The effect of applying pressure to the LIV3 and LI4 on the symptoms of premenstrual syndrome: A randomized clinical trial

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Abstract

Objective: To evaluate the effect of simple acupressure protocol in LIV3, LI4 and placebo points on the quality of life (QOL) in women with premenstrual syndrome (PMS).

Method: This paper reports a randomized, single blinded clinical trial. 97 participants (students in of Hormozgan University of Medical Sciences, Iran) with PMS were allocated to three groups to receive 20 minutes acupressure on different acupoints for 14 days before menstruation for three consecutive menstrual cycles (training and then two cycles self applied acupressure).The acupoints were LIV3 and LI4; one group received acupressure at a placebo point. Each participant completed the PSST scale (to determine PMS severity), HADS scale (for depression and anxiety), and quality of life SF12.

Results: The number of people with moderate/severe PMS decreased in LIV3 and LI4 acupressure groups by the second and third cycles compared with the placebo group ($p<0.04$).

Moreover, depression and anxiety scores significantly decreased in the LIV3 and LI4 groups by the second and third cycles compared with the placebo group ($p<0.05$).Analyzing the score of SF12 fields in the second and third cycles showed a significant difference in all dimensions between the intervention and placebo groups. There was no significant difference between LIV3 and LI4 acupressure groups in decrease of PMS symptoms, anxiety and depression and improving SF12scores ($p<0.05$).

Conclusion: Performing the simple acupressure protocol at LIV3 and LI4 is an effective method to decrease the severity of PMS symptoms, anxiety and depression, and to improve the QOL. Pressure at LIV3 and LI4 appear to be equally effective.

Key words: Premenstrual syndrome, Acupressure, Quality of life.

Introduction

Premenstrual syndrome (PMS) is the periodic recurrence of physical, cognitive, and behavioral symptoms which occurs during the luteal phase of menstruation and ends a few days' afterbleeding starts. 70-90 percent of women show different levels of PMS signs among which 20-40 percent result in dysfunction in daily activities(1). In addition, PMS results in increasing adverse educational, economic (absence of the work), and social (committing murder and crime) consequences, as well as decreasing quality of life (QOL)(2).

The cause of PMS is multi-factorial and no cure is known. Therefore, only symptomatic treatment is available. Medical treatments include selective serotonin reuptake inhibitors (SSRIs) and oral contraceptives (3). Complementary and alternative medicine is treatment methods proposed to diminish the severity of PMS symptoms(4).

In complementary and alternative medicine, the etiology and pathogenesis of PMS can be explained as stagnation of energy in the liver and pathological changes in energy level (qi) which affect other body organs. By regulating the liver function, one's mind and mood is regulated then. Therefore, when the liver qi is stagnated and cannot move easily, one's mind and mood is disturbed and psychological and emotional signs appear(4).

It's proposed several acupoint may be used for alleviate of PMS including GV24(6),LI4(6),LR3(6),SP6(6),GV20(7),CV3,4,6(7),PC6(7),GB34(7),BL23(7),Shenman(7), CV9(8),CV17(9),A5,6,8,12,16,18(10),N18(10),F6(10),GV24(11),ST36(12),BL18,19,20,21,22,47,48,49,50,51,52(13). However, there are no studies done to evaluate the effects of acupressure on PMS symptoms. The purpose of this study was to evaluate the effect of acupressure in the third hepatic (taichung), fourth large intestine (HUGO), in comparison with placebo acupressure, on PMS symptoms and QOL in females with PMS.

Methods

a) *Design and data collection*

The present study is a randomized single blinded clinical trial; we recruited students through advertisements in the campus accommodation of Hormozgan University of Medical Sciences, Iran. Sampling and allocation to groups was randomized and the sample size calculated at 30 per each group with α=0.5, 1-β=0.8, and S^2_p=2.22. Except several cases with loss to follow up, treatment compliance for the three cycles was 100%. There are not any reported adverse

effects. The researcher telephoned the participants to remind them (five days to menstruation, every day) of the timing of the interventions and follow-up visits during all two cycles.

It should be noted that the researcher (FB) had been trained in acupressure techniques and manipulation of related acupoints from a Traditional Chinese Medicine (TCM) specialist for 20 sessions at a period of four months.

