A randomized, double-blind, placebo-controlled trial of low-dose oral prednisolone for treating painful hand osteoarthritis

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Abstract

Objective. Anti-inflammatory therapies are effective analgesics for OA. This study determined whether low-dose oral prednisolone (PNL) was an effective analgesic for hand OA.

Methods. This was a randomized, double-blind, placebo-controlled trial of people with ACR criteria hand OA and baseline hand pain visual analogue scale (VAS) of >40/100 mm. Participants received 5 mg PNL or placebo daily for 4 weeks. Pain VAS, disease activity VAS, Australian/Canadian Hand Osteoarthritis Index and joint counts were performed at baseline, 4 and 12 weeks. Primary outcome was the change in hand pain VAS at 4 weeks. Analysis of covariance was used for analysis, controlling for baseline values. To explore potential mechanism of action of PNL, non-contrast 0.2 Tesla MRI was performed on the most painful hand at baseline and 4 weeks.

Results. A total of 70 participants were recruited (57 women, mean age 61 years, mean baseline pain VAS 61.5 mm); 75% had more than one joint with definite MRI synovitis/effusion. At 4 weeks the adjusted mean reduction in pain VAS was 19.9 mm (PNL group) and 16.8 mm (placebo group) (P = 0.54). There were no statistically significant differences in VAS, Australian/Canadian Hand Osteoarthritis Index or joint counts between placebo and PNL groups at 4 or 12 weeks. A total of 20 participants in each group achieved an Outcome Measures in Rheumatology-Osteoarthritis Research Society International response. Baseline synovitis/effusion did not predict response to treatment.

Conclusion. This is the first randomized controlled trial of low-dose corticosteroid alone for painful hand OA, which demonstrated that short-term low-dose oral PNL is not an effective analgesic treatment for hand OA.

Trial registration. International Standard Randomised Controlled Trial Number Register, www.isrctn.org, Trial number 99697616.

Key words: hand OA, treatment, prednisolone, MRI, randomized controlled trial.

Introduction

Symptomatic hand OA is common, with a prevalence of 16% in a large population-based study (mean age 58 years), which increases to 26% in those aged >70s [1, 2]. As the population ages, the prevalence of hand OA, along with its significant impact on quality of life [3, 4], will increase.

There has been recent interest in the potential importance of inflammation as a peripheral source of pain in hand OA. Imaging studies demonstrate a high prevalence of synovitis in painful hand OA [5, 6], with painful joints significantly more likely to have synovitis than non-painful joints [5, 7, 8].

Current pharmacological treatment options for hand OA are limited to simple analgesics, NSAIDs and corticosteroid (CS) injections [9–12]. The effect size for
these treatments is moderate at best; NSAIDs are associated with significant toxicity especially in older people, and injecting multiple small joints may not be feasible in a busy clinical setting. CSs are presumed to act via an anti-inflammatory mechanism [13], and although IA CS is an accepted treatment for knee OA, there is a lack of randomized controlled trials (RCTs) assessing CSs in hand OA [10, 11]. There is some evidence for IA steroid for first CMC joint OA [14], but RCTs of IA steroid to the first CMC joint have not demonstrated a significant difference compared with placebo [15, 16]. However, an open label study of intramuscular methylprednisolone for painful hand OA noted a short-term improvement in pain in two-thirds of participants [17], and a novel drug, combining low-dose oral prednisolone (3 mg) with dipyridamole, demonstrated a significant benefit compared with placebo in a 6-week RCT [18]. A further open label study using intramuscular CS to treat the symptoms of inflammatory hand pain, which included people with OA, noted a significant improvement in symptoms after CS [19].

We hypothesized that oral CSs would reduce pain in hand OA, and at low dose for a short time period would provide a useful and safe treatment option to the currently limited OA armamentarium, so we conducted a RCT with an exploratory study using MRI to evaluate synovitis and its relationship to therapeutic response.

Methods

Research ethics committee approval was granted by the Leeds (West) Research Ethics Committee. All participants gave written informed consent according to the Declaration of Helsinki (2008). People attending rheumatology hospital outpatient clinics in the West Yorkshire region (UK), whose main symptom was OA hand pain, were invited to participate in this study.

