The Efficacy and Safety of Treatments for Acute Gout: Results from a Series of Systematic Literature Reviews Including Cochrane Reviews on Intraarticular Glucocorticoids, Colchicine, Nonsteroidal Antiinflammatory Drugs, and Interleukin-1 Inhibitors

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**ABSTRACT.** **Objective.** To determine the efficacy and safety of glucocorticoids (GC), colchicine, nonsteroidal antiinflammatory drugs (NSAID), interleukin-1 (IL-1) inhibitors, and paracetamol to treat acute gout.

**Methods.** We searched MEDLINE, EMBASE, and Cochrane Central Register of Controlled Trials to September 2011. Randomized controlled trials (RCT) or quasi-RCT in adults with acute gout that compared GC, colchicine, NSAID, IL-1 inhibitors, and paracetamol to no treatment, placebo, another intervention, or combination therapy were included. Two authors independently extracted data and assessed risk of bias. Primary endpoints were pain and adverse events. Data were pooled where appropriate.

**Results.** Twenty-six trials evaluating GC (N = 5), NSAID (N = 21), colchicine (N = 2), and canakinumab (N = 1) were included. No RCT assessed paracetamol or intraarticular (IA) GC. No RCT compared systemic GC with placebo. Moderate quality evidence (3 trials) concluded that systemic GC were as effective as NSAID but safer. Low quality evidence (1 trial) showed that both high- and low-dose colchicine were more effective than placebo, and low-dose colchicine was no different to placebo with respect to safety but safer than high-dose colchicine. Low quality evidence (1 trial) showed no difference between NSAID and placebo with regard to pain or inflammation. No NSAID was superior to another. Moderate quality evidence (1 trial) found that 150 mg canakinumab was more effective than a single dose of intramuscular GC (40 mg triamcinolone) and equally safe.

**Conclusion.** GC, NSAID, low-dose colchicine, and canakinumab all effectively treat acute gout. There was insufficient evidence to rank them. Systemic GC appeared safer than NSAID and lower-dose colchicine was safer than higher-dose colchicine. (J Rheumatol Suppl. 2014 Sept; 92:15–25; doi:10.3899/jrheum.140458)

**Key Indexing Terms:**
GOUTY ARTHRITIS  GLUCOCORTICOIDS  COLCHICHINE
NSAID  PARACETAMOL  INTERLEUKIN-1 INHIBITORS

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Gout is an inflammatory disease that affects millions of people worldwide. It is characterized by the presence of monosodium urate crystals in the joints, leading to acute pain and swelling. The natural history of gout is composed of three periods: asymptomatic hyperuricemia, episodes of acute gout, and chronic gouty arthritis. Hyperuricemia results from either increased urate production or decreased urate excretion, or a combination of these two factors. Gout heralds its presence by an exquisitely painful, acute monoarthritic attack, commonly in the big toe; subsequent attacks tend to be longer lasting, polyarticular, and tend to affect upper limb joints as well.

Pharmacologic treatment options to treat gout include glucocorticoids, colchicine, nonsteroidal antiinflammatory drugs (NSAID), paracetamol, and more recently, interleukin 1 (IL-1) inhibitors, alone or in combination. Preference and usage of these drugs differ across regions. Despite the common occurrence of acute gout, few guidelines have a multinational, in contrast to a more regional, perspective. It is in this context that a series of systematic reviews were conducted to address this question as an evidence base for developing multinational clinical practice recommendations.

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ences (MD) between the intervention and comparator groups, with corresponding 95% confidence intervals (95% CI). For dichotomous data, a risk ratio (RR) with corresponding 95% CI was calculated. We assessed studies for clinical homogeneity with respect to type of therapy, control group, and outcomes, and only studies judged to be clinically homogeneous were pooled. Statistical heterogeneity was assessed using the I² statistic.

