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SUBCUTANEOUS SODIUM SALICYLATE THERAPY FOR CERVICAL SPINE PAIN IN RHEUMATOID ARTHRITIS

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ABSTRACT

Background: Rheumatoid arthritis (RA) frequently causes pain in the cervical spine that is difficult to treat. Anecdotal evidence suggests that subcutaneous sodium salicylate therapy (SSST) may be effective in reducing the symptoms of the condition. This treatment can be administered by nurse practitioners as well as physicians.

Objective: We performed a pilot study to determine if a controlled trial of the therapy is justified.

Method: Seven patients with pain in the neck due to RA were recruited to an open label pilot study of SSST. All patients received 3 weekly subcutaneous sodium salicylate injections. Assessments were made at weeks 4, 8 and 12.

Results: In 4 out of 7 patients there was an improvement in neck pain scores following injection with SSST. There was also a trend towards improved neck rotation and overall pain scores.

Conclusion: Injections of sodium salicylate may help to alleviate cervical spine pain in some patients with RA. The results of this pilot study indicate that a controlled trial of this therapy is justified.

KEY WORDS: rheumatoid arthritis, pain, cervical spine, subcutaneous patches, sodium salicylate

INTRODUCTION

Cervical spine involvement can be a major symptomatic problem for patients with rheumatoid arthritis (RA) . A study undertaken by Bland suggested that 42% of patients who have rheumatoid arthritis for 20 years or more were likely to have involvement of the cervical spine (1). Currently, treatment options are limited. The use of analgesics and anti-inflammatory agents has its limitations in terms of efficacy and tolerability. This study set out to examine the efficacy of subcutaneous sodium salicylate therapy (SSST) for cervical spine pain in this group of patients.

The presence of thickened and tender areas of cutaneous tissues can be found in many forms of arthritis. These have been described by different names such as interstitial fibrositis, myofasciitis, myofascial trigger points and rheumatic patches (1-4). These are commonly identified in the field of acupuncture (2). They are generally found near to and on occasion distal to the site of an inflamed joint and are palpable by employing a light pinching technique by the examiner.

Following a pilot study (3), a randomised study of 40 participants was undertaken by our group looking at the administration of SSST for osteoarthritis of the 1st CMC joint (5). Tender myofascial areas as described by Fox (6) on the same side as the affected CMC joint were injected with 20ml of 0.5% solution of sodium salicylate or were given sham injections. The results showed that both pain and tenderness were significantly lower in the sodium salicylate group.

These promising results suggested that SSST might be helpful for cervical spine pain in RA. This relatively simple treatment can be administered by nurse practitioners as well as physicians. The present pilot study was performed in order to obtain efficacy data for determining if a controlled trial of the therapy would be justified and to provide information for designing such a trial.

METHODS

Patient selection

Male and female patients who had rheumatoid arthritis as determined by the American College of Rheumatology classification criteria (7) were approached for recruitment. All patients had RA involvement of cervical spine (determined radiologically). All had persistent neck pain with an inadequate response to paracetamol and codeine. All patients had the presence of tender subcutaneous patches in the cervical region, and/or upper scapular region. Patients were recruited from Charing Cross Hospital and Chelsea and Westminster Hospital, London, England. Further inclusion and exclusion criteria are summarised below:

Inclusion criteria

- Age over 18 years
- Disease modifying therapy (including methotrexate, sulfasalazine, hydroxychloroquine or biological agents) stable for the previous two months.
- Radiological features of RA in the cervical spine, including erosion or (on MRI scanning) active inflammatory change).

Exclusion criteria

- History of asthma
- Neurological lesion or symptoms attributable to RA in the cervical spine
- Atlanto-axial subluxation on forward flexion of neck, determined radiologically as being greater than 4 mm, or causing neurological symptoms;
- Other instability of the cervical spine, determined radiologically;
- Pregnancy or current breast-feeding; any patient of child-bearing potential who was not taking adequate contraceptive measures;
- Allergy to aspirin, other salicylates or other non-steroidal anti-inflammatory agents;
- Haematological disorders leading to impaired haemostasis;
- Widespread rashes, dermatological conditions affecting the tender areas, and those expressing the Köbner phenomenon;
- Active peptic ulceration or history of peptic ulcer;
- Local sepsis;
- Any condition in which an anti-platelet action might be harmful (e.g. recent stroke);
- Known underlying conditions such as malignancy, renal failure or serious infection;
- The concomitant administration of an anticoagulant;
- Any change in arthritis therapy within two months of starting the study.