After approval by the ethics committee of Hormozgan University of Medical Science in Iran, all the students in Hormozgan University of Medical Science received a pamphlet with general information about PMS and acupressure. Then, participants who were eligible entered the study after referring to researcher and giving the written consent.

Two training sessions in the accommodation selected on the field of PMS pathology, treatment methods, and introducing acupressure. Students only did the training if they were selected to the study.

b) Recruitment of participants

Inclusion criteria were age18-45, menstruation cycle intervals 21-35 days, lack of infectious skin diseases, absence of acute rheumatoid arthritis, absence of lesions or dermatitis at the acupressure sites, absence of visual or auditory impairment, avoidance of NSAIDs or other analgesics three hours before starting the intervention, absence of severe depression and anxiety(based on HADs questionnaire), absence of severe psychological tension during the last six months(loss of relatives, surgery), absence of heart disease, renal disorder, diabetes, asthma, hypo/hyper thyroidism, respiratory disorders, lack of any genital disease, having moderate to severe PMS according to the score of PSST questionnaire [one item of the questions number 1-4 scored moderate to severe; in addition, at least four items are scored moderate to severe from question 1 to 14; one item is scored moderate to severe in the part of impact on life (the 5 latter questions)].

c) Acupressure

First cycle: Participants were randomly divided into the study groups using a table of random numbers, and trained how to apply pressure on the points of LIV3, LI4, and the placebo (which is not in the line of meridian). Participants were blinded to their allocation to the intervention groups.

The LIV3 or third hepatic acupoint is of hepatic meridian which is located at dorsal surface of the foot between the first and second toes at the point of bones junction(14) (Figure 3). The LI4 or long intestine acupoint is located at the dorsal surface of the hand between thumb and index finger approximately at the middle of the second metacarpal bone(14) (Figure 2). The placebo point is located at dorsal surface of the foot between the third and the forth toes which is not in the line of meridian (Figure 4). As bleeding started, each of participants completed the Premenstrual Symptoms Screening Tool (PSST), Hospital Anxiety and Depression Scale (HADS), and SF12 questionnaires. In this cycle, only participation's division and questionnaire completion were done.

Second cycle: participants laid down in the supine position (in order to avoiding hypotension and dizziness). At first, the participant sat down for 10-15 minutes to adapt to the room temperature. All the windows and the doors were closed and nobody was allowed to inter the room to avoid the impact of external stimulus. Applying pressure on the given points of the right foot started 14 days before menstruation at the time period of 19-21 o'clock taking 20 minutes and it was repeated daily until the bleeding started. The pressing pattern consisted of two minutes harmonic pressure (one minute in a clockwise direction and one minute in a counter clock-wise direction). In the next two minutes the researcher manipulated the point without any pressure in order that meridian stimulation did not stop. Applying pressure continued until the participant felt a light pain in the acupoint. Pressing stopped and the amount of color change in the nail was observed as a marker and showed to the participant to know how much pressure should herself apply in the next cycle. In addition, the acupressure technique for the given point was taught to the subjects. When menstrual bleeding started, PSST, SF12, and HADs questionnaires were completed by each participant.

Third cycle: As shown in the previous cycle, the participant herself applied pressure on the given point in sitting position by the third cycle. At the onset of bleeding, each participant was requested to complete PSST, SF12, and HADs questionnaires.

The researcher telephoned the participants to remind them (five days to menstruation, every day) of the timing of the interventions and follow-up visits during all two cycles.

Measures

1. PSST questionnaire: this questionnaire turns diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSMIV) classified criteria to a rating scale based on the PMS

severity. This questionnaire indicates disease severity and the impact of PMS symptoms on the individual's life (15). PSST has 19 questions in two parts, 14 questions related to the mood, body, and behavior and five questions based on the potential impact of these symptoms on individual's life. The answers range across a Likert spectrum (never, mild, moderate and severe) scoring zero to three respectively. The validity and reliability of the questionnaire are recognized (16).

2. QOL: SF_{12} evaluated quality of life. This includes 12 questions related to the eight domains of vitality, physical functioning, bodily pain, general health perceptions, physical role functioning, emotional role functioning, social role functioning, mental health. The scoring was done based on the RAND system from zero to 100. The score of each domain is obtained by aggregating the question scores of every domain and dividing the resulting number by the number of questions same domain. Higher score indicates better QOL(17). The validity and reliability of the questionnaire are approved(18).