Men and women fulfilling ACR hand OA classification criteria [20] were enrolled. Self-reported hand pain had to be at least 40/100 mm on a hand pain visual analogue scale (VAS), with symptoms present on most days for at least 3 months. Additional inclusion criteria included stable analgesic requirements (including NSAIDs) for at least 4 weeks, stable doses of chondroitin or glucosamine for 4 months, no CSs via any route for at least 3 months and a previous hand radiograph with a Kellgren–Lawrence (K/L) score of at least 1 [21]. Exclusion criteria included any inflammatory arthritis, known positive RF, sensitivity to PNL, current pregnancy, currently uncontrolled diabetes or hypertension, active infection, osteoporosis or taking bisphosphonates or any contraindications to MRI. Patients with isolated first CMC joint symptoms were excluded from the study (evidence of first CMC disease was documented). Some participants had previously been commenced on hydroxychloroquine as a treatment for their hand OA, and this was not an exclusion criterion, although its use was documented, and the dose must have been stable for at least 3 months.

Study design

This was a 12-week single centre, double-blind, randomized, placebo-controlled study. Within 1 week of screening, participants fulfilling criteria were randomized to receive PNL (5 mg) or matched placebo capsules. Follow-up visits were at 4 and 12 weeks. Concomitant medication was documented at each visit. Patients were asked to continue the same dose of analgesics or anti-inflammatories throughout the study.

The randomization was performed by the clinical trials pharmacist using random permuted blocks of 10 patients, using random number tables. Dispensing pharmacy technicians were not aware of treatment allocation, and capsules were provided in identical sequentially numbered containers. Unblinding occurred 24 h after the final visit of the final participant in the study.

Clinical assessments

All clinical assessments throughout the study were performed by the same rheumatologist, who was blinded to the treatment. Full clinical examination was performed at baseline and 4 weeks. Painful, swollen and tender joint counts were recorded at each visit, documenting painful joints (patient reported pain within the last 48 h), tender joints on palpation (pressure applied until the assessor’s nail bed blanched) and swollen (soft tissue swelling) joints for the MCP, PIP and DIP joints of each hand.

Questionnaires were completed by participants and a blinded assessor. Participants did not have access to scores from previous visits when completing questionnaires. The VAS version of the Australian/Canadian Hand Osteoarthritis Index (AUSCAN) [22] and Hospital Anxiety and Depression Scale (HADS) [23] were completed at the baseline, week 4 and week 12 visit. The Osteoarthritis Quality of Life questionnaire (OAQoL) [24] was completed at baseline and week 12.

Participants completed a 100-mm VAS recording the average pain in their fingers during the previous 48 h (VAS 48 h) and previous 2 weeks (VAS 2 week), a 48-h pain VAS for the most painful joint (VAS worst joint), a 48-h patient-reported disease activity VAS and, if applicable, a 48-h pain VAS for the first CMC joint. Physician-reported disease activity VAS for the last 48 h was also recorded.

Imaging

A radiograph of both hands, if not previously performed within the past 12 months, was undertaken at the screening visit using a standard posteroanterior view of both hands. Radiographs were scored using a global scoring method, whereby 32 joints in the hands are scored yes/no for the presence/absence of OA changes [25]. A Kellgren–Lawrence score for the most affected finger joint and the first CMC joint was also noted [21].

To assess the potential effect of low-dose PNL on imaging-detected synovitis and to avoid two doses of intra-venous contrast agents, an extremity MRI scan without contrast of the most painful hand at baseline
and 4 weeks was performed, using an Esaote C-scan 0.2 Tesla machine (Esaote, Genova, Italy), using a dual phased array wrist coil. The MCP, PIP and DIP joints of the second to fifth fingers were imaged (12 joints imaged for each participant). It was not possible to include the thumb because of the positioning of the hand within the scanner. A coronal Turbo 3D T1 sequence (relaxation time/excitation time, 35/16 ms; slice thickness, 4 mm; field of view, 140 x 140 x 80 mm; matrix, 192 x 160 x 72; echoes, 1; series, 3) and an axial 22 slice short tau inversion recovery (STIR) (relaxation time/excitation time, 2840/24 ms; slice thickness, 4 mm; field of view, 160 x 160 mm; matrix, 192 x 144; echoes, 1; series, 4) were performed at baseline. The axial 22 slice STIR was repeated at week 4.

