http://www.ijwhr.net
doi 10.15296/ijwhr.2020.60
Open Access Original Article
IJWHR
International Journal of Women's Health and Reproduction Sciences
Vol. 8, No. 4, October 2020, 376–382
ISSN 2330-4456

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, TNF-α, 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 $\alpha \leq 0.05$.

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 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

Received 9 April 2020, **Accepted** 17 June 2020, **Available online** 17 October 2020

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Key Messages

- SSBM is effective in reducing of menstrual pain intensity (MPI)
- SSBM can stimulate the releasing of β-endorphin levels and reducing pro-inflammatory cytokines (IL-6 and TNFα).

(21) and control group design were used to determine the effects of SSBM on β-endorphin, IL-6, and the TNFα level in dysmenorrhea. On the other hand, the pretest-posttest control group design was utilized to evaluate the SSBM effect on MPI. The duration of cutaneous stimulation by SSBM was 20 minutes (16).

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 intervention, and the pain level was measured using the numeric rating scale (NRS) on a scale of 0-10 (22). 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 kept in flat tubes with a gel at room temperature for 30 minutes and then centrifuged at 2700 g for 10 minutes. After centrifuging the blood samples at 1500 g at +4°C for 20 minutes, plasma samples were kept at -80°C until 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).

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).

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.

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 ($P> \alpha$), 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

Table 1. Respondents' Characteristics and Homogeneity

Variable	SSBM Group	Control Group	*P* value
Age (year), Mean (SD)	20.50 (1.32)	19.70 (1.42)	0.760
Age of menarche (year), Mean (SD)	1.50 (1.42)	13.10 (0.97)	0.074
Period of menstruation (day), Mean (SD)	7.95 (1.85)	8.55 (2.33)	0.224
Cycle of menstruation, No. (%)			
Regular	13 (65)	13 (65)	1.000
Irregular	7 (35)	7 (35)	
Volume of menstruation, No. (%)			
Moderate	11 (55)	13 (65)	0.257
Much	9 (45)	7 (35)	
Characteristic of pain, No. (%)			
Burnt out	4 (20)	0 (0)	0.054
Cramps	7 (35)	2 (10)	
Wind	8 (40)	7 (35)	
Oppressed	1 (5)	9 (45)	
Acute	0 (0)	2 (10)	
Treatment of pain, No. (%)			
Take medicine	1 (5)	2 (10)	0.795
Take a rest	14 (70)	17 (85)	
Ignore	5 (25)	1 (5)	

Note. SD: Standard deviation; SSBM: Slow stroke back massage.

(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 PGF2a 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.

Table 2. The Intensity of Menstruation Pain (Dysmenorrhea) Before the Intervention

Group	Mean ± SD	Mean Difference (95% CI)	*P* Value
SSBM	5.25 ± 1.62	-0.70 (-1.62 – 0.22)	0.132
Control	5.95 ± 1.23		

Note. SD: standard deviation; SSBM: slow stroke back massage; CI: Confidence interval.

Table 3. The Intensity of Menstruation Pain (Dysmenorrhea) After the Intervention

Group	Mean ± SD	Mean Difference (95% CI)	*P* Value
SSBM	2.65 ± 1.27	- 2.80 (-3.70 – 0.22)	0.000
Control	5.45 ± 1.54		

Note. SD: standard deviation; SSBM: slow stroke back massage; CI: Confidence interval.

Discussion

The pain intensity of dysmenorrhea can be at mild,

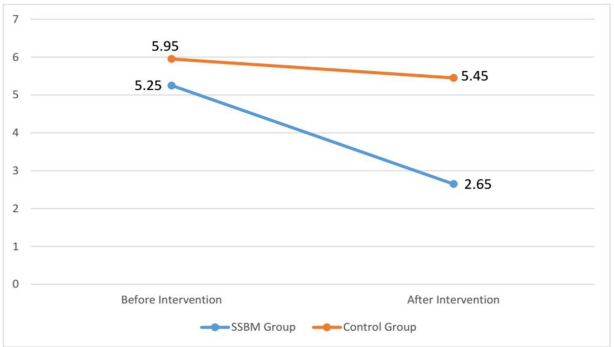

Figure 1. Differences in the Menstruation (Dysmenorrhea) Pain Rate Before and After Treatment.

