Low-Level Laser Therapy in Ankle Sprains: A Randomized Clinical Trial

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ABSTRACT. de Bie, RA, de Vet HCW, Lenssen, TF, van den Wildenberg FAJM, Kootstra G, Knipschild PG. Low-level laser therapy in ankle sprains: a randomized clinical trial. Arch Phys Med Rehabil 1998;79:1415-1420.

Objective: To test the efficacy of low-level laser therapy on lateral ankle sprains as an addition to a standardized treatment regimen, a trial was conducted in which high-dose laser (5J/cm^2), low-dose laser (0.5J/cm^2), and placebo laser therapy (0J/cm^2) at skin level were compared.

Design: Randomized, double-blind, controlled clinical trial with a follow-up of 1 year. Patients, therapists, assessors, and analysts were blinded to the assigned treatment.

Setting: An ambulatory care setting.

Patients: After informed consent and verification of exclusion criteria, 217 patients with acute lateral ankle sprains were randomized to three groups from September 1, 1993, through December 31, 1995.

Interventions: Twelve treatments of 904nm laser therapy in 4 weeks as an adjunct to a standardized treatment regimen of 4 weeks of brace therapy combined with standardized home exercises and advice. The laser therapy device used was a 904nm Ga-As laser, with 25-watt peak power and 5,000 or 500Hz frequency, a pulse duration of 200nsec, and an irradiated area of 1cm^2.

Primary Outcome Measures: Pain and function as reported by the patient.

Results: Intention-to-treat analysis of the short-term results showed no statistically significant difference on the primary outcome measure, pain ($p = .41$), although the placebo group showed slightly less pain. Function was significantly better in the placebo group at 10 days ($p = .01$) and 14 days ($p = .03$) after randomization. The placebo group also performed significantly better on days of sick leave ($p = .02$) and at some points for hindrance in activities in daily life and pressure pain, as well as subjective recovery ($p = .05$). Intention-to-treat analysis showed that total days of absenteeism from work and sports were remarkably lower in the placebo group than in the laser groups, ranging from 3.7 to 5.3 and 6 to 8 days, respectively. The total number of relapses at 1 year in the low-dose laser group ($n = 22$) was significantly higher ($p = .04$) than in the other two groups (high laser, $n = 13$; placebo, $n = 13$). Subgroup analysis to correct for possible confounders did not alter these findings.

Conclusions: Neither high- nor low-dose laser therapy is effective in the treatment of lateral ankle sprains.

EACH YEAR, 4% of the population in Western countries suffer ankle sprains, with about half of the injuries occurring during participation in sports activities. Some 20% of these patients need medical care.[1] Treatment costs and absenteeism from work are not a negligible part of direct and indirect costs. About 21% of all people who have had ankle sprain injuries are absent from school or work for about 7 days.[2] In addition, sports absenteeism and the emotional burden of sudden incapacitation influence a relatively simple injury negatively.

One of the treatment modalities for ankle sprain injuries is low-level laser therapy (LT), which is either used as an additional therapy, combined with taping or bracing, or used as a stand-alone therapy.[3,4]

WORKING MECHANISM

In the past 25 years, several authors have postulated biostimulative effects of LT. Biostimulation refers to the application of electromagnetic energy by LT to body tissues, which is supposed to influence cell functions.[5-7] The effects were thought to consist of stimulation or inhibition of biochemical, physiological, and proliferative activities. However, because both stimulation and inhibition seem possible, terminology has changed, thus rendering the term *biostimulation* obsolete.[7] The magnitude of the effect is reported to be dependent on wavelength, dosage, and dose-intensity of LT.[8] In practice, LT typically involves treatment dosages of <1 to 4J/cm^2 to treatment sites.[7]

One theory that attempts to explain effects of LT is that in the event of an impairment or disorder, the energy state of a cell is changed, consequently altering the electromagnetic communication between cells. LT is thought to influence this communication favorably.[9,10]

