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LOW POWER Ga–Al–As LASER TREATMENT OF PAINFUL OSTEOARTHRITIS OF THE KNEE

A Double-Blind Placebo-Controlled Study

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ABSTRACT. The aim of this double-blind study was to evaluate the effect of low power Ga–Al–As laser treatment on chronic pain related to osteoarthritis of the knee with periarticular tender points. Twenty-nine out-patients with uni- or bilateral osteoarthritis of the knee were included and randomly assigned to treatment with either laser or placebo laser. Fourteen patients received active laser treatment and all patients included completed the study. The effect variables were daily levels of pain, analgesic requirements, palpation tenderness and isokinetic quadriceps strength. Each patient participated in the study for 9 weeks and registered daily level of pain and consumption of analgesics. In weeks 4, 5 and 6 the patients received a total of nine treatments, each of 15 min and administered to periarticular tender points. The dose per treatment was 22.5 joule. No significant differences in any of the effect variables were found between the two groups before, during or after treatment. With regard to the patients' overall assessment there was a clearly demonstrable positive effect of treatment in both groups. This is likely to be due to a placebo effect.

Key words: low power laser, knee osteoarthritis.

During the last 10 years low power laser treatment for painful musculo-skeletal conditions has become increasingly popular despite the fact that an increasing number of controlled studies have not been able to demonstrate any significant (1, 4, 9–11, 13, 14, 17, 20) or convincing clinically relevant effects (2, 8), nor any potential biological effects which could explain the postulated pain relieving effect (6, 12).

In some of the few studies indicating a positive effect there are essential methodological weaknesses with regard to randomization, blinding etc. (7, 16, 18, 19).

The purpose of this study was to evaluate the effect of low power Ga–Al–As laser treatment applied to painful osteoarthritis of the knee with periarticular tender points.

MATERIAL AND METHODS

Out-patients with clinically and X-ray verified uni- or bilateral osteoarthritis of the knee suffering from exercise-induced pain of at least 6 months duration were invited to participate in the study. The X-ray verification was based on the assessment by a radiologist of a standard anteroposterior radiograph. The radiographic changes characteristic of osteoarthritis of the knee are joint space narrowing, osseous eburnation, subchondral cysts, marginal osteophytes and sharpening of the tibial spines (3). The X-ray verification of the diagnosis was established if the radiologist concluded that the radiographic changes were consistent with the characteristics of osteoarthritis. The severity of the radiographic changes in the medial or lateral femoro-tibial compartment or patellofemoral compartment ranged from minor in one compartment to severe in the whole knee joint. The impairment spanned the whole clinical spectrum.

The patients had to have at least five periarticular tender points and demonstrate ability to fill in the pain questionnaire. Informed consent was obtained (Helsinki declaration II), and the study was approved by the regional ethics committee. Patients who had received intra- or periarticular injection therapy, physiotherapy or who had changed medication (NSAID/analgesics) during the last 5 weeks were excluded. Patients with secondary arthrosis due to inflammatory joint disease and patients in whom routine medical examination indicated other causes for knee-related pain (e.g. osteoarthritis of the hip, arterial insufficiency, lumbar root compression) were also excluded. Twenty-nine patients, 24 women and 5 men, median age 74 years (range 60–86), were included. No patients were excluded after inclusion and randomization (see below).

Study schedule

Patients participated in the study for 9 weeks. Each day the levels of exercise-induced pain, pain at rest, and consumption of NSAID/analgesics were registered. The study was divided into pre-treatment (1), treatment (2) and post-treatment (3) periods, each of 3 weeks. To reduce the number of potential drop-outs due to inability to fill in the registration forms correctly the inclusion and randomization procedures were carried out between periods 1 and 2. Thus at

the beginning of period 2, the questionnaires for period 1 were evaluated by the physician, and, if filled in correctly, the patient was included and randomization carried out by the nurse. In period 2 (weeks 4, 5 and 6) the patients received a total of nine treatments with laser or placebo.

