



Research Article

Acupressure as an Adjunct to Pharmacological Treatment for Depression, Anxiety, and Stress in Patients with Knee Osteoarthritis

Meenu Rani, Lokendra Sharma*, Uma Advani, Susheel Kumar

Department of Pharmacology, Sawai Man Singh Medical College, Jaipur, Rajasthan, 302004, India

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ABSTRACT

Background: Osteoarthritis is the most common type of arthritis. Depression, anxiety, and stress are associated with knee osteoarthritis.

Objectives: The aim of the study was to check the effectiveness of acupressure therapy with pharmacological treatment on pain, depression, anxiety, and stress in patients with knee osteoarthritis and to assess the effect of pain improvement on psychological health.

Methods: Eligible 212 patients with knee osteoarthritis were divided into two groups (intervention and control group). The intervention group (n = 106) received acupressure therapy in combination with pharmacological treatment, whereas the control group (n = 106) continued pharmacological treatment only. Pain and psychological symptoms were measured using the visual analog scale and Depression Anxiety Stress Scale-21. Pearson's correlation was used to check the effect of pain improvement on psychological health.

Results: Patients of both groups reported severe pain initially. On analyzing the results after completion of the study, it was found that patients in the intervention group scored better on the pain scale ($p < 0.001$) and DASS-21 ($p \leq 0.0001$). However, it may be noted that reduction in the DASS-21 score was not found to be significant for the control group ($p = 0.08$). Pearson's correlation coefficients value ranged from 0.231 to 0.412 for DASS-21 ($p < 0.05$).

Conclusions: On analysis, it can be concluded that acupressure can be used as add-on therapy in combination with conventional treatment (pharmacological treatment), which may assist in pain reduction. The reduction in pain directly contributes to improvement in the physiological wellness among patients with knee osteoarthritis.

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1. Introduction

Knee osteoarthritis is most frequently reported form of arthritis among the elder and middle-aged population. It is a kind of degenerative disease in joints, which leads to breakdown of cartilage and bones. Prevalence of knee osteoarthritis increases among old people owing to physiological changes in the musculoskeletal system [1], which leads to destruction and degeneration of joints. Restricted daily activities in patients are detriments of poor quality of life [2] and poor mental health [3, 4]. The knee pain and poor physical functions are one of the major factors that cause

depression and anxiety among patients with knee osteoarthritis. These comorbidities (depression and anxiety) decline physical activities and social and psychological life of the patients [5]. A limited number of studies are available that have examined relationship between pain and development of depressive symptoms [6, 7]. Depression associated with knee osteoarthritis may worsen pain symptoms and further deteriorate physical activities [6, 7].

Symptoms of knee osteoarthritis can be managed by using pharmacological treatment although patients also opt for alternative therapies, which may be effective and safe [8, 9]. Yoga, acupuncture, Tai chi, massage, and acupressure are commonly used complementary and alternative therapies [10]. Acupressure therapy is used in many pain conditions such as dysmenorrhea pain, labor pain, and various joint pains [11, 12]. It works similar to acupuncture therapy to maintain vital energy (chi/Qi) of the body through the meridian system [11, 12]. Instead of needles, fingers or elbows are used to stimulate the acupoints in acupressure

* Corresponding author. Department of Pharmacology, Sawai Man Singh Medical College, Jaipur, Rajasthan, 302004, India.

E-mail addresses: meenusaharan23@gmail.com (M. Rani), drlokendra29@gmail.com (L. Sharma), drupadvani@gmail.com (U. Advani), susheelpn72@gmail.com (S. Kumar).

treatment [13]. Manipulation of acupoints can be done to balance the vital energy flow, which manages the dysfunctions [14]. As per modern medical science, acupressure works by stimulating acupoints that balance the concentration of neurotransmitters and hormones in the neural system. This phenomenon leads to reduction in anxiety and depression [15]. Some studies have been conducted to explore the effectiveness of acupressure for anxiety and depression management [16, 17].

The present study investigates and compares the effect of acupressure therapy in combination with pharmacological treatment on depression, anxiety, and stress among patients with knee osteoarthritis. Association between knee pain and development of depressive symptoms is evaluated during the study. Depression, anxiety, and stress symptoms are assessed by using Depression Anxiety Stress Scale-21 (DASS-21) and the most commonly used questionnaire for assessment of psychological symptoms in nonclinical and clinical practice [18].

