OBJECTIVES: To evaluate safety and effects of a new home treatment method, a whole-body cold mist treatment, on chronic inflammatory arthritis patients.

Method: Whole-body cold mist shower therapy was given to 121 voluntary patients with chronic inflammatory arthritis in this cross-over study during one week rehabilitation periods. Pain and sleep quality were assessed by a ten centimeter visual analogue scale (VAS). Mental status was assessed by DEPS -depression score. Body temperature, blood pressure, heart rate, use of occasional pain and sleep medication, and possible side effects were recorded.

Results: The differences in pain (VAS) between treatment and control periods were significant (2.0 vs 2.4, p=0.006, paired t-test) in the last measurement, when assessed the pain of the passed week as a whole. A trend could be seen to an increasing difference towards the end of the week. The treatment effect was statistically significant (LRT, p<0.0001) after controlling for period and sequence effects. There was an indication for a better sleep quality (VAS) during the treatment period (2.3 vs 2.7, p=0.058 paired t-test) when assessing the passed week as a whole. The mean depression scale (DEPS) values showed no difference between the periods (5.5 vs 5.0, p=0.1874 paired t-test, at start, and 4.5 vs 4.1 p=0.29 paired t-test, at the end). No significant side effects were recorded.

Conclusions: The new whole-body cold treatment method may offer a safe option for pain self-treatment at home, but further study is needed to find out the clinical significance of the effect after a longer use.

INTRODUCTION: Better treatment strategies and therapeutic options have changed the treatment of inflammatory arthritis during the past decades. However, pain is still the area of health in which almost 70% of the patients would like to see improvement (1). The prognosis of pain is often poor even when inflammatory disease is optimally controlled (2). Pain in inflammatory arthritis is known to rise from multiple mechanisms, involving inflammation, but also peripheral and central pain processing (3,4). Consequently, pain has wide range characteristics and is often associated with psychological distress (5). Higher depression scores are known to result in greater number of painful joints in RA (6). NSAID’s are known to improve pain in RA, but have a modest influence as monotherapy for people with centrally mediated pain (7). Adverse events frequently limit the use of analgesics in arthritis (8), new methods for pain treatment with less adverse events are welcome.

Cold therapies are a widely used self-care method among patients with arthritis, as an adjunct therapy for local and generalized pain. Several studies with cold administered locally or as a whole-body treatment have shown positive effects on pain (9) and general well-being (10). Studies on whole-body cold treatment reveal that rising levels of norepinephrine play an important role in the mechanism leading to a decrease of the pain (11). A new method for whole-body cold treatment has been introduced in Finland. In a pilot study this method has given promising effects on pain and life-quality for people with rheumatic symptoms, with an easily at home applied device (12).

