Pain Reduction After Laser Acupuncture Treatment in Geriatric Patients with Knee Osteoarthritis: a Randomized Controlled Trial

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ABSTRAK

Tujuan: membandingkan efektivitas laserpunktur aktif dengan plasebo dalam menurunkan intensitas nyeri dan perbaikan fungsional pada pasien geriatri dengan osteoartritis (OA) genu. *Metode:* uji klinis acak dengan kontrol tersamar ganda dilakukan pada pasien geriatri dengan OA genu di poliklinik Akupunktur Medik, poliklinik Geriatri Terpadu serta poliklinik Reumatologi RS. Cipto Mangunkusumo, Jakarta, periode Mei 2015 – Oktober 2015. Enam puluh dua pasien OA genu secara acak dibagi menjadi dua kelompok: kelompok laserpunktur aktif atau kelompok laserpunktur plasebo. Intervensi menggunakan laser gallium aluminium arsenida pada titik ST35 Dubi, ST36 Zusanli, SP9 Yinlingquan, GB34 Yanglingquan dan EX - LE - 4 Neixiyan, pada lutut yang terdiagnosis OA selama 10 sesi terapi, dua kali seminggu. Visual Analogue Scale (VAS) dan indeks Lequesne digunakan untuk mengukur keluaran penelitian yang dinilai pada saat sebelum perlakuan, setelah 4 sesi, setelah 9 sesi dan 2 minggu pasca perlakuan dihentikan. *Hasil:* terdapat perbaikan luaran VAS yang bermakna pada kelompok laserpunktur aktif dibandingkan dengan kelompok laserpunktur plasebo pada penilaian setelah 4 sesi (beda rerata 0,39; p<0,001), setelah 9 sesi (beda rerata 37,48; p<0,001) dan 2 minggu pasca perlakuan dihentikan (beda rerata 39,15; p<0,001). Terdapat perbaikan keluaran indeks Lequesne yang bermakna pada kelompok laserpunktur aktif dibandingkan dengan kelompok laserpunktur plasebo pada penilaian setelah 4 sesi (beda rerata 4,68; p<0,001), setelah 9 sesi (beda rerata 5,90; p<0,001) dan 2 minggu pasca perlakuan dihentikan (beda rerata 6,48; p<0,001). *Kesimpulan:* laserpunktur aktif efektif dalam menurunkan intensitas nyeri.

Kata kunci: osteoartritis genu; laserpunktur; VAS; indeks Lequesne.

ABSTRACT

Aim: to compare the effectiveness of active laser acupuncture with placebo on reducing pain intensity and improving functional outcome in geriatric patients with knee osteoarthritis (OA). *Methods:* a double-blind randomized controlled trial was conducted in geriatrics with knee OA at Medical Acupuncture Outpatient Clinic, Integrated Geriatric Outpatient Clinic, Rheumatology Outpatient Clinic of Cipto Mangunkusumo Hospital, Jakarta, during May to October 2015. Sixty two patients with knee OA were randomly assigned into two groups: active laser acupuncture group or placebo laser acupuncture group. Interventions were carried out using a gallium aluminum arsenide laser device at the ST35 Dubi, ST36 Zusanli, SP9 Yinlingquan, GB34 Yanglingquan and EX - LE - 4 Neixiyan acupuncture points on the affected knee for ten sessions of treatment,

i.e. twice a week. Patients were assessed using a visual analogue scale (VAS) and Lequesne index at baseline, after four sessions, after nine sessions and at 2 weeks after the treatment had been stopped. **Results:** *the VAS scores were significantly improved in the active laser acupuncture group compared to the placebo group. The evaluation of VAS scores was carried out after four treatment sessions (mean difference: 0.39; p<0.001), after nine treatment sessions (mean difference: 37.48; p<0.001) and at 2 weeks post intervention (mean difference: 39.15; p<0.001). The evaluation also showed significant improvement of Lequesne index after four treatment sessions (mean difference: 4.68; p<0.001), after nine treatment sessions (mean difference: 5.90; p<0.001) and at 2 weeks post intervention (mean difference: 6.48; p<0.001).* **Conclusion:** *active laser acupuncture is effective in reducing pain.*

Keywords: knee osteoarthritis, laser acupuncture, VAS, Lequesne index.