2. Materials and methods

2.1. Study strategy

The nonblinded comparative study was conducted on patients with knee osteoarthritis. The approval was taken from the institutional ethics committee (reference number: 3706/MC/EC/2018 dated on 26/02/2018). Prospective patient consent was obtained in written form. A total of 212 patients were recruited from the outdoor clinic of the orthopedic department. Recruited patients with knee osteoarthritis were randomly divided into the intervention group ($n = 106$) and control group ($n = 106$). Randomization was performed by flipping a coin, wherein heads indicate the intervention group and tails indicate the control group. Intervention group patients took acupressure as add-on therapy to the pharmacological treatment (nonsteroidal anti-inflammatory drugs), whereas control group patients continued usual pharmacological treatment.

2.2. Population of the study

2.2.1. Inclusion and exclusion criteria of the study

The inclusion criteria were as follows: (1) patients aged (both genders) from 45 to 70 years, (2) patients with unilateral knee osteoarthritis (from the last 5–6 months), (3) patients scoring grade 2 and grade 3 on the Kellgren–Lawrence scale, and (4) patients having a pain score ≥ 2 on the visual analog scale (VAS).

The exclusion criteria were as follows: (1) patients taking intra-articular injection to manage knee osteoarthritis, (2) patients taking acupressure or acupuncture treatment for knee osteoarthritis, (3) patients who underwent knee replacement, (4) pregnant females, and (5) patients having rheumatoid arthritis and other autoimmune disorders.

2.3. Acupressure intervention

A protocol for acupressure technique was designed by the investigators on the basis of literature review [19]. The self-designed protocol was checked and approved by two trained and qualified acupuncturists. The principles of the self-designed protocol were as follows: Pressure on selected acupoints was performed with the help of the fingertip. A total of six acupoints (ST34, ST35, ST36, SP9, SP10, and GB34) [20] were chosen to reduce the pain level among patients with knee osteoarthritis. Accuracy of applied pressure on each acupoint was confirmed by feeling of soreness, numbness, heaviness, distention, and warmth. The total duration of each session of acupressure therapy was limited to 15 minutes,

consisting of 3 minutes of initial message around acupoints and 12 minutes of pressure applied on acupoints (2 minutes for each acupoint). Frequency of acupressure application was two times a day for five days in a week, for which a record was kept by patients in the logbook.

The patients were given 3 training sessions (two acupressure training sessions and one conclusion session) to get trained in self-administered acupressure therapy. The first training session was conducted during the first week of the study, in which the acupressure procedure was taught by the investigator to the patients as per the protocol. At the end of this session, almost all patients revealed expertise in acupressure technique. A self-designed booklet on the acupressure protocol was also distributed to the patients for reference. The second training session of acupressure was initiated during the second week. A basic review on acupressure therapy was imparted again to the patients, which was followed by a doubt-clearing session. To assess the understanding, feedback was taken from the participants. Finally, a concluding session was conducted during the third week, wherein the logbook maintained by the patients was evaluated for adherence. In addition, the side effect of acupressure therapy if any was inquired.

2.4. Classification of patients as per VAS score improvement

To correlate VAS (pain) improvement with that of DASS-21, patients of both the groups were subcategorized into four groups depending on VAS improvement from baseline (i.e. $<10\%$ improvement in pain, ≥ 10 to $<25\%$ improvement in pain, ≥ 25 to $<50\%$ improvement in pain, and $\geq 50\%$ improvement in pain).

2.5. Measurement tools

The VAS and DASS-21 were used as measurement tools. The VAS ranged from 0 (no pain) to 10 (worst pain). DASS-21 contains 21 questions, 7 questions in each parameter (depression, anxiety, and stress). Each question of DASS-21 was scored from 0 (does not apply to me at all) to 3 (applied to me very much or most of the time). The total score and score of each parameter (depression, anxiety, and stress) were obtained as mentioned by Lee et al. [18].