3. Depression and anxiety: the HADs questionnaire contains 14 questions. Seven questions on the domain of depression and seven questions for the field of anxiety. Each answer scored zero to three based on likert spectrum, and the total score of both fields are 0-21. The validity and reliability of the questionnaire are approved(19).

4. Body mass index (BMI) was measured by weight (kg)/Height^2 (m).

5. Socio-economic status: The number of years of formal education of each participant was taken as an indicator of socio-economic status.

d) Data analysis

Data analysis were done using descriptive statistics (frequency, percent, mean, standard deviation), kruskawallis (to analyze qualitative variable), and ANOVA (to analyze quantative variables). Intergroup comparison was done using the Sheffe test. Data were analyzed using Statistical Package for the Social Sciences 21.0 (SPSS Inc., Chicago, IL, USA). Significance level of $p<0.05$ was considered.

Results

The process of allocating participants during 2015 -2016 is shown in Figure 1.

a) Sample characteristics

90 participants completed treatment and follow-up, and were included in the analysis. There was no significant difference between groups in age, BMI, education, the score of QOL fields, depression and anxiety scores (P>0.05) (Table 1).

b) Severity of PMS, depression and anxiety

Table 2 shows a significant decrease in the number of PMS symptoms (moderate to severe) according to PSTT in LIV3 (23 vs. 21) and LI4 (18 vs. 16) compared with the placebo group (30 vs. 29) after intervention (second and third cycles) (P<0.05).

Moreover, there was a significant difference in depression score in the second and third cycles in LIV3 (11.50±2.16 vs. 10.17±0.46) and LI4 (11.60±2 vs. 10.36±2.23) compared with the placebo group (12.33±0.72 vs. 11.46±2.54) (P<0.05) (Table 3).

There was a significant difference in anxiety score in the second and third cycles in LIV3 (9.73±1.52 vs. 9.43±1.13) and LI4 (10.20±2.48 vs. 10.90±6.33) compared with the placebo group (9.22±2.02 vs. 8.72±2.90) (P<0.05) (Table 3).

The Sheffe test showed no significant difference between LIV3 and LI4 groups in severity of PMS, depression and anxiety (P>0.05).

c) Quality of life

There was a significant difference between groups in all fields of quality of life (P<0.05). Table 4 shows that QOL score was better in LIV3 and LI4 acupressure groups compared with the placebo.

The Sheffe test showed no significant difference between LIV3 and LI4 groups in QOL (P>0.05).

Discussion

The current study is the first study which evaluates the effect of applying acupressure in two separate acupointsLIV3 and LI4 in comparison with placebo on QOL in women with PMS. The results show the number of PMS cases (moderate/severe) according to PSST scale significantly decreased in acupressure groups compared with the placebo in the second and third menstrual cycles. In other words, the severity of PMS symptoms according to PSST scale dramatically decreased in acupressure groups. In a study of Fong etal (date) the PMS signs and symptoms improved in acupuncture groups of LR3, CV4, 6, SP6, GV24 acupoints in comparison with the control group (using herbal medications)(21).Habek et al reported that PMSsymptoms significantly decreased ($p<0.001$) in acupuncture groups (Shemun, BT23, GB39, PC6, CV3,4,10, LK3, LI4 and GV_2acupoints) compared with the control group (acupuncture sham)(22). However, acupuncture is associated with some complications such as pain, and bleeding at the puncture site, damage to internal organs, and increasing the risk of infectious disease such as hepatitis and AIDS. Acupressure has no side effects and disadvantages even in the case of incomplete performance. Acupressure is a non-invasive treatment method, easy to apply, and it can be done by individual.

Xuand Sun(2006) showed that PMS severity was significantly decreased in intervention group (acupuncture in the acupoints of GV3,4,5,6,7,8, BL18,23,47,49,50,52for 14 days before menstruation during three cycles) in comparison with the control group (Medroxyprogestron acetate 6 µgr/ day from 16^{th}d to 25^{th} day ofmenstrual cycle) ($p<0.001$)(23). Although, in our study intervention done by individuals themselves in the third cycle and only one acupoint is allocated to each intervention group in order to avoid participant's confusion.