RESULTS
A total of 564 potentially relevant articles were identified: 153 for IA and systemic GC, 308 for colchicine, 410 for NSAID, 42 for IL-1 inhibitors, and 20 for paracetamol (Figures 1A-1F). Of these, 5 trials for systemic GC, 2 for colchicine, 21 for NSAID, and 1 for IL-1 inhibitors met our inclusion criteria. No trials of IA GC or paracetamol met our inclusion criteria. Of 9 ACR and EULAR abstracts of potential relevance, none were suitable for inclusion. The characteristics of studies included in the final review are summarized in Table 1. A list of excluded studies and reasons for exclusion are included in the online Appendix available from www.3egout.com.

Systemic Glucocorticoids
All 5 included trials that met our inclusion criteria...
were parallel RCT; no trials compared systemic GC to placebo. Three trials compared systemic GC to NSAID\textsuperscript{19,20,21}, one compared 1 systemic GC to another\textsuperscript{23}, and 1 (reported in 2 articles) compared systemic GC to canakinumab, an IL-1 inhibitor\textsuperscript{22,24}. Risk of bias of included trials is shown in supplementary Figure 2A in the Appendix available from www.3egout.com.

Figure 1. C. Results of the search strategy. Literature search for colchicine in acute gout. A total of 308 studies were identified by the initial search; of these, 2 studies met the criteria for inclusion in the final review. D. Literature search for NSAID in acute gout. A total of 410 studies were identified by the initial search; of these, 21 studies met the criteria for inclusion in the final review.

Systemic GC versus NSAID. Of the 3 trials that compared systemic GC to NSAID, one\textsuperscript{21} (n = 90; low risk of bias) compared oral prednisolone (35 mg daily for 5 days) to indomethacin (indomethacin 50 mg and diclofenac 75 mg on day 1 followed by indomethacin 150 mg for 2 days and 75 mg for 3 days). Outcomes (pain reduction in mm/h and AE) were evaluated every 30 min for 2 h, at 24 h, and on day
5 and 14. Another low risk of bias trial (n = 120)\textsuperscript{20} compared oral prednisolone (35 mg daily for 5 days) to naproxen (1 g daily for 5 days). Outcomes measured (on a 100 mm VAS) over 90 h were pain, general disability and walking disability, and AE. The third trial (n = 100)\textsuperscript{19} (high risk of bias) compared 40 IU intramuscular (IM) adrenocorticotropic hormone (ACTH) to indomethacin (up to 200 mg daily till pain relief). Outcomes were evaluated at 0–5 h and at 5–7 days; followup was for 1 year. Primary outcome was time to complete pain relief on ambulation; other outcomes were time to complete pain relief, intervals between attacks during trial period, and AE.

One systemic GC versus another. A single trial\textsuperscript{23} (n = 31; high risk of bias) compared a single IM dose of 40 IU of
Table 1. Characteristics of studies included in the final review.