2.6. Estimation of the sample size

An 8-week pilot study was conducted on 24 participants (12 in the intervention and 12 in the control group) for sample size calculation. The evaluated mean difference and standard deviation (pain scores of the VAS) before and after intervention were -6.2 and 14.8 . Two-tailed group comparison equation for evaluating the sample size is given by Eq. 1.

$$n = \frac{2S^2(Z_{\alpha/2} + Z_{\beta})^2}{(\mu_1 - \mu_2)^2} \quad (1)$$

where $Z_{\alpha/2}$ is 1.96, Z_{β} is 0.84, $\mu_1 - \mu_2$ is -6.2 , and S is 14.8.

To maintain 80% power and 0.5 type 1 error, a minimum of 89 participants is needed for the intervention and control group. A total of 212 participants were enrolled in the present study (considering a 20% dropout rate).

2.7. Data collection and evaluation

Demographic data were collected by using a self-developed questionnaire. Initially, VAS and DASS-21 data were collected and compared at baseline. Subsequently, the records (VAS and DASS-

21) were evaluated during the follow-up period (2 months of follow-up, 4 months of follow-up, 6 months of follow-up, and 8 months of follow-up).

2.8. Analysis of data

IBM SPSS software, version 21 (Chicago, USA[®]), was used for analysis. Before evaluation, all records were checked for normal distribution, missing values, outliers, and extreme values. Continuous data were denoted as mean and standard deviation, and categorical data were represented in the form of frequency and percentage at baseline. It may be noted that data of age and body mass index at baseline were not distributed normally; therefore, a nonparametric test (Mann–Whitney U test) was used to evaluate its characteristics. The remaining data at baseline were evaluated and compared by using the Chi-square test. Data of the VAS and DASS-21 of both groups were compared by using the Student t-test at each time. The effects of therapy over time in both groups were analyzed by performing repeated measure analysis of variance. To check the effect of pain improvement on depression, anxiety, and stress, Pearson's correlation coefficient was used. Correlations between pain improvement and symptoms of depression, anxiety, and stress were analyzed by Pearson's correlation coefficient. The score of all the subcategories of pain was correlated with improvement in DASS-21 using Pearson's correlation coefficient. The intention-to-treat design was used. The significance level was set at a *p*-value less than 0.05.

3. Results

A total of 212 patients were selected for the study. The dropout rate of the study was 3.77% (8 from the intervention group and 3 from the control group, as shown in Fig. 1). The mean age of all the selected patients was 58.07 ± 11.2 years. The duration of the knee osteoarthritis disease was 5.11 for the intervention group and 4.87 for the control group, which is nearly similar. The average rate of consumption of nonsteroidal anti-inflammatory drugs was similar for both the groups. The common comorbid diseases were hypertension ($n = 135$, 63.6%) and diabetes ($n = 77$, 36.3%). The statistical data related to comparison of baseline characteristics have been provided in Table 1. It may be noted that no significant difference was observed for baseline parameters between the intervention and control group ($p > 0.05$).

Patients of both the intervention and control group experienced severe pain at baseline (8.97 ± 5.27 , 8.12 ± 4.67). A significant decrease in the VAS pain score was observed for the intervention group for the second month (T_1) until the last follow-up of the study (T_4) ($p < 0.001$). The VAS pain score reduced by 24.4% at T_1 , 34.6% at T_2 , 42.9% at T_3 , and 53.4% at T_4 when compared from baseline. It may be noted that improvement in the pain score was also observed for the control group but comparatively less than for the intervention group ($p > 0.05$).

The record of the DASS-21 score was analyzed to assess the physiological symptoms (depression, anxiety, and stress). Of the total of 212 patients, 48.1% experienced depression, 28.3% experienced anxiety, and 25.5% experienced stress. Depression among patients could be further classified into four categories based on the severity [extremely severe depression (3.9%), severe depression (2.9%), moderate depression (51.9%), and mild depression (41.1%)]. Likewise, the anxiety score [extremely severe anxiety (3.3%), severe anxiety (3.3%), moderate anxiety (41.6%), and mild anxiety (51.6%)] and stress score [extremely severe stress (2.0%), severe stress (4.0%), moderate stress (46.1%), and mild stress (48.0%)] were divided into four subtypes based on the level of intensity.

