The Effect of Slow Stroke Back Massage on Primary Dysmenorrhea: Levels of Beta-Endorphin, Interleukin-6, Tumor Necrosis Factor-α, and Pain Intensity

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Abstract

Objectives: Dysmenorrhea is one of several gynecological issues that occur among women of reproductive age. In addition, it appears as pain that forms in the pelvis or lower abdomen and spreads to the back and thighs. The peripheral blood among women with dysmenorrhea increases the synthesis and the concentration of oxytocin, F2α prostaglandin hormone, vasopressin, interleukin-6 (IL-6), and tumor necrosis factor-α (TNFα). In this regard, this study aimed to determine the effect of slow-stroke back massage (SSBM) on the levels of β-endorphins, IL-6, TNFα, and menstrual pain intensity (MPI).

Materials and Methods: Based on the aim of the study, the posttest only quasi-experimental method with the control group design approach, pretest-posttest control group approach, and purposive sampling techniques were applied for sample selection. The samples were divided into SSBM and control groups each containing 20 subjects. The numeric rating scale (NRS), β-endorphin, IL-6, and TNFα levels were measured using the indirect enzyme-linked immunosorbent assay. Then, data were analyzed by paired sample t test and independent-samples t test with α ≤ 0.05.

Results: The results revealed that SSBM had an effect on the intensity of menstrual pain (P<0.05), and differences were found between β-endorphin levels, IL-6, TNFα, and MPI among SSBM and control (P<0.05) groups. Accordingly, SSBM can stimulate releasing β-endorphin levels and reducing pro-inflammatory cytokines (IL-6 and TNFα).

Conclusions: In general, SSBM is a nonpharmacological action that is effective in primary dysmenorrhea.

Keywords: β-Endorphin, IL-6 level, Menstruation pain intensity, Slow-stroke back massage, TNFα level

Introduction

Dysmenorrhea, as one of the gynecological problems that appears before or during the menstruation period among reproductive women, shows symptoms in the lower abdomen and spreads to the back pain, and its severity varies from mild, moderate, and severe levels (1,2). School absence and severe pain felt at the time dysmenorrhea can have psychological, physical, and social consequences among adolescents (3,4). The primary dysmenorrhea commonness is up to 90% (5) and varies in different regions. For instance, its range was reported by 78.3% (6), 69.3% (7), 85.1% (8), and 90.1% (9) in Korea, Ethiopia, Palestine, and Jordan, respectively.

The high level of F2α prostaglandin hormone (PGF2α) release from endometrium was one reason for the appearance of primary dysmenorrhea with symptoms such as abdominal pain, uterine cramps, and uterine muscle contraction (10-13). Studies have shown that the pro-inflammatory cytokines, including interleukin 1 β, tumor necrosis factor (TNF), interleukin (IL)-6, and IL-8, significantly increase on the first day of menstruation. These cytokines can induce PGF2α and oxytocin synthesis, and uterus hypercontractility and reduce endometrial blood flow, and eventually pain (14,15).

Contraceptive pills and nonsteroidal anti-inflammatory drugs commonly consumed to treat dysmenorrhea have several side effects. Based on the gate control theory, acupressure, warm or cold compress, and slow-stroke back massage (SSBM) can be an alternative treatment for dysmenorrhea. A skin stimulation by SSBM causes endorphins releases that block pain transmission (16). Several studies also suggested that SSBM and acupressure at the Sanyinjiao point effectively reduced the intensity of menstrual pain (17-19), and traditional Malay massage could reduce several pro-inflammatory mediators (i.e., TNF-α, IL-1β, IL-8, monocyte chemotactic protein-1, IL-6, and IL-10) related to dysmenorrhea (20). So far, no research has examined the SSBM effect on pro-inflammatory cytokines levels in dysmenorrhea. Therefore, this study aimed to observe the SSBM effect on β-endorphin levels, IL-6, TNF-α, and menstrual pain intensity (MPI).

Materials and Methods

Design

In this study, the posttest only quasi-experimental method...
SSBM is effective in reducing menstrual pain intensity (MPI) and can stimulate the releasing of β-endorphin levels and reducing pro-inflammatory cytokines (IL-6 and TNFα).

