Using warm compresses to reduce IL-1β levels in dysmenorrhea: An evaluation of quasy experimental study

Mukhoirotin Mukhoirotin*, Siti Uridah
1Nursing Science Program, Faculty of Health Science, University of Pesantren Tinggi Darul Ulum, Jawa Timur, Indonesia
*email: mukhoirotin@fik.unipdu.ac.id

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ABSTRACT

Primary dysmenorrhoea is a gynochological problems that occured among adolescents and women of reproductive age. In primary dysmenorrhea an increase of pro-inflammatory cytokine IL-1β levels. The aim of this study was determine the effect of warm compresses to reduce IL-1β levels in primary dysmenorrhea. Research desaign used quasy experiment with pretest-posttest control group design and post test only control group design. The population of this study were all students of Health Science Faculty of Unipdu Jombang who experienced dysmenorrhoea, with a total sample of 24 respondents taken by using simple random sampling techniques and met inclusion and exclusion criteria. Hot water bag were the equiptments of this study. The instrument for measuring pain used NRS (Numeric Rating Scale), IL-1 β levels used the ELISA method. The data analyzed by using Wilcoxon test and Mann-Whitney Test with α ≤ 0.05. The results of study showed there was an effect of warm compresses on dysmenorrhea with a significant value (p) of 0.000 (p ≤ 0.05). There were significant differences of the intensity of menstrual pain and IL-1β levels between warm compress group vs. control group (p≤0.05). Warm compresses are effectively to reduce IL-1β levels on primary dysmenorrhea, it can be used as an alternative intervention to overcome complaints of primary dysmenorrhea. The recommendation for next research is the research wich focus on an observation of IL-1β levels before and after giving intervention.

Keywords: Compresses; interleukin-1beta; dysmenorrhea

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Primary dysmenorrhea is menstrual pain and it not based on pathological conditions in pelvis. Primary dysmenorrhea also one of gynecological problems that occurred among adolescents and women of reproductive age. Dysmenorrhea divided into two, namely primary dysmenorrhea and secondary dysmenorrhea. Primary dysmenorrhea starts a few hours before or shortly after menstruation begins. Usually, pain and painful cramps suffer during the first 2 days of menstruation (De Sanctis, Soliman, Bernasconi, Bianchin, Bona, Bozzola, et al., 2015). Primary dysmenorrhea generally occurs among adolescents, which occurs 6-12 months after menarche.

The prevalence of dysmenorrhea was 94% occurred among adolescents who aged 10-20 years, and 8.8% of women should be hospitalized because of dysmenorrhea (De Sanctis, Soliman, Bernasconi, Bianchin, Bona, M, et al., 2015). In some countries such as the UK, 41-97% of women experienced dysmenorrhea and 11-14% experienced severe pain and cramps due to dysmenorrhea (Zondervan et al. 1998 in De Sanctis et al., 2015). In Japan, at least 46% of high school students who aged 12-15 years experienced moderate level of pain due to dysmenorrhea and 17.7% experienced severe pain due to dysmenorrhea. Other countries like Giorgia at least 70% of students didn't went to school due to menstrual pain. In Indonesia, the prevalence of primary dysmenorrhea was 54.89% and 45.11% secondary dysmenorrhea (Proverawati & Misa, 2009).