Comparison of DASS-21 scores (depression, anxiety, and stress) has been carried out for the intervention and control group (Table 2 and Table 3). Baseline scores of depression, anxiety, and stress were found to be comparable ($p > 0.05$). A total of 30.5% reduction in the DASS-21 score (40.85 ± 22.32 at baseline, 28.36 ± 18.76 after completion of treatment) was reported among intervention group patients, which is higher than that among control group patients ($p = 0.08$). Mean scores of depression, anxiety, and stress scored better for intervention group patients ($p < 0.05$).

For analysis, patients of both the groups were classified into four subgroups on the basis of pain improvement starting from baseline (Fig. 2). Approximately 47% patients of the intervention group showed $\geq 50\%$ improvement in pain from T_0 to T_4 (47.1% versus 29.3% respectively, odds ratio: 2.17). Nearly 58% patients of the intervention group reported $\geq 25\%$ improvement from T_0 to T_4 (58.2% versus 43.7%, odds ratio: 1.83).

Relationship between magnitude of pain (VAS) and symptoms of depression, anxiety, and stress is shown in Fig. 3. Magnitude of pain showed moderate correlation with symptoms of depression ($r = 0.320$, $p = 0.008$), anxiety ($r = 0.231$, $p = 0.01$), and stress ($r = 0.246$, $p = 0.01$). The correlation between pain level and psychological symptoms in the intervention group was found to be statistically higher than in the control group. Among all the psychological variables (depression, stress, and anxiety), highly significant relation was found between depression and pain improvement ($p = 0.008$). Patients of the intervention group reported more improvement in pain (≥ 50) and better mental health (DASS-21 score) ($r = 0.412$, $p = 0.0001$).

4. Discussion

The present study found more prevalence of depression (approximately 50%) in patients with knee osteoarthritis. However, occurrence of both anxiety and stress among patients with knee osteoarthritis (approximately 33.5%) is comparatively lower than occurrence of depression symptoms.

It was found that the pain score reduced significantly among participants receiving acupressure with pharmacological treatment. The results of the analysis obtained in the present study is similar to those obtained in the study by Li et al. [21], wherein a significant improvement in the WOMAC pain score and NRS score was noticed among patients with knee osteoarthritis in the intervention group.

Patients with knee osteoarthritis suffer from depression symptoms owing to less physical activity [22]. As a consequence, psychological and physical health of the patient gets deteriorated [23]. Therefore, a reduction in pain alleviates depression-related symptoms among patients with osteoarthritis [24]. Acupressure therapy improved the depression score in intervention group participants. This could be attributed to reduction in pain, which improves physical activities and makes them more self-dependent.

Anxiety is another major psychological symptom that affects social and emotional well-being of patients with knee osteoarthritis. Honda et al. [25] concluded that self-administered acupressure therapy lowers the level of depression and anxiety. Later, Beikmoradi et al. [16] noticed improvement in the anxiety score after applying acupressure. Recently, Fadawy et al. [17] reported reduction in both the anxiety and depression level in patients with knee osteoarthritis. In the present study, a similar trend was observed, wherein the level of anxiety was found to be less in patients receiving acupressure as an add-on therapy with pharmacological treatment. This can be attributed to the lower pain level, which directly affects the anxiety level. Moreover, acupressure therapy may produce relaxation and decrease sympathetic

