The Effect of Ginger Candy (Zingiber Officinale Rosc.) on PGF2\(\alpha\) Levels in Adolescents with Primary Dysmenorrhea

Eka Tri Wulandari\(^1\); Desi Kumalasari\(^1\)

\(^1\) Program Studi Kebidanan Universitas Aisyah Pringsewu

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ABSTRACT

Primary dysmenorrhea is a common complaint that is commonly experienced by women around the world, especially teenagers. One of the causes of primary dysmenorrhea is the hyperactivity of the myometrium which is modulated by the synthesis of prostaglandins, especially PGF2\(\alpha\). Some herbs are known to work as prostaglandin inhibitors, one of them are ginger. Giving ginger in adolescents who experience dysmenorrhea is expected to lower the levels of PGF2\(\alpha\) so that dysmenorrhea pain can be reduced. Generally ginger can be developed in a variety of food and beverage products such as jelly candy. The purpose of this study was to analyze the effect of ginger candy on PGF2\(\alpha\) levels in adolescents with primary dysmenorrhea. This research is an analytic research which used randomize pre post group design experimental approach. The object of the research is 38 adolescents with primary dysmenorrhea. The object is divided into two groups, 19 treatment group and 19 control group. The treatment group was given jelly candy containing 100 mg of ginger extract, while the control group was given jelly candy without ginger. The candy was given on the first day of menstruation until the second day of menstruation. The measurement of PGF2\(\alpha\) level was on the second day of menstruation after the candy was given to the groups. The results showed that after administration of candy, the average levels of PGF2\(\alpha\) in the treatment group decreased from 482.9 ng/ml to 370.5 ng/ml or down by 11%. Whereas in the control group, the PGF2\(\alpha\) level 483.3 become 409.2. The difference in the percentage of decreasing in the levels of PGF2\(\alpha\) using mann whitney test showed significant result (\(\rho\)=0.002). The conclusion of this research is ginger candy can reduce levels of PGF2\(\alpha\) in adolescents with primary dysmenorrhea.

Kata kunci:
PGF2\(\alpha\)
Dismenorea Primer
Permen Jeli Jahe

\(^1\) corresponding author

Eka Tri Wulandari
Program Studi Sarjana Terapan Kebidanan
Fakultas Kesehatan, Universitas Aisyah Pringsewu

Email: fatihnyaumi@gmail.com

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INTRODUCTION

Dysmenorrhea is pain associated with the menstrual process, and is a common gynecological complaint in women of reproductive age. (Proctor & Murphy, 2001), (Bettendorf, Shay, & Tu, 2008), (Wallace, Keightley, & Gie, 2010) Dysmenorrhea can be divided into two types, namely primary and secondary. Primary dysmenorrhea is a pain during normal menstruation and is not associated with any pathological conditions (MY., 2006), (Lindeque BG, 2015) while secondary dysmenorrhea is a menstrual pain due to pathological conditions. (Wallace et al., 2010), (Lindeque BG, 2015)

Primary dysmenorrhea is a common complaint experienced by women all over the world, especially teenagers. In a study, it was reported that almost 90% of adolescents experienced dysmenorrhea and more than 50% of adult women also reported experiencing it, 10-20% of them complained of being very suffering and anxious about their condition. (Berkley, 2013) The data of dysmenorrhea case and the impact of dysmenorrhea on daily activities days on adolescents in Indonesia it self is not definite. In a preliminary study conducted at Aisyah Pringsewu University Lampung on 61 nursing students, it was found that 58 people or 95% experienced dysmenorrhea, using the VAS (Visual Analog Scale) scale for pain measurement, the results were obtained; 22% experienced mild pain, 47% moderate pain, 29% severe pain and 2% severe pain.

Primary dysmenorrhea is not a life-threatening disease, but dysmenorrhea pain can have an impact on a person's quality of life, even in severe conditions that will affect daily activities, being absent from school or work, mental and psychological disturbances, and even the choice of the desired type of baby delivery. (Liu et al., 2013) A study reported that dysmenorrhea is the reason for 34-50% of adolescent girls to be absent from school. (Mahvash et al., 2012).