INTRODUCTION

Knee osteoarthritis (OA) is the most common form of arthritis and a leading cause of impaired mobility in elderly. The prevalence of knee OA with the longer life expectancy.[1] In Indonesia, there are 5% of people age older than 65 years old and it is estimated to increase up to 10.6% of population by the year 2035, which will become a burden.[2]

There is currently no available disease-modifying therapy for knee OA. Non-steroidal anti inflammatory drugs (NSAIDs) are used for patients with knee OA, but they only reduce knee pain with a tendency of inducing gastrointestinal bleeding.[3,4] Moreover, the population of elderly also has co-morbidities, which may lead to increased side effects due to drug interactions.

Recently, there is an increasing number of studies that investigate the efficacy of acupuncture for knee OA (KOA). Moreover, a systematical review by Osteoarthritis Research International Society (OARSI) has stated that acupuncture may have a symptomatic benefit in patients with knee OA.[5] Acupuncture itself is a technique involving fine needle and using current knowledge of anatomy, physiology and pathology and the principles of evidence-based medicine.[6]

Acupuncture has several techniques, while one of the most popular is laser acupuncture. This non-invasive technique has a positive effect on degenerative process at neurovascular bundle on the acupuncture points (acupoints) and has almost no complications or side effects.[7] There are only three published studies, which have investigated the efficacy of laser acupuncture

on KOA with conflicting results.[8-10] Those studies had many important factors that affect effectiveness of laser acupuncture including the wavelength, treatment duration, dosage and the number of acupoints. Variations in those factors make it difficult to conclude.[11] In our study, we only performed laser acupuncture without exercise or any other interventions. Therefore, the results could be more objective that they were the outcomes of laser acupuncture treatment. None of published studies has the same protocol as ours.

Our study investigated the efficacy of laser acupuncture applied to acupoints in geriatrics with knee OA by comparing the outcomes between the placebo laser group and the active laser group.

METHODS

We conducted a double-blind randomized controlled trial in geriatric patients with knee osteoarthritis who visited the Geriatric Outpatient Clinic, Acupuncture Outpatient Clinic and Rheumatology Outpatient Clinic at Cipto Mangunkusumo Hospital, Jakarta, Indonesia from May 2015 to October 2015.

Subjects

The sample size was calculated using formula of mean difference with type I error of 5% and type II error of 20%. Based on the experiences from previous studies, we defined the minimum difference of reduction as clinically significant when there was 30 mm of difference with 3.49 standard deviation.[8,12] The minimum total subjects needed were 28 patients for each group. However, we decided to

collect 31 samples for each group to anticipate the 10% lost.

We included patients aged more than 60 years old who had been diagnosed with grade 2 and grade 3 knee osteoarthritis based on the Kellgren-Lawrence grading scale, either unilateral or bilateral and who also had average pain intensity of more than 40 on a 100-mm visual analogue scale (VAS). We excluded patients who had a previous knee replacement surgery, consumed opioids as well as the patients who had a previous corticosteroid intraarticular injection in the last 4 months or those with hyaluronic acid intrarticular injection in the last 6 months or local-oral NSAIDs medication in the last 3 days or topical capsaicin treatment prior to study entry. Patients who received TENS, ultrasound or laser therapy in the previous 2 weeks or those with conditions of laser treatment contraindication (cancer, infections with high fever, untreated epilepsy, acute solaris dermatitis, increased photoallergic responsiveness, congestive heart failure) as well as those with conditions that would interfere outcome measures (e.g. psychotic, moderate-severe cognitive impairment) were excluded. Patients were allowed to take acetaminophen as required for severe pain (with a maximum dose of 4 g/day). All of the participants had given written informed consent. The participants were considered drop out when they missed two consecutive treatment sessions.