The MR images, anonymized to patient demographics and time order, were scored by two experienced musculoskeletal radiologists. The STIR images were used to assess for synovitis/effusion. Reader one (A.J.G.) scored joints for increased signal (synovitis and/or effusion) for both time points. Scores were defined as 0 = normal, 1 = probable synovitis/effusion and 2 = definite synovitis/effusion. The two time points were then viewed together by both readers (A.J.G. and R.H.), and an opinion as to whether the appearances had improved, deteriorated or were unchanged were reported for each group of MCPs, DIPs and PIPs.

**Statistical analysis**

**Sample size calculation.** The change in 48-h hand pain VAS after 4 weeks was the predefined primary outcome. We postulated that the smallest detectable difference between placebo and PNL, which was likely to be clinically significant, was a reduction on a pain VAS of 15 mm [26]. To achieve a 15-mm clinical difference in mean VAS score between placebo and PNL group, assuming a s.d. of 22.3 [27], using the 5% significance level and 80% power, required 35 people per group. To account for a potential 10% dropout rate, recruitment of 77 people was planned: during study recruitment, 70 participants completed the 4-week visit, so no further recruitment was required.

An intention to treat analysis was used. Data were analysed using the statistical package SPSS version 19.0.0 and Stata 11.2. Analysis of covariance (ANCOVA) was used to compare changes between groups at 4 and 12 weeks, controlling for baseline values. Student’s t-test was used for normal distributed data and Mann–Whitney U test for ordinal data. Multilevel binary logistic models were constructed taking clinical assessment of the presence of joint pain, joint swelling or joint tenderness as the outcome each time and including MRI synovitis/effusion score (normal/probable/definite) as the explanatory factor for each. Clustering of joints within each patient was controlled for by allowing for random intercepts at the patient level within each model.

A secondary analysis was undertaken using the Outcome Measures in Rheumatology-Osteoarthritis Research Society International (OMERACT-OARSI) D criteria [28], whereby a person is classed as a responder if there is a 50% reduction in pain (VAS 48h) or function (AUSCAN functional subscale) or a 20% reduction with an absolute reduction of at least 10 mm in two of three of VAS 48h, AUSCAN functional subscale or patient activity VAS.

**Results**

A total of 115 people were invited to join the study, and 70 participants were recruited (August 2009–September 2010). Of the 70 participants, 57 were women, mean age 61.5 years (range 43–81), median (interquartile range [IQR]) disease duration (months) 60 (30–120). The flow chart of participants throughout the study is demonstrated in Fig. 1. One participant withdrew (placebo group) at 2 weeks because of severe vertigo. Data were collected from this participant at 4 weeks to assess the primary outcome. One participant in each group failed to attend the final 12-week visit and was unable to be contacted. No imputation was made for missing data; hence, data from the final visit are available for 67 participants.

**Concomitant medication**

By week 4, eight participants (11.4%) (four from each group) had altered their concomitant medication. Six participants reduced their analgesics, as they reported a subjective improvement in hand pain. Two participants who increased their analgesics were in the placebo group. At 12 weeks, seven participants (10%) had altered their analgesics from baseline. Six participants had increased their analgesics (three from the PNL group and three from the placebo group), two because of increased hand pain and four for other reasons. One subject had altered their NSAID (diclofenac to ibuprofen).

**Clinical**

Baseline characteristics are shown in Table 1. The randomization was effective, with no substantive differences at baseline between the two groups. Overall, most people had improved at 4 weeks. There were no statistically significant differences in pain VAS or AUSCAN pain scores between placebo and PNL groups at either 4 or 12 weeks. Likewise, there were no significant differences in patient- or physician-reported disease activity VAS, AUSCAN stiffness or function scores, painful joint count (PJ), tender joint count (TJ), swollen joint count (SJ), HADS or quality of life scores at either 4 or 12 weeks (see Table 2). A total of 20 participants (57%) in each group achieved OMERACT-OARSI responder criteria at 4 weeks. Repeat ANCOVA analysis after removing the eight participants who altered concomitant medication at 4 weeks did not alter the primary outcome.

**Radiographs**

All radiographs were reviewed by a radiologist to confirm the presence of radiographic hand OA before enrolling a participant in the trial. However, formal radiographic scoring was performed after the trial was completed; at this point, radiographs were available for scoring for 66 of 70 participants. The mean (s.d.) number of joints with radiographic OA was 9.9 (6.4) and median 10. Fourteen of 70 participants were classified as erosive (one or more
erosive joints), whereby an erosion was defined as a focal area of bone loss associated with disruption of the cortex.