One of the causes of primary dysmenorrhea is an increase in uterine prostaglandins derived from cyclooxygenase (COX)-2. The COX enzyme consists of 2 iso-enzymes, namely COX-1 and COX-2. COX-1 enzyme is constitutive to maintain normal physiology and homeostasis, while COX-2 is an enzyme that is induced in injured cells by cytokines, endotoxins, and growth factors (Zukhrullah & Aswad, 2012) COX-1 is found in most tissues that functions to catalyze prostaglandin E-2 (PGE-2) which has a cytoprotective function and helps in maintaining the integrity of the gastrointestinal mucosa. While COX-2 is induced by pro-inflammatory cytokines and produces prostaglandins (PGF2α) which mediate the inflammatory response, vasoconstriction (reduced oxygen flow), ischemia and the onset of pain. (Connolly, 2003) Clinical evidence also shows that women with severe dysmenorrhea have PGF2α.

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prostaglandin synthesis (van Breemen, Tao, & Li, 2011). (Chrubasik, Pittler, & Roufogalis, 2005) Therefore, ginger can reduce prostaglandin levels that cause hyperactivity of myometrium causing uterine ischemia causing pain. In an RCT (randomized clinical trial) study of 150 adolescents, it was stated that there was a significant difference in pain levels between the groups which were given ginger and those which were given a placebo. (Rahnama, Montazeri, Huseini, Kianbakht, & Naseri, 2012) Another study that compared the use of ginger, tamarind, mefenamic acid, and ibuprofen for the treatment of dysmenorrhea in 150 students found that ginger was as effective as mefenamic acid and ibuprofen for relieving dysmenorrhea pain. (Ozgoli, Goli, & Moattar, 2009).

Ginger has anti-inflammatory properties. The main compounds of ginger that are anti-inflammatory are gingerol and zingerone, but in vivo almost all components of ginger have anti-inflammatory effects. Ginger works by influencing the modulation of leukotrienes and prostaglandin synthesis. (Lakhan, Ford, & Tepper, 2015) In one study, the administration of [6] gingerol (25 mg-50 mg/kg) intraperitoneally could inhibit inflammation in the paws of animals that were given carrageenan. (Singh, Duggal, Singh, & Katekhaye, 2010) It is well known that excessive prostaglandin production of prostaglandins (especially PGF2α) will stimulate abnormal myometrial contractions which will reduce blood flow to myometrial cells, causing pain. (MY., 2006).

In some literature it is stated that the use of ginger dosage for the treatment of dysmenorrhea is 1000-2000 mg with variations in the administration of 2x per day, 3x per day, and 4 times per day, and in the form of a powder or capsule. (Lakhan et al., 2015 ) Other dosage forms that are simpler and more acceptable by the public, such as in the form of candy, or biscuits, have not been found in many literature studies. In general, ginger can be developed in various food and beverage products. Domestic products made from ginger include dried ginger, ginger candy, ginger powder, ginger oil and oleoresin. (Supriadi, Yusron, & Wahyudi, 2011).

In a preliminary study conducted by researchers nationally on adolescents in several provinces to find out which form of processed ginger was preferred by adolescents, it was found that adolescents preferred processed ginger in the form of candy preparations.

METHOD

The research subjects were 38 Diploma 3 Midwifery students at Aisyah Pringsewu University who experienced dysmenorrhea. Subjects will be divided into 2 groups. 19 people in the control group and 19 in the treatment group, who met the inclusion criteria and were willing to become respondents by signing the consent form after the explanation.

The research sample was taken by simple random sampling. Inclusion criteria were patients with primary menstrual pain aged 18-21 years, no organic abnormalities were found through ultrasound examination, experienced menstrual pain on a VAS scale of 4-6, had never been married and gave birth, had regular menstrual cycles for the last 3 months (28-30 days), and volunteered to participate in this study.

The exclusion criteria in this study were adolescents who had other complaints in the uterus and pelvis, adolescents who were undergoing treatment with painkillers, adolescents who had undergone surgery on the abdomen and pelvis, and adolescents who used contraceptives and other drugs.

