



Laser acupuncture in children with headache: A double-blind, randomized, bicenter, placebo-controlled trial

Sven Gottschling ^{a,*}, Sascha Meyer ^b, Inessa Gribova ^c, Ludwig Distler ^c, Jens Berrang ^d,
Ludwig Gortner ^b, Norbert Graf ^a, M. Ghiath Shamdeen ^e

^a University Children's Hospital, Department of Pediatric Hematology and Oncology, Saarland University, Kirrbergerstr., 66421 Homburg, Germany

^b University Children's Hospital, Department of Neonatology and Pediatric Intensive Care Medicine, Saarland University, Homburg, Germany

^c Caritas Hospital St. Theresia, Pain Clinic, Saarbruecken, Germany

^d Gemeinschaftskrankenhaus Herdecke, Department of Pediatrics, Herdecke, Germany

^e University Children's Hospital, Section of Neuropediatrics, Saarland University, Homburg, Germany

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Abstract

To investigate whether laser acupuncture is efficacious in children with headache and if active laser treatment is superior to placebo laser treatment in a prospective, randomized, double-blind, placebo-controlled trial of low level laser acupuncture in 43 children (mean age (SD) 12.3 (\pm 2.6) years) with headache (either migraine (22 patients) or tension type headache (21 patients)). Patients were randomized to receive a course of 4 treatments over 4 weeks with either active or placebo laser. The treatment was highly individualised based on criteria of Traditional Chinese medicine (TCM). The primary outcome measure was a difference in numbers of headache days between baseline and the 4 months after randomization. Secondary outcome measures included a change in headache severity using a 10 cm Visual Analogue Scale (VAS) for pain and a change in monthly hours with headache. Measurements were taken during 4 weeks before randomization (baseline), at weeks 1–4, 5–8, 9–12 and 13–16 from baseline. The mean number of headaches per month decreased significantly by 6.4 days in the treated group ($p < 0.001$) and by 1.0 days in the placebo group ($p = 0.22$). Secondary outcome measures headache severity and monthly hours with headache decreased as well significantly at all time points compared to baseline ($p < 0.001$) and were as well significantly lower than those of the placebo group at all time points ($p < 0.001$). We conclude that laser acupuncture can provide a significant benefit for children with headache with active laser treatment being clearly more effective than placebo laser treatment.

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1. Introduction

Headache is a common health problem, often with an onset in childhood. An increasing prevalence of headache in children has been reported [4,23,33,39,45]. In a crossnational study of the World Health Organization (WHO) including 12,000 children, the prevalence of

headache increased 5% in 4 years [36]. The prevalence rates for migraine and tension-type headache (TTH) vary considerably (0.9–72.8%) depending on how strict criteria of the International Headache Society (IHS) were applied [1,3–5,33]. In a recent large Swedish study the prevalence of TTH and migraine in children and adolescents was 9,8% and 11%, respectively [23]. TTH is essentially defined as bilateral headache of a pressing or tightening quality without a known medical cause. TTH is defined as episodic if it occurs on less than 15 days a month and as chronic if it occurs more often

* Corresponding author. Tel.: +49 6841 16 28399; fax: +49 6841 16 28424.

E-mail address: ksigot@uniklinikum-saarland.de (S. Gottschling).

[16]. Migraine typically manifests as attacks of severe, pulsatile, one-sided headaches, often accompanied by nausea, phonophobia or photophobia [16]. Treatment for headaches includes a wide variety of drugs and non-pharmacological methods [44]. Acupuncture is the most widely used non-pharmacological intervention to prevent or treat episodes of TTH or migraine attacks [24–26,28]. Recently, a number of adequately powered studies showed that acupuncture could be effective in an adult population [2,7,8,11,12,20,21,27,40,42,43]. However, there is only one study in children fulfilling the criteria of a randomized controlled trial (RCT). In this study by Pintov and colleagues [32], 22 patients aged 7–15 years with migraine received either true or superficial (in this trial defined as placebo) acupuncture. The results showed that true acupuncture clearly reduced migraine frequency and severity. No such changes were observed in the placebo group. In our double-blind, randomized, bicenter, placebo-controlled trial we investigated whether active laser acupuncture reduced headache frequency more effectively than placebo laser acupuncture in children with migraine or tension-type headache.