Randomization

Before commencing the study, a randomization list was created using a computer generated table containing random numbers. Both investigator and participants did not know whether laser acupuncture active treatment or placebo treatment was being administered. Only the researcher and her assistant had the code to determine which treatment was given. Both groups used the same laser device and the same study site. Participant blinding was optimized by using eye mask and headset during treatment session so that participant could not see the red light from laser device and also could not hear the sound from laser device.

Laser Acupuncture and Lequesne Index

Our study used a single-probe gallium aluminum arsenide laser device (Handylaser Trion RJ-Laser®, Waldkirch, Germany) with 50 mW output power and 25 mW/cm^2 power density. The device produces an infrared laser with a wavelength of 785 nm. Probe and laser device were checked before starting the laser acupuncture treatment.

Laser acupuncture was performed at the acupuncture points of ST35 Dubi, ST36 Zusanli, SP9 Yinlingquan, GB34 Yanglingquan and EX-LE-4 Neixiyan. A laserpuncture dose of 4 Joule was carried out for 80 seconds at each point. The treatment was given twice a week as many as 10 sessions. The same procedures were applied in placebo group but the device was inactive. In both groups, patients were not allowed to see the red light that came out from the instrument and they were also not allowed to hear the sound from device; therefore, they wore eye mask before wearing a protective goggle and also headset.

VAS was measured at the baseline, after four treatment sessions, after nine treatment sessions and at 2 weeks post intervention. The investigator asked participants to rate their pain on a horizontal 100-mm line, "no pain" on the left and "worst pain possible" on the right.[12] Participants marked a line to represent their pain level.

Lequesne index has been developed as an interview format and consists of three aspects: pain, maximum distance walked and activities of daily living. The score for pain contains five questions for each scale and ranges from 0 (no pain or functional limitation) to 2 (pain at rest). The maximum distance walked aspect is graded from 0 = unlimited to 6 = less than 100 m. The score was upgraded one point if the participant used one walking stick or two point if participant used two walking sticks or crutches. The activities of daily living aspect is graded from 0 = no limitation; 0.5 = able with mild limitation; 1 = able with moderate limitation; 1.5 = able with severe limitation; 2 = unable. Lequesne index directly aggregates symptoms and function, which results in a single global index score ranging from 0 to 24.[13]

Ethics

The study protocol has been approved by the Research Ethics Committee of the Faculty of Medicine, University of Indonesia – Cipto Mangunkusumo Hospital (345/UN2.F1/ETIK/2015).

Statistical Analysis

Statistical analysis was performed using SPSS version 20.0 (IBM Corp., New York, USA). A student t-test was applied when the variables were numerical data with normal distribution. A "per-protocol" analysis was used in this study.

RESULTS

Fifty nine of 62 eligible participants completed the study. One participant from the laser acupuncture active group was unable to complete the protocol because of having cerebrovascular accident. Two participants from the placebo laser group refused to complete the protocol because they felt no improvement after 2 sessions (**Figure 1**). The demographic and baseline clinical characteristics of the groups were similar (**Table 1**).