Pain assessment

Patients indicated the level of exercise-induced pain in the (most) painful knee by choosing one of the following alternatives: No pain (score = 0), mild pain (score = 1), moderate pain (score = 2) or severe pain (score = 3). Registration was based on the level of pain experienced during the previous 24 hours and patients were asked to fill in the questionnaire at approximately the same time each evening (8 p.m.). Pain at rest was registered similarly. A period index based on the pain registration was calculated for each 3-week period by summation of the daily values for exercise-induced pain and pain at rest. Thus the maximum pain index value for one subject in a period could be $(3 + 3) * 21 = 126$.

At the end of weeks 4 to 9 of the study the patients made an overall assessment of whether the treatment had reduced the pain or not.

Medicine requirements

The consumption of analgesics and NSAID was registered with regard to product name and number of tablets per 24 hour. A medicine index was calculated for each period, and was designed with the intention of compensating for differences in the analgetic potency between different groups of medicaments. Thus, the number of standard 24-hour doses for each medicament was multiplied according to the following: Weak simple analgesics × 1, NSAID and dextropropoxifen × 2 and opioids × 3 (one 24-hour standard dose of opioids being equivalent with 60 mg morphine given orally). The period index was calculated as the sum of the individual values for the respective periods. To illustrate: A patient on one particular day took the following tablets: paracetamol 3 g, ibuprofen 600 mg and morphine 60 mg. This gives a medicine index based on the following values: One 24-hour standard dose of a simple analgesic $\Rightarrow 1 \times 1 = 1$, one half standard 24-hour dose NSAID $\Rightarrow 1/2 \times 2 = 1$ and 1 standard 24-hour dose opioid $\Rightarrow 1 \times 3 = 3$. This gives a total for that day of $1 + 1 + 3 = 5$.

Palpation tenderness assessment

Before the first treatment (week 4), after the last treatment (week 6) and 3 weeks after the last treatment (end of week 9) the patients' knee was palpated in the region 10 cm proximal to and 10 cm distal from the joint line. At palpation a pressure of approximately 4 kg was applied. The localization of tender points was registered and tenderness graded as light (i), moderate (ii), or severe (iii).

A palpation index was calculated as the sum of tenderness-scores for all the periarticular tender points. The palpation of the knee of each patient was carried out by the same physician. We did not carry out a study of the intra observer within-day variation in the palpation index as it was not possible to blind the observer with respect to the score obtained a few hours before in the same patient.

Muscle strength measurements

If there is a pain relieving effect of the laser treatment better walking is to be expected and because of this, training based improvement of the muscle strength (15), or simply higher performance because of a reduced pain level. Therefore isokinetic quadriceps strength was measured on the treated side before the first and after the last treatment. A Kin-com dynamometer was used. The muscle strength was measured at the angle velocity 60°/s. The highest peak-torque in three measurements was chosen as the effect parameter (5).

Equipment

The active laser was a Ga–Al–As infra-red laser, class 3B, wavelength 830 nm, mean effect 25 mW, continuous beam. The irradiation area of the diodes was 0.28 cm^2. The active and placebo laser units were identical, except that the probe of the placebo laser had been inactivated. The two laser units were checked by the manufacturer just before the first patient started and after patient no. 12 of the study. After patients 25 and 29 the units were checked by the medico-technical department at Rigshospitalet, University of Copenhagen. All four measurements confirmed the active laser probe as having an output of 25 mW and the placebo as being inactive.

Randomization and exposure schedule

In period 2 (weeks 4, 5 and 6), the patients received a total of nine treatments with laser or placebo laser, 2–4 treatments a week. Each treatment consisted of 15 minutes of irradiation applied to tender points, each tender point receiving between one and three minutes of irradiation. Thus, a minimum of five- and a maximum of fifteen tender points was irradiated and the dose per tender point varied between 1.5 and 4.5 joule. If there were less than the inclusion criteria of five tender points, the area around previous tender points was irradiated. The total dose per treatment with active laser was $15 \times 60 \times 25/1000 = 22.5$ joule, and the accumulated dose for all nine treatments 202.5 joule.