2. Patients and methods

2.1. Ethical approval

The study was done in accordance with the ethical standards of the Helsinki Declaration of 1975, as revised in 1983. The Human Ethics Committee of the Saarland University approved all aspects of the study. Written informed consent was obtained from all patients and their parents or persons having the care and custody of the child.

2.2. Patient recruitment and selection

The study was carried out between October 2006 and March 2007 at two medical centers, the University Children's Hospital Homburg and the Caritas Hospital Saarbruecken, Germany. Patients admitted either to the neuropediatric section of the University Hospital or to the pain clinic of the Caritas Hospital with the diagnosis of headache were contacted to participate in this study. Interested families received a phone number and had to themselves contact the trial coordinator for further information. Potential subjects for the study were then offered a face-to-face appointment for formal assessment. When fulfilling the inclusion criteria patients received a headache diary and the pre-randomization phase of 4 weeks was started. After evaluation of the headache diaries the first 48 patients still meeting the inclusion criteria were enrolled in the study.

2.3. Inclusion and exclusion criteria

Patients were included if they were 17 years of age or under; had unilateral or bilateral headache, either migraine (2 to 8 migraine attacks per month), with or without aura, or tension-type headache (at least eight days with headache a month) in accordance with the diagnostic criteria of the International

Headache Society (IHS) [16] present for at least 12 months. Secondary causes for headache were excluded by adequate means (EEG, brain-MRI, ophthalmologist, otorhinolaryngologist). Exclusion criteria: age 18 or older; headache other than migraine or tension-type; less than 2 migraine attacks per month or less than 8 days with headache per month for tension-type headache; use of analgesics on more than 10 days per month; prophylactic migraine treatment with drugs; relevant organic or mental disorders; participation in any clinical research study in the preceding 6 months; history of seizures (except febrile convulsions). Patients with less than 2 documented migraine attacks or less than 8 documented days with headache during the 4 weeks of pre-randomization baseline phase. The first 48 patients who fulfilled the inclusion criteria were recruited for the study.

2.4. Randomization and blinding

Patients were randomized to one of two identical lasers (labelled A or B) following allocation using 48 sequentially numbered, opaque, sealed envelopes which were prepared earlier by a third party, using a computerized table of random numbers and balanced to ensure equal numbers in each group. The contents stated which laser had to be used (A or B) and each envelope was opened immediately before the first treatment. In this bicenter study the acupuncturists had to contact the trial co-ordinator by phone to receive the results of the randomization. The digital display of both lasers, the visible red guiding light and the sound emitted during operation were identical, but only one emitted an invisible laser beam.

2.5. Laser device

The patients were treated with a class 3B laser. The laser used was a schwa-medico Modulas-Handy 2/99, 30 mW, 830 nm, continuous wave, power density 3.8 W/cm², 1 mm laser beam diameter, REF 205237, schwa-medico, Ehringshausen, Germany. Before the laser was switched on, the patient, the acupuncturist and any other person in the room (e.g. parents) put on protective glasses specific for 830 nm wavelength. The glasses were used for eye protection, as required for Class 3B lasers. For both, the acupuncturist and the patient, it was impossible to differentiate between active and placebo laser because of the invisible infrared laser beam, being subthermal. Therefore no perceptible physiological changes occurred.

2.6. Treatment protocol

One hundred and three patients contacted the trial coordinator. Patients fulfilling the inclusion criteria had a personal interview. Patients received a headache diary and started with a 4-week-pre-randomization phase, keeping a headache diary focussing mainly on: days per month with headache, duration of headache per day, severity of pain (on a 10 cm visual analogue scale (VAS)) and type and amount of rescue medication. Those patients still fulfilling the inclusion criteria after pre-randomization phase were randomized and the patient recruitment was stopped. Patients were randomized into Laser A or B and received once a week a laser acupuncture treatment by one of three experienced acupuncturists (between 4 and 18 years of experience, between 250 and 1500 h of training). A