Acupressure and acupuncture provide more relaxation and less tension. Moreover, acupressure decreases blood levels of serotonin, increases endorphins and neuro-peptide Y; stimulates the nerves located inmuscle and other tissues, and helps release endorphins and other neuro-hormones. Acupressure can also change the pain process in the brain and spinal cord, and reduce information by stimulating the release of vascular and immunity factors(22).

In this study, the QOL score was better in all subscales in acupressure groups compared with the control group which is probably due to the improved physical and mental health in the acupressure groups. This is the first study to show this finding. Moreover, the level of

depression and anxiety in the acupressure groups significantly decreased compared with the placebo group. This finding was similartothe results of the previous studies reporting that acupressure reduces depression in hemodialysis patients (25), chronic pulmonary obstruction disease(26), and chronic knee pain in the patients of elderly care centers(27). Acupoint stimulation increases the release of serotonin and endorphins, and regulates the level of serum cortisol. These hormonal changes reduce depression and result in more relaxation which directly changes the mechanisms leading to depression(28).

The strengths of the present study include following-up the subjects during three consecutive menstrual cycles, considering the placebo group, and applying pressure on the placebo point similar to the intervention groups in order to continuous meridian stimulation. The present study had some limitations. Oral, written, and practical training were used in this study to help subjects identify the location of acupoint and learn the pressing technique. We studied the students of one university while the results may vary with the results obtained from young women with lower education level or other ethnic groups in other universities. Randomized studies with larger sample size and longer follow-up period would improve the existing knowledge on the benefits and mechanism of acupressure in PMS.

Funding

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RCT code

IRCT2016060828038N2 (http://www.irct.ir/searchresult.php?keyword=IRCT2016060828038N2&id=28038&number=2&field=a&prt=1&total=1&m=1)

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Figure 1: flow chart of study