The nurse in charge of the randomization key selected the laser or placebo laser before each treatment, checking the effect meter of the instrument each time to ensure that correct apparatus was handed to the physician. The blinded settings for patients and physician were maintained until the last patient had completed the study. As a rule, all treatments for any one patient were given by the same physician.

Statistics

The period indexes for pain, medicine and palpation tenderness were used for ranking and the Wilcoxon-Mann-Whitney test (non parametric, unpaired, rank sum test) was applied to test for differences between the two groups for each of the three periods of the study. Friedman's one-way analysis of variance was used to test for changes in index values between the three periods in each group for pain, medicine and palpation, respectively. Index intervals across the entire scale were regarded as being equal. On the basis of this assumption the Mann-Whitney two sample rank sum test was also used to compare the two groups with respect to the individual changes in period indexes from periods (1) to (2) and (3), respectively. The student's *t*-test was used to compare muscle strength before and after treatment. Fisher's exact test was used to compare results of patients' overall assessment of the treatment. The *p*-values of the different tests are given in parentheses, the placebo group mentioned

Table I. *Pain, medicine and palpation index in the placebo ($n = 15$) and laser ($n = 14$) groups in the pre-treatment, treatment and post-treatment periods*

Median and inter quartile range are given.

	Pre-treatment		Treatment		Post-treatment	
	Placebo	Laser	Placebo	Laser	Placebo	Laser
Pain	71 63–101	82 60–99	69 42–91	61 46–100	61 29–98	66 42–104
Medicine	11 0–46	24 2–44	8 0–34	19 3–46	7 0–35	24 6–41
Palpation	21 14–29	20 14–33	20 8–39	18 8–28	22 10–38	15 10–28

Table II. *Individual changes in pain, medicine and palpation indexes in the placebo ($n = 15$) and laser ($n = 14$) groups from the pre-treatment to treatment period and post-treatment period, respectively*

Median and inter quartile range are given

	Pre-treatment to treatment period			Pre-treatment to post-treatment period		
	Placebo	Laser	*p*-value	Placebo	Laser	*p*-value
Pain	2 −1–18	8 −2–16	1.00	11 0–27	1 −6–21	0.51
Medicine	0 −1–4	0 −2–5	0.98	0 −1–4	−3 −7–7	0.40
Palpation	0 −7–10	3 0–7	0.18	−1 −20–3	7 0–13	0.07

first and then the laser group unless otherwise indicated. 0.05 was chosen as the level of significance.

RESULTS

No significant differences between the two groups were found in the three periods (1, 2 and 3) regarding pain ($p = 0.85$, $p = 0.85$, $p = 0.59$), medicine ($p = 0.51$, $p = 0.48$, $p = 0.43$) and palpation tenderness ($p = 0.88$, $p = 0.94$, $p = 0.31$).

Within each group (placebo, laser) only small, insignificant changes between periods were observed in the pain ($p = 0.16$, $p = 0.55$) and the medicine ($p = 0.74$, $p = 0.25$) indexes, whereas changes in the palpation index ($p = 0.88$, $p = 0.03$) were significant in the laser group (Table I). We found no significant differences between the two groups with respect to the individual changes in period indexes (Table II).

The muscle strengths (Table III) were not significantly different when we compared laser with placebo before ($p = 0.47$) and after ($p = 0.25$) treatment. No changes were observed within each group when we compared the paired data before and after treatment ($p = 0.32$, $p = 0.77$).

Patients' overall assessment (Table IV) showed no significant difference between those treated with laser and the placebo group.

In neither group were side effects reported by the patients.