combination of traditional Chinese body acupuncture and auriculotherapy was applied. Treatment was based on TCM criteria (history, pulse diagnosis, tongue diagnosis) in some patients combined with a computer-based measurement of skin resistance differences (Acussana Proacus, Acussana GmbH & Co. KG, Dautphetal, Germany) at defined points to narrow down the range of applicable points. Basic points for patients with frontal headache were large intestine 4 (He Gu) and stomach 36 (Zu San Li), for patients with lateral headache Sanjiao 5 (Zhi Gou) and gallbladder 34 (Yang Ling Quan), for patients with occipital pain small intestine 3 (Hou Xi) and bladder 60 (Kun Lun), and for patients with holocephalic pain Du Mai 20 (Bai Hui). Additional body acupuncture points (e.g. locus dolendi points) and ear acupuncture points could be chosen individually. There was no limitation of points in this study. The acupuncturist was allowed to decide whether to laser uni- or bilaterally. The settings and technique of laser radiation used on each patient were: continuous wave mode, using vertical contact with the skin and a duration of 30 s resulting in an intensity of ~ 0.9 J/point. During all stages of the study patients were allowed to treat acute headaches as needed. During the treatment patients had to document all of the above-mentioned variables in the headache diary until 16 weeks from baseline. We assured participants compliance as follows: all study participants had a history of headache since at least 12 months and were already seen by a couple of specialists expressing a considerable psychological strain leading to a high motivation to receive acupuncture free of charge. Both patients and parents were instructed on how to record the data. Both parents and patients received paper headache diaries in case a diary got lost. Diaries had to be filled in daily. Parents were instructed to remind their child every headache day to assess and to write down the parameters together with them. Pain intensity was measured using a 10 cm visual analogue scale (VAS). Headache duration should be estimated the day following a headache attack. Weekly phone calls during the whole study phase between the trial coordinator and every study participant were performed and patients/parents were advised to send the filled in diaries back to the trial coordinator monthly. In case of a delay or missing data patients/parents were contacted immediately. After receiving the completed diaries the patients were unblinded to what treatment they had received. Patients that had received placebo acupuncture were given the opportunity to experience 4 treatments of active laser acupuncture.

2.7. Outcome measurement

Primary outcome measure was the difference in number of days with headache between the placebo and verum group. Secondary outcome measures were: change in headache duration and headache severity at different time phases compared to baseline and in comparison of active laser acupuncture with placebo laser acupuncture for all mentioned parameters.

2.8. Statistical methods

Assuming that the active treatment group would show a 70% improvement and the placebo treatment group a 25% improvement, a sample size of 20 patients in each group was

needed to yield a power of 80% with a type I error of 5%. The power calculation was based on the only double-blinded trial of acupuncture for children with headache with 22 participants [32] and other blinded trials on needle/laser acupuncture in children for various other conditions ranging from 36 to 50 participants in total [12,15,19], as well as on personal experience. With an estimated dropout rate of 20% 48 patients were needed for randomization. Statistical analysis was performed using SPSS (SPSS 11.0. SPSS Inc., Chicago, IL). Data are presented as means \pm standard deviation (SD) or \pm standard deviation of the mean (SDOM) as indicated in the text and figures. Biometric data were compared using the χ^2 test. For statistical comparison between the two groups, the Mann–Whitney *U*-test was employed. To compare data within the two groups one-way analysis of variance (ANOVA) was performed. As more statistical tests were conducted, the likelihood that one or more are significant just due to chance increases (so-called “alpha inflation”). Therefore, the post hoc Scheffe correction for multiple testing was employed to compensate for spurious significant results that occur with multiple comparisons. The test gives a measure of the difference between all means for all combinations of means. A *p*-value < 0.05 was considered significant.

3. Results

One hundred and three patients contacted the trial coordinator after being pre-screened by either the neuro-pediatric section of the University Children’s Hospital Homburg or the pain clinic of the Caritas Hospital Saarbruecken. The first 48 patients who met the eligibility criteria were included in the study (Fig. 1).

3.1. Characteristics of the study group

The baseline characteristics of the groups after randomization are detailed in Table 1. There were no significant differences concerning age, gender, baseline headache frequency, headache type, severity and duration of headache attacks between the active and the placebo laser group. A mean (SD) of 8.4 (± 4.7) acupuncture points per patient and session was stimulated.