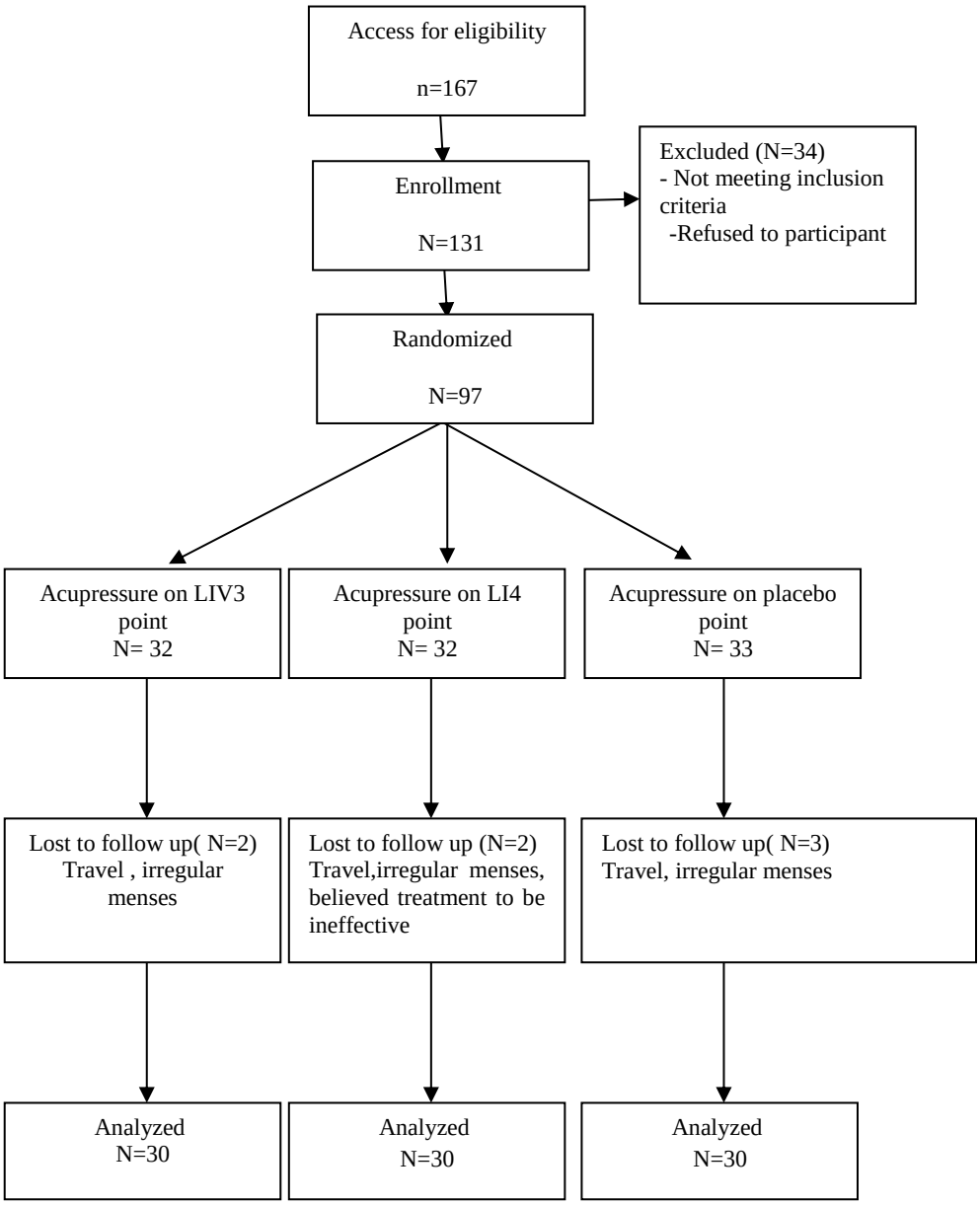

Figure 2: Location of LI4 point

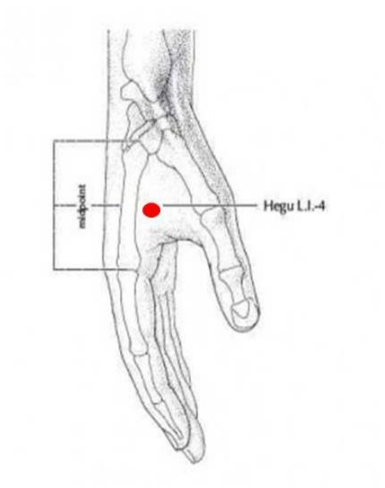

Figure 3: Location of LIV3 point

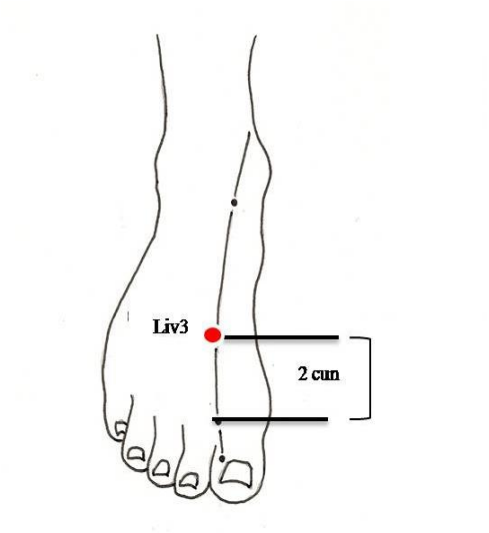

Figure 4: Location of placebo point

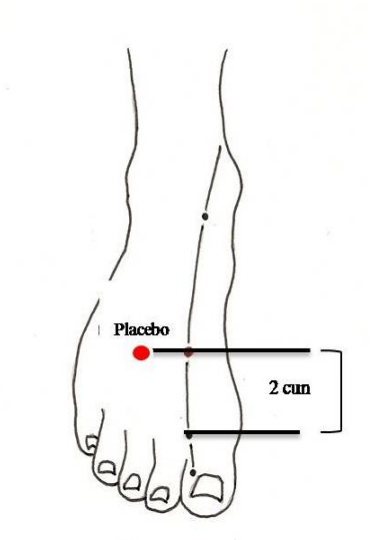

Table1: Demographic and baseline characterizes of participants

Variable		Group			P value
		placebo	Liv_3	LI_4	
Age (years)**		22.06±1.86	21.77±1.18	22.03±1.97	0.79
Education (years)**		15.68±0.96	16±1.2	15.23±0.89	0.8
BMI**		19.598±2.41	19.45±2.18	19.70±3.07	0.15
HADS**	Anxiety	10.79±2.04	10.72±1.25	10.36±7.70	0.7
	Depression	11.31±1.78	11.51±1.24	11.36±7.86	
SF12 domains**	PF	63.33±22.10	66.96±25.39	65±23.67	0.09
	RP	63.79±31.04	67.02±12.49	62.08±23.32	0.47
	RE	71.98±26.01	74.16±13.10	62.50±25.21	0.51
	VE	75.83±12.25	69.13±23.60	69.83±12.45	0.87
	SF	45.50±12.01	50±25.87	48.33±23.42	0.27
	BP	65.34±20.61	67.50±12.01	68.33±23.61	0.6
	GH	65±16.86	70.55±24.75	69.16±20.43	0.52
	MH	70.86±24.76	66.66±7.14	64.58±18	0.07
	MSC	63.22±9.44	65.17±18.47	68.64±15.53	0.53
	PSC	66.66±8.42	65.49±9.13	66.56±12.23	0.64

**Mean±SD

physical functioning (PF), role limitations due to physical problems (29), bodily pain (BP), general health perception (GH), social functioning (SF), role limitations due to emotional problems (RE), vitality (VT), and mental health (MH), mental subscale component (MSC), physical subscale component (PSC)

Table2: PSST scores in the second &third cycles between groups

Variable*		Group			P value**
		Placebo	Liv_3	LI_4	
Second cycles	NO/Mild	_	6(24.15)	12(40)	0.001
	Moderate/severe	30(100)	23(79.3)	18(60)	
Third cycles	NO/mild	1(3.3)	9(31)	14(46.7)	<0.001
	Moderate/severe	29(96.7)	21(72.45)	16(53.3)	

**ANOVA

*Mean±SD