VAS scores showed a statistically significant improvement for the active laser acupuncture group after four sessions of treatment (mean difference 0.39, 95% CI 0.20 to 0.58, p<0.001), after nine-treatment sessions (mean difference 37.48, 95% CI 29.05 to 49.50, p<0.001) and at 2 weeks post intervention (mean difference 39.15, 95% CI 31.14 to 47.16, p<0.001) compared to the placebo group (**Table 2** and **Figure 2**). On the contrary, VAS scores showed no statistically significant improvement for the placebo laser group at all assessment periods (p=0.48). These
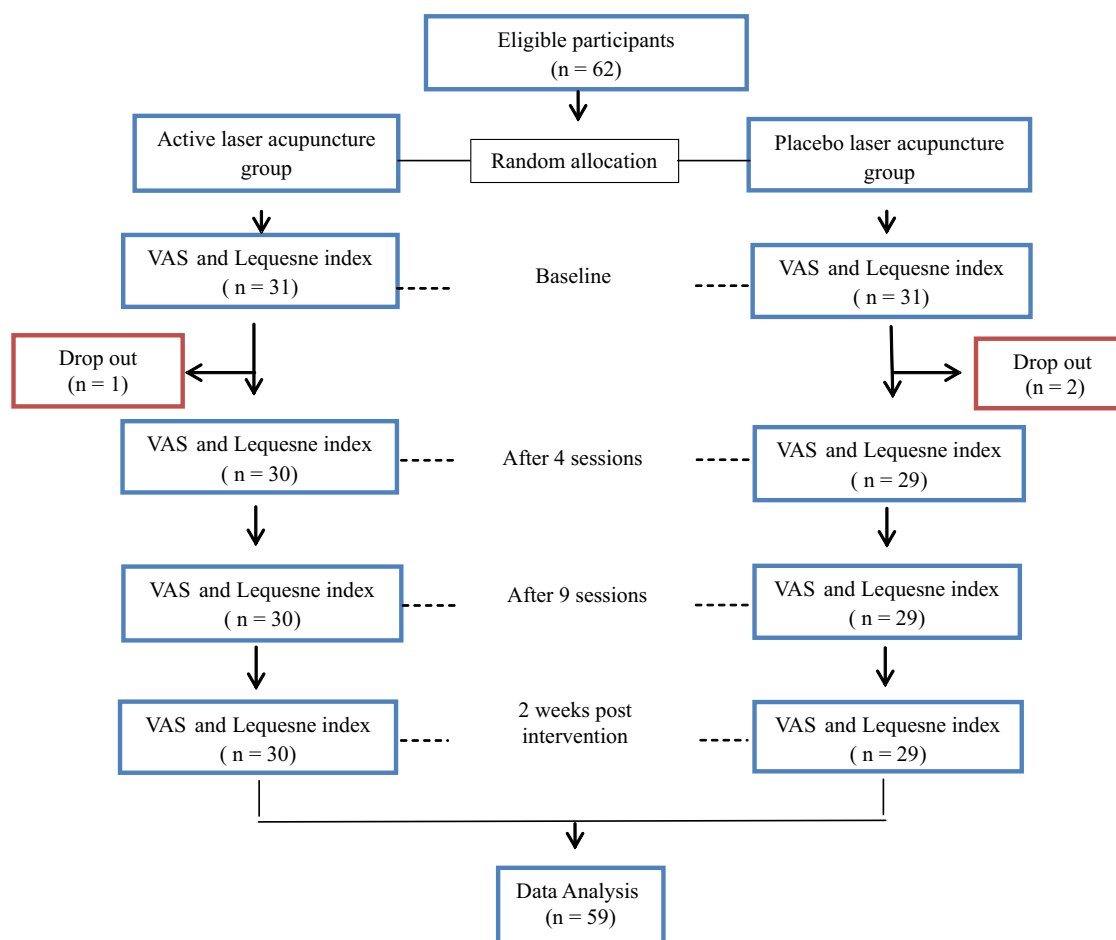

Figure 1. A flow chart of study protocol

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Table 1. Baseline characteristics between groups

Characteristics	All subjects (n=59)	Active laser acupuncture group (n=30)	Placebo laser acupuncture group (n=29)
Age (years), mean (SD)	69 (5)	69 (6.0)	68 (5.0)
Gender (n)			
- Male	17	12	5
- Female	42	18	24
Body mass index (kg/m^2), mean (SD)	26.1 (4.3)	25.8 (4.3)	26.3 (4.3)
Grade of OA			
- Grade 2	23	14	9
- Grade 3	36	16	20
Visual analogue scale (mm), mean (SD)	57.2 (11.9)	60.2 (12.2)	54.1 (10.8)
Lequesne index, mean (SD)	10.8 (4.3)	10.7 (5.0)	11.0 (3.6)
Acetaminophen medication (n)			
- Had medication	29	14	15
- No medication	30	16	14