<table>
<thead>
<tr>
<th>Study, Country</th>
<th>Gout Diagnosis; No. Joints Involved</th>
<th>Total No. (dropouts)</th>
<th>Duration</th>
<th>Design</th>
<th>Intervention</th>
<th>Comparator</th>
<th>Overall Risk of Bias</th>
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</thead>
<tbody>
<tr>
<td><strong>Systemic glucocorticoids</strong>&lt;br&gt;Systemic glucocorticoids vs NSAID&lt;br&gt;Axelrod 1988(^\text{19}), USA&lt;br&gt;Colchicine&lt;br&gt;Ahern 1987(^\text{27}), Australia&lt;br&gt;Terkeltaub 2010(^\text{28}), USA&lt;br&gt;NSAID&lt;br&gt;NSAID vs placebo&lt;br&gt;Garcia de la Torre, 1987(^\text{34}), Mexico&lt;br&gt;NSAID vs alternate NSAID (for NSAID vs systemic glucocorticoids, please see above)&lt;br&gt;Altman 1988(^\text{29}), USA&lt;br&gt;Butler 1985(^\text{30}), UK&lt;br&gt;Cheng 2004(^\text{31}), China&lt;br&gt;Douglas 1970(^\text{32}), UK&lt;br&gt;Eberl 1993(^\text{33}), Austria&lt;br&gt;Lederman 1980(^\text{34}) Brazil&lt;br&gt;Lomen 1986(^\text{36}), USA</td>
<td>No studies of systemic glucocorticoids vs placebo&lt;br&gt;Expert opinion, MSU crystals; mono/oligo&lt;br&gt;MSU crystals; mono&lt;br&gt;MSU crystals; study predefined clinical criteria; mono in 85&lt;br&gt;MSU crystals; mono&lt;br&gt;ACR 1977; 126 mono, 56 oligo, 18 poly&lt;br&gt;MSU crystals; mono/oligo&lt;br&gt;MSU crystals/mono&lt;br&gt;ACR 1977; Mono/oligo/ poly&lt;br&gt;ACR 1977; clinical criteria; n/a&lt;br&gt;MSU crystals/clinical / ACR 1977; n/a&lt;br&gt;MSU crystals/clinical; n/a&lt;br&gt;ACR 1977; Mono/oligo&lt;br&gt;Clinical criteria; n/a&lt;br&gt;MSU crystals/ NY criteria; n/a&lt;br&gt;MSU crystals/ NY criteria; n/a&lt;br&gt;MSU crystals/ NY criteria; mono</td>
<td>100 (24)</td>
<td>7 days (1 yr)</td>
<td>Parallel RCT</td>
<td>ACTH 40 IU</td>
<td>Indomethacin 50 mg × 4/d, till pain relief</td>
<td>High</td>
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<td></td>
<td></td>
<td>120 (2)</td>
<td>3 weeks</td>
<td>Parallel RCT</td>
<td>Prednisolone 35 mg/d × 5 days</td>
<td>Naproxen 1 g × 5 days</td>
<td>Low</td>
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<tr>
<td></td>
<td></td>
<td>90 (0)</td>
<td>14 days</td>
<td>Parallel RCT</td>
<td>Prednisolone 30 mg/ paracetamol 1 g × 5 days</td>
<td>Indomethacin 50 mg/diclofenac IM 75 mg/paracetamol 1 g, then indomethacin 150 mg/d × 2 days, then 75 mg/d × 3 days</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td></td>
<td>200 (9)</td>
<td>8 weeks</td>
<td>Parallel RCT</td>
<td>Triamcinolone 40 mg IM</td>
<td>Canakinumab 10-150 mg S/C</td>
<td>Unclear</td>
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<tr>
<td></td>
<td></td>
<td>31 (1)</td>
<td>30 days</td>
<td>Parallel RCT</td>
<td>ACTH 40 IU IM</td>
<td>Triamcinolone 60 mg IM</td>
<td>High</td>
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<tr>
<td></td>
<td></td>
<td>43 (2)</td>
<td>48 h</td>
<td>Parallel RCT</td>
<td>Oral colchicine 1 mg, then 0.5 mg 2 hourly till symptom relief or GI toxicity; High dose colchicine 1.2 mg, then 0.6 mg q 1 h for 6 h (total 4.8 mg)</td>
<td>Placebo; low dose colchicine 1.2 mg, then 0.6 mg in 1 h</td>
<td>Unclear</td>
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<tr>
<td></td>
<td>62 (n/a)</td>
<td>8 days</td>
<td>Parallel RCT</td>
<td>Diclofenac SR, 75 mg/d × 7 days</td>
<td>Placebo</td>
<td>High</td>
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<tr>
<td></td>
<td></td>
<td>25 (1)</td>
<td>14 days</td>
<td>Parallel RCT</td>
<td>Phenylbutazone, 800 mg 2 times, then 400 mg till resolution of attack</td>
<td>Placebo</td>
<td>Low</td>
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<tr>
<td></td>
<td>20 (n/a)</td>
<td>14 days</td>
<td>Parallel CCT</td>
<td>Meclofenamate, 200 mg then 600 mg x 1 day, then 300 mg/d × 6 days</td>
<td>Placebo</td>
<td>High</td>
<td></td>
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<tr>
<td></td>
<td>60 (0)</td>
<td>7 days</td>
<td>Parallel CCT</td>
<td>Etofolic acid 600 mg/d × 7 days</td>
<td>Naproxen 1.5 g/d x 7 days</td>
<td>High</td>
<td></td>
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<tr>
<td></td>
<td>29 (3)</td>
<td>5 days</td>
<td>Parallel RCT</td>
<td>Flurbiprofen 400 mg/d, then 200 mg/d × 5 days</td>
<td>Placebo</td>
<td>Low</td>
<td></td>
</tr>
</tbody>
</table>
Table 1. Continued.

