The effect of nerve mobilization exercise in patients with rheumatoid arthritis: a pilot study

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SUMMARY

Rheumatoid arthritis (RA) is an autoimmune disorder characterized by chronic inflammation of the joints. The neurogenic inflammatory mechanism plays an important role in the inflammatory process of RA, and pathological changes in neural tissues in RA have also been noted. We aim to investigate treatment of the nervous system to relieve joint pain and inflammation in RA. Nerve mobilization, a nervous system-specific therapeutic exercise, was applied on RA patients to determine the effect of nerve mobilization on joint inflammation. Twelve RA patients were recruited from the community and were randomised into an experimental and a control group. In the experimental group, the subjects were taught a set of nerve mobilization exercises while the subjects in the control group were taught a set of gentle joint mobilization exercises. Both groups were instructed to practice the exercises daily. After a 4-week period, their RA pain scale (RAPS) and pain scores were examined, as well as the C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Subjects in the experimental group showed improvements in RAPS and pain scores after 4 weeks of nerve mobilization exercises, while CRP and ESR values remained unaffected.

These preliminary data showed that nerve mobilization exercises might be beneficial in controlling joint pain in RA patients.

Key words: CRP; ESR; Nerve mobilisation; Neurogenic inflammation; Rheumatoid arthritis.

INTRODUCTION

Rheumatoid arthritis (RA) is one of the most prevalent chronic autoimmune diseases. The symptoms of RA are characterized by joint inflammation and deformities that are associated with pain and functional disability (1). The aetiology of RA remains unclear, but an increasing number of investigations have provided evidence that disease perpetuation could be due to a mixture of both immunogenic (1) and neurogenic (2, 3) inflammation. The mechanism of neurogenic inflammation has been described as an inflammation that is initiated by the nervous system (4-6). The neurogenic inflammation is triggered in the tissues by the cutaneous nerves (4, 7-10). The evidence of neurogenic inflammation in RA is supported by a small but significant number of tyrosine hydroxylase-positive sympathetic nerve fibres, which have a negative correlation with the inflammation index, a large number of substance P-positive nerve fibres (11) and immunoreactive sensory nerve fibres with calcitonin gene-related peptide (CGRP) (12).

The current treatment algorithms for RA involve the use of both traditional and biological disease-modifying antirheumatic drugs (DMARDs) to control the disease (13). Physical treatments are also beneficial for patients to optimize physical functions, decreasing pain and improving quality of life (14-16). A paradigm is named as neurodynamic, which is a series of movements that produce physiological and mechanical events in the nervous system. They are used in physical testing to gain a response to the mechanical performance and sensitivity of the nervous sys-
Table I - Actions for nerve mobilizations.

<table>
<thead>
<tr>
<th>Nerve Mobilization</th>
<th>Actions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median nerve (Figure 1)</td>
<td>Sit on a plinth, supported by elbows, with wrists and fingers extended and arms by the sides. Shift the body weight to the left and right sides to give a pulling sensation along the palm side of the arm on the same side.</td>
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<tr>
<td>Musculocutaneous nerve (Figure 2)</td>
<td>Clench a fist, bend the fist down, straighten the elbow and extend the shoulder as though marching. Perform the actions with left and right arm oppositely and simultaneously.</td>
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<tr>
<td>Saphenous nerve (Figure 3)</td>
<td>Stand with feet apart, stretching the leg out behind; place the ankle of the stretched leg in dorsiflexion and eversion with the use of a towel role. The saphenous nerve is mobilised when the front of the knee is bent and driven forwards.</td>
</tr>
<tr>
<td>Entire nervous system (Figure 4)</td>
<td>In a sitting position, slump the body, bend the head down and place the arms behind the body. The stretched leg is actively kicked up with ankle dorsiflexion until a stretching sensation occurs in the posterior thigh and calf.</td>
</tr>
</tbody>
</table>

Table I - Actions for nerve mobilizations.
Subjects in the experimental group were taught a set of active nerve mobilization exercises, the two types of which are classified as slider and tensioner applications. The former implies less challenge and allows the nervous system a large degree of neural movement; the tensioner places a load on both ends of the nervous system and is a more aggressive technique. In this study, the tensioner technique was applied because patients with RA usually had no active neurogenic symptoms and the technique produces a larger excursion on the nerve (17, 22).