MATERIAL AND METHODS: The study was implemented in Rehabilitation Center Apila, Kangasala, Finland. All the patients entering the center in 2013-2014 with clinical diagnosis of rheumatoid arthritis (RA), psoriatic arthritis (PsA) or ankylosing spondylitis/spondylarthropathy (AS/SpA)
participating the institutional rehabilitation groups were asked to be volunteers in the study (n=208). The study did not change the multidisciplinary rehabilitation program. The program consisted of lectures, discussion groups and physical training in groups. The rehabilitation groups gathered three times during one year and each period lasted 5 days. The medications of the patients varied from only non-steroidal anti-rheumatic drugs to biological agents. The anti-rheumatic or pain relieving medications were not changed during the rehabilitation periods. The patients were in chronic stage of the disease. The number of volunteers was 156 (75%). Altogether 121 participants (91 female) completed the study. The rheumatologist given diagnosis for 65 patients was RA, for 44 patients AS/ and for 12 it was PsA. Randomly chosen half of the study patients were first in the treatment cohort at the first rehabilitation period and 6 months later at the second rehabilitation period they were in the control cohort. For the other half of the study patients the order was vice versa. This is called the AB-BA cross-over design in statistical literature (13). In this statistical method every patient serves as a personal control for him/herself. Some patients started the rehabilitation period in autumn 2013 (period 1), and continued in spring 2014 (period 2). Others started in spring 2014 (period 2) and they continued in autumn 2014 (period 3). The cold treatment was carried out with Amandan-device twice a day, in the mornings and in the evenings. Amandan® is a new Finnish innovation for supplying cold therapy at home. It is device, adjustable to a standard bathroom, equipped with nozzles which disperse cold water into mist particles (14). The patients used a swimming suit and were controlled to stay 2 minutes in the whole-body cold mist shower each time. Pain and sleep quality were assessed by a ten centimeter visual analogue scale (VAS). Both at the treatment and at the control periods the patients were asked on day 1 to assess their pain and sleep-quality during the former week, and on day 5 to assess the pain and sleep-quality of the past week, as a whole. In addition, during the days 1-5 they were asked to assess their current sleep-quality in the mornings and pain three times a day. Mental status was assessed by DEPS depression score (15) on days 1 and 5, in both cohorts. Body temperature was measured two times from upper arm and sternum both before and immediately after the cold treatment. Blood pressure and heart rate were measured at the beginning and at the end of the study period. The use of occasional pain and sleep medication as well as extra local cold treatments were recorded. Univariate analyses were performed using paired t-test applied over difference of treatment and control weeks. To analyze the ABBA cross-over design over the whole study week we utilized the linear mixed model, where treatment/time interaction -, period - and sequence were taken as fixed effects while the intercept and time were considered as random effects. The treatment/time interaction was tested using the likelihood ratio test. The basic advantage of this kind of modeling frame is that it can be used for repeated measures of data and it can also utilize all the information available, e.g. not only the complete measurement sequences.

Results: Mean (±SD) skin temperature at sternum skin before and immediately after treatment was 34.8 C (±1.3) and 26.7 C (±2.0), respectively. No difference was found in mean blood pressure and heart rate between treatment and control periods during the study (Table 1). The mean pain (VAS) value was 3.4 at the start in both periods. A statistically significant difference could be seen between the treatment and the control periods in pain (VAS) in the last measurement, when assessing the pain of the past week as a whole (2.0 vs 2.4, p=0.006 paired t-test, Table 1). A trend can be seen to an increasing difference towards the end of the week (Fig. 1). Testing for the mixed linear model shows that the treatment effect was statistically significant (LRT, p<0.0001) after controlling for period and sequence effects. As expected the sequence effect is not statistically significant while the third period seems to differ of the other two (t=-2.813; p=0.0049). No difference could be seen according to the patient’s clinical diagnosis. When assessed on gender
basis, a difference could be seen. The cold therapy was significantly more effective for women, and the effect was greatest during last days of the study period (p=0.005, likelihood ratio test, Fig. 2A, 2B). There was an indication for a better sleep-quality (VAS) during the cold treatment period (2.3 vs 2.7, p=0.058 paired t-test) when assessing the past week as a whole. The mean depression scale (DEPS) values showed no difference between treatment and control periods (5.5 vs 5.0, p= 0.1874 paired t-test, at start, and 4.5 vs 4.1 p=0.29 paired t-test, at the end). No gender difference could be seen in sleep quality or mental status in the study. The last day 16%, 47%, 17% and 1% of the participants found the treatment very pleasant, pleasant, unpleasant or very unpleasant, respectively. No significant side effects were recorded. No difference according to treatment was found in the use of extra pain medication or in the use of additional local cold treatment.

Ethics and consent: The plan for this study has been approved by the research ethical panel of Tampere University Hospital. All the patients signed a consent form.