Photochemical theory offers an alternative explanation. The absorption of laser light takes place in tissue chromophores (photo acceptors). These chromophores may be enzymes, membrane molecules, or any other cellular or extracellular substances. Activation of these chromophores by LT is considered responsible for the postulated bioeffects.[11]

Neither theory has been thoroughly confirmed in research; the supposed working mechanism remains unclear. Moreover, recent research on tissue samples, using various dosages, has failed to show any effects on cell metabolism, and hence has not provided corroborative evidence.[12]

The lack of a convincing biological background that explains the clinical effects induced by LT not only hampers further explanation, but also generates uncertainties about proper dosage and treatment indications.

In a preliminary trial[13] published in 1988 with 38 patients, LT was found to have substantial pain-relieving qualities. After 5 days, patients in the laser group showed 20% more pain relief than persons in the placebo group. To reproduce these results,

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with a power of 80% (1-β) and a two-tailed level of significance (α) of 5%, 50 persons per group would be needed. In view of what we perceived to be clinically relevant effects, we opted for a larger trial with 75 persons per group.

PATIENTS AND METHODS

Study Design

We compared the effect of high-dose and low-dose LT with that of a placebo in patients with acute lateral ankle sprains. LT acted as an additional therapy, applied upon a standardized treatment regimen that consisted of 4 days' elastic wrapping followed by 3.5 weeks of bracing with a Push ankle brace.[a] The Push ankle brace consists of a nonstretch sock with a zipper, with short and long adjustable Velcro straps to imitate the ankle ligaments and ensure sufficient stability. Efficacy was evaluated on the basis of 4 weeks and results at 3, 6, 9, and 12 months. The 4-week follow-up period was intended to reflect the actual healing process and to provide preliminary information about resumption of work and sports participation. Follow-up to 1 year was carried out to detect long-term effects and possible relapses.

The study was approved by the medical ethics committee of Maastricht University and the University Hospital of Maastricht (the Netherlands). A detailed description of the protocol is available from the authors.

Selection of Patients

Patients who reported between September 1, 1993, and December 31, 1995, to the accident and emergency department of a university hospital with acute lateral ankle sprain, who were between 18 and 65 years old, and whose injury was not older than 24 hours were selected by the physician on call. In addition, patients with fractures (confirmed by obligatory radiography), direct open trauma, and underlying abnormalities of the foot and/or legs were excluded. Finally, those with systemic diseases (eg, rheumatoid arthritis or diabetes) and mental handicap were excluded, as well as people with difficulties with the Dutch language. Patients could also be excluded for practical reasons, for instance, if they lived too far away or if they could be expected not to attend all therapy sessions (eg, going on holiday, working abroad).

Eligible patients were given a detailed description of the intended treatment procedure and were informed about the chance of receiving a placebo therapy as well as about their right to withdraw from the trial at any time. After receiving this information in writing, the patients gave their informed consent to participate. The next morning they were seen by a trained research assistant who checked inclusion and exclusion criteria. The research assistant also kept a record of the baseline interview and physical examination, and the patient filled out a questionnaire to provide baseline data.

Randomization

Patients were stratified by severity of injury (mild or severe) and sports participation (participation or nonparticipation in sports activities) to prevent unequal distributions by chance for these prognostic factors between treatment groups.[14] After informed consent, 217 consecutive patients were randomly allocated to one of three groups by means of a computer-generated table, with a random permuted block size of 3. The first group (n = 74) received low-dose LT, the second group (n = 72) received high-dose LT, and the third group (n = 71) received placebo LT. Patients, therapists, outcome assessors, and analysts were blinded to the treatments given.