The series of nerve mobilization exercises comprised four actions (Table I; Figures 1-4) that focus to a greater extent on the major innervating cutaneous nerves: the median nerve, musculocutaneous nerve, saphenous nerve and the entire nervous system (21, 23, 30, 31). Each action of the mobilization exercises was repeated 10 times but was not continued when subjects experienced the stretching sensation and then returned to the starting position. The subjects were instructed to perform the series of exercises daily, twice a day (23).

In the control group, subjects were given a set of joint mobilization exercises that comprised five actions to mobilize the fingers, wrists, elbows and shoulders, the spine and
the entire lower limbs. The movements were gentle, not touching the end range of the joints. The subjects were instructed to repeat the actions 10 times; the whole series of actions took about 5 minutes or less. The mobilization exercises were not supposed to impose any stress on the joints, muscles or the cardiopulmonary system. An exercise log book was provided for each subject to record compliance with the exercises. Recorded exercise DVDs were also given to the subjects for them to follow and practice daily.

Patients’ anti-rheumatic therapies were recorded throughout the study period. Subjects were instructed to suspend the exercises and contact the investigator if symptoms flared up during the period.

**Pain assessment tools and inflammatory biomarkers**

The Rheumatoid Arthritis Pain Scale (RAPS) was used to rate the severity of pain, before and after the study period. The questionnaire comprised 24 items with a scale from 0 to 6 to quantify the severity of pain and inflammation (32, 33), where 0 represents a condition that always occurs, and 6 represents a condition that never occurs. For items 1-24, the lowest total score was 0 and the highest score was 144 (Appendix 1). This questionnaire was chosen because the questions concern both pain, which is the greatest concern of patients with RA (34), and joint inflammation. Cronbach’s alpha for the total RAPS was found to be 0.91 while the subscale alpha coefficients were between 0.64 and 0.86. The visual analogue scale–numeric rating scale (VAS-NRS) is listed in RAPS as the last item and is a subjective pain measurement rated from 0 to 10 to describe the level of pain: 0 represents none, and 10 represents severe. The RAPS correlations with VAS-NRS and that with total joint count were 0.67 and 0.52, respectively (33). The total joint score in RAPS was not recorded as a rheumatologist was not available on the site. Inflammatory biomarkers C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were tested in either the university clinic or in the public hospitals where the subjects were being followed up (35-37).

**Statistics**

Results were analysed using IBM SPSS 23. The nonparametric Mann-Whitney U test was applied to analyze differences between the groups and the Wilcoxon test was used for within-group comparisons.

**RESULTS**

A total of 12 RA patients were recruited into the study, with two subjects in the experimental group subsequently dropped out: one lost contact during follow-up, and one developed an infection after the first screening. One subject was excluded from the control group due to disease flare. No statistical difference in demographics and baseline measurements was found between the two groups (Table II). After 4 weeks, the subjects in both groups demonstrated good compliance with the

<table>
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<tr>
<th>Table II - Characteristics of patients with rheumatoid arthritis.</th>
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<tbody>
<tr>
<td>Characteristics</td>
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<tr>
<td>Age (years, mean ± S.D.)</td>
</tr>
<tr>
<td>Male:Female</td>
</tr>
<tr>
<td>Disease duration (years, mean ± S.D.)</td>
</tr>
<tr>
<td>Therapy</td>
</tr>
<tr>
<td>Methotrexate</td>
</tr>
<tr>
<td>Sulfasalazine</td>
</tr>
<tr>
<td>Leflunomide</td>
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<tr>
<td>Corticosteroids (Prednisolone)</td>
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<td>Non-steroidal anti-inflammatory drugs (NSAID)</td>
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exercises according to the exercise log. The changes in values of RAPS and pain level, CRP and ESR were compared between the 2 groups, before and after intervention (Tables III and IV). The experimental group reported a better maintenance or improvement of the RAPS and pain level scores (Table III). However, it should be noted that the inconsistency in values at baseline might induce a favourable or unfavourable bias to the groups. Both groups presented fluctuation in CRP and ESR values, but no particular trend could be observed. Overall, the outcomes of the two groups after the study period showed no statistical difference.