Discussion: The new whole-body cold treatment method may offer a safe option for pain self-treatment, easily implemented at home. Winter swimming and whole body cryotherapy are known to be helpful for rheumatic patients (10) but they have many limitations for use, economical and geographical to be mentioned first. The former methods can also be considered to be extreme and may often have psychological barriers. This method can be seen to serve a low-threshold possibility for self-treatment, according to the high rates of volunteers starting and completing the study. The majority of the studied patients found this treatment pleasant. This can be understood by the mechanism of this cold treatment. Cold water mist on the skin can be understood to be more easily tolerated compared to ice cold water. This study also finds no serious side effects during five days of regular use. On the other hand, the primary question of the study was the efficacy of the treatment. During the five days, a statistically significant effect for pain can be seen, but the effect size does not seem to be clinically relevant between the groups during the one week study. However, the impact seems to increase towards the end of the treatment period (Fig 1). This could give some indication of a better effect in continuation. In winter swimming studies a regular repeat has been shown to give a better result both in biological and psychological measures (16,17).The unexpected result that women reacted in a different way in this study is, however, in line with the earlier findings that women with inflammatory disease score higher subjective but not objective disease activity measures than men (18). This may be partly due to the central component of the patient’s pain (19). Central pain may both play a more significant role by women (17) and central pain may also be more affected by this kind of treatment. This indicates that this gender difference should be taken into account in therapeutic decision-making process: at the same level of disease activity women may have more symptoms. This should be considered both in the specific treatment of the disease and in the pain treatment. Accordingly women might also gain more from self-treatment methods for pain.

In this study all the patients expressed lower pain assessments towards the end of the week, which can be understood to be due to the multidisciplinary rehabilitation as well as the peer support. In home environment the benefit of the treatment could be even better noticeable, also for sleep quality and mental status. This study needs continuation with a longer follow-up and to be carried out in home environment.

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References


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14) Amandan (www.amandan.fi)


Table 1. Results for main variables (mean ± SD) and p-value of the paired t-test over treatment and control weeks.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment (n=121)</th>
<th>Control (n=121)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS pain (previous week)</td>
<td>3.4 (±2.4)</td>
<td>3.4 (±2.2)</td>
<td>0.98</td>
</tr>
<tr>
<td>VAS pain (study week)</td>
<td>2.0 (±1.6)</td>
<td>2.4 (±1.8)</td>
<td>0.006*</td>
</tr>
<tr>
<td>VAS sleep (whole former week)</td>
<td>3.7 (±2.5)</td>
<td>3.7 (±2.6)</td>
<td>0.97</td>
</tr>
<tr>
<td>VAS sleep (whole study week)</td>
<td>2.3 (±2.0)</td>
<td>2.7 (±2.2)</td>
<td>0.058</td>
</tr>
<tr>
<td>DEPS day 1</td>
<td>5.5 (±4.5)</td>
<td>5.0 (±4.7)</td>
<td>0.184</td>
</tr>
<tr>
<td>DEPS day 5</td>
<td>4.5 (±4.4)</td>
<td>4.1 (±4.2)</td>
<td>0.29</td>
</tr>
<tr>
<td>Systolic blood pressure day 1</td>
<td>134 (±17)</td>
<td>133 (±19)</td>
<td>0.38</td>
</tr>
<tr>
<td>Systolic blood pressure day 5</td>
<td>133 (±17)</td>
<td>131 (±17)</td>
<td>0.063</td>
</tr>
<tr>
<td>Diastolic blood pressure day 1</td>
<td>81 (±0)</td>
<td>79 (±11)</td>
<td>0.002</td>
</tr>
<tr>
<td>Diastolic blood pressure day 5</td>
<td>80 (±9)</td>
<td>79 (±10)</td>
<td>0.08</td>
</tr>
<tr>
<td>Heart rate day 1</td>
<td>75 (±12)</td>
<td>74 (±12)</td>
<td>0.61</td>
</tr>
<tr>
<td>Heart rate day 5</td>
<td>73 (±11)</td>
<td>75 (±11)</td>
<td>0.05</td>
</tr>
</tbody>
</table>
EFFECTS OF COLD MIST SHOWER ON INFLAMMATORY ARTHRITIS PATIENTS; A CROSS-OVER CONTROLLED CLINICAL TRIAL

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Fig. 2A Mean pain expressed on visual analogue scale (VAS) for males (N=30) for treatment and control weeks.

Fig. 2B Mean pain expressed on visual analogue scale (VAS) for females (N=91) for treatment and control weeks.