# Effects of cold mist shower on patients with inflammatory arthritis: a crossover controlled clinical trial

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**Objectives**: To evaluate the safety and effects of a new home treatment method, a whole-body cold mist treatment, on patients with chronic inflammatory arthritis.
**Method**: Whole-body cold mist shower therapy was given to 121 voluntary patients with chronic inflammatory arthritis in this crossover study during 1-week rehabilitation periods. Pain and sleep quality were assessed by a 10-cm visual analogue scale (VAS). Mental status was assessed by the Depression Scale (DEPS). 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 assessing the pain of the past week as a whole. A trend could be seen of an increasing difference towards the end of the week. The treatment effect was statistically significant [likelihood ratio test (LRT), $p < 0.0001$] after controlling for period and sequence effects. There was an indication of better sleep quality (VAS) during the treatment period (2.3 vs. 2.7, $p = 0.058$ paired t-test) when assessing the past week as a whole. The mean DEPS scores showed no difference between the treatment 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 self-treatment of pain at home but further study is needed to determine the clinical significance of the effect after longer use.

Better treatment strategies and therapeutic options have changed the treatment of inflammatory arthritis over the past decades. However, pain is still the area of health in which almost 70% of patients would like to see an 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 a wide range of characteristics and is often associated with psychological distress (5). Higher depression scores are known to result in a greater number of painful joints in rheumatoid arthritis (RA) (6). Non-steroidal anti-inflammatory drugs (NSAIDs) 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), and 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 in 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 quality of life for people with rheumatic symptoms, with a device applied easily at home (12).

## Method

This study was implemented in the Rehabilitation Centre Apila, Kangasala, Finland. All of the patients entering the centre in 2013–2014 with a clinical diagnosis of RA, psoriatic arthritis (PsA), or ankylosing spondylitis/spondylarthropathy (AS/SpA) and participating in the institutional rehabilitation groups were asked to be volunteers in the study (n = 208). The study did not change the multidisciplinary rehabilitation programme, which consisted of lectures, discussion groups, and physical training in groups. The rehabilitation groups met three times a year and each period lasted 5 days. The medications of the patients varied from NSAIDs to

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biological agents. Their anti-rheumatic or pain-relieving medications were not changed during the rehabilitation periods. The patients were in the chronic stage of the disease. The number of volunteers who agreed to participate in the study was 156 (75%). In total, 121 participants (91 females) completed the study. The rheumatologists' diagnoses were RA for 65 patients, AS for 44 patients, and PsA for 12 patients. Half of the randomly chosen 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 reversed. This is known as the AB/BA crossover design in the 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 continued in autumn 2014 (period 3).

The cold treatment was carried out with the Amandan® device twice a day, once in the morning and once in the evening. This device is a Finnish innovation for supplying cold therapy at home. It is adjustable to a standard bathroom, equipped with nozzles that disperse cold water into mist particles (14). The patients wore a swimsuit and were instructed to stay for 2 minutes in the whole-body cold mist shower each time. Pain and sleep quality were assessed on a 10-cm visual analogue scale (VAS). For both the treatment and control periods, the patients were asked on day 1 to assess their pain and sleep quality during the previous week, and on day 5 to assess their pain and sleep quality of the past week as a whole. In addition, during days 1–5 they were asked to assess their current sleep quality in the mornings and their pain three times a day. Mental status was assessed by the Depression Scale (DEPS) (15) on days 1 and 5 in both cohorts. Body temperature was measured twice from the upper arm and sternum before and immediately after the cold treatment. Blood pressure and heart rate were measured at the beginning and end of the study period. The use of occasional pain and sleep medication, as well as extra local cold treatments, was recorded.

Univariate analyses were performed using a paired t-test applied over the difference between treatment and control weeks. To analyse the AB/BA crossover design over the whole study week, we used a 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 (LRT). The basic advantage of this kind of modelling frame is that it can be used for repeated measures of data and it can also make use of all of the information available, for example not only the complete measurement sequences.

The plan for this study was approved by the research ethical panel of Tampere University Hospital. All of the patients signed a consent form.

## Results

The mean (± standard deviation) skin temperature at the sternum before treatment was 34.8 ± 1.3°C, and immediately after treatment 26.7 ± 2.0°C. No differences were 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 of an increasing difference towards the end of the week (Figure 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

Table 1. Results for main variables and p-values of the paired t-test over treatment and control weeks.

| | Treatment (n = 121) | Control (n = 121) | p |
|---|---|---|---|
| VAS pain (previous week) | 3.4 ± 2.4 | 3.4 ± 2.2 | 0.98 |
| VAS pain (study week) | 2.0 ± 1.6 | 2.4 ± 1.8 | 0.006* |
| VAS sleep (whole former week) | 3.7 ± 2.5 | 3.7 ± 2.6 | 0.97 |
| VAS sleep (whole study week) | 2.3 ± 2.0 | 2.7 ± 2.2 | 0.058 |
| DEPS score day 1 | 5.5 ± 4.5 | 5.0 ± 4.7 | 0.184 |
| DEPS score day 5 | 4.5 ± 4.4 | 4.1 ± 4.2 | 0.29 |
| Systolic blood pressure day 1 | 134 ± 17 | 133 ± 19 | 0.38 |
| Systolic blood pressure day 5 | 133 ± 17 | 131 ± 17 | 0.063 |
| Diastolic blood pressure day 1 | 81 ± 10 | 79 ± 11 | 0.002 |
| Diastolic blood pressure day 5 | 80 ± 9 | 79 ± 10 | 0.08 |
| Heart rate day 1 | 75 ± 12 | 73 ± 11 | 0.61 |
| Heart rate day 5 | 73 ± 11 | 75 ± 11 | 0.05 |

VAS, Visual analogue scale; DEPS, Depression Scale.
Values given as mean ± standard deviation.
*A statistically significant finding.