3.2. Dropouts

Five subjects withdrew from the study during the course of treatment (two of the active and three of the placebo group). In no case was the reason related to headache or treatment complications (Fig. 1).

3.3. Primary and secondary outcome measures

3.3.1. Headache frequency

There was a significant decrease in headache frequency compared to baseline in the active laser treatment group. The mean improvement in headache

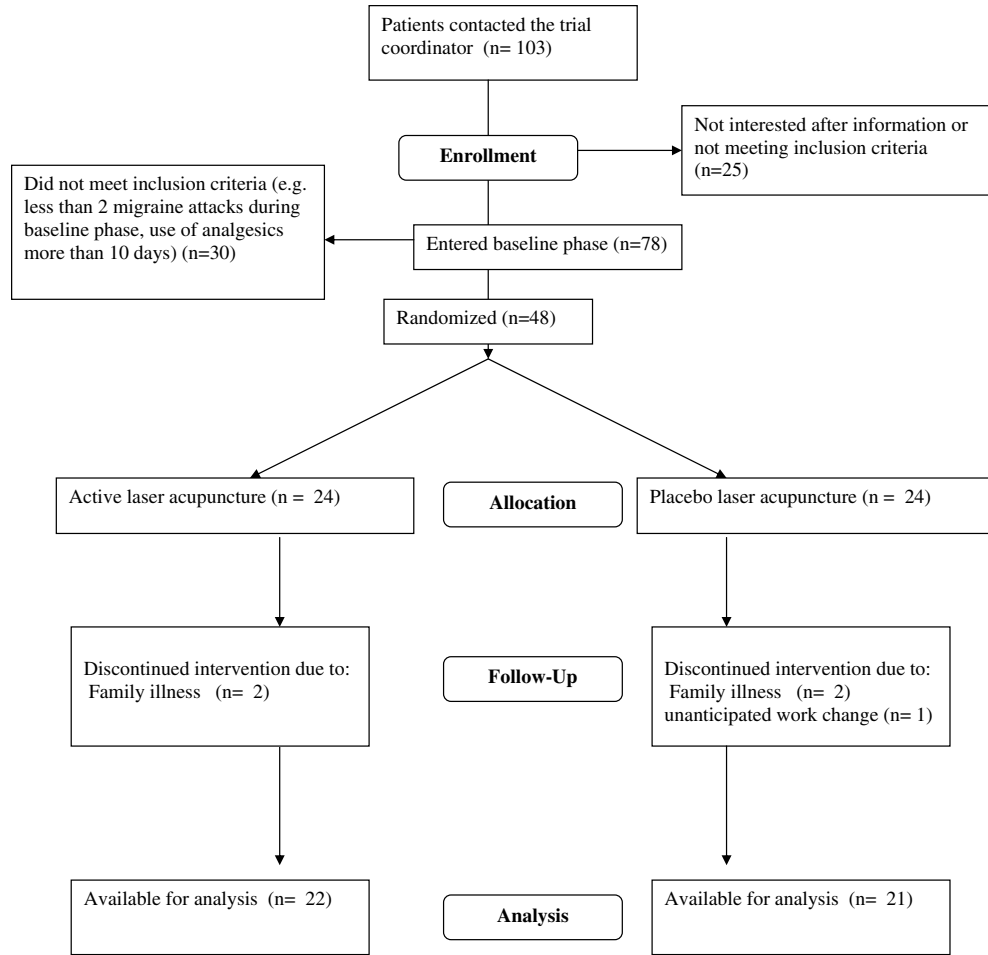


Fig. 1. Flow chart of patient recruitment.

frequency was significantly greater in the treatment group than the placebo group. From baseline to week 5–8 the number of days decreased by 7.0 days in the active acupuncture group compared to 1.2 days in the placebo group. The difference active acupuncture vs. placebo acupuncture was 5.4 days ($p < 0.001$). The decrease in headache frequency in the placebo group was not significant compared to baseline ($p = 0.145$)

(Fig. 2). Whereas, the headache frequency in the placebo group reached baseline level in weeks 9–12, headache frequency in the active acupuncture group stayed low until the study endpoint ($p < 0.001$) (Fig. 2).

