Chapter 10: Aluminum foil for the prevention of post-amputation pain: A randomised, double-blind, placebo-controlled, cross-over trial

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Abstract

Introduction: Phantom limb pain (PLP) is a painful sensation perceived in the missing limb after amputation. The underlying pathophysiology remains unclear. Up to now, only opioid analgesics have proven effective in prospective studies. Anecdotally, PLP patients employ self-help measures, sometimes including “wrapping-up” or rubbing their stump with aluminium foil for relief of PLP. Our hypothesis is that wrapping up an amputation stump with aluminium foil perioperatively will prevent PLP in the postoperative period.

Methods: From September 2007 to September 2009, 32 consecutive patients were included in a crossover, double-blind, randomized clinical trial. Perioperative fitting of an aluminium stump bandage was compared with a placebo paper foil. Scores were noted daily in a variable diary. The observation period was 2 weeks: first week double-blinded, second week change of bandage: aluminium to placebo or vice versa. A visual analogue scale (VAS) score was used as primary research variable. Secondary variables were use of analgesics, VAS measure of wound pain and wound infections. Statistical analysis was done by means of Student’s t-test for non-paired observations.

Results: Baseline characteristics were similar between groups. A period effect (p=0.84) and treatment-period interaction (p=0.79) were not present. There was no significant difference (mean difference 0.42) between both treatments in PLP VAS scores (95% CI -2.56 - 1.81, p=0.71). VAS measure of wound pain showed no significant difference between both groups (95% CI -2.32 - 1.66, p=0.72). Also the other secondary endpoints did not differ.

Conclusion: Patients receiving an aluminium foil stump wrapping do not experienced less PLP as compared with a placebo.
Introduction

Phantom limb pain (PLP) is a painful sensation perceived in the missing limb after amputation. [1] It must be differentiated from non-painful phantom phenomena and residual-limb pain (pain in the residual portion of the limb or stump).

The incidence of PLP varies from 50% to 90%, [2,3] but diminishes with time. [4] PLP is complex, multidimensional and the underlying pathophysiology remains unclear. Factors associated with PLP are [4,5]: lower leg amputation, amputation on both legs and preoperative pain. In approximately 50%, the onset of PLP occurs within the first 24 hours. For another 25%, PLP begins within the first week and in a minority of patients, the onset of PLP occurs many months, or even years after amputation. [6]

The mainstay treatment for PLP is predominately pharmacological. However, most studies have been uncontrolled short-term assessments of small patient samples. [7] A maximum benefit of about 30% has been reported from treatments such as surgical interventions (e.g., sympathectomy, rhizotomy), pharmacological approaches (e.g., nerve blocks, local anesthetics), physical therapy (e.g., ultrasound, transcutaneous electrical nerve stimulation [TENS]), and psychological treatments (e.g., psychotherapy, biofeedback, hypnosis). These reports of beneficial interventions have been generally supported by small research samples, flawed research designs, transient effects, or with below the expected rate of placebo response. [8,9]

As of yet only opioids have proven to result in pain reduction in a randomized trial. [10,11] Two trials have found a positive effect with the use of an electromagnetically shielding stump stocking interwoven with metal. [12,13]

Anecdotally, PLP patients employ self-help measures, sometimes including "wrapping-up" or rubbing their stump with aluminium foil for the relief from PLP. In our practise we have encountered multiple amputees, claiming a benefit from this method. Also, entering ‘tin foil AND phantom pain’ or
‘aluminium foil AND phantom pain’ in an internet search engine will yield several hits, referring to blogs and personal websites describing patients’ both positive and disappointing experiences with aluminium foil stump wrapping. The mechanisms underlying this supposed effect are unclear. In contrast with the metal interwoven stump stockings used in two prior investigations, [12,13] aluminium foil does not carry any ferromagnetic properties.