Interventions

All patients received a standardized treatment regimen that consisted of 4 days' elastic wrapping followed by 3.5 weeks of bracing with a Push ankle brace. We also provided standardized patient information and standardized home exercises. The home exercises consisted of simple mobility exercises for the ankle, learning to bear weight on the injured foot, and later learning to regain balance and ensure a proper gait pattern. The additional 904nm LT was similar in all three groups, except for the dose. Laser specifications are given in table 1.

Laser dose at skin level was 0.5J/cm^2 in the low-dose group, 5J/cm^2 in the high-dose group, and 0J/cm^2 in the placebo group. The target tissue was considered to lie a maximum of 1cm under the surface of the skin. Energy density at tissue level was calculated to be 0.07J/cm^2, 0.7J/cm^2, and 0J/cm^2 for each dose, respectively. Laser output was validated before the start and at the end of the trial and was checked at regular intervals during the trial by an independent party.

The laser device was also equipped with a calibration sensor that was independent of the treatment settings. Each morning, laser output was checked. Blinding of the treatment setting was ensured by randomizing the three settings (high, low, or placebo) over 21 treatment codes (7 for each group) so that in the event of unmasking one of the codes, the trial did not have to be halted. This, however, did not occur.

The most painful area on the lateral side of the ankle was chosen as the target location. The patient indicated the painful area. This was consequently checked by an algometer. The target area was circumscribed with a waterproof marker during the first visit. Before LT was applied, the area was cleaned with alcohol (96%) to minimize backscatter and reflection from fatty skin. Then the probe was placed perpendicularly in the center of the circumscribed area, directly on the skin, thereby preventing energy loss due to divergence. All three groups followed the same treatment schedule: 5 treatment sessions in the first week, 3 treatment sessions in the second week, and 2 treatment sessions per week in the third and fourth weeks, adding up to 12 treatment sessions during a 4-week intervention period.

At each treatment session, every patient received 200 seconds of laser therapy. Both patient and therapist were fully blinded. In all three groups, the laser apparatus produced a soft sound and the display read, "Warning: laser beam active!" Both patients and therapists also wore protective glasses. In addition, 904nm laser light is invisible to the human eye. After therapy, the patient replaced the brace or elastic wrapping.

We allowed patients to take standardized pain medication (Paracetamol,[b] 500mg; maximum dosage 1 tablet every 4 hours). These drugs were provided at intake, and the patients kept a record of the amount they took.

Table 1: Laser Parameters of Uniphy Phyaction 740 Laser Device[c]

	Low Laser	High Laser	Placebo Laser
Medium	Ga-As	Ga-As	NA
Wavelength	904nm	904nm	NA
Waveform	Block	Block	NA
Irradiated area	1cm^2	1cm^2	1cm^2
Frequency	500Hz	5,000Hz	NA
Peak power	25W	25W	NA
Pulse duration	200nsec	200nsec	NA
Average output	1W	1W	NA
Treatment time	200sec	200sec	200sec
Dose at skin level	0.5J/cm^2	5J/cm^2	0J/cm^2
Dose at tissue level	.068J/cm^2	.68J/cm^2	0J/cm^2

Outcome Measures

In this trial, we considered the most important outcome measures those that were capable of reflecting the actual state of the complaint from the patients' point of view. Therefore, the primary measures of effect were perceived pain measured on a scale of 0 to 10 and function. For measurement of pain, we specifically chose a scale of 0 to 10 because this way of grading pain is familiar and easy to use for patients and other assessors. Moreover, it is quite similar to the Dutch report-mark system. Numerical rating scales, with a range from 0 to 10 points, provide reliable and consistent measures of clinical pain intensity compared with visual analogue scales in both acute and chronic pain measurements.[14-16] Function was scored on a 100-point scale that combined the items pain, instability, weight bearing, swelling, and gait pattern. The scale has been validated and is used as both a diagnostic and a prognostic instrument.[17]