3.3.2. Duration of headache

There was a significant decrease in monthly headache hours in the active acupuncture group compared to

Table 1
Patient demographic characteristics (mean ± standard deviation (SD))

Patient characteristics	verum acupuncture	placebo acupuncture	P-value
Number of patients	22	21	n.s.
Age (years)	12.5 ± 2.8	12.0 ± 2.4	n.s.
Headache since when (years)	5.3 ± 3.7	3.9 ± 2.6	n.s.
How often per month during the last year	9.4 ± 6.6	9.0 ± 5.2	n.s.
Duration of an attack (hours)	8.7 ± 4.0	7.8 ± 3.6	n.s.
Severity (VAS 0–10)	7.7 ± 1.6	7.3 ± 1.2	n.s.
Type of headache			
Migraine	11	11	n.s.
Tension-type Headache	11	10	n.s.
Sex (F/M)	14/8	16/5	n.s.

n.s., non-significant.

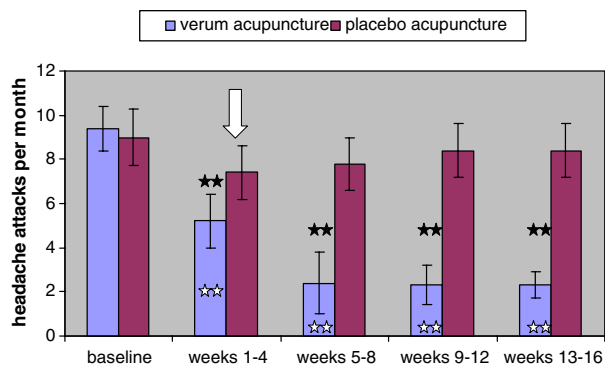


Fig. 2. Headache frequency. Arrow indicating time phase when weekly acupuncture sessions took place. White stars indicating significant changes compared to baseline. Black stars indicating significant differences between placebo and active acupuncture with * indicating ($p < 0.05$) and ** indicating ($p < 0.001$). Data are presented as means. Error bars indicate standard error of the mean (SODM).

baseline with the mean improvement being greater in the active acupuncture group (Fig. 3). The mild benefit of placebo acupuncture disappeared after eight weeks from baseline whereas the beneficial effect of active laser acupuncture lasted until the end of the follow up (Fig. 3). Interestingly, there was no significant change concerning the daily duration of headache on headache days. The monthly headache hours decreased almost solely due to a reduction of the headache frequency.

3.3.3. Pain intensity during an attack

Pain intensity in the active treatment group decreased significantly compared to baseline. Again the improvement in the active acupuncture group was greater than in the placebo group. Nevertheless, there was a significant beneficial effect of placebo laser acupuncture in weeks 1–4 and 13–16 from baseline ($p = 0.024$;

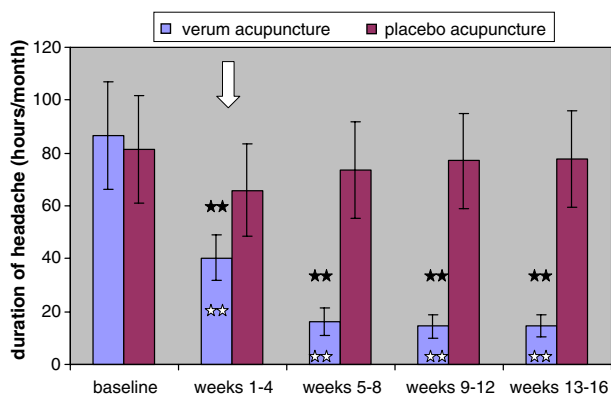


Fig. 3. Headache duration. Arrow indicating time phase when weekly acupuncture sessions took place. White stars indicating significant changes compared to baseline. Black stars indicating significant differences between placebo and active acupuncture with * indicating ($p < 0.05$) and ** indicating ($p < 0.001$). Data are presented as means. Error bars indicate standard error of the mean (SODM).