Some studies mentioned that the age of menarche, menstrual volume, smokers, obesity, heredity and alcohol consumption were considered as the main factors causing dysmenorrhea (De Sanctis, Soliman, Bernasconi, Bianchin, Bona, M, et al., 2015; Habibi, Huang, Gan, Zulida, & Safavi, 2015; Ju, Jones, & Mishra, 2015). In primary dysmenorrhea, the level of pro-inflammatory expression of cytokine genes (IL1β, TNF, IL6 and IL8) significantly increase at the first day of menstruation, whereas anti-inflammatory cytokines (ILF5 and IL11) are reduced. Many studies showed that proinflammatory cytokines stimulated the synthesis or released of PGE2 and OT, which induce uterine hypercontractility, decrease endometrial blood flow, and cause pain (Fribe-Hoffmann, Chiao, & Rauk, 2001). Pro-inflammatory cytokines also increase oxytocin / Ca2 + signaling, this has an important role in myometrial contractions. For example, IL-1β (interleukin-1beta) increases OT secretion in the decidua of humans through prostaglandin production (Fribe-Hoffmann et al., 2001 in H. Ma et al., 2013). Proinflammatory cytokines (IL-1β, TNF-α and IL-6) were cause blood vessel constriction (Ahnstedt, Stenman, Cao, Henriksson, & Edvinsson, 2012), increased procoagulant activity (Aksu, Donmez, & Keser, 2012) and induced sensory neuron stimulation (Ji, Gereau IV, Malcangio, & Strichartz, 2009).

Pharmacological intervention to alleviate or treat primary dysmenorrhea can be used non-steroidal anti-inflammatory drugs (NSAIDs), this drugs work by inhibiting the activity of the cyclooxygenase enzyme in that prostaglandin production is reduce (Marjoribanks, Ro, Farquhar, & Proctor, 2015). The regularly NSAID consumption have an impact on the metabolic processes in the body. The addicted of NSAID and large expenditure of money are severe consequences caused by primary dysmenorrhea. Especially gastric reflux (Marjoribanks et al., 2015). Moreover, the consumption of NSAIDs in patients with chronic disease can increase the risk of angina, acute myocardial and nerve bleeding (Hochberg et al., 2012). Therefore, non-pharmacological interventions are recommended because it is easy, cheap and effective to reduce pain due to primary dysmenorrhea, non-pharmacological interventions are including the use of warm compresses, cold compress, slow stroke back massage, acupuncture and acupressure. Warm compres is a compress using warm water, and it causes dilation of blood vessels (vasodilation) and decreases muscle tension so the dysmenorrhea pain will decrease or disappear (Potter, Perry,
Cold compress is an ice therapy which reduces prostaglandin that strengthen the pain and other subcutaneous sensitivity at injury place by inhibiting the inflammatory process. This because of cold compresses can reduce blood flow in a part and reduce edema bleeding which it gives analgesic effect by slowing down the speed of nerve conduction, less pain impulses reaching the brain (Price & Wilson, 2005). Slow-stroke back massage is a back massage with slow strokes. Skin stimulation causes delivery of endorphins so it will block the transmission of pain stimulation (Potter et al., 2013). Acupressure is an action by applying pressure or massage and stimulation at certain points in the body (Fengge, 2012). Acupressure at Sanyinjiao Point, Hegu Point, Tai Chong and Guanyuan Point were effective to reducing the intensity of menstrual pain (Mukhoirotin, Fatmawati, & Prihartini, 2018; Pangastuti & Mukhoirotin, 2018).

Some studies mentioned that warm compresses intervention for 20 minutes with a temperature of 40°C in adolescents who experienced primary dysmenorrhea were reduced the intensity of pain from level 6.5 to 4.2 from a scale of 4-9 that is described as moderate to severe dysmenorrhea (Murtiningsih & Karlina, 2015). Another research found that warm compress was effective decreased the intensity of menstrual pain (Dahlan & Syahminan, 2016; Dhirah & Sutami, 2019; Mahua, Mudayatiningsih, & Perwiraningtyas, 2018; Maidartati, Hayati, & Hasanah, 2018; Rahmadhayanti, Afriyani, & Wulandari, 2017). The results of previous studies showed that no differences in levels of β-endorphin, IL-6 and TNF-α among adolescents who experienced dysmenorrhea after being given cold compresses and warm compresses (Mukhoirotin, Kurniawati, & Fatmawati, 2018). Some previous research mentioned that warm compress influenced menstrual pain. But so far the effect of warm compresses on IL-1β levels has not been clearly known, in that researchers are interest to conducting this research with the aim of this study to finding the effect of warm compresses on IL-1β levels on primary dysmenorrhea.