**DISCUSSION**

Our preliminary data demonstrate the positive effect of nerve mobilization exercises on subjective pain scores in RA patients while ESR and CRP remains unmodified. The use of nerve mobilization on patients with RA was based on the idea that RA involves neurogenic inflammation which can be influenced by mechanical stimulation of immune-reactive sensory nerve fibres (11, 12, 35). Cutaneous nerves are physiologically inelastic and mechanically sensitive followed by inflammation (26, 36, 37), chronic arthritis such as RA implies mechanical stress which induces degenerative changes in the nerves (2, 3) and possibly exaggerates the release of inflammatory neuropeptides (11, 12, 35). Experimental studies discovered more physiological mechanisms of the nerve mobilization. The mobilization was shown to redistribute the sodium ion channels of sensory axons (25), increase neural growth factor and myelin protein zero in injured nerves (38, 39). Overall, the therapeutic effects of the nerve mobilization could be accounted for by reduction of physical stress through the movements of the nerves (17, 18) and intraneural fluid dispersion (19, 20), normalization of sensory axons excitability (25), and promotion of nerve regeneration by stimulating expression of neural growth factor and myelin protein zero (38, 39).

As a pilot study, the methodology had several limitations such as sample size, subjects’ homogeneity and the length of the follow-up period. Due to the limited sample size, although randomization was conducted and the baseline CRP and ESR

<table>
<thead>
<tr>
<th>Subject</th>
<th>Pre ESR (mm/hr)</th>
<th>Post ESR (mm/hr)</th>
<th>Pre CRP (mm/L)</th>
<th>Post CRP (mm/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject 1</td>
<td>10</td>
<td>16</td>
<td>1.3</td>
<td>1</td>
</tr>
<tr>
<td>Subject 2</td>
<td>34</td>
<td>45</td>
<td>4.5</td>
<td>17.4</td>
</tr>
<tr>
<td>Subject 3</td>
<td>22</td>
<td>29</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Subject 4</td>
<td>10</td>
<td>4</td>
<td>3.3</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table IV - Comparison of CRP and ESR values.**

<table>
<thead>
<tr>
<th>Subject</th>
<th>Pre ESR (mm/hr)</th>
<th>Post ESR (mm/hr)</th>
<th>Pre CRP (mm/L)</th>
<th>Post CRP (mm/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject 5</td>
<td>23</td>
<td>19</td>
<td>4.8</td>
<td>4.5</td>
</tr>
<tr>
<td>Subject 6</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Subject 7</td>
<td>10</td>
<td>12</td>
<td>6.5</td>
<td>6.5</td>
</tr>
<tr>
<td>Subject 8</td>
<td>38</td>
<td>15</td>
<td>13.9</td>
<td>1</td>
</tr>
<tr>
<td>Subject 9</td>
<td>30</td>
<td>35</td>
<td>3.3</td>
<td>0.43</td>
</tr>
</tbody>
</table>
were similar in two groups, a minor and statistical insignificant (p>0.05) inequality in RAPS and VAS-NRS was noted. When compared to the control group, the experimental nerve mobilization appeared to be positive after the intervention. Disease activity score such as 28 joints (DAS28) is a standard clinical tool in evaluating RA disease activity, and may serve as a reference in RA medication adjustment (40). Although CRP, ESR and subjects’ response were available, the study was not conducted in a hospital setting with the support of either a rheumatologist or a specialized trained nurse, thus reliable swollen joint counts were not available (41).

**CONCLUSIONS**

Early pharmaceutical treatments have been the major intervention for RA, such as biological and new non-biological DMARD. Patients benefit from better control of the disease and prevention of early joint damage (13). Our preliminary data has demonstrated the use of nerve mobilization exercise in patients with RA to as additional modalities in managing pain and inflammation, and merit further investigation.

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**Conflict of interest:** the authors declare no conflict of interest.

**REFERENCES**

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