Exploratory imaging study of potential mechanism of action of PNL

A total of 65 participants underwent MRI at baseline. Five participants were not imaged because of technical difficulties with the eMRI machine on the day of the study visit. In total, 701 joints were imaged at baseline. Of these, 39% imaged normally, 43% demonstrated probable synovitis/effusion and 18% definite synovitis/effusion. All subjects had at least two joints with probable synovitis/effusion, and 49 of 65 participants (75%) had at least one joint with definite synovitis/effusion. The median number of abnormal joints (score ≥1) on MRI was 7. A joint with imaging-detected synovitis/effusion...
(relative to a joint with no imaging-detected synovitis/effusion) was significantly more likely to be painful [definite synovitis/effusion odds ratio (OR) = 3.7 (95% CI 2.2, 6.2), P < 0.001; overall Wald \( \chi^2 = 24.6, P < 0.001 \)] or swollen [definite synovitis/effusion OR = 12.6 (95% CI 5.9, 26.9), P < 0.001; overall Wald \( \chi^2 = 51.4, P < 0.001 \)] or tender [definite synovitis/effusion OR = 4.7 (95% CI 2.8, 7.9), P < 0.001; overall Wald \( \chi^2 = 35.3, P < 0.001 \)] (Fig. 2).

There was no significant difference in baseline synovitis (defined by the mean number of joints with definite synovitis/effusion) between placebo and PNL groups (Mann–Whitney U, P = 0.59). Baseline synovitis (defined as the number of joints with definite synovitis/effusion) did not correlate with baseline hand pain VAS and did not predict OMERACT-OARSI response (Fig. 3). There was little change in the repeat MR images at 4 weeks. The images of only three participants had altered, showing the appearance or resolution of definite synovitis/effusion.

**Adverse events**

There was no significant difference in the number of adverse events reported in the two groups. Two adverse events were probably related to CS (bruising and gastric reflux).

One serious adverse event was reported, unrelated to the study drug (total knee replacement).

**Discussion**

This is the first RCT of low-dose CS alone in hand OA, and despite adequate powering (for a moderate effect), this study demonstrated that there is no significant benefit for this dose of PNL compared with placebo for short- to medium-term relief of painful hand OA. The placebo group showed marked improvement in symptoms, consistent with a recent meta-analysis of placebo effect in OA trials [29]. An additional explanation for the lack of significant benefit compared with placebo may be a low dose of CS at the individual joint level; however, the dose and length of treatment were deliberately limited to reduce potential side effects. Pain in OA is complex, and recently identified potential peripheral sources of nociceptive pain in hand OA include the presence of bone marrow lesions, erosions and bone attrition [8], which were not assessed in this study. However, the most responsive outcomes in hand OA trials have been demonstrated to be patient-reported disease activity and change in pain on a VAS [30]. Neither measure showed a significant difference