Table 2. Changes in VAS and Lequesne index between groups

Characteristics	Active laser acupuncture group (n = 30)	Placebo laser acupuncture group (n = 29)	Mean difference (95% CI)	P value
Δ VAS1	1.36 (0.27)	0.97 (0.30)	0.39 (0.20 to 0.58)	<0.001
Δ VAS2	41.1 (15.3)	3.6 (17.0)	37.48 (29.05 to 49.50)	<0.001
Δ VAS3	40.5 (14.8)	1.3 (6.0)	39.15 (31.14 to 47.16)	<0.001
Δ Lequesne 1	3.7 (2.4)	-1.0 (3.7)	4.68 (3.07 to 6.29)	<0.001
Δ Lequesne 2	5.2 (3.9)	-0.7(4.2)	5.90 (3.78 to 8.02)	<0.001
Δ Lequesne 3	5.3 (4.5)	-1.2 (3.7)	6.48 (4.34 to 8.46)	<0.001

Δ VAS1: changes in VAS between baseline and the fourth treatment session; Δ VAS2: changes in VAS between baseline and the ninth treatment sessions; Δ VAS3: changes in VAS between baseline and at 2 weeks post intervention; Δ Lequesne 1: changes in Lequesne index between baseline and the fourth treatment session; ΔLequesne 2: changes in Lequesne index between baseline and ninth treatment sessions; Δ Lequesne 3: changes in Lequesne index between baseline and at 2 weeks post intervention

improvements were clinically significant for the active laser acupuncture group after nine sessions of treatment and at 2 weeks post intervention.

Similar to the VAS scores, the Lequesne index was improved significantly after four sessions of treatment (mean difference 4.68, 95% CI 3.07 to 6.29, p<0.001), after nine-treatment sessions (mean difference 5.90, 95% CI 3.78 to 8.02, p<0.001) and at 2 weeks post intervention (mean difference 6.48, 95% CI 4.34 to 8.46, p < 0.001) compared to the placebo group (**Table 2** and **Figure 3**). There was no statistically significant improvement of Lequesne index for the placebo laser group at all assessment periods (p=0.89).

DISCUSSION

Our study found that the laser acupuncture treatment has a beneficial effect on reducing pain intensity and improving functional outcome in patients with knee OA. Infrared light with 785 nm wave length was used as it provides deeper penetration compared to the visible red light.[7]
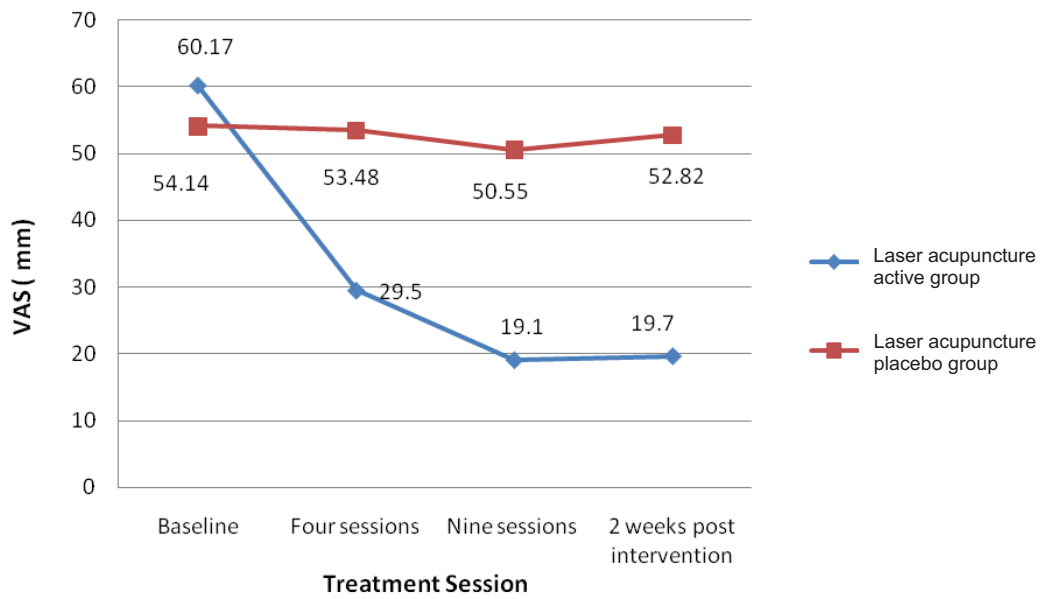
The dose was given based on consideration

