Alfredo PP, Bjordal JM, Dreyer SH, and et al. Efficacy of low level laser therapy associated with exercises in knee osteoarthritis: a randomized double-blind study. Clinical Rehabilitation 2011; 26(6) 523–533.

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Design: Randomized double-blind placebo-controlled clinical trial

Objective: To evaluate the effectiveness of low level laser therapy in combination with a program of exercise in reducing pain, improving functionality, range of motion, muscular strength, and quality of life in patients with osteoarthritis of the knee.

Population /sample size/setting:

- A total of 40 participants (31 females, 9 males, mean age 61.7 years) with knee osteoarthritis (OA) were recruited into the study from the Special Rehabilitation Services in Taboao da Serra, Sao Paulo, Brazil, and randomized to a treatment group (n = 20) or to a control group (n = 20).
- Study design was a randomized, investigator and outcomes assessor blinded, placebo controlled trial with sequential allocation of patients to different treatment groups. Randomization was performed by using sealed, randomly filled envelopes describing the treatment group. Patients and the physiotherapist responsible for the evaluation were unaware of the group allocation.
- Inclusion criteria included knee OA with OA grades 2 to 4 according to Kellgren–Lawrence grade, aged 50 to 75 years, knee pain and functional disability for at least 3 months, and defined according to the criteria of the American College for Rheumatology.
- Exclusion criteria included cancer, diabetes, symptomatic hip osteoarthritis, or use of antidepressants, anti-inflammatory medications or anxiolytics during six months prior to enrollment.

Methods/Interventions/Outcome Measures:

- The intervention for the treatment group consisted of low level laser (LLL) therapy and exercises and the control group or placebo group intervention consisted of placebo laser and exercises. Participants in both groups received either LLL therapy or placebo laser therapy three times a week for the first three weeks following the initial baseline assessment. No exercise therapy was given to either group during this first 3 weeks. After laser or placebo laser treatments were complete at the end of 3 weeks, the exercise program began. Both groups followed the same exercise training program and exercised three times a week for the remaining eight weeks of the program. Each session lasted 45 minutes and consisted of warm-ups, range of motion exercises, strengthening, stretching, and balance exercises.
- The primary outcome measurement of the study was the change in VAS pain score from baseline at 3 and 8 weeks. Pain was assessed using a visual analogue scale (VAS) consisting of a 10 cm ruler (without numbers).

- The secondary outcome measures included functionality using the Lequesne questionnaire, range of motion (ROM) for knee flexion using a goniometer, muscular strength of the quadriceps using a dynamometer, and activity using the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) questionnaire.
- Subjects in both the treatment and control groups underwent assessments of all outcome measures at three time points by the same blinded physiotherapist: at the start of the study (baseline), after the end of laser therapy (three weeks), and at the end of the exercise program (11 weeks).
- All patients were treated by the same physiotherapist who did not take part in the assessments.
- In the laser group, energy was irradiated over the joint line onto 5 points of the synovial region of the medial side of the knee and in 4 points at the lateral side, at 3 J per point. Total dose per knee was 27 J per treatment. In the placebo group, procedures were identical but without emission of energy. The laser equipment had two identical pens, one for the active treatment and one for the placebo treatment (sealed). The LLL dose utilized was a wave length of 904 nm, frequency of 700 Hz, average power of 60 mW, peak power of 20 W, pulse duration 4.3 ms, 50 seconds per point (area 0.5 cm^2). The parameters followed the recommendation of the World Association of Laser Therapy (WALT) for osteoarthritis.
- Sample size was calculated assuming 80% power to detect a 20% improvement in pain (VAS), with a standard deviation of 2 points and a significance level of 5%. The required sample size would be 17 patients per group.