Treatment protocol

Patients were screened as per the inclusion/exclusion criteria. After the obtaining of written consent, they were assessed (week -4) for the presence of tender subcutaneous areas in the neck and scapular regions. Patients were also asked to complete a series of questionnaires (see below in the assessment section for details). At weeks 0, 1 and 2 the patients were given subcutaneous injections of sodium salicylate (see below for details of technique). At weeks 4 and 12 patients attended for follow-up visits when were asked to complete a series of questionnaires (see below), together with a 28 joint assessment and measurement of erythrocyte sedimentation rate (ESR).

The study participants were requested not to alter their current analgesic medication during the course of the trial. All participants were aware that they could leave the study at any time.

Injection technique
Tender subcutaneous patches were identified by palpation in the posterior area of the neck and upper scapular region on both sides. Injections were administered to these areas as follows. On the first occasion 1% lignocaine up to a dose of 10ml was injected into the tender neck areas bilaterally. Two minutes later 0.5% of sodium salicylate (Northwick Park Hospital Pharmacy, Harrow Middlesex) was administered into the same areas. The solution was delivered through a 23-gauge needle subcutaneously so as to produce a firm wheal. 20mls were injected on any one occasion, given all into one large patch, or, more typically, divided between two to four smaller patches. One week later, the upper scapular areas were injected with the same dose of lignocaine and sodium salicylate. The following week, any further tender areas that had been identified were injected as per protocol. Sticking plaster (e.g. Bandaid) was put over all of the injection sites, and patients were instructed to keep this on for 24 hours.

Assessment
Participants in the study completed questionnaires and assessments at weeks -4, 0, 1, 2, 4 and 12.

Neck pain and neck rotation were measured at all assessments. The patient was asked to use 10cm visual analogue scales (VAS) from 0 (none) to 10 (greatest) to record the severity of neck pain over the preceding 24 hours. Neck rotation to right and left was also measured in degrees. For each variable the results obtained at weeks 4 and 12 were compared with the mean of the results obtained at weeks -4 and 0.

Immediately after each injection, patients were asked to assess the pain of the injection by VAS.

An American College of Rheumatology (ACR) Core Data Set (7) was gathered at weeks -4, 4 and 12. This involved the patient's global assessment of disease activity using VAS, the assessor's global assessment of disease activity using VAS, the patient's functional assessment using a health assessment questionnaire ("HAQ") and the number of swollen and tender joints was determined by physical examination of 28 joints.

Ethics approval
The study was approved by the Hammersmith Hospital Research Ethics Committee

RESULTS
Patient Selection
Out of 8 patients invited to take part in the study 7 female patients consented to do so. Their median age was 57 years at the time of recruitment, (range 38 to 66). All participants were white British.

Neck Pain
Table 1 demonstrates the neck pain scores at baseline and at 4 and 12 weeks post injection as determined using VAS, as well as the percentage change in these values from baseline. In 4 out of 7 patients, there was improvement in neck pain scores at week 4, and this was sustained in 3 patients at 12 weeks (Patients 1, 6 and 7). The mean percentage change in VAS compared to baseline was 18.5% reduction at week 4 and 22.79% reduction at week 12.

Neck Rotation
Table 2 demonstrates the neck rotation values at baseline and at 4 and 12 weeks as well as the percentage change in these from baseline. In patients 1, 6 and 7 there was improvement in neck rotation at 4 weeks which was sustained at 12 weeks. Patients 4 and 5 showed a sustained deterioration in neck rotation. The mean percentage change in neck rotation was a 10.89% increase in rotation from baseline at week 4 and 23.78% increase in rotation at week 12.

DAS-28-ESR
Table 3 demonstrates the overall disease activity scores for each patient using DAS-28-ESR at baseline and 4 and 12 weeks post injection. The overall trend is towards an improvement in DAS over the course of the study. The mean DAS-28-ESR improved by 23.9% from baseline at week 4, and 8.61% by 12 weeks post treatment.

HAQ, patient and physician global assessment scores
The average HAQ score at the start of the study was 10.9. At week 4 post injections, this score was 11.0 and at week 12 it was 12.1. Similarly, there was no particular trend in the change in patient and physician global assessment scores over time (data not shown).

Injection Site Pain
Patients reported varying degrees of pain at the injection sites at weeks 1, 2 and 3 (data not shown). There was no correlation between the degree of pain caused by the injection and neck pain or rotation scores.