<table>
<thead>
<tr>
<th>Study, Country</th>
<th>Gout Diagnosis; No. Joints Involved</th>
<th>Total No. (dropouts)</th>
<th>Duration</th>
<th>Design</th>
<th>Intervention</th>
<th>Comparator</th>
<th>Overall Risk of Bias</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maccagno 1991, Argentina</td>
<td>MSU crystals/ NY criteria; n/a</td>
<td>28 (n/a)</td>
<td>Not described</td>
<td>Parallel RCT</td>
<td>Phenybutazone 800 mg/d, then 400 mg/d, then 100 mg/d</td>
<td>Naproxen, 200 mg/d, then 600 mg/d</td>
<td>Low</td>
</tr>
<tr>
<td>Rubin 2004, USA</td>
<td>ACR 1977; mono 144, poly 49</td>
<td>41 (n/a)</td>
<td>7 days</td>
<td>Parallel CCT</td>
<td>Naproxen, 750 mg, then 500 mg/d</td>
<td>Phenybutazone, 800 mg/d, then 600 mg/d</td>
<td>High</td>
</tr>
<tr>
<td>Schumacher 2002, USA</td>
<td>ACR 1977; mono/ oligo</td>
<td>34 (n/a)</td>
<td>7 days</td>
<td>Parallel CCT</td>
<td>Piroxicam, 40 mg/d, then 20 mg/d</td>
<td>Piroxicam, 40 mg/d, then 20 mg/d</td>
<td>High</td>
</tr>
<tr>
<td>Shrestha 1995, USA</td>
<td>ACR 1977; n/a</td>
<td>10 (n/a)</td>
<td>6 days</td>
<td>Parallel RCT</td>
<td>Tenoxicam, 20 mg/d</td>
<td>Tenoxicam, 40 mg/d</td>
<td>High</td>
</tr>
<tr>
<td>Sturtevant 1996, USA</td>
<td>MSU crystals; clinical criteria; n/a</td>
<td>30 (n/a)</td>
<td>4 days</td>
<td>Parallel RCT</td>
<td>Phenybutazone, 700 mg, then 400 mg</td>
<td>Fenoprofen, 3.6 g, then 3 g</td>
<td>Low</td>
</tr>
<tr>
<td>Willburger 2007, Germany</td>
<td>ACR 1977; Mono 187, poly 48</td>
<td>235 (12)</td>
<td>7 days</td>
<td>Parallel RCT</td>
<td>Lumiracoxib, 400 mg/d</td>
<td>Indomethacin, 150 mg/d</td>
<td>Low</td>
</tr>
<tr>
<td>IL-1 inhibitors</td>
<td>So 2010, Switzerland USA</td>
<td>ACR 1977; 126 mono, 56 oligo, 18 poly</td>
<td>200 (9)</td>
<td>8 weeks</td>
<td>Triamcinolone, 40 mg IM</td>
<td>Canakinumab, 10–150 mg SC</td>
<td>Unclear</td>
</tr>
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</table>

ACTH to a single dose of 60 mg IM triamcinolone; outcomes (grading of pain, swelling, function and mobility as improved by < or > 50%, unchanged, or worse) were assessed at days 1–2, 3–4, 10–14, and 30.