Secondary outcome measures were total days of sick leave from work, school, or housekeeping because of trauma and moment of reuptake of sports (measured in days since onset of trauma). We also measured limitation in activities of daily living (ADL) by use of a scale of 0 to 10, swelling of the ankle by means of the volumetric difference between swelling at intake and at several points during the intervention, pressure threshold test (in kg/cm^2) by means of an algometer,[18,19] subjective recovery by use of a scale of 0 to 10, and satisfaction about recovery rate and received treatment by use of a scale of 0 to 10. Measurements were collected at intake, during 4 weeks of treatment, and at 3, 6, 9, and 12 months. Success of blinding, side effects, and relapses were evaluated at the end of the intervention period. All measurements were carried out in a blinded fashion by means of a standardized protocol.

Data Management and Statistical Analysis

Data were stored on a personal computer in dBASE IV[20] and were checked for completeness, inconsistencies, range of possible values, and protocol deviations. Subsequently, the data were analyzed with SPSSWIN/PC statistical software.[21] Analysis was performed in a blinded manner and according to the intention-to-treat principle: all participants, including those with poor compliance and those who had withdrawn from therapy, remained in the group to which they were assigned by randomization. Subsequently, a per-protocol analysis was performed to see whether protocol deviations influenced the results.

The primary and secondary outcome measures were compared between the three treatment groups. Differences between the means of groups at 5, 10, 14, and 28 days and at 3, 6, 9, and 12 months, respectively, were compared by use of a two-tailed analysis of variance (ANOVA) model. Decreases in the primary outcome measure pain were compared between groups by regression analysis. For each patient, the individual curve was estimated, whereafter mean group scores of the estimated regression coefficients were compared by ANOVA.

Subgroup analyses were carried out to determine whether particular subgroups showed other outcomes than the treatment groups as a total. Dichotomized subgroups were formed according to age (cut-off, 35yrs), sports participation (yes/no), gender (female/male), and occupation (sitting/standing work). The coding was broken after final analyses had been carried out.

RESULTS

Short-Term Results

From September 1, 1993, through December 31, 1995, 217 consecutive patients were included and randomized. All patients were present for baseline measurements, yet 2.1% of all treatment sessions were missed and thus formed gaps in the data set (43 of 2,064 treatment sessions; 0.4% from the low-dose group, 0.7% from the high-dose group and 1% from the placebo group).

Seven patients missed only one treatment session because of illness or work. These missing data were substituted by the

Table 2: Comparison of Treatment Groups With Respect to Demographic and Prognostic Variables

	Low-Dose Laser	High-Dose Laser	Placebo
No. of patients	74	72	71
Mean age, yrs (SD)	30.2 (9.6)	33.2 (10.4)	30.9 (10.3)
Sex (F/M)	30/44	17/55	22/49
Baseline measurements			
Mean pain score (SD)*			
During the day	3.7 (2.7)	3.8 (2.5)	3.6 (2.8)
In the morning	4.8 (2.9)	4.4 (2.9)	4.2 (3.0)
Mean no. of pain tablets (SD)	0.5 (1.0)	0.8 (1.4)	0.7 (1.4)
Mean pressure pain, kg/cm^2 (SD)			
Calcaneo fibular ligament	3.2 (1.9)	3.3 (1.9)	3.5 (1.9)
Anterior talofibular ligament	1.7 (1.3)	1.8 (1.4)	1.6 (1.0)
Posterior talofibular ligament	3.6 (2.0)	3.1 (2.0)	3.3 (1.8)
Mean sports category (SD)†	2.2 (0.8)	2.1 (0.8)	2.1 (0.8)
Mean prognosis on recovery (SD)‡			
2wks	7.2 (1.2)	6.9 (1.2)	7.4 (1.2)
4wks	9.4 (0.8)	9.2 (0.8)	9.4 (0.9)
Mean function score (SD)‡	13.1 (10.6)	12.1 (10.8)	13.4 (11.8)
Blue/white collar ratio§	37/35 (2)	37/30 (5)	35/32 (4)
Work load			
Light	21	17	20
Normal	19	18	19
Heavy	28	30	27
Very heavy	6	7	5

* Measured on a scale of 0 to 10 (0, no pain; 10, extremely painful).
† Measured on a 4-point scale (0, no sports participation; 1, recreational; 2, competition sports; 3, professional).
‡ Measured on a scale of 0 to 100 (0, no function; 100, perfect function).
§ Numbers in parentheses indicate number unemployed.

