its potential in prevention and treatment of diabetes and prediabetic states Hindawi Publish. Corp. N. J. Sci.

[21] Kim, et al. 2005 [6]-gingerol inhibits COX-2 expression by blocking the activation of p38 MAP kinase and NF-kB in phorbolester-stimulated mouse skin Oncogen Nat. Publish. Group

[22] Fortier, et al. 2008 A postgenomic integrated view of prostaglandins in reproduction: implications for other body systems J. Physiol. Pharmacol.

[23] Lundstrom and Green 1978 Endogenous levels of prostaglandin F2α and its main metabolites in plasma and endometrium of normal and dysmenorrheic women Am. J. Obstet. Gynecol. 130 640

[24] Aryaeian and Tavakkoli 2015 Review: ginger and its effects on inflammatory diseases Adv. Food Technol. Nutr. Sci.