Participants
The population in this study consisted of students who studied at the Faculty of Health Sciences, Unipdu Jombang, and experienced menstruation pain (dysmenorrhea). In addition, the study sample comprised 40 respondents who met the inclusion and exclusion criteria. The inclusion criteria entailed students who received no anti-pain therapy, along with cooperative students. On the other hand, the exclusion criteria were female students who refused to obtain treatment during the middle phase of the study. The samples of the study were randomly grouped into SSBM (n = 20) and control (n = 20) groups and a purposive sampling method was employed in this study.

Data Collection Procedure
After obtaining permission from the head of the research institute, the researchers approached the students who experienced menstrual pain (dysmenorrhea) to obtain their approval for participating in this study. The students were then divided into two groups. The treatment group received the SSBM intervention while the control group received no SSBM although they were provided with information regarding menstrual pain management. SSBM was given only once on the first day of dysmenorrhea, by gently rubbing the skin of the respondent’s back, starting from the middle of the lower back then toward the left and right hemispheres from the head to the sacrum area with circular movements at a speed of 60 times per minute for 20 minutes. Next, both groups were observed after the SSBM intervention (Table 3), in which the levels of β-endorphins, IL-6, and TNFα were checked after applying the intervention technique.

In addition, whole blood samples (3 mL) were drawn from a peripheral vein (median basilic) after the intervention. Further, serum samples for clotting were drawn from a peripheral vein (median basilic) after the SSBM intervention while the control group received no SSBM although they were provided with information regarding menstrual pain management. SSBM was given only once on the first day of dysmenorrhea, by gently rubbing the skin of the respondent’s back, starting from the middle of the lower back then toward the left and right hemispheres from the head to the sacrum area with circular movements at a speed of 60 times per minute for 20 minutes. Next, both groups were observed after the SSBM intervention (Table 3), in which the levels of β-endorphins, IL-6, and TNFα were checked after applying the intervention technique.

Measurement of Pain Level
The level of pain was measured using the NRS on a scale of 0-10 with the 0 response meaning no pain. Moreover, 1-3, 4-6, and 7-9 demonstrated mild, moderate, and severe pain levels which could be controlled, and finally, scale 10 represented a severe pain level which was uncontrollable (22).

Results
Respondents’ characteristics (Table 1) were age, the age of menarche, the period of menstruation, the cycle of menstruation, the volume of menstruation, the characteristic of pain, and the treatment of pain. The characteristics of the two groups showed no significant differences (P >0.05), meaning that the characteristics of the two groups were balanced or homogeneous.

The average MPI before the intervention was found to be moderate in both groups, representing that MPI was comparable in treatment and the control groups before the intervention (P > α), the details of which are provided in Table 2.

Based on the data in Table 3, the average intensity of menstrual pain was mild in the treatment group while it was moderate in the control group (with no SSBM intervention) after the SSBM intervention (Table 3), which is in line with the findings of the previous study further use. Then, data were measured using an NRS instrument.

Measurement of Serum Level β-endorphin
The level of β-grade serum endorphins was determined by test kits from the enzyme-linked immunosorbent assay (ELISA, Product LSBio, catalog number 124733).

Measurement of Serum Level IL-6
The serum level assay of IL-6 was quantitatively detected by the ELISA in duplicate for each subject according to the manufacturer's procedure (Biolegend).

Measurement of Serum Level TNFα
Moreover, the serum level assay of TNFα was quantitatively detected by the ELISA in duplicate for each subject according to the manufacturer’s instruction (Biolegend).

Statistical Analysis
The obtained data were analyzed using SPSS, version 11.5 (SPSS Inc., Chicago, IL, United States). The Shapiro-Wilk test was used to test the normality of the distribution for continuous variables. Additionally, data were expressed as mean ± standard deviation, where applicable. The variable data including the mean level of β-endorphin, IL-6, and TNFα were compared by an independent sample t test, and the paired sample t-test was applied to evaluate pain levels. The resulting P<0.05 was considered statistically significant.
(17), suggesting that SSBM treatment can decrease dysmenorrhea pain. However, pain intensity was still at a moderate level in the control group because there was no SSBM intervention, and they were only provided with information regarding menstrual pain management.