Systemic GC versus IL-1 inhibitors. One trial (n = 200; unclear risk of bias) compared systemic GC to canakinumab; patients received either a single IM dose of 40 mg triamcinolone (n = 57) or canakinumab [10–150 mg subcutaneously (SC) at differing doses; n = 143]. Outcomes were assessed at 72 h, 7 days, 4 weeks, and 8 weeks post-dose. Primary outcome was determination of the canakinumab dose that produced equivalent efficacy to that achieved with triamcinolone acetone 40 mg 72 h after treatment, according to patient assessment of pain on a 100 mm visual analog scale; other outcomes were time to 50% reduction in pain, time to recurrence of flare, reductions in C-reactive protein and serum amyloid A protein levels, use of rescue medication, physician and patient global assessments, and HRQOL. An updated literature search for the related Cochrane review identified 2 more articles [reporting 3 studies; 2 comparing 150 mg canakinumab with 40 mg triamcinolone, and one comparing 320 mg of rilonacept (an IL-1 inhibitor) with indomethacin].

Effects of systemic GC. Systemic GC versus NSAID. There was moderate quality evidence based on 2 trials of no between-group difference in pain reduction over 2–6 hours [mean difference –1.77 (95% CI –4.80 to 1.26)] and difference in clinical criteria; n/a. The third trial reported evidence, based upon 1 trial, of no difference between systemic GC and another.

NSAID than systemic GC in 1 trial (22/40 vs 1/36 for GI bleeding). The third trial reported faster pain relief in the ACTH group compared with the indomethacin group, although it was not possible to extract and independently verify the presented data. Gastrointestinal (GI) and non-GI AE were more common with NSAID than systemic GC in 1 trial (22/40 vs 1/36 for GI and 27/40 vs 1/36 for non-GI AE). SAE were also more common with NSAID than systemic GC in another trial (7/40 vs 0/40); 5 SAE in the NSAID group were related to GI bleeding.

One systemic GC versus another. There was low quality evidence, based upon 1 trial, of no difference between ACTH and triamcinolone in time to average resolution of symptoms (8 days in both groups) and triamcinolone.
Systemic GC versus IL-1 inhibitors. Canakinumab at the highest dose used (150 mg) was significantly better than triamcinolone for reduction in pain at 72 h [24/27 vs 6/11 (numbers in the triamcinolone group have been adjusted to account for multiple comparisons); mean difference 26.80 (95% CI 2.35 to 51.25)]; there were no between-group differences in efficacy outcomes between triamcinolone and the lower doses of canakinumab (10 mg, 25 mg, 50 mg, and 90 mg) and no between-group differences in AE comparing triamcinolone to any dose of canakinumab24.

Colchicine

Both included colchicine trials were parallel RCT: 1 with low-27 and the other with unclear26 risk of bias (see supplementary Figure 2B in the Appendix available from www.3egout.com). One trial (n = 43) randomized participants to either high-dose colchicine (n = 22) or placebo (n = 21)27. The other (n = 575) randomized participants to either low- (n = 192) or high-dose colchicine (n = 193) or placebo (n = 190)28. Both trials converted pain to a dichotomous measure of success (proportion improved by ≥ 50%); pain reduction measurements were taken at 12, 24, 36, and 48 h in the first27 trial and at 24 and 32 h in the second28. Secondary outcomes in the first trial were 50% reduction in a compounded score comprising pain, joint tenderness, swelling, redness, and AE; for the second study, secondary outcomes were treatment response based on at least a 2-unit reduction in target joint pain score at 24 and 32 h and AE.  

Effects of colchicine. There was low quality evidence based upon 2 trials that showed significantly more people taking high-dose colchicine compared with those taking placebo obtained pain relief at 24 h [26/74 vs 6/50, RR 2.88 (95% CI 1.28 to 6.48)] and 36 hours [35/74 vs 12/50, RR 2.16 (95% CI 1.28 to 3.65)]27,28. There was low quality evidence based upon 1 trial that low-dose colchicine was also significantly more effective than placebo for pain relief at 24 h [28/74 vs 4/29, RR 2.74 (95% CI 1.05 to 7.13)] and 36 h [31/74 vs 5/29, RR 2.43 (95% CI 1.05 to 5.64)] in 1 trial, but there was no between-group difference in pain relief at 24 h or 36 h for those taking high- versus low-dose colchicine28.