Table 3: HADS Scores in the second & third menstrual cycles between groups

Variable**		groups			P value*
		placebo	Liv_3	LI_4	
Second Cycle	Anxiety	9.22±2.02	9.73±1.52	10.20±2.48	<0.001
	Depression	12.33±0.72	11.50±2.16	11.60±2	0.02
Third Cycles	Anxiety	8.72±2.90	9.43±1.13	10.90±6.33	<0.001
	Depression	11.46±2.54	10.17±0.46	10.36±2.23	0.05

*ANOVA

**Mean± SD

Table 4: quality of life subscales in the second & third menstrual cycles between groups.

Variable**		groups			P value*
		placebo	Liv_3	LI_4	
Second Cycle **	PF	75±32.04	65.83±23.19	64.83±32.48	0.01
	RF	70.25±25.11	85.83±15.65	82.50±21.52	0.01
	RE	63.33±25.41	78.75±10.03	63.33±25.41	0.01
	VE	56.25±25.11	65.83±15.65	62.50±21.52	0.04
	SF	51.55±14.52	57.93±28.83	55±25.08	0.05
	BP	60.34±21.66	81.66±11.24	87.50±18.74	0.01
	GH	69.50±28.35	78.33±10.45	76±21.21	0.01
	MH	50.89±13.99	54.16±5.99	52.50±11.08	0.04
	PSC	70.47±18.23	78.68±8.75	76.29±17.22	0.05
	MSC	53.79±12.18	62.50±6.78	63.33±17	0.03
Third Cycles**	PF	65.83±28.97	80.17±27.04	94.16±12.40	<0.001
	RP	65.66±245.98	89.39±28.65	90±9.5	<0.001
	RE	67±23.11	72.41±11.87	70.08±32.15	0.01
	VE	58.62±28.56	59.16±12.60	61.66±6.04	0.04
	SF	29.16±10.75	34.16±24.98	33.31±26.78	0.05
	BP	74.83±22.84	87.69±20.50	84.86±23.60	0.05
	GH	70.83±22.82	87.50±20.52	85.86±24.20	0.02
	MH	79.43±27.42	90±12.45	90.86±17.96	<0.001
	PSC	67.29±17.59	90.41±7.99	92.67±20.15	<0.001
	MSC	52.34±10.01	69.87±4.47	69.27±10.59	<0.001

*ANOVA

**Mean ± SD

physical functioning (PF), role limitations due to physical problems, bodily pain (BP), general health perception (GH), social functioning (SF), role limitations due to emotional

problems (RE), vitality (VT), and mental health (MH), mental subscale component (MSC), physical subscale component(PSC).