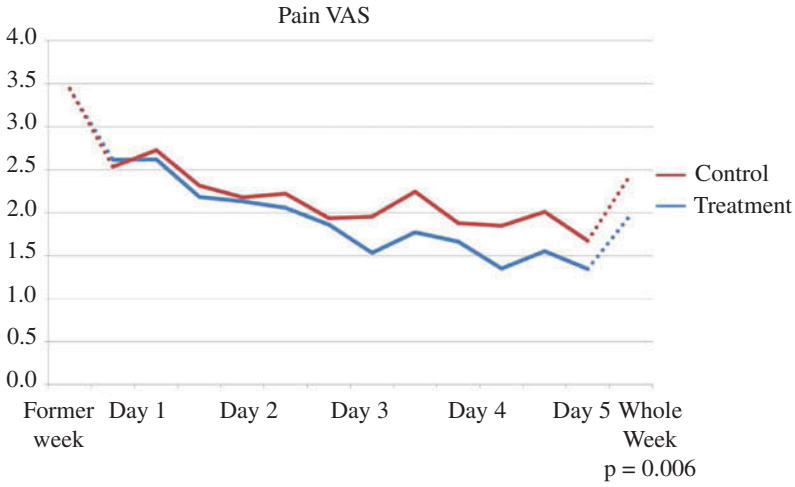


Figure 1. Mean pain expressed on a visual analogue scale (VAS) during testing over treatment and control weeks (n = 121). Last point on the x-axis is the mean of the overall assessment with the p-value of the paired t-test.

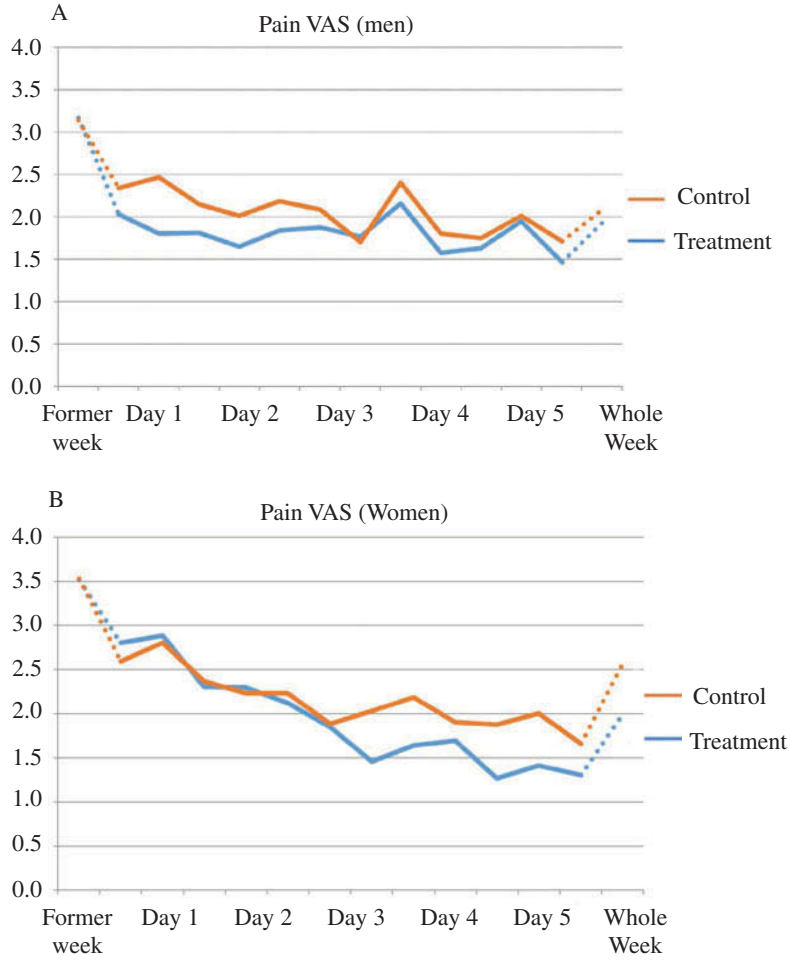


Figure 2. Mean pain expressed on a visual analogue scale (VAS) for (A) males (n = 30) and (B) females (n = 91) for treatment and control weeks.

not statistically significant while the third period seems to differ from the other two (t = −2.813, p = 0.0049). No difference could be seen according to the patient's clinical diagnosis. When assessed on a gender basis, a difference could be seen. The cold therapy was significantly more effective for women, and the effect was greatest during the last days of the study period (p = 0.005, LRT, Figures 2A and 2B). There was an indication of 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 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. On 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.

## Discussion

The new whole-body cold treatment method could 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 there are many limitations with regard to use, both economic and geographic, that should be noted. The former methods can also be considered to be extreme and may often have psychological barriers. The current 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 the cold treatment. Cold water mist on the skin can be understood to be more easily tolerated compared to ice cold water. This study also found no serious side-effects during 5 days of regular use. However, the primary question of the study was the efficacy of the treatment. During the 5 days, a statistically significant effect for pain could be seen, but the effect size did not seem to be clinically relevant between the groups during the 1-week study period. However, the impact did seem to increase towards the end of the treatment period (Figure 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 for both biological and psychological measures (16, 17). The unexpected result that women reacted in a different way in this study is, however, in line with earlier findings that women with inflammatory disease score higher on 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 play a more significant role in women (18) 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 the therapeutic decision-making process because women may have more symptoms at the same level of disease activity. 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 of 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 peer support. In the home environment the benefit of the treatment could be even more noticeable not only with regard to pain but also for sleep quality and mental status. Further study of this treatment method is needed in the home environment and with a longer follow-up time.

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