High-dose colchicine was associated with significantly more GI AE than placebo in both trials: 22/22 versus 5/51 [RR 3.91 (95% CI 1.89 to 8.09)] in 1 trial27 and 40/52 versus 8/29 [RR 3.72 (95% CI 1.80 to 7.70)] in the other trial28. However, participants were instructed to continue taking colchicine until either pain relief or toxicity in the first trial. This may have inflated the risk of GI AE because all participants in this trial developed diarrhea and/or vomiting with median time to onset of toxicity being 24 h or after a mean dose of 6.7 mg of colchicine27. High-dose colchicine was associated with significantly more GI AE than low-dose colchicine [40/52 vs 19/74, RR 3.00 (95% CI 1.98 to 4.54)]; with regard to GI AE, low-dose colchicine was no different from placebo [19/74 vs 6/29, RR 1.24 (95% CI 0.55 to 2.79)]28. For colchicine, we found a FDA warning of the association of potentially fatal AE with IV colchicine (including bone marrow, renal, and cardiac toxicity) and a significant drug interaction between drugs metabolized with CYP3A4 and P-glycoprotein enzyme systems (such as clarithromycin, erythromycin, ketoconazole, ritonavir, verapamil, and diltiazem), particularly in the presence of hepatic or renal dysfunction.

NSAID

Trial duration of the 21 NSAID trials (n = 1621) that met our inclusion criteria varied between 90 h and 14 days19,20,29-33,34-38,39-43,44,45,46,47. Risk of bias of the included trials is shown in supplementary Figure 2C in the Appendix available from www.3egout.com. Only 1 trial (high risk of bias) compared an NSAID (tenoxicam) to placebo34; the primary outcomes were time to improvement and resolution of symptoms; secondary outcomes were pain and inflammation. Seventeen trials compared 1 NSAID to another29-33,35-39,40,42-46,47. There were 3 trials, all judged to be at low risk of bias, that compared a conventional NSAID (indomethacin) to a selective COX-2 inhibitor (etoricoxib38, celecoxib39, or lilmuracoxib47). The duration of treatment ranged from 5 to 10 days, and followup from 24 h to 14 days. The primary efficacy endpoint in 3 trials was the proportion of participants improved by ≥ 50%.33,34,36 (pain reported on ordinal scales) and the primary safety endpoint of withdrawals due to AE in 13/18 trials29-33,34-38,39,40,47. Other endpoints were variably reported. Seven trials31,32,33,35,36,37,37,42 variably assessed inflammation as an outcome. Function was assessed in 5 trials29,31,33,35,37,37; of these, two29,31 assessed function as part of a total inflammatory score while the other three33,35,37 trials reported whether there was a limitation of motion of the index joint. Five trials29,31,35,36,37 included a measure of the patient global assessment; no trials included a measure of HRQOL. Eleven trials29-33,35,36,37,40,42,43 included the number of participants with AE and provided a description of these. All 3 trials of NSAID versus cyclooxygenase-2 selective drugs measured pain as a primary outcome using a Likert scale38,47 or 5-point ordinal scale39 and measured inflammation, PGA, and AE as secondary outcomes; function was not assessed in any of the trials and only 1 trial14 measured HRQOL as a secondary outcome. The description of the 3 trials20,21,48 that compared an NSAID to GC (oral or systemic) is given above. An updated literature search for the related Cochrane review identified 1 more study49 (n = 86, low risk of bias) comparing celecoxib to indomethacin.

Effects of NSAID. There was low quality evidence based upon 1 trial (n = 50) that NSAID (tenoxicam) was no different from placebo with respect to ≥ 50% reduction in pain and joint swelling at 24 h and at day 434. Only 2 trials that compared etodolac to naproxen (n = 121) could be pooled; and there were no between-group differences with
respect to proportion who considered themselves markedly improved at the end of treatment [etodolac 53/60 vs naproxen 53/61, RR 1.01 (95% CI 0.89 to 1.15)]\(^{35,37}\). In the 3 trials (n = 108) that compared indomethacin to another NSAID (flurbiprofen\(^{36}\), meclofenamate\(^{33}\), or ketoprofen\(^{29}\)), there were no between-group differences in efficacy. There was moderate quality evidence, based upon 3 trials (n = 574), of no between-group differences between indomethacin and coxibs with respect to pain [MD 0.02 (95% CI –0.10 to 0.13)], inflammation [MD 0.02 (95% CI –0.08 to 0.11)], or global assessment of treatment success [MD –0.02 (95% CI –0.15 to 0.12)], while 1 trial reported no between-group differences with respect to HRQOL (data not provided)\(^{47}\).