Results:

- Forty-six patients were assessed at baseline and randomly allocated in two different groups (laser group=24 and placebo group=22). Six patients discontinued the intervention and 40 patients completed the treatment and attended the last assessment.
- Both groups did not differ significantly in demographic characteristics as well as in baseline measurements of all outcome measures.
- The between group results showed that the laser group presented significant improvement compared to the placebo group in the WOMAC activity subscales of pain (P=0.033), function (P=0.002) and total score (P=0.008) at the 3 week time point, and pain (P=0.001), function (0.002) and total score (0.003) at the 11 week time point compared to baseline.
- No other statistically significant differences between groups were found in any of the other primary or secondary outcome measures including VAS pain score, function, ROM, and muscle strength (P>0.01).
- The within group results showed that the laser group presented significant improvement at the different measurement time points,r elative to baseline, in VAS pain scores, functionality, and ROM (P<0.05), and the WOMAC activity subscales of pain, function, and total score (P<0.001).
- The within group results showed that the placebo group presented no significant improvements in any of the primary or secondary outcome measures (P>0.05).

Authors' conclusions:

- Positive results were found in low level laser therapy when associated with exercises in yielding pain relief, improvement in function, and activity compared to the placebo group. LLL when associated with exercises is effective in yielding pain relief, and improved function and activity in patients with knee osteoarthritis.
- The application of LLL 3 times per week for 3 weeks can assist in the execution of exercises in patients with knee osteoarthritis. The combination of laser and exercise can improve pain, function and activities in patients with knee osteoarthritis.
- The effects on pain relief experienced in the laser group after laser therapy may have been a consequence of the anti-inflammatory properties of the low level laser at 3 J, applied onto specific points on the articular capsule, or it may have resulted in improved exercise performance, and this combination resulted in prolonged analgesic effects.
- This study also demonstrated functional improvements and improvements in activity parameters in the laser group compared to placebo.
- This study did not demonstrate improvements in quadriceps muscle strength even though functionality improved in the laser group following the exercise therapy. These results may be due to the fact that the exercise program was focused not only on quadriceps muscle strength gain, but on the overall strengthening of the lower limb.
- Although no significant difference was observed between groups for range of motion, within group results showed improvement in the laser group after exercise.
- Future studies should increase the number of patients, include a control group, add a group which receives low level laser therapy and exercise simultaneously from the very beginning, and include a long-term follow-up assessment.

Comments:

- The primary outcome measurement of the study was the change in VAS pain score from baseline at 3 and 8 weeks. This is documented by the trial's registration on ClinicalTrials.gov(https://clinicaltrials.gov/ct2/show/NCT01306435?term=low+power+laser+exercise+osteoarthritis&rank=1). The results of this study indicate that there was no significant difference in VAS pain scores after 3 weeks of LLL or after 8 weeks of exercise between the laser group and the placebo group. The primary outcome measure does not show an effect. Thus, the effect of laser on pain is negative in this study.
- The author purports that LLL when associated with exercises is effective in yielding pain relief, and improved function and activity in patients with knee osteoarthritis based on the positive results of a secondary outcome measure, WOMAC activity. The author is treating the WOMAC results as though they were the primary outcome. This is selective reporting of outcomes and used especially when several outcomes are designated for a study and only one or a few outcomes are associated with positive results. This introduces reporting bias, and decreases our confidence in the internal validity of the study. The author is erroneously ignoring the negative results of the primary outcome. The positive effects of secondary outcomes seldom rise to the level of an evidence statement.
- It is not clear if the single physiotherapist treating all of the patients was blinded to group allocation. If the physiotherapist was not blinded, this could introduce performance bias,

since the physiotherapist could push patients in the laser group to enhance their exercise performance.

- It is also not clear who administered the laser and placebo laser treatments to the participants and it is not known if they were blinded to group allocation. This could also introduce performance bias.
- The authors failed to report why 6 participants discontinued the intervention and did not complete their participation in the study.
- It is interesting to note that only the laser group displayed significant improvements over time in several of the outcome measures.
- Although no significant difference was observed between groups for range of motion, within group results showed improvement in the laser group for ROM only after 8 weeks of exercise. No improvement was seen in the laser group for ROM after the 3 weeks of LLL treatment and before exercise.
- Strengths of this study included investigator and outcomes assessor blinding, trial registration, and an adequate sample size powered to detect significant differences. This increases our confidence in the internal validity of the study.
- An important limitation of the study was the exclusion of reporting the raw scores and mean differences for between group differences at each follow-up time point. This exclusion limits the interpretability of the results.

Assessment*:*

- This study does not support an evidence statement because the primary outcome measure (VAS pain score) identified by the authors did not show a positive effect.