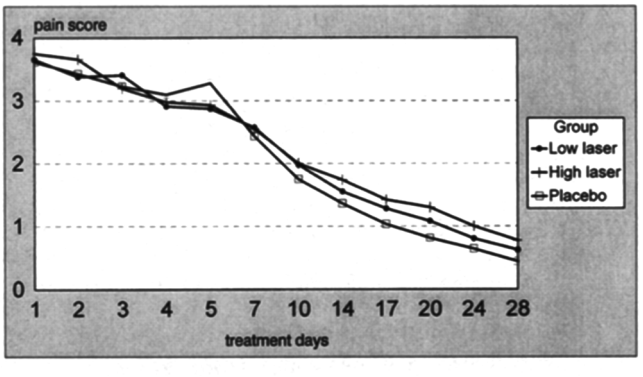

Fig 1. Daily pain score of the treatment groups for 4 weeks (0, no pain; 10, extremely painful).

mean value of preceding and following measurements in the data set in both intention-to-treat and per-protocol analyses.

Eight patients missed 21 treatment sessions because they believed they were cured. For these patients, the last known entry was substituted for the intention-to-treat analysis. Two of these patients were in the low dose group, 1 was in the high-dose group, and 5 were in the placebo group.

Three patients withdrew from the trial without being cured. These were 2 patients from the low-dose group, 1 of whom missed two treatment sessions in a row and one of whom stayed away 10 days after trauma; 1 patient from the high-dose group stayed away 8 days after initial trauma. For these patients, the last known value was substituted for the intention-to-treat analysis.

The three treatment groups were similar with respect to demographic characteristics and baseline measures, although age and gender differed slightly in the high-dose group compared with the other two groups (table 2).

Figure 1 shows scores of the groups for "pain during the day." All treatment groups improved, and the placebo group showed consistently more improvement from day 8 on than the other groups. However, comparison of the entire curves using regression analysis showed no significant differences between the three groups ($p = .41$).

Table 3 provides information about recovery on primary and secondary measures of effect. As seen in table 3, the outcomes on function scores on days 10 and 14, days of sick leave, hindrance in ADL on day 10, pressure pain on anterior talofibular ligament on day 14, and subjective recovery reached statistical significance. In all of these cases, the placebo group performs better than the LT groups.

No side effects of LT were reported or observed during or after treatment. The per-protocol analysis in which missing data were not substituted and the intention-to-treat analysis showed similar results.

Table 3: Measures of Effect (Mean and SD) on Several Days During Treatment and *p* Values of Differences in Means Using ANOVA