The process of this research is to give ginger jelly candy and jelly candy without ginger for 2 days, namely the first day and the second day of menstruation to adolescents who are menstruating and experiencing primary dysmenorrhea. The dose used in this study was 100 mg of ginger extract which was made in 1 package of 6 pieces of candy which was given twice a day with 3 pieces of candy per serving. Subsequently, blood samples were taken to measure PGF2α levels. The data were collected directly by the researcher. Data collecting was conducted by using questionnaires, checklists and blood collection. PGF2α examination was carried out in the Molecular Genetics Laboratory, Faculty of Medicine, Unpad, using the ELISA method. The data collected were analyzed descriptively and analytically to analyze the effect of ginger candy on decreasing PGF2α levels.

The design used in this research is true experimental. The approach used in this study was a randomized pretest-posttest group design. Data analysis used Wilcoxon test and Mann-Whitney test.

RESULTS

Table 1
Characteristics of Subjects in Both Research Groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Treatment (n=19)</th>
<th>Control (n=19)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>x (SD)</td>
<td>19.0 (12.0)</td>
<td>19.0 (0.88)</td>
<td>0.795*</td>
</tr>
<tr>
<td>Median</td>
<td>19.0</td>
<td>19.0</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>18-21</td>
<td>18-21</td>
<td></td>
</tr>
<tr>
<td>Menarche</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>x (SD)</td>
<td>12.2 (0.78)</td>
<td>13.3 (0.94)</td>
<td>0.001*</td>
</tr>
<tr>
<td>Median</td>
<td>12.0</td>
<td>13.0</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>11-13</td>
<td>11-15</td>
<td></td>
</tr>
<tr>
<td>Weight</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>x (SD)</td>
<td>51.6 (7.49)</td>
<td>58.0 (25.25)</td>
<td>0.644*</td>
</tr>
<tr>
<td>Median</td>
<td>50.0</td>
<td>50.0</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>40-66</td>
<td>43-157</td>
<td></td>
</tr>
<tr>
<td>Height</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>x (SD)</td>
<td>156.4 (54.4)</td>
<td>146.9 (30.41)</td>
<td>0.644*</td>
</tr>
</tbody>
</table>
Based on the table, the characteristics of the research subjects were equal between the control and treatment groups, including in terms of age, height, weight, and PGF2α levels.

### Table 2
Differences in PGF2α Levels Before and After Dysmenorrhea Adolescents Given Ginger Candy

<table>
<thead>
<tr>
<th>Description</th>
<th>Group</th>
<th>Predicates (n=27)</th>
<th>Controls (n=27)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre test</td>
<td>Post test</td>
<td>Control</td>
<td></td>
</tr>
<tr>
<td>PGF2α level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>x (SD)</td>
<td>482.9(509.76)</td>
<td>370.5(190.34)</td>
<td>483.3(443.51)</td>
<td>0.506*</td>
</tr>
<tr>
<td>Median</td>
<td>378.9</td>
<td>308.41</td>
<td>347.2</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>293.47-2543.08</td>
<td>253.16-1090.76</td>
<td>253.16-2215.06</td>
<td></td>
</tr>
<tr>
<td>Δ PGF2α level</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>x (SD)</td>
<td>112.3(327.81)</td>
<td>6.9(42.62)</td>
<td>0.003**</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>-23.79</td>
<td>2.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>-1452.32-35.27</td>
<td>-61.76-94.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PGF2α percentage</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>x (SD)</td>
<td>11.5(11.11)</td>
<td>2.6(12.20)</td>
<td>0.002**</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>-7.34</td>
<td>0.67</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>-57.11-10.33</td>
<td>-14.55-34.83</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Test used: Mann Whitney*

### DISCUSSION

Ginger is a type of herb that has many benefits, cheap and relatively safe to use. One systemic review reported that subjectively ginger can be used for pain relief in certain conditions, one of which is dysmenorrhea. (Terry et al., 2011)

In a randomized clinical trial (RCT) study of 150 adolescents, it was stated that there was a significant difference in pain levels between the groups that were given ginger and those who were given a placebo. (Rahnama et al., 2012) The use of ginger for dysmenorrhea therapy is widely practiced. Compounds contained in ginger such as gingeroil, shogaol and their derivatives can inhibit the cyclooxygenase (COX) pathway in the process of prostaglandin synthesis, (van Breemen et al., 2011). In addition, they can also inhibit the synthesis of pro-inflammatory cytokines such as IL-1, TNF-α, and IL-8. (Mashhadi et al., 2013) Therefore, ginger can reduce prostaglandin levels which cause myometrial hyperactivity which results in uterine ischemia causing pain.