METHOD

This research used Quasy Experiment Design with pretest-posttest Control Group Design and Post Test Only Control Group Design (Nursalam, 2016). The population of this study were all students in Health Science Faculty of Unipdu Jombang who experienced dysmenorrhea, with a total sample were 24 respondents and they divided into two groups namely the warm compress group (n = 12) and the control group (without giving intervention, n = 12) and it was taken by using simple random sampling (Nursalam, 2016).

Inclusion criteria of the study were: 1) Students who have primary dysmenorrhea; 2) Students who have not received anti-pain therapy; and 3) The first day experiencing dysmenorrhea. Exclusion criteria were female students who refused in the middle of intervention.

Warm compresses are given by using warm water with temperature of 40-45°C and put in a hot water bag than compressed on the abdomen for 20 minutes. The equipments for measuring temperature uses a thermometer and hot water bag for warm compresses. The instrument for measuring pain used NRS (Numeric Rating Scale)(Berman, Synder, & Fradsen, 2015), IL-1 β levels used the ELISA (Enzyme Linked Immunosorbet Assay) method. NRS instrument was valid and reliable with the validity number (r = 0.71–0.99), and reliable number (0.673–0.822) (Li, Liu, & Herr, 2007). The data were analyzed by using Wilcoxon test and Mann-Whitney Test with α ≤ 0.05 (Nursalam, 2016). This research was obtained the Ethical clearance of Nursing Faculty, Airlangga University, Surabaya with certificate number of 1336-KEPK.

RESULTS
The menarche age of all respondents were 11-13 years old or in normal of age menarche (79.2%). Almost all respondents have regular of menstrual cycle (70.8%) with 8-15 das of menstrual period (62.5%) and responden had excessive volume of menstruation (75%) (table 1). The intensity of menstrual pain in the warm compresses before intervention was mostly (58.3%) in moderate pain, almost half at severe pain (41.7%) and after intervention was almost entirely at mild pain (83.3%), few experienced moderate pain (16.7%). The intensity of menstrual pain in the control group before intervention was half (50%) in moderate and severe pain and after intervention was mostly at moderate pain (58.3%), almost half experienced severe pain (41.7%). The results of wilcoxon test obtained p = 0.001, this mean that there was an effect of warm compresses on the reduction of dysmenorrhea (p<0.05) (Table 2).

Table 1. Respondent characteristics (n=24)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Menarche Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal Menarche (11-13 years old)</td>
<td>19</td>
<td>79.2</td>
</tr>
<tr>
<td>Slow Menarche (&gt;13 years old)</td>
<td>5</td>
<td>20.8</td>
</tr>
<tr>
<td>Menstrual cycle</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Regular</td>
<td>17</td>
<td>70.8</td>
</tr>
<tr>
<td>Unregularly</td>
<td>7</td>
<td>29.2</td>
</tr>
<tr>
<td>Menstrual length</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (1-7 hari)</td>
<td>9</td>
<td>37.5</td>
</tr>
<tr>
<td>Long (8-15 hari)</td>
<td>15</td>
<td>62.5</td>
</tr>
<tr>
<td>Menstrual bleeding</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>6</td>
<td>25</td>
</tr>
<tr>
<td>Heavy</td>
<td>18</td>
<td>75</td>
</tr>
</tbody>
</table>

Table 2. Effects of warm compress on dysmenorrhea

<table>
<thead>
<tr>
<th>Group</th>
<th>Pre Median (Minimum - Maximum)</th>
<th>Post Median (Minimum - Maximum)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warm compress</td>
<td>2 (2-3)</td>
<td>1 (1-2)</td>
<td>0.001</td>
</tr>
<tr>
<td>Control group</td>
<td>2.5 (2-3)</td>
<td>2 (2-3)</td>
<td>0.317</td>
</tr>
</tbody>
</table>