	Low-Dose Laser	High-Dose Laser	Placebo	*p* (Two-Sided)
Perceived pain, mean (SD)*				
Day 5	2.8 (2.2)	2.9 (2.1)	3.3 (2.4)	.6
Day 10	2.0 (2.0)	2.1 (1.9)	1.7 (1.9)	.48
Day 14	1.6 (1.9)	1.7 (1.7)	1.4 (1.7)	.42
Day 28	0.6 (1)	0.8 (1.2)	0.4 (1)	.14
Function score, mean (SD)†				
Day 5	25.1 (15)	24.7 (15.1)	25.7 (14.8)	.92
Day 10	42.2 (16.1)	44.1 (14.9)	49.9 (15.9)	.01
Day 14	56.3 (16.1)	56.0 (15.7)	60.0 (17.1)	.03
Day 28	73.6 (14.7)	74.3 (17.5)	76.4 (14.9)	.50
Days of sick leave, mean (SD)	12.5 (11.1)	11.2 (10.0)	7.8 (9.2)	.02
Reuptake of sports in days, mean (SD)	27.3 (7.9)	27.4 (7.5)	25.3 (9.8)	.26
Hindrance in ADL, mean (SD)*				
Day 5	4.4 (2.6)	4.9 (2.8)	4.8 (2.7)	.42
Day 10	3.7 (2.7)	3.3 (2.4)	2.6 (2.2)	.03
Day 14	2.8 (2.6)	2.7 (2.1)	2.0 (2.1)	.08
Day 28	0.9 (1.5)	1 (1.5)	0.8 (1.6)	.83
Decrease in swelling of the ankle in % of total foot volume, mean (SD)				
Day 5	1.6 (2.6)	2.1 (2.5)	2 (2.6)	.44
Day 10	3.5 (2.8)	4.3 (3.2)	4.1 (2.6)	.20
Day 14	4.4 (2.9)	4.8 (3.3)	4.9 (3.0)	.55
Day 28	5.2 (3.8)	4.5 (3.5)	5.2 (3.2)	.39
Pressure pain in kg/cm^2, mean (SD)				
Day 5				
On calcaneo fibular ligament	4 (1.8)	4 (1.8)	4 (1.8)	1
On anterior talofibular ligament	2.3 (1.7)	2.4 (1.4)	2.2 (1.4)	.71
On posterior talofibular ligament	3.9 (1.8)	3.9 (1.8)	4.2 (1.8)	.71
Day 10				
On calcaneo fibular ligament	5.0 (1.4)	4.8 (1.5)	5.0 (1.4)	.81
On anterior talofibular ligament	3.4 (1.7)	3.6 (1.6)	3.5 (1.5)	.68
On posterior talofibular ligament	4.9 (1.5)	5.1 (1.3)	5.0 (1.4)	.56
Day 14				
On calcaneo fibular ligament	5.3 (1.3)	5.5 (1.2)	5.5 (1.1)	.69
On anterior talofibular ligament	3.9 (1.7)	4.6 (1.4)	4.5 (1.6)	.01
On posterior talofibular ligament	5.3 (1.2)	5.4 (1.2)	5.4 (1.1)	.65
Day 28				
On calcaneo fibular ligament	5.7 (0.8)	5.8 (0.7)	5.7 (0.7)	.91
On anterior talofibular ligament	5.3 (1)	4.9 (1.4)	5.1 (1.2)	.09
On posterior talofibular ligament	5.7 (0.9)	5.4 (1.2)	5.7 (0.8)	.32
Subjective recovery, mean (SD)*	8.6 (0.9)	8.7 (0.9)	8.9 (0.8)	.05

* Measured on a scale of 0 to 10 (not limited, 0; severely limited, 10).
† Measured on a 100-point scale (no function, 0; perfect function, 100).

Long-Term Results

All patients were present for baseline measurements, yet in the follow-up 3.6% to 8.3% of the patients were lost to follow-up as time passed. Table 4 shows the numbers per group compared with baseline attendance, as well as outcome measures at 3, 6, 9, and 12 months of follow-up. The low-dose group showed 6 losses to follow-up after 1 year; 4 patients had moved, 1 patient did not respond to either written or telephoned requests, and 1 patient's telephone was disconnected. In the high-dose group, 2 patients had moved and 1 patient had left an erratic telephone number; thus 3 patients in total were missed. The placebo group showed 8 losses to follow-up after 1 year; 6 patients had moved, 1 patient's telephone was disconnected, and 1 patient had no telephone and did not respond to written requests.