Figure 2. Mean visual analogue scores. Assessments were made at baseline, after four sessions, nine sessions and at 2 weeks post intervention.
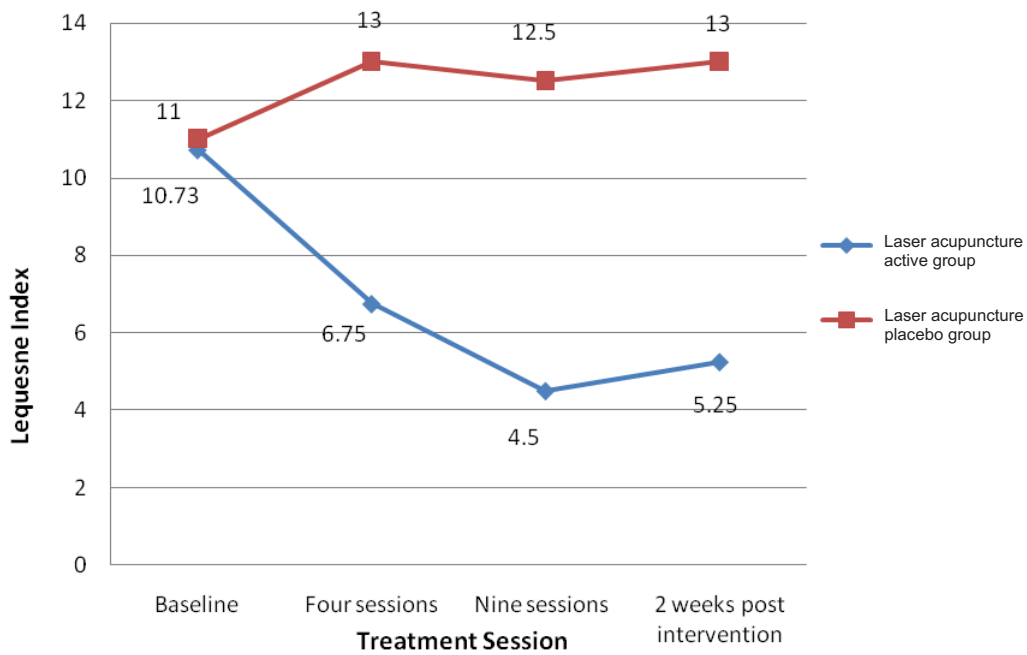

Figure 3. Mean Lequesne index. Assessments were made at baseline, after four sessions, nine sessions and at 2 weeks post intervention.

of minimum dose as defined by WALT for knee OA.[14] The treatment intervention was performed in 10 sessions twice a week; therefore, it can be applied for outpatient clinic units.