Our hypothesis is based on the experience of patients with established PLP, who employ aluminium foil stump wrapping, claiming a reduction of their symptoms. We hypothesized that wrapping an amputation stump with aluminium foil perioperatively will prevent or diminish phantom pain in the postoperative period.

Patients and methods

Thirty-two consecutive patients were included in a prospective single-center cross-over, double-blind, placebo controlled, randomised clinical trial from September 2007 to September 2009. (Figure 1) Inclusion criteria were: Consenting adults over the age of 18 years, ability to communicate adequately, with a single lower extremity amputation due to peripheral vascular disease or diabetic neuropathy. Patients with a recurrent or second amputation or guillotine amputation were excluded. The randomisation was stratified by the level of amputation and diabetic neuropathy without macrovascular disease. After completing a preoperative pain questionnaire, patients were allocated to one of the two treatment groups, aluminium first or placebo first, using sealed opaque envelopes with computer generated randomization numbers. An independent research fellow performed the randomization. The surgeon was informed about the randomisation outcome in the operating room. Stratification for amputation level and reason for amputation (critical ischemia or diabetic neuropathy) was performed. Patients, nurses and
residents on the ward were kept blinded to the allocated treatment sequence. The local medical ethical committee approved this study (WO 07017).

*Surgical technique*

Skin closure was done with staples in all patients. Immediately after surgery, the patients had a stocking fitted to their amputation stumps, consisting of a sterile wound dressing, a wrap of aluminium foil or paper, covered by a stump cotton wool bandage in the operating room. Qualities of the stocking - exterior view, size, weight, compression and lining - were identical.

*Postoperative care*

Postoperatively, all patients were treated equally with regard to feeding, pain regulation, mobilization, and postoperative care. The wound was inspected on day 5, at which patients and nursing staff were unblinded. The trial bandage was changed on day 7; patients with aluminium wrapping were given the placebo paper and vice versa. After 14 days the bandages were removed for final inspection and analysis. Pain medication consisted of standard paracetamol 6 times 500 milligrams (mg) or piritramide 10 mg or tramadol 50 mg three times per day, when demanded by the patient. The use of other analgesics and neuroleptics was avoided. The use of any analgesics was recorded prospectively.

*Primary and secondary research variables*

A visual analogue scale (VAS) measure of PLP served as primary research variable, which was scored daily. Secondary variables were the use of analgesics, VAS measure of wound pain (scored daily) and the incidence of wound infections (scored on day 5 and 14). A mean VAS measure was
calculated for both treatments. For the analysis this mean of the daily scores for aluminium bandage and placebo were compared. Incomplete follow-up was defined as 3 or more absent daily scores by any cause per treatment per patient. Comorbidities present were diabetes mellitus (type I or II), cardiovascular disease (angina pectoris or heart failure), chronic kidney disease (creatinine > 180 µmol/l), hypercholesterolemia and hypertension. The manuscript was written with the Consort Statement as guidance.

Figure 1. Trial flow diagram
Statistical analysis

Patients were analysed according to the intention-to-treat principle. A power analysis ($\alpha$ 0.05, $\beta$ 0.2) was based on the VAS score of PLP. A difference in 2 points on the VAS measure ($\pm$ 2 SD) between the two groups was considered as a clinical significant difference. This difference revealed that a sample size of 23 treatments had to be included in each arm. In anticipation of a drop-out rate of 10%, a group size of 30 in each treatment arm was considered necessary. Due to the crossover design of this study, 2 times 15 patients were randomised; aluminium first or placebo first. Both treatments were compared using Chi-squared test or Student’s t-test, one or two sample when appropriate. Association with the primary research variable was tested by means of analysis of variance (linear regression) and Pearson’s correlation coefficient. A p-value of < 0.05 was considered statistically significant. For statistical analyses, the SPSS 17.0 software package (SPSS, Chicago, IL) was used.