Table 4: Outcome Measures at 3, 6, 9, and 12 Months of Follow-Up

	Low-Dose Laser	High-Dose Laser	Placebo	*p* (Two-Sided)
Total days of sick leave due to ankle sprain, mean (SD)				
No. of patients	74	72	71	
At 1yr follow-up	13.1 (12.3)	11.5 (10.7)	7.8 (9.3)	.013‖
Days until reuptake of sports, median (range)§				
No. of patients	51	54	48	
At 9mo follow-up	41 (7-274)	40 (10-272)	33.5 (3-275)	.36#
At 1yr follow-up	42 (7-365)	40 (10-272)	34 (3-365)	.26#
3mo results				
No. of patients	72	72	66	
Activity level*	5.6 (2.3)	5.7 (2.3)	5.4 (2.6)	.82‖
Free of complaints†	8.7 (1.7)	8.8 (1.8)	8.6 (2.2)	.80‖
Function score‡	85.3 (15.7)	85.5 (15.9)	84.5 (21.5)	.94‖
Use of brace in ADL (yes/no)	7/65	6/66	6/60	.96¶
Use of brace during sports (yes/no)§	28/17	27/21	18/21	.33¶
6mo results				
No. of patients	69	70	63	
Activity level	5.7 (2.2)	6.0 (2.2)	6.1 (2.3)	.54‖
Free of complaints	9.2 (1.2)	8.9 (1.7)	9.3 (1.1)	.38‖
Function score	88.5 (13.5)	88.4 (13.6)	89.8 (15.1)	.83‖
Use of brace in ADL (yes/no)	3/66	3/67	5/57	.49¶
Use of brace during sports (yes/no)§	23/21	24/24	15/27	.25¶
9mo results				
No. of patients	68	69	63	
Activity level	5.8 (2.3)	5.9 (2.2)	5.9 (2.3)	.93‖
Free of complaints	9.4 (1.3)	9.4 (1.1)	9.5 (1.1)	.91‖
Function score	89.16 (13.9)	89.8 (13.5)	88.8 (15.2)	.92‖
Use of brace in ADL (yes/no)	2/66	2/67	2/60	.99¶
Use of brace during sports (yes/no)§	14/31	18/30	10/31	.41¶
12mo results				
No. of patients	68	69	63	
Activity level	5.8 (2.3)	6.2 (2.2)	5.9 (2.2)	.61‖
Free of complaints	9.5 (1.2)	9.5 (1.0)	9.7 (0.8)	.59‖
Function score	89.6 (14.8)	91.5 (13.0)	88.9 (14.5)	.53‖
Use of brace in ADL (yes/no)	0/68	0/69	2/59	.15¶
Use of brace during sports (yes/no)§	15/29	8/31	11/37	.31¶

* Measured on a scale of 0 to 10.
† Measured on a report mark scale of 0 to 10 (10, free of complaints).
‡ Measured on a scale of 0 to 100 (0, no function; 100, perfect function).
§ Only applicable in patients who participate in sports.
‖ ANOVA.
Kruskal-Wallis.
¶ χ^2.

Table 5: Number of Relapses in the Three Groups at 3, 6, 9, and 12 Months

Relapses Per Period	Low-Dose Laser N	Low-Dose Laser Cumulative	High-Dose Laser N	High-Dose Laser Cumulative	Placebo N	Placebo Cumulative	Total	χ^2
3mo	11/72		6/72		5/66		22/210	.26
6mo	7/69	18	2/70	8	4/63	9	13/202	.22
9mo	4/68	22	2/69	10	1/62	10	7/199	.39
12mo	0/68	22	3/69	13	0/62	10	3/199	.04

As seen in table 4, there is a striking difference between the two laser groups and the placebo group in absenteeism from work and sports. Other outcome measures do not show large differences. Correction for baseline differences in sex and age with ANOVA did not alter the results. The per-protocol analysis showed similar results.

Table 5 shows the number of relapses per 3 months in the three groups. No patient had more than one relapse. The total number of relapses was 45 (20.7% to 22.6%, depending on comparison of number of patients at baseline or at the end of follow-up), 22 of which occurred in the low-dose group. From a Cox regression model, a significant trend ($p = .04$) toward a greater relapse ratio in the low-dose LT group than in the high-dose LT group or placebo group was found.