After the SSBM intervention, the average of MPI decreased (from 5.25 to 2.65) significantly ($P < 0.05$) in the treatment group compared with before the intervention. A reduction (from 5.25 to 2.65) was also observed in MPI in the control group after providing information about menstrual pain management. The average reduction of MPI in the treatment group was higher in comparison with the control group, where the differences in the average before and after the intervention were 2.60 and 0.5 in the treatment and control groups, respectively (Figure 1).

The results demonstrated that β-endorphin, IL-6, and TNFα levels significantly differed ($P < 0.05$) between the treatment and control group after SSBM treatment. The β-endorphin levels in the treatment group were higher compared to the control group while IL-6 and TNFα levels were lower in the treatment group in comparison to the control group (Table 4). IL-6 and TNFα related to the stimulations of PGF2α and oxytocin, which induce uterine hypercontractility, decrease endometrial blood flow, and cause pain. On the other hand, the SSBM intervention increases endorphin, IL-6, and TNFα levels and leading to a decline in the intensity of pain among the respondents.

**Discussion**

The pain intensity of dysmenorrhea can be at mild,
moderate, or severe levels. The mild dysmenorrhea pain occurs in a person but it does not disturb the person’s daily activities, thus it needs no medicine for pain reduction. The moderate dysmenorrhea pain slightly interferes with daily activities but it can be managed by using a medicine or painkillers while severe dysmenorrhea is painful and disturbs daily activities (2). The results of previous studies indicated the average intensity of menstrual pain among respondents at a moderate level (23). Some factors influencing the high risk of menstrual pain (dysmenorrhea) include the younger age of menarche, the longer duration of menstruation, excessive menstrual volume, a low body mass index, smoking and alcohol consumption, low social support, family history of dysmenorrhea, a high caffeine diet, depression, anxiety, and stress (24-28). However, the prevalence of dysmenorrhea was low among women who experienced long-term pregnancy and lactation, married women, and those who experienced childbirth. Other studies also found that childbirth decreases adrenergic receptors in the uterus (29,30).

The average intensity of menstrual pain after SSBM intervention represented a significant decrease. This occurred because the applied SSBM was accompanied by a sweep technique to the back skin of the respondent with a circular motion for 60 times per minute. In this technique, the movement starts from the middle of the lower back and then moves toward the left and right hemispheres from the head to the sacrum area and for 20 minutes. In addition, SSBM makes the respondent feel comfortable so that it stimulates the release of β-endorphins and decreases the intensity of menstrual pain. If the person perceived touch as a stimulus for relaxation, then he/she responds with relaxation (26). The correct use of cutaneous stimulation could reduce the perception of pain and help reduce muscle tension. Otherwise, muscle tension could increase pain (16). Based on the results of a previous study, acupressure at the Sanyinjiao point and SSBM were effective in reducing the intensity of menstrual pain (17). Another study also showed that giving a massage for 15 minutes was effective in alleviating menstrual pain (31).

Regarding the average intensity of menstrual pain in the control group, after providing information, the majority of participants mentioned that they were not experiencing menstrual pain and a small number of them experienced light menstrual pain. This occurs because giving information to the respondents allowed them to understand the provided intervention. Moreover, providing the information is an effort for dealing with the pain thus the intensity of pain among most respondents did not demonstrate a decrease (55%) although a small number of them indicated a decrease from previous intensity (45%). The decline in MPI occurred because the respondents understood more about the received intervention; thus they became calmer and comfortable.

The β-endorphin levels among the SSBM group were higher compared to the control group, because the SSBM group worked by encouraging the release of endorphins and blocked the transmission of pain stimuli. The differences of β-endorphin levels can be explained based on the endogenous opiate theory, where opiate receptors in the brain and spinal cord determined where the central nervous system activated morphine substances called ‘endorphins’ and ‘enkephalins’ if they received pain. The output of opiate endogenous could be stimulated by the stimulation of the skin and the muscle. These opioid receptors are located on the sensory peripheral nerve (19). Endorphins inhibit C fibers in pre- and post-synapses and Aδ fibers (delta A) on the dorsal horn and activate larger sensory nerve fibers Aß (A-beta). Therefore, the pain gate closes or blocks pain signals which enter the spinal cord thus the pain perception represents a decrease (32). Marzouk et al concluded that an aromatherapy abdominal massage intervention for 10 minutes once a day within 7 days effectively reduced menstrual pain, excessive bleeding, and its duration (33). Other studies also suggested that the SSBM intervention was effective in decreasing menstrual pain (dysmenorrhea) intensity (17,34), increasing β-endorphin levels, and reducing the pain transmission process (19,35).