Wilcoxon Test

Table 2. Differences of menstrual dysmenorrhea after intervention

<table>
<thead>
<tr>
<th>Group</th>
<th>Median (Minimum - Maximum)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warm compress</td>
<td>1 (1-2)</td>
<td>0.000</td>
</tr>
<tr>
<td>Control group</td>
<td>2 (2-3)</td>
<td></td>
</tr>
</tbody>
</table>

Mann-Whitney Test

The results of mann-whitney test obtained p = 0.000, this means that there are significant differences the intensity of menstrual pain in warm compress vs. control group (p<0.05). The analysis results showed that warm compresses are effective to reducing the intensity of menstrual pain.

Table 4. Differences of IL-1 β level after intervention

<table>
<thead>
<tr>
<th>Group</th>
<th>Median (Minimum - Maximum) pg/ml</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warm compress</td>
<td>11.14 (6.40 – 45.60)</td>
<td>0.021</td>
</tr>
<tr>
<td>Control group</td>
<td>19.20 (8.48 – 38.40)</td>
<td></td>
</tr>
</tbody>
</table>
Mann-Whitney Test

The results of mann-whitney test obtained p = 0.021, this means that there are significant differences of IL-1 β levels in warm compress vs. control group (p<0.05). The analysis results showed that warm compresses are effective to reducing IL-1β levels in primary dysmenorrhea.

DISCUSSION

PGF2α and leukotriene levels are significantly increase in primary dysmenorrhea where in menstruation period occurred secretory endometrial contains arachidonic acid which are converted to prostaglandin F2α (PGF2α), Prostaglandin E2 (PGE2) and Leukotrients (Adeyemi & Adekanle, 2007; Y.-X. Ma et al., 2010). In addition, the concentration of IL-6 and oxytocin plasma also were increased among women with dysmenorrhoa compared with healthy women (Yeh, Chen, So, & Liu, 2004), this make an increasing of uterine contraction (Aguilar & Mitchell, 2010; Henriet, Chevrannay, & Marbaix, 2012; Jabbour, Kelly, Fraser, & Critchley, 2006), decreased blood flow to uterus, and it were gave an impact like ischemia and pain. In primary dysmenorrhea, IL-6, there was also a significant increased at the first day of menstruation because of proinflammatory cytokine levels (IL-1β, TNFo and IL8). IL-1β and TNFo were increased prostaglandin and oxytocin stimulation at the first day of the menstrual phase (Friebe-Hoffmann, Baston, Hofmann, Chiao, & Rauk, 2007; Tamura. Mitsutoshi et al., 2002; Terzidou, Blanks, Kim, Thornton, & Bennett, 2011; Thompson et al., 2004).

The intensity of menstrual pain before giving intervention was in moderate and severe level of pain. Moreover, moderate level of pain was found among respondents with normal age of menarche, regular menstrual cycle, long menstrual duration (8-15 days), and excessive menstrual volume. Severe level of pain was found among respondents who had long menstrual duration (8-15 days) and excessive menstrual volume. Several risk factors can increase the incidence of dysmenorrhea are early age of menarche, longer menstrual duration, excessive menstrual volume, smoking, alcohol consumption, low social support, family history of dysmenorrhea, high caffeine diet, depression, anxiety and stress (Mukhoirotin, 2018). The results of this study showed that severe dysmenorrhea was found among respondents with long menstrual duration and excessive menstrual volume. Long menstrual periods and heavier menstrual flow are determined by prostaglandin (Habibi et al., 2015; Ibrahim et al., 2015). The increasing of production and the release of endometrial prostaglandins during menstruation can inducing uterine hypercontractility, reduce uterine blood flow, and hypersensitivity of pain fibers (Y.-X. Ma et al., 2010).