**TABLE 1** Baseline characteristics of the two groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo n = 35</th>
<th>PNL n = 35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (s.d.), years</td>
<td>61.1 (9.0)</td>
<td>61.9 (6.6)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>31 (89)</td>
<td>26 (74)</td>
</tr>
<tr>
<td>RF, n</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>32</td>
<td>33</td>
</tr>
<tr>
<td>Positive</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Unknown</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Disease duration, median (IQR), months</td>
<td>60 (30–120)</td>
<td>60 (36–108)</td>
</tr>
<tr>
<td>BMI, mean (s.d.)</td>
<td>27.7 (5.4), n = 34</td>
<td>27.5 (4.2)</td>
</tr>
<tr>
<td>NSAID (oral and/or topical) usage, n (%)</td>
<td>19 (54)</td>
<td>19 (54)</td>
</tr>
<tr>
<td>Oral</td>
<td>16</td>
<td>17</td>
</tr>
<tr>
<td>Topical</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Opioid usage, n (%)</td>
<td>10 (29)</td>
<td>12 (34)</td>
</tr>
<tr>
<td>Hydroxychloroquine usage, n (%)</td>
<td>4 (6)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Joints with radiographic OA global score (range 0–32), mean (s.d.)</td>
<td>10 (7)</td>
<td>10 (6)</td>
</tr>
<tr>
<td>K/L score of worst finger joint (n = 63), n</td>
<td></td>
<td></td>
</tr>
<tr>
<td>K/L ≤ 2</td>
<td>17</td>
<td>14</td>
</tr>
<tr>
<td>K/L 3</td>
<td>6</td>
<td>13</td>
</tr>
<tr>
<td>K/L 4</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Pain VAS 2 week, mean (s.d.), mm</td>
<td>58 (17)</td>
<td>62 (15)</td>
</tr>
<tr>
<td>Pain VAS 48 h, mean (s.d.), mm</td>
<td>61 (16)</td>
<td>62 (19)</td>
</tr>
<tr>
<td>Pain VAS worst joint, mean (s.d.), mm</td>
<td>67 (19)</td>
<td>71 (21)</td>
</tr>
<tr>
<td>Patient reported disease activity VAS, mean (s.d.), mm</td>
<td>59 (18)</td>
<td>65 (22)</td>
</tr>
<tr>
<td>Physician reported disease activity VAS, mean (s.d.), mm</td>
<td>54 (13)</td>
<td>59 (7)</td>
</tr>
<tr>
<td>PJC (range 0–28), median (IQR)</td>
<td>6 (4–8)</td>
<td>7 (5–11)</td>
</tr>
<tr>
<td>SJC (range 0–28), median (IQR)</td>
<td>1 (0–3)</td>
<td>2 (1–4)</td>
</tr>
<tr>
<td>TJC (range 0–28), median (IQR)</td>
<td>6 (3–8)</td>
<td>6 (4–12)</td>
</tr>
<tr>
<td>AUSCAN pain VAS, mean (s.d.)</td>
<td>60 (15)</td>
<td>66 (16)</td>
</tr>
<tr>
<td>AUSCAN stiffness VAS, mean (s.d.)</td>
<td>56 (21)</td>
<td>55 (30)</td>
</tr>
<tr>
<td>AUSCAN function VAS, mean (s.d.)</td>
<td>62 (15)</td>
<td>61 (23)</td>
</tr>
<tr>
<td>OAQoL (Rasch) (range 0–24), mean (95% CI), n = 34</td>
<td>7 (5, 9)</td>
<td>6 (4, 9)</td>
</tr>
<tr>
<td>HADS anxiety (Rasch) (range 0–21), mean (s.d.)</td>
<td>12 (4)</td>
<td>11 (11)</td>
</tr>
<tr>
<td>HADS depression (Rasch) (range 0–21), mean (s.d.)</td>
<td>12 (4)</td>
<td>11 (5)</td>
</tr>
</tbody>
</table>
between PNL and placebo in this study. The previous study demonstrating efficacy of intramuscular CS in hand OA was open label [17], and the different pharmacokinetics may result in a higher circulating level of CS, although the overall total dose of CS is similar. The previous study using the novel drug CRx-102, an oral CS (3 mg PNL) combined with dipyridamole (200–400 mg) [18], which may potentiate the action of CS, thereby requiring a lower dose, did demonstrate a benefit compared with placebo in symptom relief for hand OA. The degree of radiographic damage in this study is markedly different from our study. Eighty-five percent of the finger joints in the CRx-102 participants had moderate to severe radiographic OA changes (K/L score of 3 or 4). This is in contrast to our study in which the median number of joints with radiographic OA was 10/32 (31%). Our cohort therefore may represent milder radiographic disease than previous studies.

One of the inclusion criteria of the CRx-102 study was more than one swollen finger joint on examination, with a resultant baseline mean number of swollen joints of five. There is a paucity of data available for the mean number of clinically swollen joints in population studies of hand OA. Sixteen participants (23%) in the current cohort did not have a swollen joint at baseline, and the mean number of swollen joints was much lower than in the study listed earlier (mean 2.5, median 2). The current study did not use swollen joints as an inclusion criteria, as it was designed to target and treat people with hand OA pain, regardless of clinical joint swelling. Furthermore, in a recent study using the very effective anti-inflammatory anti-TNF therapy in hand OA, the mean number of swollen joints was 2.85, and yet, although structure modification was obtained in terms of reduced erosion progression, a statistical reduction in symptoms was not achieved [31].