The IL-6 and TNFa levels of the SSBM group are lower than those of the control group. IL-6 increases oxytocin (OT) secretion (36) whereas TNFa increases prostaglandin and OT on the first day of menstruation (37,38). Additionally, OT and prostaglandin stimulate uterine contractions (39) thus this has a sensation similar to the pain from primary dysmenorrhea. Lower IL-6 and TNFa levels lead to lower prostaglandin and OT secretion which will decrease pain sensation. Therefore, SSBM intervention can reduce the levels of IL-6 and TNFa, which occurs because SSBM is a skin massage action that can stimulate the release of β-endorphin. In addition, β-endorphins can activate opioid receptors which activate analgesia through the inhibition of Ca2+ and K+ channels, thus it inhibits the release of neurotransmitters including

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### Table 4. Differences between the Levels of β-Endorphin, IL-6, and TNFα in SSBM and Control Groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>SSBM Group Mean (SD)</th>
<th>Control Group Mean (SD)</th>
<th>Mean Difference (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>β-Endorphin</td>
<td>166.13 (2.70)</td>
<td>96.32 (1.78)</td>
<td>69.8148 (29 - 91.34)</td>
<td>0.000</td>
</tr>
<tr>
<td>IL-6</td>
<td>183.63 (3.12)</td>
<td>198.21 (6.08)</td>
<td>-618.5 (-1181.46 - -55.49)</td>
<td>0.034</td>
</tr>
<tr>
<td>TNFα</td>
<td>265.57 (4.82)</td>
<td>417.57 (1.62)</td>
<td>-152 (-303.04 - -0.96)</td>
<td>0.049</td>
</tr>
</tbody>
</table>

Note: SD: standard deviation; SSBM: slow stroke back massage; CI: confidence interval; IL: interleukin; TNFα: tumor necrosis factor-α.
substance P and prostaglandins (32,40).

In another study, Crane et al showed that massage therapy has effectively reduced the production of NF-κB, TNF-α, and other inflammatory cytokines (41). Besides, massage therapy was found to improve immunological function by increasing natural killer and lymphocyte cell circulations (42). Other research also demonstrated that Swedish massage therapy can reduce several mitogen-stimulation cytokines levels such as IL–1ß, IL-2, IL-4, IL-5, IL-6, IL-10, IL-13, and interferon-γ (43).

Based on the findings of another study, the level of IL-6, TNFα, and other pro-inflammatory cytokines including IL1ß and IL8 increased in primary dysmenorrhea (44). IL1ß expression stimulates the PGF2α, OT, and endothelin synthesis which leads to the vasoconstriction of blood vessels and uterine contractions and causes pain (14,15). Further, it was found that moxibustion intervention can reduce PGF2α and OT expression. The results of similar research also showed that herb-partitioned moxibustion intervention can effectively reduce prostaglandin levels in primary dysmenorrhea (45).

These study results are extremely useful in the women’s health field because SSBM is an effective intervention for reducing dysmenorrhea by affecting the regulation of hormones and proinflammatory cytokines. Furthermore, SSBM can act as an analgesic, easy-to-do, and non-invasive approach. However, this study only provides data on several variables (i.e., β-endorphin, IL-6, and TNFα) related to dysmenorrhea thus further research is needed to measure other ovarian hormones and proinflammatory cytokines related to dysmenorrhea and compare them with other nonpharmacological methods.

Conclusions
In general, the results of this study indicated that there was an effect of SSBM on MPI and there were differences in the levels of β-endorphin, IL-6, TNFα, and the intensity of menstrual pain among the SSBM and control groups. It was found that SSBM can stimulate the release of β-endorphin levels and reduce proinflammatory cytokines (i.e., IL-6 and TNFα). Therefore, it can be argued that SSBM is an effective nonpharmacological intervention for primary dysmenorrhea.

Authors’ Contribution
All authors contributed equally to the study.

Conflict of Interests
The authors declare that they have no conflict of interests regarding the publication of this paper.

Ethical Issues
This study obtained ethical clearance from the Ethics Committee of the Nursing Faculty, Airlangga University, Surabaya.

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