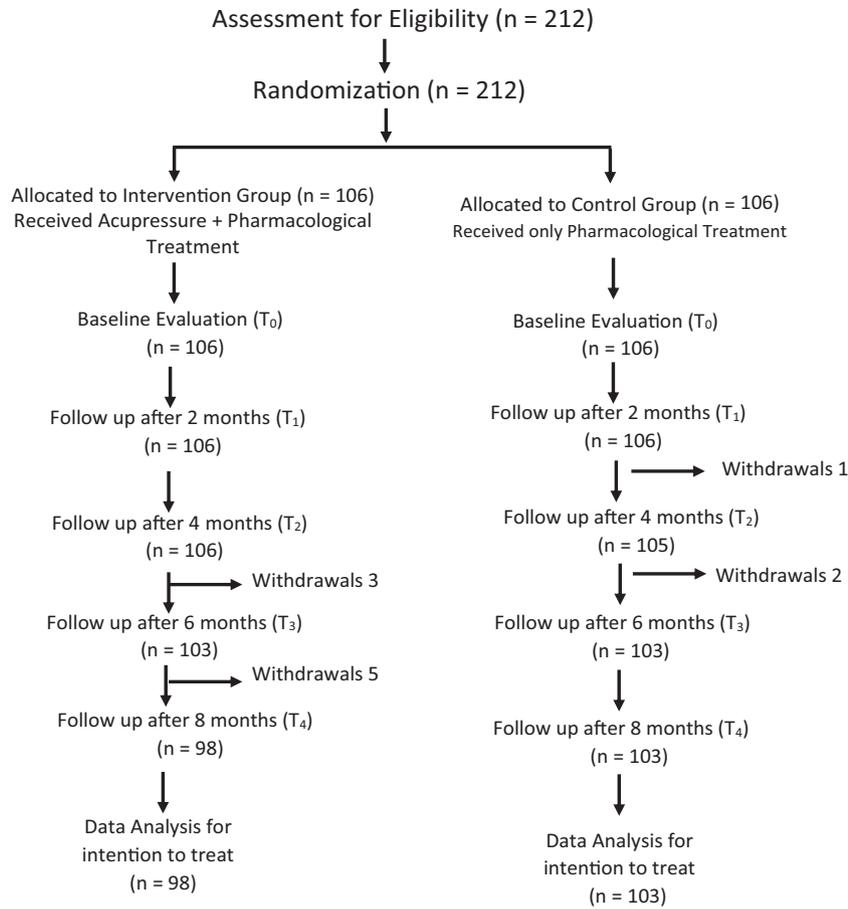


Figure 1. Consort flow chart indicating the participants' screening, allocation, follow-up, and analysis.

Table 1
Comparison of baseline characteristics of the intervention and control group.

Participant's characteristics	Total sample (n = 212)	Intervention group (n = 106)	Control group (n = 106)	p
Age	58.07 ± 11.2	57.82 ± 11.61	59.21 ± 9.87	0.37 [*]
Gender				
Male	49.62%	47.98	53.26	0.44
Female	50.38	52.02	46.74	
Body mass index	29.21 ± 14.67	30.15 ± 8.72	28.13 ± 9.26	0.10 [*]
Knee affected				
Right knee	51.08%	52.72%	51.25%	0.83
Left knee	48.92%	47.28%	48.75%	
Employment				
Employed	45.17%	42.43%	44.82%	0.86
Retired	47.23%	46.89%	45.73%	
Other	7.60%	10.68%	9.45%	
Comorbidity score[†]				
0	17.34%	12.72%	20.98%	0.54
1	49.60%	54.98%	50.81%	
≥2	33.06%	32.30%	28.21%	

The Chi-square test was applied for comparison of all baseline data except age and body mass index.

^{*} The significance level was checked by using the Mann–Whitney U test.

[†] The Charlson index was used to measure the comorbidity score.

system activities, which also leads to decrease in the anxiety level [26].

Pain directly affects psychological symptoms (depression and anxiety) in patients with knee osteoarthritis. In the present study, patients of the acupressure group were classified into different groups on the basis of improvement in the VAS pain score. A strong

correlation was observed between pain improvement and total score of DASS-21 ($r = 0.412$). It was found that the group showing maximum improvement in the VAS pain score also showed largest improvement in DASS-21 scores.

It was found that acupressure therapy in combination with pharmacological treatment further reduces depression, anxiety,

Table 2
Comparison of mean scores of pain and DASS-21 for the intervention and control group at different time periods.