DISCUSSION

We found no significant differences between the effect of low power laser biostimulation and placebo with

Table III. *Isokinetic (60°/s) knee-extensor muscle strength (Nm) on the treated side*

	Before treatment		After treatment	
	Placebo $n = 14$	Laser $n = 13$	Placebo $n = 14$	Laser $n = 13$
Mean	72	64	76	62
SD	26	37	28	34

Table IV. *The overall assessment by the patients once weekly in the treatment and post-treatment period*
The frequencies of the two possible answers are given.

Week number	Treatment	Overall assessment by the patient: Treatment did help	Overall assessment by the patient: Treatment did not help	*p*-value
4	Placebo	7	8	
	Laser	3	11	0.30
5	Placebo	9	6	
	Laser	6	8	0.58
6	Placebo	9	6	
	Laser	7	7	0.87
7	Placebo	8	7	
	Laser	4	10	0.33
8	Placebo	6	9	
	Laser	4	10	0.80
9	Placebo	6	9	
	Laser	4	10	0.80

respect to pain and medicine requirements. Regarding the palpation tenderness we found a significant reduction in the laser group, when the tenderness before treatment was compared with the tenderness after the treatment, whereas no significant differences at any time occurred between the two groups. This observation should be interpreted with care since it was the only parameter which gave an indication of a positive effect of the laser treatment. We were unable to find any changes in muscle strength that could imply a positive effect of the laser treatment. The overall assessment by the patients also failed to show a positive effect of the laser treatment. Neither did this study, which was specially designed to demonstrate a long lasting effect with a late onset, show any sign of such an effect, except on palpation tenderness.

In this study we set out to evaluate the effects of low power laser treatment on one of the many painful conditions it is currently applied to. In planning the design we wanted to administer treatment according to the usual clinical setting in a commercial laser clinic, ensuring on empirical grounds that the accumulated dose given was "enough" and that the treatment was rendered exactly as indicated by the manufacturers of the laser apparatus.

In osteoarthritis, the pain probably derives from the subchondral bone, the joint capsule and extra articular structures, e.g. ligaments, tendons, bursae, muscles (3). Because only a minor fraction of the laser beam penetrates more than a few millimeter below the surface (12) we made no attempt to irradiate the subchondral bone. Instead, we intended to reduce the pain originating from the joint capsule and the extra articular structures by irradiating periarticular tender points. Thus, we only used the extra articular tender points to localize the areas most probably relevant to benefit from irradiation.

The correlation between the palpation index and the clinical impairment of the patient was not very strong. To avoid large variations between patients of the total dose given, all patients in the active group received the same total dose, and not the same dose per tender point. The total dose was high compared with what was given in most other studies (1, 2, 4, 7, 8–11, 13, 14, 16–20). Applying the treatment to periarticular tenderness points and not randomly around the knee joint might have improved our chances of demonstrating a positive effect of the treatment.

All variables improved slightly in both groups, and as demonstrated in Table IV, this effect is most likely a placebo effect.

The number of patients participating in the study was, admittedly, relatively small. However, when planning the study and calculating of the sample size (number of patients) it is necessary to decide the size of the minimal relevant difference (effect of the laser treatment), which should not be overlooked. Regarding the main variable, the pain index, we chose a minimal clinically relevant improvement to be 42, corresponding to a mean change in the daily pain from one level to the level below, e.g. from moderate to mild pain. The risk of committing a type I error was set at 5% and the risk of committing a type II error 20%. This calculation gave the number of patients which actually participated in the study. To exclude very small effects, hundreds of patients would have to be included. We do not find it relevant at this moment to search for such small effects as the great economic costs of the treatment cannot be justified by such small (hypothetical) benefits of the treatment.

From a clinical point of view this study adds to the growing list of blinded controlled studies failing to demonstrate any clinically relevant effect of low power laser beams on painful musculoskeletal conditions. The only convincing positive effect we could demonstrate was a placebo effect. This cannot justify the

great economic costs of low power laser treatment which takes public health resources from other—truly efficacious—treatment regimens. In our opinion, low level lasers should not be used in routine treatment nor approved by the health authorities before more solid scientific evidence documenting any beneficial effects is available.

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