Table 4. Differences Between the Levels of β-endorphin, IL-6, and TNFα in SSBM and Control Groups

Variable	SSBM Group Mean (SD)	Control Group Mean (SD)	Mean Difference (95% CI)	*P* value
β-Endorphin	166.13 (2.70)	96.32 (1.78)	69.8148.29 – 91.34)	0.000
IL-6	1363.6 (3.12)	1982.1 (6.08)	-618.5 (-1181.46 – -55.49)	0.034
TNF-α	265.57 (4.82)	417.57 (1.62)	-152 (-303.04 – -0.96)	0.049

Note. SD: standard deviation; SSBM: slow stroke back massage; CI: confidence interval; IL: interleukin; TNF-α: tumor necrosis factor-α.

moderate, or severe levels. The mild dysmenorrhea pain occurs in a person but it does not disturb the person's daily activities, thus 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 TNFα levels of the SSBM group are lower than those of the control group. IL-6 increases oxytocin (OT) secretion (36) whereas TNFα 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 TNFα levels lead to lower prostaglandin and OT secretion which will decrease pain sensation. Therefore, SSBM intervention can reduce the levels of IL-6 and TNFα, 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 Ca^{2+} and K^{+} channels, thus it inhibits the release of neurotransmitters including

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 IL1β and IL8 increased in primary dysmenorrhea (44). IL1β expression stimulates the PGF2a, 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 PGF2a 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.

Financial Support

This research was funded by the Directorate of Research and Community Service, Directorate General of Research and Development Strengthening, Ministry of Research, Technology, and Higher Education (Kemenristekdikti).

Acknowledgments

The authors would like to thank Universitas Perguruan Tinggi Darul 'Ulum Jombang and Kemenristekditi, Indonesia for facilitating this study.

References

1. Esimai O, Esan GO. Awareness of menstrual abnormality amongst college students in urban area of ile-ife, osun state, Nigeria. Indian J Community Med. 2010;35(1):63-66. doi:10.4103/0970-0218.62559
2. Turk DC, Melzack R. Handbook of Pain Assessment. New York: Guilford Press; 2011.
3. Deb S, Raine-Fenning N. Dysmenorrhoea. Obstet Gynaecol Reprod Med 2008;18(11):294-299. doi:10.1016/j.ogrm.2008.08.007
4. Wong LP, Khoo EM. Dysmenorrhea in a multiethnic population of adolescent Asian girls. Int J Gynaecol Obstet. 2010;108(2):139-142. doi:10.1016/j.ijgo.2009.09.018
5. Grandi G, Ferrari S, Xholli A, et al. Prevalence of menstrual pain in young women: what is dysmenorrhea? J Pain Res. 2012;5:169-174. doi:10.2147/jpr.s30602
6. Kim HO, Lim SW, Woo HY, Kim KH. Premenstrual syndrome and dysmenorrhea in Korean adolescent girls. Obstet Gynecol Sci. 2008;51(11):1322-1329.
7. Muluneh AA, Nigussie TS, Gebreslasie KZ, Anteneh KT, Kassa ZY. Prevalence and associated factors of dysmenorrhea among secondary and preparatory school students in Debremarkos town, North-West Ethiopia. BMC Womens Health. 2018;18(1):57. doi:10.1186/s12905-018-0552-x
8. Abu Helwa HA, Mitaeb AA, Al-Hamshri S, Sweileh WM. Prevalence of dysmenorrhea and predictors of its pain intensity among Palestinian female university students. BMC Womens Health. 2018;18(1):18. doi:10.1186/s12905-018-0516-1
9. Mukattash TL, Tahaineh L, AlRawi N, Jarab A, Hammad H, Nuseir K. Behaviors and attitudes towards dysmenorrhea: a crosssectional survey of 2,000 Jordanian university students. Jordan Med J. 2013;47(1):26-34. doi:10.12816/0001066
10. Dawood MY. Primary dysmenorrhea: advances in pathogenesis and management. Obstet Gynecol. 2006; 108(2):428-441. doi:10.1097/01.AOG.0000230214.26638.0c
11. Lowdermilk D, Perry S, Cashion MC. Maternity Nursing. Singapore: Elsevier; 2013.
12. Shi GX, Liu CZ, Zhu J, Guan LP, Wang DJ, Wu MM. Effects of acupuncture at Sanyinjiao (SP6) on prostaglandin levels in primary dysmenorrhea patients. Clin J Pain. 2011;27(3):258-261. doi:10.1097/AJP.0b013e3181fb27ae
13. Turhan N, Celik H, Duvan C, Onaran Y, Aydın M, Armutcu F. Investigation of oxidative balance in patients with dysmenorrhea by multiple serum markers. J Turk Ger Gynecol Assoc. 2012;13(4):233-236. doi:10.5152/jtgga.2012.36
14. Ahnstedt H, Stenman E, Cao L, Henriksson M, Edvinsson