After given a warm compress, the intensity of menstrual pain among respondents was almost entirely at mild pain. The results of statistical tests showed that there was an effect of warm compresses on the intensity of menstrual pain and there was a significant difference of menstrual pain in warm compress group and the control group. The decreasing of menstrual pain occurs because of warm compresses intervention because it makes dilation of blood vessels (vasodilation), the increasing of blood supply throughout the body and providing a sense of comfort to the respondent. A warm compress is an action that can reduce pain by using a dilation blood vessels and increasing blood supply throughout the body (Berman, Synder, & Fradsen, 2015). The warm compresses are independent intervention of nursing. As a care giver, the nurses could giving warm compresses as an effort to reducing menstrual pain and as an educator, the nurses could giving health education about non-pharmacology therapy to reducing menstrual pain by using warm compresses.

The results of this study showed that there were difference of IL-1β levels between warm compress groups vs. control group (p<0.05). The warm compresses intervention can speed up blood circulation because of the effects of vasodilation and muscle relaxation
The increasing of blood circulation to uterus has an impact on the dilution of bradykinin, prostaglandins and intravascular histamine (Steen and Cooper, 1998 in Yang et al., 2017). Prostaglandins can increase oxytocin release without affecting synthesis (Arulkumaran et al., 2012). Thus, decreased of prostaglandin production will give an impact like the reducing of oxytocin release. The mechanism of decreasing IL-1β levels after warm compresses intervention may occur due to the delusional effects of prostaglandins in that the IL-1β levels also decrease. The results of previous studies mentioned that the local heat intervention same as effective as NSAIDs (ibuprofen and acetamenophen), but it was safety for used because it does not cause potential effects like NSAIDs (Mark Akin et al., 2004; MD Akin et al., 2001). The mechanism of NSAIDs to relieve primary dysmenorrhoea depends on inhibition of cyclooxygenase (COX), an enzyme that is responsible for the formation of prostaglandins. Excessive prostaglandins cause contractions of dysrhythmias in the uterus, thereby decreasing local blood flow and increasing peripheral nerve sensitivity (Dawood, 2006; Dawood & Khan-Dawood, 2007). Thus, warm compresses can inhibit the activity of cyclooxygenase (COX) in that the formation of prostaglandins is also reduced.

The results of previous studies showed that after Herb-Partitioned Moxibustion (HPM) intervention there was an increase of regulation of 20α-dihydroprogesterone, pregnenolone, Prostaglandin E2 and gamma-aminobutyric acid and decreased regulation of estrone, 16-oxotrone and prostaglandin H2. Thus HPM can regulate internal secretion in primary dysmenorrhoea (Y. X. Ma et al., 2015; Xue, Liu, Gao, & Ma, 2014), in addition HPM can regulate the metabolism of arachidonic acid which produces prostaglandins and leukotrienes through the function of cyclooxygenase and lipoxygenase. Herb-Partitioned Moxibustion is an external therapy in Traditional Chinese medicine (TCM), the therapy process is a giving moxibustion with herbs on CV8 (shenque). Local heat intervention and warm compresses are easy to apply, but warm compresses are more efficient because they don't need money and more easy to find the ingredients. However, Herb-Partitioned Moxibustion are requires assistance from an expert and also need of money. Thus, warm compresses are more efficient in their application when compared to local heat intervention and Herb-Partitioned Moxibustion. Warm compresses are more beneficial because it can reduce proinflammatory cytokines (IL-1β levels) so the synthesis or released of PGF2α and OT decreases, decreases uterine contractions, increases endometrial blood flow, and decreases the intensity of menstrual pain. A limitation of this study was the IL-1β levels were only observed after giving intervention.

CONCLUSIONS
Warm compresses are effectively to reduce IL-1β levels on primary dysmenorrhea, it can be used as an alternative intervention to overcome complaints of primary dysmenorrhea. The recommendation for next research is the observation of IL-1β levels before and after giving intervention.

DISCLOSURE STATEMENT
All the author contributed to this study. There are no ghost writer included during the manuscript preparation process.

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