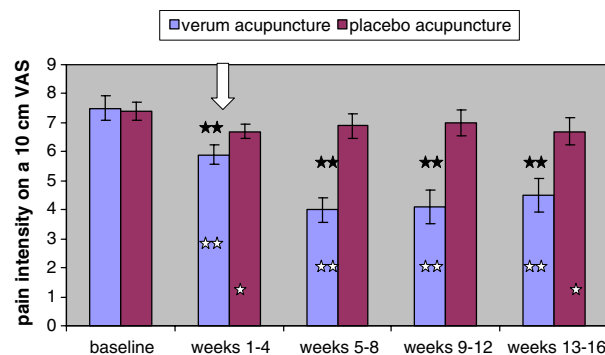


Fig. 4. Pain intensity. Arrow indicating time phase when weekly acupuncture sessions took place. White stars indicating significant changes compared to baseline. Black stars indicating significant differences between placebo and active acupuncture with * indicating ($p < 0.05$) and ** indicating ($p < 0.001$). Data are presented as means. Error bars indicate standard error of the mean (SODM).

$p = 0.004$) (Fig. 4). The effect of the active laser acupuncture on pain severity was weaker than on the above-mentioned parameters but still significantly superior compared to placebo acupuncture at all time points ($p < 0.001$).

3.3.4. Adverse effects

Adverse effects of acupuncture were an item in the headache diary. Moreover, patients had an additional telephone interview in the context of unblinding also with a focus on adverse effects of laser acupuncture. No study participant reported any adverse effects of the treatment.

4. Discussion

Over the past two decades, several studies have investigated the efficacy of acupuncture in relieving headache. Some of the studies suggested that acupuncture may be useful [8,12,27,42], others showed no superiority to sham acupuncture or other types of alternative treatment [2,20,25,28,43]. It remains still partly unexplained how acupuncture can have an influence on acute and chronic pain. Proposed mechanisms are an activation of descending inhibitory pain control systems [19], an activation of the propriospinal heterosegmental antinociceptive system [35], and alterations of β -endorphin plasma levels [32]. There are data about laser–tissue interactions inducing an inhibition of $\text{Na}^+ - \text{K}^+ - \text{ATPase}$, exerting influence on the resting potential of cells. Moreover laser can induce a reversible blockade of mitochondrial transport, resulting in a neurotransmission failure in A-delta and C fibres leading to pain relief [9].

As headache is known to be particularly responsive to placebo treatment, the choice of a suitable placebo for acupuncture is difficult [13,46]. Sham acupuncture and placebo needle acupuncture proved to be quite problematic because double-blind studies are impossible, and the

quality of the study results of non-blinded or single-blinded studies has to be challenged. Laser acupuncture offers distinct advantages over traditional needling apart from the possibility of a double-blind setting [6,41]. The procedure is painless and non-traumatic and therefore especially suitable for children of all ages. Laser acupuncture is devoid of common side effects of needle acupuncture like nausea and syncope and even more important no fatal complications like septicaemia and pneumothorax can occur [10,14,31].

This prospective, randomized, placebo-controlled double-blinded study provides evidence for the efficacy of a 30 mW, 830 nm low level laser in the treatment of children with chronic headache. Our study is, to date, the first pediatric double-blinded study on the efficacy of laser acupuncture in children with chronic headache. Our two groups were comparable concerning age, gender, type of headache and the baseline values for primary and secondary outcome parameters. The verum acupuncture laser group reported a statistically significant and clinically relevant improvement concerning the primary outcome measure, headache frequency. Interestingly, the beneficial effects of real laser acupuncture persisted until the endpoint of the study. Placebo laser acupuncture was, as expected, not without influence on the disease pattern [13]. Especially during weeks 1–4 when patients received weekly acupuncture sessions, changes in headache frequency, severity and duration were observable, but most of the beneficial effects diminished after 8 weeks. The clinical effects of placebo acupuncture could be possibly explained by the weekly contact of the patients with the acupuncturist. Although acupuncture has a high rate of acceptance in the pediatric population [22] there are very few studies of higher quality concerning the efficacy of acupuncture in children for different diseases [34,37]. One possible reason for the paucity of acupuncture studies in younger populations may be the conventional view that children are afraid of acupuncture and researchers are concerned regarding patient enrolment and/or retention. Studies on laser acupuncture in children are also rare, even though the results were as well promising [6,30,41]. Compared to the study results in adult patients, our results support the experience of the authors that children seem to be more sensitive to acupuncture, even to laser acupuncture which is said to be efficacious to a lesser extent than needle acupuncture [12,18]. In our study population, we applied 0.9 J/point once a week on four consecutive weeks. Compared to other studies on laser acupuncture the energy dosage per acupuncture point was in a median dosage range and the treatment intensity (acupuncture treatments/patient) was quite low [6,12,15,41]. From a clinical point of view it is very important that the beneficial effects of active laser acupuncture lasted for at least a couple of months in this group of chronic pain patients whereas the beneficial