Characteristics	T ₀	T ₁	T ₂	T ₃	T ₄	p [†]
VAS pain						
Intervention group	8.97 ± 5.27	6.96 ± 3.46	5.86 ± 3.87	5.12 ± 2.65	4.18 ± 2.11	<0.001
Control group	8.12 ± 4.67	7.89 ± 3.24	7.67 ± 4.31	7.43 ± 4.11	7.31 ± 2.45	0.10
p [*]	0.21	0.04	0.001	<0.001	<0.001	-
Depression						
Intervention group	14.56 ± 8.63	14.28 ± 8.67	13.45 ± 7.89	12.32 ± 4.56	10.98 ± 4.34	0.001
Control group	16.54 ± 9.87	16.42 ± 8.90	15.61 ± 6.84	15.28 ± 5.78	14.56 ± 4.23	0.14
p [*]	0.12	0.07	0.03	0.0001	<0.0001	-
Anxiety						
Intervention group	9.78 ± 5.18	9.34 ± 5.12	6.98 ± 4.87	6.12 ± 7.98	5.87 ± 4.20	<0.0001
Control group	8.76 ± 5.29	8.12 ± 5.58	8.35 ± 4.18	7.67 ± 4.34	7.55 ± 4.89	0.25
p [*]	0.15	0.09	0.02	0.01	0.01	-
Stress						
Intervention group	16.51 ± 9.85	15.23 ± 9.78	14.34 ± 9.87	12.86 ± 8.67	11.51 ± 8.13	0.001
Control group	17.65 ± 8.25	17.16 ± 7.81	16.43 ± 7.64	15.97 ± 6.78	15.87 ± 7.45	0.36
p [*]	0.36	0.11	0.08	0.004	0.0009	-
DASS-21, total						
Intervention group	40.85 ± 22.32	38.85 ± 22.34	34.77 ± 21.47	31.30 ± 20.85	28.36 ± 18.76	<0.0001
Control group	42.95 ± 22.47	41.70 ± 24.65	40.39 ± 25.31	38.92 ± 24.78	37.98 ± 17.25	0.08
p [*]	0.49	0.37	0.08	0.01	0.0001	-

DASS-21 = Depression Anxiety Stress Scale-21; T₀ = data at baseline; T₁ = follow-up after 2 months; T₂ = follow-up after 4 months; T₃ = follow-up after 6 months; T₄ = follow-up after 8 months; VAS = visual analog scale.

* Mean scores of both groups compared by using the Student t-test at each time point.

† Repeated measure analysis of variance was performed.

Table 3
Comparison of mean scores of DASS-21 and pain for the intervention and control group from baseline.

Outcome measures	Intervention group				Control group			
	p-value [*]							
	(T ₀ vs T ₁)	(T ₀ vs T ₂)	(T ₀ vs T ₃)	(T ₀ vs T ₄)	(T ₀ vs T ₁)	(T ₀ vs T ₂)	(T ₀ vs T ₃)	(T ₀ vs T ₄)
VAS	0.001	<0.0001	<0.0001	<0.0001	0.67	0.46	0.25	0.11
Depression	0.81	0.32	0.01	0.0002	0.92	0.42	0.25	0.09
Anxiety	0.55	0.002	<0.0001	<0.0001	0.39	0.53	0.10	0.08
Stress	0.30	0.12	0.004	<0.0001	0.65	0.26	0.10	0.10
DASS-21, total	0.51	0.04	0.001	<0.0001	0.70	0.43	0.21	0.08

DASS-21 = Depression Anxiety Stress Scale-21; (T₀ vs T₁) = comparison of the baseline score versus follow-up (2 months) mean score; (T₀ vs T₂) = comparison of the baseline score versus follow-up (after 4 months) mean score; (T₀ vs T₃) = comparison of the baseline score versus follow-up (after 6 months) mean score; (T₀ vs T₄) = comparison of the baseline score versus follow-up (after 8 months) mean score; VAS = visual analog scale.

* The Student t-test was used for comparison of baseline data.

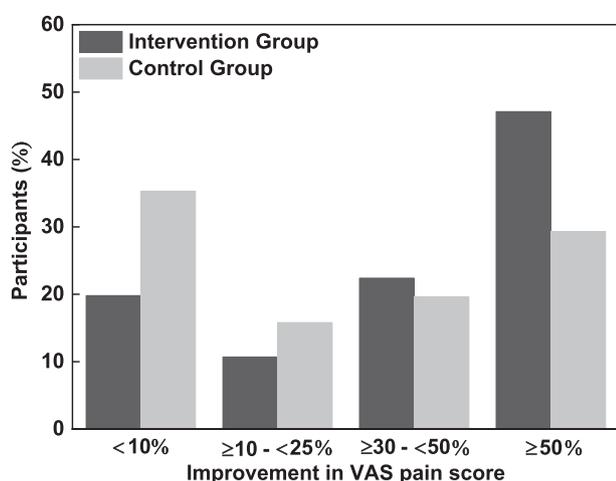


Figure 2. Categorization of the participants of both groups on the basis of pain improvement from baseline to the 8th month of the study. VAS = visual analog scale.