There was no between-group difference in number of AE in the trial that compared NSAID to placebo\(^{34}\), or in the trials that compared 1 conventional NSAID to another. There were no withdrawals due to AE in either arm of the placebo-controlled NSAID trial. There was moderate quality evidence, based upon pooled data from 3 trials\(^{38,39,47}\), that coxibs are associated with significantly fewer GI events [20/296 (coxibs) vs 44/278 (NSAID), RR 0.42 (95% CI 0.26 to 0.70)], and fewer total AE [74/296 (coxibs) vs 110/278 (NSAID), RR 0.57 (95% CI 0.44 to 0.74)].

II-1 inhibitors

The one trial (n = 200) that met our inclusion criteria was a parallel RCT judged to be at unclear risk of bias [see supplementary data (Fig. 2D) in the online Appendix available from www.3egout.com\(^{22,24}\)]. This trial compared canakinumab to systemic GC and is described in the systemic GC section above.

DISCUSSION

This article synthesizes the existing evidence on various treatments for acute gout. These results were combined with expert opinion from the panel of rheumatologists taking part in the 3e Initiative to generate 1 of the 10 clinical recommendations on the management of gout. A detailed description of all the final recommendations can be found elsewhere\(^{6}\).

Our review highlights the paucity of high-quality evidence regarding efficacy of commonly used treatments for acute gout. Despite their perceived effectiveness\(^ {1}\) and endorsement by various guidelines and literature reviews\(^ {3,4,5,8,50}\), there are no published RCT or quasi-RCT that have assessed the efficacy and safety of either IA GC therapy or paracetamol (vs placebo or other interventions) in people with acute gout, and we identified only a single placebo-controlled trial of NSAID\(^ {34}\), one placebo-controlled trial of low-dose colchicine\(^ {28}\), and no placebo-controlled trials of systemic GC. We found moderate quality evidence from 3 trials that systemic GC were as effective as NSAID but had a better safety profile. Low-dose colchicine was as effective as high-dose colchicine (1 trial) but had a better safety profile. No NSAID was more effective than another. While the coxibs were as effective as conventional NSAID (based on 3 trials), they had a safer GI profile. Based on 1 trial, 150 mg canakinumab was more effective than a dose of 40 mg triamcinolone, with a similar safety profile.

Several systematic reviews and guidelines on the management of acute gout have been published over the last few years including those by the EULAR\(^ {5}\), by Hamburger, et al\(^ {3}\), and more recently by the ACR\(^ {4}\). The ACR guidelines differed methodologically from the others in using the RAND/UCLA (University of California at Los Angeles) Appropriateness Method, rather than the Delphi approach. The EULAR guidelines recommended oral colchicine and/or NSAID as first-line agents, and IA GC (on the basis of 1 uncontrolled trial) in patients with a severe mono-articular attack and in those with contraindications to NSAID and colchicine. The conclusions of the reviews by Hamburger, et al and the ACR are broadly consistent with our review, and recommend oral colchicine, NSAID, or GC as appropriate first-line therapeutic options.

Following presentation of the evidence for the use of the above treatments in acute gout, notwithstanding the variable quality of the evidence, the consensus opinion from the multinational experts from the 3e Initiative gout project was that equal weight be given to NSAID, low-dose colchicine, and GC (given as IA, oral, or IM therapy), as there was insufficient evidence to prioritize them. Although there was early evidence that canakinumab may be useful in the treatment of acute gout, further evidence was required prior to making a formal recommendation. Paracetamol, although not recommended as first-line therapy, could be a useful analgesic adjunct. Individual treatment decisions should be made on the basis of an individual’s comorbidities and in consideration of each drug’s safety profile.

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REFERENCES


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