effects of placebo acupuncture lasted only short time. The clarity of the superiority of active acupuncture was quite distinct in comparison with studies on adult headache patients [7,11,20,40]. No patient in either group reported any adverse effects of acupuncture. This is in line with reports on the safety of acupuncture [14,29]. The use of laser acupuncture in children is non-traumatic, could be applied to children of all ages, regardless of platelet count and coagulation status and even more importantly the symptom of pain is not treated with a painful or frightening procedure like, e.g. needle acupuncture.

The advantages of this study include strictly concealed central randomization, blinded experienced medical acupuncturists and blinded diary evaluation. Furthermore patients received a highly individualised acupuncture. Patients were not treated standardized, with the so-called formula acupuncture, a treatment regime that is often practised in Western countries. Formula acupuncture implies that patients with the same Western diagnosis share a pathology that is sufficiently similar to be treated with the same acupuncture points. In TCM a special kind of diagnosis mainly based on constitutional factors leads to an individually tailored acupuncture as it was applied in this study. Applying TCM criteria could be one of the main reasons for the favourable results in the active laser acupuncture group. The German acupuncture trials (GERAC) for various conditions provided only weak evidence for specific acupuncture-point related effects leading to an intense debate about the relevance of using specific acupoints [26]. The only single-blinded GERAC trials used formula acupuncture only partially in accordance with TCM criteria. In our trial we had no group receiving active laser treatment at non-acupuncture points. Therefore, we cannot rule out that the laser treatment as such and not stimulating meridian-associated acupoints was important. Nevertheless there is growing evidence for specific acupoint-related effects. It has been shown that the stimulation of vision-related acupoints led to an activation in the visual cortex demonstrated with functional magnetic resonance imaging [38]. Similar results were found concerning the hypothalamic–lymbic system when analgesic acupoints were stimulated [17]. Furthermore it has been shown that cerebral cortical activity was ipsilateral to the body side to which acupuncture was applied [38]. This leads to the assumption that acupuncture is really mediated by meridians, all but one not crossing to the other side.

4.1. *Clinical relevance*

Facing the percentage of children and adolescents with headache (at least 20%) [23,45], headache and the treatment of headache in this age group are of enormous socioeconomic importance. Laser acupuncture is a cheap

treatment option that is nearly devoid of side effects when applied within a common energy dosage range per acupuncture point and combined with an appropriate eye protection. For many parents the regular use of rescue medication for headache and even more the prophylactic treatment with a drug seems to be more or less unacceptable for their children [47]. Moreover a couple of drugs like, e.g. some triptans are not licensed for children and therefore a large amount of pediatric headache sufferers does not receive an adequate headache prevention or therapy leading to further pain chronification.

4.2. Limitations

Our study population was rather small with only 43 patients enrolled. Our inclusion criteria consisted of two different types of headache: migraine and TTH and we cannot rule out mixed forms (e.g. a migraine patient occasionally experiencing TTH), but patients with either migraine or TTH were balanced in both groups and we found no significant differences concerning efficacy of acupuncture between both types of headache. It is unclear why the daily duration of headache did not decrease in the treatment group whereas the other parameters significantly did. It could not be ruled out that it might be due to an ambiguity on how to exactly define headache duration.

Unfortunately, we were not able to look for long-term effects because we had to stop blinding 16 weeks after randomization due to a demand of the Human Ethics Committee of the Saarland University.

5. Conclusions

Three main conclusions can be drawn from the results of the present study.

First, laser acupuncture appears to be a safe, non-invasive treatment and therefore especially suitable for children.

Second, even a short-term acupuncture treatment with a low level acupuncture laser has good and at least medium-term lasting effects on headache frequency, severity and monthly hours with headache.

Third, active laser acupuncture treatment was clearly superior to placebo laser acupuncture treatment.

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