Table 2 shows that at the beginning of the study the mean of serum PGF2α level in the treatment group was higher (378.9 ng/ml) than the control group (347.2 ng/ml), but statistically there was no significant difference between the control and treatment groups. This shows that the initial serum PGF2α level before candy administration was homogeneous. This condition is probably due to the fact that the researchers respondents had almost the same characteristics. Meanwhile, at the end of the study, the mean of serum PGF2α level in the treatment group was lower (308.41 ng/ml) than the control group (334.8 ng/ml). This average value indicates the success of giving ginger candy to reduce PGF2α levels. This table also shows that in the treatment group there was a significant decrease in PGF2α levels before and after the study (p=0.002) and the decrease in PGF2α levels in the group given ginger candy therapy was greater than in the group given candy without ginger (p<0.05).

Giving ginger to reduce pain has been mentioned in several studies. Research by Amritpal Singh et al 2010 on experimental pharmacology for gingeroil compounds and their derivatives showed that ginger is considered to have an anti-inflammatory effect because it inhibits cyclooxygenase and 5-lipoxygenase, thereby reducing the synthesis of prostaglandins and leukotrienes. (Singh et al., 2010) Research by Richard et al. about Cyclooxygenase-2 inhibitors in ginger also show the results that by using liquid chromatography-tandem mass spectrometry (LC-MSMS) compounds 10-gingeroil, 8-shogaol, and 10-shagoal are compounds in ginger that may be responsible for the anti-inflammatory process by inhibiting COX-1 and COX-2. (van Breemen et al., 2011)

The existence of a correlation between prostaglandins and menstrual pain is supported by the research of Fortier et al., in their research it was found that prostaglandins and leukotrienes cause an inflammatory response, which will cause uterine muscle spasm and systemic complaints such as nausea, vomiting, flatulence and headaches. (Fortier, Krishnaswamy, Danyod), Boucher-Kovalik, & Chapdalaine, 2008). A study conducted by Dawood and Khan-Dawood, by measuring the levels of PGF2α in menstrual blood contained in tampons, it was found that PGF2α levels were twice as high in women who experienced menstrual pain compared to those who experienced no menstrual pain. Giving ginger to adolescents who experience dysmenorrhea is expected to reduce PGF2α levels so that the perceived dysmenorrheal pain will be reduced. (MY., 2006), (Ozgoli et al., 2009)

Based on the table, it is observed that there are respondents who experience a decrease in PGF2α levels in...
the control group and conversely there is an increase in PGF2α levels in the treatment group. Many factors can influence this, including hormone levels, nutritional status, stress, and physiological conditions of the body, sports activities and diet. (Mayo, 1997) Besides that, humans are unique individuals and have different biological characteristics so that their response to stimuli are also different.

During the luteal phase, there is excessive production of endometrial prostaglandins. Prostaglandins (especially PGE2 and PGF2α) diffuse into the endometrial tissue which then stimulates abnormal uterine/myometrial muscle contractions, this excessive contraction will reduce blood flow resulting in ischemia in myometrial cells resulting in spasmodic pain. PGF2α levels are highest in the first 2 days of the menstrual period. (GUIDELINE, 2005)

Based on the explanation above, it can be concluded that there is an effect of giving ginger jelly candy to the decreasing of serum PGF2α levels in adolescents with primary dysmenorrheal.

**CONCLUSION**

In the ginger candy group there was a decreasing of PGF2α levels before and after the study and the decreasing of PGF2α levels in the group which was given ginger candy therapy was greater than in the group which was given candy without ginger.

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