L. Cytokines and growth factors modify the upregulation of contractile endothelin ET(A) and ET(B) receptors in rat cerebral arteries after organ culture. Acta Physiol (Oxf). 2012;205(2):266-278. doi:10.1111/j.1748-1716.2011.02392.x
15. Arulkumaran S, Kandola MK, Hoffman B, Hanyaloglu AC, Johnson MR, Bennett PR. The roles of prostaglandin EP 1 and 3 receptors in the control of human myometrial contractility. J Clin Endocrinol Metab. 2012;97(2):489-498. doi:10.1210/jc.2011-1991
16. Potter PA, Perry AG, Stockert PA, Hall A. Fundamentals of Nursing. US: Mosby; 2012.
17. Mukhoirotin, Fatmawati DA. Pengaruh akupresur pada titik sanyinjiao dan slow stroke back massage terhadap penurunan intensitas nyeri haid (dismenorrhea). Seminar Nasional dan Muswil Kedua Ikatan Perawat Maternitas Indonesia (IPEMI) Provinsi Jawa Tengah "Membangun Etos Kerja Profesional Keperawatan Maternitas dalam Mengisi Era Masyarakat Ekonomi ASEAN" Magelang, Indonesia: Faculty of Medicine, University of Diponegoro; 2016. [Indonesian].
18. Rahayu D, Santoso B, Yunitasari E. The difference in breastmilk production between acupresure point for lactation and oxytocin massage. Jurnal Ners. 2015;10(1):9-19. doi:10.20473/jn.v10i1.1852
19. Rahayu D, Yunarsih Y. Perubahan Kadar β endorphine pada pasien primigravida inpartu kala I fase aktif dengan penerapan "Comfort food: Slow-stroke back massage" berbasis teori kenyamanan Kolcaba di RSUD Kabupaten Kediri. The Indonesian Journal of Health Science. 2017;7(1):17-25. [Indonesian].
20. Sejari N, Kamaruddin K, Ramasamy K, Lim SM, Neoh CF, Ming LC. The immediate effect of traditional Malay massage on substance P, inflammatory mediators, pain scale and functional outcome among patients with low back pain: study protocol of a randomised controlled trial. BMC Complement Altern Med. 2016;16:16. doi:10.1186/s12906-016-0988-1
21. Nursalam. Metodologi Penelitian Ilmu Keperawatan. Jakarta: Salemba Medika; 2016.
22. Kozier B. Buku Ajar Fundamental Keperawatan Konsep Proses & Praktik. 7th ed. Jakarta: EGC; 2010.
23. Atallahi M, Amir Ali Akbari S, Mojab F, Alavi Majd H. Effects of wheat germ extract on the severity and systemic symptoms of primary dysmenorrhea: a randomized controlled clinical trial. Iran Red Crescent Med J. 2014;16(8):e19503. doi:10.5812/ircmj.19503
24. Faramarzi M, Salmalian H. Association of psychologic and nonpsychologic factors with primary dysmenorrhea. Iran Red Crescent Med J. 2014;16(8):e16307. doi:10.5812/ircmj.16307
25. Iliyasu Z, Galadanci HS, Abubakar IS, Ismail AO, Aliyu MH. Menstrual patterns and gynecologic morbidity among university students in Kano, Nigeria. J Pediatr Adolesc Gynecol. 2012;25(6):401-406. doi:10.1016/j.jpag.2012.08.006
26. Ju H, Jones M, Mishra G. The prevalence and risk factors of dysmenorrhea. Epidemiol Rev. 2014;36:104-113. doi:10.1093/epirev/mxt009
27. Perry M. Treatment options for dysmenorrhoea. Pract Nurs. 2012;23(4):195-198. doi:10.12968/pnur.2012.23.4.195
28. Sahin N, Kasap B, Kirli U, Yeniceri N, Topal Y. Assessment of anxiety-depression levels and perceptions of quality of life in adolescents with dysmenorrhea. Reprod Health. 2018;15(1):13. doi:10.1186/s12978-018-0453-3
29. Chiu MH, Hsieh HF, Yang YH, Chen HM, Hsu SC, Wang HH. Influencing factors of dysmenorrhoea among hospital nurses: a questionnaire survey in Taiwan. BMJ Open. 2017;7(12):e017615. doi:10.1136/bmjopen-2017-017615