Yurtkuran et al[8] conducted a clinical trial to investigate the effects and minimum effective dose of laser acupuncture in knee OA and to determine whether it is superior to placebo treatment. Their study used a laser device with 904-nm low-level laser irradiation, 10 mW/

cm^2 power density, 4 mW output power and 0.4 cm^2 spot size. Acupuncture point of Sp9 was irradiated for 120-sec (0.48 J) treatment time per session for the laser and placebo groups. The patients in both groups had treatment as many as 10 sessions with an interval of 5 days per week. The patients in both groups were also given 10 sets of isometric exercises and active range of motion exercises for knee every day. The result showed that there is an improvement of knee swelling as shown by better knee circumference measurement in the laser group compared to the placebo group at the 2nd week.[8]

Our study showed a statistically significant difference on VAS after four sessions, nine sessions and at 2 weeks post intervention between two groups. VAS improvement was shown clinically significant after nine sessions (41.1 mm) and at 2 weeks post intervention (40.5 mm) in the laser acupuncture active group. Similar result has also been shown for Lequesne index. Our results are different from the study conducted by Yurtkuran et al. The difference may be due to lower laser doses. The dose may be too low as WALT has set 4 joules as the minimum dose for KOA.[14] In addition, power density also plays an important role. Yurtkuran et al[8] used a laser device with a power density of 10mW/cm^2. The power density may be too low to be able to induce mast cell degranulation, which is important to stimulate the acupuncture point.[15]

Al Rashoud et al[10] conducted a clinical trial to evaluate the efficacy of laser acupuncture when applied to five acupuncture points combined with exercise. The study use lower dose and power density. The number of acupuncture points and also therapy sessions used in the study are similar with our study. The study demonstrated a significant reduction of pain level in laser acupuncture active group and placebo group at the 9th session and 6 months post intervention.[10]

Pain reduction can occur through several mechanisms. Low level laser therapy has biostimulation effects, which increase cell proliferation and migration, particularly fibroblasts. It also can cause modulation of cytokines, growth factors and inflammatory mediators as well as improving tissue oxygenation.[16] Bjordal et al stated that low-intensity laser therapy modulates inflammation by decreasing the levels of biochemical markers (PGE2. m-RNA COX-2. IL1β. and TNFα), the influx of neutrophils, oxidative stress and edema.[17] Serra et al[18] found that the analgesia effect of laser acupuncture comes from the release of opioid through the migration of immune cells releasing local beta endorphins. Brosseau et al[19] also suggested that laser acupuncture can disrupt sensory input to the central nervous system as a result of the increased activity of the Na - K pump and therefore, it increases the pain threshold.

Laser acupuncture with minimal power density of 20 W/cm^2 can cause needle-equivalent acupuncture effects.[15] Moreover, laser irradiation will stimulate peripheral DRG neurons and mast cells. Stimulation of the peripheral DRG neurons will inhibit pain transmission to central nervous system.[20] Laser irradiation will cause mast cell degranulation and release of histamine, which has been known to have the effect of stimulating the Aβ and non - nociceptive C fibers that play a role in the inhibition of pain.[20,21]

A systematic review indicates that infrared laser light irradiation has some effects on Aδ and C nociceptive nerve fibers including direct inhibition of nerve conduction and reduced pain intensity. The laser irradiation can also increase serotonin level in the CNS and decrease bradykinin activities.[22]

Side effects such as infection and shock are not found. Pain was once reported by 17 of 30 subjects (56.67%) in the laser acupuncture active group, i.e. after they had the first two or three sessions. However, the complaint was not reported in subsequent sessions.

There were no previous studies reported similar issues. The pain may be experienced due to the accumulated effects of histamine release by mast cell degranulation, which was triggered by laser irradiation.[15]

The limitation of our study is the short-term follow-up period and therefore, we do not know when exactly the laserpuncture effect will diminish.

CONCLUSION

Laser acupuncture has a more effective effect on reducing VAS and Lequesne index in the elderly patients with KOA compared to placebo treatment. Larger sample size or longer follow-up period are still necessary for further studies to evaluate more effect on the efficacy of the treatment modality.

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