Results

Baseline characteristics are shown in table 1. Fifteen right limbs and 17 left limbs were included. There were no differences between the two groups. First of all, a period effect was tested by a two sample t-test in order to compare the differences between the treatment 2 weeks in the 2 patient groups. Differences were excluded (confidence interval [CI] of the difference -1.68–1.39; $p=0.84$). Also, no treatment-period interaction was present, excluding any interaction between the patients’ average response, regardless of the order in which they were received, to the two treatments (95% CI of the difference -2.12–1.63; $p=0.79$). The mean difference in PLP score at the end of the study period was 0.42 points: aluminium scored slightly more PLP. (Table 2) However, this was not significant. Also, VAS measures of wound pain at the end of the study
period did not show any significant difference between both groups. There was no association between PLP and wound pain (p=0.32, Pearson’s correlation test). In the entire study population, 3 patients did not experience any PLP, 2 patients had a mean VAS measure above 4. There were no predictive factors associated with PLP (linear regression analysis). On day 5 (wound inspection) patients treated with aluminium foil experienced more PLP and wound pain, the latter difference being significant (95% CI 0.27–3.36, p=0.023). The rate of uncomplicated wound healings did not differ between both groups (p=0.31). Three patients underwent a second amputation due to wound infections. In the entire study population, 8 patients received morphine analgesics, 2 patients had epidural analgesia, 7 patients required tramadol hydrochloride and the remaining group used paracetamol. There was no significant difference between both treatments in use of analgesics (p=0.69).
### Table 1. Baseline characteristics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>group 1 (18)</th>
<th>group 2 (14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age [mean (SD)]</td>
<td>72 (11)</td>
<td>74 (12)</td>
</tr>
<tr>
<td>Male</td>
<td>14</td>
<td>7</td>
</tr>
<tr>
<td>Comorbidity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>10</td>
<td>4</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Smoking</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Failed recent bypass</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Indication of amputation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>peripheral artery occlusive disease III</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>peripheral artery occlusive disease IV</td>
<td>10</td>
<td>9</td>
</tr>
<tr>
<td>Diabetes</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>other</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>VAS score preoperative [mean (SD)]</td>
<td>3.3 (3.2)</td>
<td>5.2 (3.2)</td>
</tr>
<tr>
<td>Level of amputation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>transtibial</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>transfemoral</td>
<td>9</td>
<td>8</td>
</tr>
</tbody>
</table>

### Table 2. PLP and wound pain at the end of the study period

<table>
<thead>
<tr>
<th>Variable</th>
<th>Aluminium treatment</th>
<th>Placebo treatment</th>
<th>mean difference</th>
<th>95% CI, p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean phantom VAS score [mean (SD)]</td>
<td>2.05 (1.83)</td>
<td>1.73 (2.50)</td>
<td>0.42</td>
<td>-2.56–1.81, 0.71</td>
</tr>
<tr>
<td>Mean wound VAS score [mean (SD)]</td>
<td>2.94 (1.61)</td>
<td>3.28 (2.22)</td>
<td>0.34</td>
<td>-2.32–1.66, 0.72</td>
</tr>
</tbody>
</table>
Discussion

We demonstrated that patients who received an aluminium foil stocking experienced a mean of 0.42 VAS points more PLP compared to placebo in the immediate postoperative period. This difference was not statistically significant. Also there was no difference in wound pain, use of analgesics, wound healing or stump infections over the complete study period.