30. Jang IA, Kim MY, Lee SR, Jeong KA, Chung HW. Factors related to dysmenorrhea among Vietnamese and Vietnamese marriage immigrant women in South Korea. Obstet Gynecol Sci. 2013;56(4):242-248. doi:10.5468/ogs.2013.56.4.242
31. Bakhtshirin F, Abedi S, YusefiZoj P, Razmjooee D. The effect of aromatherapy massage with lavender oil on severity of primary dysmenorrhea in Arsanjan students. Iran J Nurs Midwifery Res. 2015;20(1):156-160.
32. Londhey VA. Pathophysiology of Pain. J Assoc Physicians India. 2015;63(2 Suppl):5-7.
33. Marzouk TM, El-Nemer AM, Baraka HN. The effect of aromatherapy abdominal massage on alleviating menstrual pain in nursing students: a prospective randomized cross-over study. Evid Based Complement Alternat Med. 2013;2013:742421. doi:10.1155/2013/742421
34. Zuliani, Mukhoirotin, dan Pujiani. Pengaruh stimulasi kutaneus (slow stroke back massage) terhadap penurunan nyeri haid (dismenorea). Jurnal Eduhealth. 2013;3(2):130-134. [Indonesian].
35. Rahayu D. Perubahan tingkat nyeri pada pasien primigravida inpartu kala i dengan penerapan slow stroke back massage berbasis teori kenyamanan kolcaba. Jurnal Ilmu Kesehatan. 2015;4(1):102-109. doi:10.32831/jik.v4i1.81. [Indonesian].
36. Rauk PN, Friebe-Hoffmann U, Winebrenner LD, Chiao JP. Interleukin-6 up-regulates the oxytocin receptor in cultured uterine smooth muscle cells. Am J Reprod Immunol. 2001;45(3):148-153. doi:10.1111/j.8755-8920.2001.450305.x
37. Skarzynski DJ, Miyamoto Y, Okuda K. Production of prostaglandin f(2alpha) by cultured bovine endometrial cells in response to tumor necrosis factor alpha: cell type specificity and intracellular mechanisms. Biol Reprod. 2000;62(5):1116-1120. doi:10.1095/biolreprod62.5.1116
38. Thompson M, Barata da Silva H, Zielinska W, et al. Role of CD38 in myometrial Ca2+ transients: modulation by progesterone. Am J Physiol Endocrinol Metab. 2004;287(6):E1142-1148. doi:10.1152/ajpendo.00122.2004
39. Henriet P, Gaide Chevronnay HP, Marbaix E. The endocrine and paracrine control of menstruation. Mol Cell Endocrinol. 2012;358(2):197-207. doi:10.1016/j.mce.2011.07.042
40. Kirkpatrick DR, McEntire DM, Hambsch ZJ, et al. Therapeutic basis of clinical pain modulation. Clin Transl Sci. 2015;8(6):848-856. doi:10.1111/cts.12282
41. Crane JD, Ogborn DI, Cupido C, et al. Massage therapy attenuates inflammatory signaling after exercise-induced muscle damage. Sci Transl Med. 2012;4(119):119ra113. doi:10.1126/scitranslmed.3002882
42. Billhult A, Lindholm C, Gunnarsson R, Stener-Victorin E. The effect of massage on immune function and stress in women with breast cancer--a randomized controlled trial. Auton Neurosci. 2009;150(1-2):111-115. doi:10.1016/j.

autneu.2009.03.010
43. Rapaport MH, Schettler P, Breese C. A preliminary study of the effects of a single session of Swedish massage on hypothalamic-pituitary-adrenal and immune function in normal individuals. J Altern Complement Med. 2010;16(10):1079-1088. doi:10.1089/acm.2009.0634
44. Ma H, Hong M, Duan J, et al. Altered cytokine gene expression in peripheral blood monocytes across the menstrual cycle in primary dysmenorrhea: a case-control study. PLoS One. 2013;8(2):e55200. doi:10.1371/journal.pone.0055200
45. Ma YX, Yang XY, Guo G, Du DQ, Yu YP, Gao SZ. Research of herb-partitioned moxibustion for primary dysmenorrhea patients based on the LC-MS metabonomics. Evid Based Complement Alternat Med. 2015;2015:621490. doi:10.1155/2015/621490