and stress. Acupressure acts by regulating functions of hormones and neurotransmitters by stimulating acupoints [27]. Consistent pressure by the fingertip on acupoints regulates nervous system

functions, which leads to improvement in psychological and general health [27].

Therefore, clinicians may implement acupressure therapy with conventional treatment in patients with knee osteoarthritis to manage pain and improve psychological illness. Furthermore, this noninvasive therapy can be self-administered by patients suffering from knee osteoarthritis.

4.1. Limitations

One of the limitations of this study is that blinding technique could not be taken into account because the primary researcher was involved in all the processes. A lack of blinding may overestimate the effect of acupressure as an adjunct to medication. In addition, the participants were not blinded, and subjective outcomes such as stress and anxiety may have introduced performance bias. Another limitation is that the sample size was computed on the basis of difference in the VAS score. The VAS score was calculated using a smaller number of patients owing to lack of relevant literature. Finally, the data collected for pain, depression, anxiety, and stress are subjective in nature, which makes their quantification quite challenging.

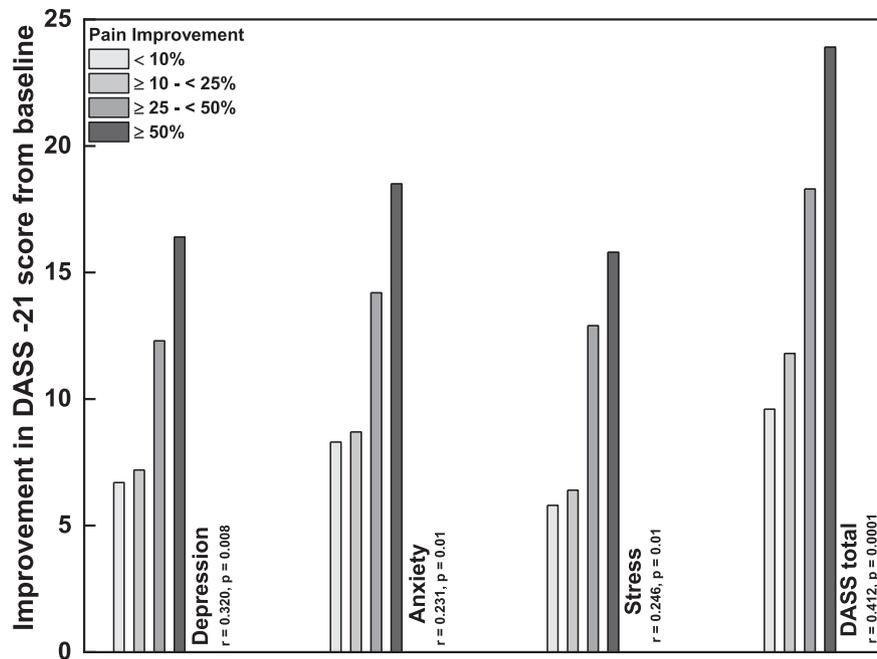


Figure 3. Improvement in the DASS-21 score from baseline in participants of the intervention group categorized into four groups on the basis of pain improvement. The r-value symbolizes Pearson's correlation coefficient. DASS-21: Depression Anxiety Stress Scale-21.

5. Conclusion

From the present study, it can be concluded that acupressure in combination with pharmacological treatment improves psychological and general health of patients with knee osteoarthritis. This is due to reduction in pain, which has proportional effect on psychological health. Therefore, acupressure as an add-on therapy is recommended with conventional treatments to control psychological symptoms (depression, anxiety, and stress) more efficiently. The study gives a prospect for implementing alternative and complementary therapies (acupressure and acupuncture) to improve quality of life.

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Declaration of competing interest

None.

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