Analysis for success of blinding showed that placebo laser therapy was not unmasked by the patients (table 6). Subgroup analyses showed no difference in outcome when corrected for age (cut-off, 35yrs), sports participation (yes/no), gender (female/male), or occupation (sitting/standing work).

DISCUSSION

In this study, we tried to overcome flaws encountered in a systematic review of 36 randomized trials of LT.[22] Attention was paid to prognostic comparability at baseline level, group size, and blinding of the entire procedure. Furthermore, explicit details were given about dose and intensity of LT. An independent party checked for adequate dosimetric output of the laser device before, during, and after the trial.

In this trial, we compared a low-dose, a high-dose, and a placebo group. To determine whether the claimed effects of LT were present, we incorporated a placebo group because new technologies are known to be surrounded by novelty effects and thus have the potential of enhancing placebo responses. We opted for a low-dose and a high-dose group because of the ongoing debate on adequacy of dose. The low dose represented a dose and intensity used in current physiotherapy practice and was derived from a previously undertaken metaanalysis.[22] Because there are claims that this dose is too low to be effective, we also incorporated a high-dose group in the trial. In this fashion we would be able to determine a dose-response relationship in case of cumulative effects, an inadequate dose-response relationship in case of too low a dose, or perhaps a rebound effect in case of too high a dose. Although no adverse effects of LT were reported by the patients themselves, the outcome measures clearly showed delayed recovery in the LT groups.

Table 6: Success of Blinding per Group

Which Treatment Did You Get?	Low-Dose Laser	High-Dose Laser	Placebo
Do not know	61%	60%	69%
Low-dose	21%	19%	13%
High-dose	12%	14%	13%
Placebo	6%	7%	3%
	100%	100%	100%

The chosen wavelength was derived from the results of previous trials. It seemed that trials on musculoskeletal diseases and sports injuries that used 632nm laser showed, on average, less positive results than trials using 904nm laser.[22] The relative lack of penetration depth of 632nm laser may have played a part in these findings, although other factors such as inadequate dosimetry may also have influenced these results.[23] The expert in the field might notice that 820nm and 830nm laser therapy was not considered. When the protocol was developed (1992), insufficient evidence about these lasers existed.

In a pilot study ($n = 38$), with a dose setting that was comparable to that of our low-dose group, we found that LT had beneficial effects.[13] After 5 days of treatment, the pain score appeared to have decreased significantly more in the laser group than in the placebo group. In the present investigation, a slight effect of LT on decreasing pain score was also found (fig 1). However, this difference was only 4%, whereas in the pilot trial a difference of 33% was noted. In the present investigation, both laser groups performed more poorly than the placebo group. All patients were allowed to take standardized pain medication provided by us at intake. Pain medication was registered throughout the trial. After 2 days of intervention, most patients had stopped using medication, in spite of the rather serious injuries as estimated by the function score at intake. Moreover, drug intake was comparable between the groups. Because the differences in effect described here started to take place after 5 days of treatment, drug intake could not have influenced the outcome.

Among secondary measures of effect, days of sick leave shows a worrying difference between placebo and laser groups. Compared with placebo, a mean difference of 3.4 days for high-dose LT and 4.7 days for low-dose LT may be regarded as highly cost-ineffective, especially taking into account the extra medical costs of laser treatment. For the total trial, it meant for the LT groups a loss of 593 working days compared with the placebo group.

The number of relapses in this trial is substantial but is to be expected. Other trials report corresponding figures.[24,25] No explanation for the low-dose group being responsible for half the relapses is given.

We conclude that LT is not effective in the treatment of ankle sprains. On the basis of this trial, therapists should reconsider the use of LT in the treatment of ankle sprains.

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Suppliers

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