These results are in contrast with two randomised trials investigating local stump care in order to prevent PLP, reporting significant differences using a metal-interwoven stump liner. [12,13] Kern et al. performed a double blind crossover trial in a total of 30 leg amputees compared a stump stocking interwoven with metal with a dummy. Each stump stocking was worn for two weeks after a two-week baseline period without stocking. Stump stocking interwoven with metal versus dummy stocking reduced pain significantly more often (77.3% versus 36.4%, respectively, p< 0.008). [13] Conine et al. used a linen fabric with ultra thin steel threads (Farabloc) to be worn over the stump. In this second randomized double blind crossover trial, 34 patients reported their pain relief level on a VAS during a pre-treatment period, Farabloc or placebo treatment period, a no-treatment or "washout" period for the control of any carry-over effect, and an alteration of treatment period. The results were statistically significant (p< 0.001) in favour of the Farabloc period. Of the 34 subjects, 21 reported their greatest pain relief during Farabloc intervention. [12]

Another single-blind cross-over study in untrained subjects on delayed onset muscle soreness demonstrated significantly reduced pain, strength loss, and serum inflammatory markers when double Farabloc wrapping of the thigh post exercise was compared to placebo fabric. [14] These research studies have not determined the mechanism by which Farabloc reduced PLP or delayed onset muscle soreness. The possible explanation of our negative results is the use of aluminium instead of a ferrous metal. If changes in the electromagnetic field are assumed to have an analgesic effect, aluminium will fail due to the absence of ferromagnetic properties.
Farabloc is made of 9.5% steel wire consisting of iron, nickel and chromium, all of which have ferromagnetic properties.

Also chronic pelvic pain, whiplash injuries and lumbar radiculopathies responded favorably to electromagnetic fields. [15-17] In patients with Complex Regional Pain Syndrome I, however, a beneficial effect could not be demonstrated. [18]

Whereas several small randomized controlled studies have reported a reduction of the proportion of patients with PLP when additional epidural anesthesia was used before and during surgery, one large randomized controlled study found no beneficial effect on PLP. [19] Epidural analgesia use was equally divided in our patients, so this did not disturb the outcomes.

Descriptive studies have identified factors that may contribute to the development of PLP: The degree of preamputation pain, below knee amputation, bilateral amputation, acute postoperative pain (including pain due to proinflammatory processes) and psychological factors. [4,5,20]

PLP has a negative effect on the quality of life (QoL) and is related to depressive symptoms. [21,22].

A recent systematic review found a summary quality score of 50% or more in ten studies, with the maximum being 81%. [23] However, these fifteen cross-sectional studies and four prospective studies were found to be heterogeneous with respect to the study objectives and instruments used to assess QoL. Additionally, some obscurities were found in the methodological aspects and study population characteristics of most of these studies.

At the moment only opioids have shown proven efficacy in randomised trials in the treatment of PLP, [10,11,24] with a pain reduction of more than 50% in more than 40% of the patients. This supports the theory that PLP originates from the central nervous system. [25] Accordingly, the key to success is influencing cortical reorganization and preventing or extinguishing a pain memory. Flor et al. maintained that defective stump
information is likely to generate ectopic discharge from the posterior root ganglion, with the consequent result of PLP. [26]

Our study has limitations. Firstly, blinding was interrupted at day 5, due to the regular wound inspection. Secondly, 12 of 32 patients could not be analyzed for the primary variable. This was due to early hospital discharge, complications (delirium) and death (figure 1). Five patients were lost to follow up. The fact that this study is therefore underpowered, unfortunately weakens our conclusions and may warrant further investigations on this topic in a larger sample of patients. Considering all patients – including those who failed to meet the inclusion criteria - we can conclude that we investigated a patient group with severe morbidity. Thirdly, the preoperative pain score was (non-significantly) lower in the patients who started with the aluminum foil. A type II error, however, is unlikely, because although pain scores were lower in the aluminum first group, postoperatively they tended to be higher during aluminum treatment.

In conclusion, there are small, non-significant differences in the perception of PLP and wound pain in favour of placebo foil stocking, compared to aluminium foil after a lower limb amputation. There is a tendency to more wound pain. The use of aluminium foil stump wrapping in wound bandages for lower leg amputations for the reduction of PLP cannot be recommended based on the results of this study.
References

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25. Haug M. [Postamputation phantom limb pain -- comes the solution into view?]. Zentralbl Chir 2005;130:55-9