DISCUSSION
This pilot study shows a tendency towards improved neck pain and neck rotation following the injection of subcutaneous sodium salicylate in patients with RA. This was noted at 4 weeks, and was sustained at 12 weeks. The data therefore support carrying out a randomised controlled trial of this therapy in such patients.

This study demonstrated a small improvement in average DAS-28-ESR following SSST injections.. This could be attributed to the improvement in neck pain, as rheumatoid arthritis activity was otherwise generally stable. This is perhaps expected, as SSST is likely to only affect the region close to where it is administered, rather than providing an overall improvement in disease activity.

The mechanism of action of SSST remains unclear. One possibility is an effect on central sensitisation. Supporting this is the observation that patients frequently report immediate relief following the injection (5). Another potential mechanism is through the neurogenic control of inflammation, which is often disturbed in rheumatic diseases (8-9). This could occur via an irritant effect of salicylate similar to that of topical capsaicin (10-12). Another possibility is that SSST injections could act in a similar way to acupuncture. Evidence supporting the use of acupuncture in the management of chronic pain and arthritis is well documented (13). This could be especially true as tender subcutaneous patches often occur at common acupuncture sites. The sustained effect of salicylate seen in this study suggests an added benefit from substances being injected in the tissues. For the same reason it is unlikely that the benefit of SSST is purely due to a systemic anti-inflammatory effect. There is likely to be a placebo effect from an injection therapy. However, there was no correlation between the recorded pain of the injections and the changes in clinical outcome variables.

It is interesting to note that patient 5 consistently demonstrated poor response to the SSST. She experienced considerable social stress during the course of the study. It is clear that some patients may fail to respond to treatment due to confounders such as medical comorbidities and social factors. As with other treatments, careful patient selection may be needed if SSST is to be used further in this patient group.

In terms of efficacy assessment this study was limited by its small sample size. However it achieved its aim of determining if a controlled trial should be performed. Another limitation was the demographic of our patient population: they were all Caucasian females, which is reflective of the majority of the local patient population.

Our results justify a randomised controlled trial of SSST in patients with painful RA of the cervical spine. Since this therapy can be administered by nurse practitioners as well as physicians, formal demonstration of its efficacy would represent a significant advance the options for treatment.

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TABLE 1
Neck pain scores measured using VAS at baseline and at 4 weeks and 12 weeks post-injections. Baseline scores are the mean of scores obtained at weeks -4 and 0. Negative values represent an improvement compared to baseline.

Patient	Baseline	Week 4	Percentage Change (%)	Week 12	Percentage Change (%)
1	7.15	4	-44.06	4.3	-39.86
2	2.7	2.9	7.41	0.3	-88.89
3	7.4	5.5	-25.68	8.5	14.86
4	6.85	7.2	5.11	9.5	38.69
5	4.95	8.7	75.76	8.9	79.80
6	7.25	2.6	-64.14	2.6	-64.14
7	9.3	1.5	-83.87	0	-100.00
Average		-18.50		-22.79	

TABLE 2
Neck rotation measured using degrees at baseline and at 4 weeks and 12 weeks post-injections. . Baseline scores are the mean of scores obtained at weeks -4 and 0.

Patient	Baseline	Week 4	Percentage Change (%)	Week 12	Percentage Change (%)
1	15.25	20	31.15	22.5	47.54
2	26.25	25	-4.76	30	14.29
3	17.5	37.5	114.29	17.5	0.00
4	48.75	42.5	-12.82	37.5	-23.08
5	22.5	10	-55.56	22	-2.22
6	60	80	33.33	85	41.67
7	42.5	30	-29.41	80	88.24
Average		10.89		23.78	

TABLE 3

Overall Disease Activity Scores measured using ESR (DAS-28-ESR) at baseline and at 4 weeks and 12 weeks post-injections. . Baseline scores are the mean of scores obtained at weeks -4 and 0. Negative values represent an improvement in DAS-ESR.

Patient	Baseline	Week 4	Percentage Change (%)	Week 12	Percentage Change (%)
1	4.46	5.1	14.35	4	-9.87
2	5.96	5	-16.11	4.6	-23.15
3	7.15	6.2	-13.15	5.8	-18.88
4	4.85	3.6	-26.80	4.8	-1.24
5	2.54	2	-20.47	4.2	66.54
6	4.19	3.7	-12.17	2.4	-42.00
7	1.42	0.1	-92.96	1	-31.69
Average		-23.90		-8.61	

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