The imaging in this study was an exploratory outcome to help examine the potential anti-synovitis mechanism of action of PNL. Imaging data from this study confirmed the findings of previous studies: there was a high prevalence of synovitis in painful hand OA, with 75% of participants demonstrating definite synovitis/effusion in at least one joint on imaging. Despite the high prevalence of synovitis, CS did not have any effect on imaging-detected synovitis for the 4-week period. It has been previously demonstrated that the extent of changes in individual joints on ultrasonographic imaging does not correlate with the degree of symptoms [5, 19]. The MRI findings in this study confirmed that not all joints with imaging evidence of synovitis were painful or swollen; however, a joint that had MR evidence of synovitis/effusion was significantly more likely to be reported by the participant as painful, tender or swollen. This is in agreement with a recent publication demonstrating an association between MR-detected synovitis and joint tenderness in hand OA [8]. However, at the patient level, there was no association between baseline synovitis and pain or patient-reported disease activity VAS scores. This is also in agreement with a recent publication [8]. This study was of course not designed to determine the pathological associations of MR.

### Table 2

<table>
<thead>
<tr>
<th>Variable</th>
<th>Placebo (n = 35)</th>
<th>PNL (n = 34)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain VAS 2 weeks</td>
<td>-17 (24, -11)</td>
<td>-8 (24, -11)</td>
<td>0.009 P = 0.77</td>
</tr>
<tr>
<td>Pain VAS 48h</td>
<td>-20 (29, -13)</td>
<td>-10 (15, -3)</td>
<td>0.027 P = 0.61</td>
</tr>
<tr>
<td>Patient disease activity VAS</td>
<td>-20 (27, -12)</td>
<td>-10 (15, -3)</td>
<td>0.027 P = 0.60</td>
</tr>
<tr>
<td>Physician disease activity VAS</td>
<td>-16 (24, -9)</td>
<td>-8 (15, -3)</td>
<td>0.027 P = 0.60</td>
</tr>
<tr>
<td>AUSCAN pain VAS</td>
<td>-10 (16, -4)</td>
<td>-8 (15, -3)</td>
<td>0.008 P = 0.82</td>
</tr>
<tr>
<td>AUSCAN function VAS</td>
<td>-8 (14, -2)</td>
<td>-2 (8, 1)</td>
<td>0.008 P = 0.82</td>
</tr>
</tbody>
</table>

Data are given as mean change in variable (95% CI), mm.
pain at the patient level, as this would have required a matched cohort with no symptoms. This study did have limitations. Eleven percent of participants altered their concomitant analgesia at 4 weeks, although there was no increase in NSAID use in any participant. Furthermore, repeat analysis after removing all eight participants who had altered medication did not alter the primary outcome. It would be unethical to insist on maintaining stable analgesic doses in participants who complain of increased pain or to require that participants remain on potentially toxic analgesics if they do not require them. Paracetamol as rescue therapy, if additional analgesia was required, was not thought to be appropriate, as participants were recruited from a hospital secondary care setting, where many people with symptomatic hand OA have not had sufficient pain relief from paracetamol. This was the case in that 50% of participants were already using paracetamol at baseline, yet still had a baseline pain VAS score of >40 mm.

The MR data were limited by the low resolution of the scanner and the resultant quality of the MRI scans. The imaging was non-contrast enhanced, and the resolution of the STIR images and the slice thickness of 4 mm did not allow us to use the recently proposed Oslo Hand OA MRI scoring system [32]. In several participants, joints could not be scored because of incorrect positioning of the hand in the scanner or movement artefact. However, to avoid bias, we excluded from the analysis any group of joints (MCP, PIP and DIP) in which two or more joints could not be scored or any patient who had four or more joints missing on MR images. For these reasons, the degree of synovitis in this cohort may be underestimated.

In summary, low-dose (5 mg) PNL for 4 weeks is not an effective analgesic treatment for hand OA compared with
placebo. This study has demonstrated a high prevalence of synovitis/effusion in painful hand OA. Further studies to find effective and safe treatments for painful hand OA and to further explore the relationship between imaging-detected synovitis and symptoms are required.

Rheumatology key messages
- Short-term low-dose oral PNL is not an effective analgesic treatment for hand OA.
- There is a high prevalence of imaging-detected synovitis/effusion in painful hand OA.
- The relationship between imaging-detected inflammation and symptoms in hand OA warrants further study.

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