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## **Pharmacological treatment of acute Gout attacks: Which treatment is effective? Review the latest systematic reviews using the AMSTAR tool**

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**Abstract**--Gout is an inflammatory condition of the joints caused by deposition of crystallized monosodium urate (MSU) in the joint which leads to Arthritis. there are many debates about the suitable pharmacological therapy for the acute inflammatory gout attacks. The Pharmacological treatment included colchicine, non steroidal anti-inflammatory (NASIDS) and corticosteroid injection. The aim of this study is to review the evidences which studied the effect of Colchicine, NASID and corticosteroid injections and discuss their effectiveness in treating the acute flares of Gout. After evaluation the validity of the latest best evidences presented in the database by using the AMSTAR tool. There was no best drug and no optimal dose identified in treating acute Gout attacks. Doctors should be careful in selecting the treatment considering the side effect of each medication and deal with each patient individually to provide the best health care.

**Keyword**--pharmacological, gout attacks, treatment, AMSTAR tool.

## **Introduction**

Gout is an inflammatory condition of the joints caused by deposition of crystallized monosodium urate (MSU) in the joint which leads to Arthritis. (1). The incidence of the inflammatory Gout in the whole world is 0.3% , and the percentage varies from country to country. These differences are due to environmental and genetic factors. In American 5-13 cases are affected for every 1000 men and 1-6 cases are affected for every 1000 in women with rate of 0.27% in general population (2).The deposition of these crystals leads to pain ,swelling, redness, and joint stiffness (3). Although the big toe is mostly effected, other joints can also be affected .Polyarticular gout is more prevalent in males greater than 40 years who have hypertension and Females in their menopausal period (4).The main source of crystallized monosodium urate is Purine, which is found steaks, meat, and seafood. Other food may increase uric acid content, especially beer, and fructose-rich beverage.

Many therapies have been reported the treatment of Acute Gout attacks as Ice, prevent diuretics, and high BMI. Furthermore, dietary restrictions of carbon dehydrate , increased protein and use of unsaturated fat may also limit the frequency of acute attacks (tug well 2002)(4).However, there are many debates about the suitable pharmacological therapy for the acute inflammatory gout attacks (5). The Pharmacological treatment included colchicine , non steroidal anti- inflammatory (NASIDS) and corticosteroid injection (6). The aim of this study is to review the evidences which studied the effect of Colchicine, NASID and corticosteroid injections and discuss their effectiveness in treating the acute flares of Gout in patients with multiple co-morbidities as hypertension, organ failure, and obesity, after evaluation the validity of the latest best evidences presented in the database by using the AMSTAR tool. The AMSTAR tool for critical appraisal the systematic reviews is a validated and well known tool as it used most frequently in the assessment of the methods quality, for this reason, it was used to evaluate the quality of the systematic reviews which have been used in this review.

## **Material and Methods**

This review included the the studies which are relevant to Gout and their management (Pharmacological) as injections therapy, NSAID, and Colchicines. No restriction on patient's age or gender, only human. The evidence has been searched from Cochrane database for systematic reviews, Pubmed database. Words used were "treatment", "management", "Gout", "inflammatory", "conservative", "acute", "attack" , " Injection" .The time limitation was for the last 10 years, English literatures were included. The abstracts have been read and the relevant articles were included in the study after collecting them in the Mandalay programme. The initial search showed 173 study, after exclusion the duplicated studies and the studies which are not relevant to our case after reviewing the abstracts, the result were 14 reports, only one result has been found in the Cochrane database of systemic review. Other 5 systematic reviews were considered in our review for further analysis as they were relevant to the case.

**Discussion**

Table 1  
Assessment of multiple systematic reviews' (AMSTAR)

| No. | AMSTAR questions  | Khanna et al | Shekelle et al | Seth et al | Li et al | Van Durme et al |
|-----|---|--------------|----------------|------------|----------|-----------------|
| 1   | Was an 'a priori' design provided?  | Yes          | Yes            | Yes        | Yes      | Yes             |
| 2   | Was there duplicate study selection and data extraction?  | Yes          | Yes            | Yes        | Yes      | Yes             |
| 3   | Was a comprehensive literature search performed?  | Yes          | Yes            | Yes        | Yes      | Yes             |
| 4   | Was the status of publication (i.e. grey literature) used as an inclusion criterion?              | Yes          | Yes            | Yes        | Yes      | Yes             |
| 5   | Was a list of studies (included and excluded) provided?   | Yes          | Yes            | Yes        | Yes      | Yes             |
| 6   | Were the characteristics of the included studies provided?  | Yes          | Yes            | Yes        | Yes      | Yes             |
| 7   | Was the scientific quality of the included studies assessed and documented?                       | Yes          | Yes            | No         | Yes      | Yes             |
| 8   | Was the scientific quality of the included studies used appropriately in formulating conclusions? | Yes          | Yes            | No         | Yes      | Yes             |
| 9   | Were the methods used to combine the findings of studies appropriate?                             | Yes          | Yes            | Yes        | Yes      | Yes             |
| 10  | Was the likelihood  | Yes          | Yes            | No         | Yes      | Yes             |

|    |  |       |       |      |       |       |
|----|--|-------|-------|------|-------|-------|
|    | of publication bias assessed?          |       |       |      |       |       |
| 11 | Was the conflict of interest included? | Yes   | Yes   | No   | Yes   | ?     |
|    | Score                                  | 11/11 | 11/11 | 7/11 | 11/11 | 10/11 |

? cannot answer

The systematic review from Khanna et al (7) shows high validity. Because of the controversy about the effectiveness of corticosteroid injections, NSAID and Colchicine. The authors in this systematic review assessed the effect of these three different therapies. The NSAIDs included in the study were: Indomethacin, naproxen, Cox 2 inhibitors. There were 23 studies (19 double-blind RCT's, 2 single-blind RCT) not included. The studies showed the benefit of Indomethacin in treatment of acute gout attack. Moreover, there was a superiority of Naproxen over etodolac. However, the Naproxen was similar to Prednisone in its effectiveness. celecoxib was statistically less effective than indomethacin. The study reported the effectiveness of Corticosteroid injection compared to NSAID. Furthermore, the study showed the effectiveness of colchicines especially when it used in small doses. However, the duration of Colchicine was not assessed. However, there were some important weakness aspects in the Khanna study. Firstly, the lack of the long-term effectiveness of the treatment. Secondly, they did not assess the type and the severity of the Inflammatory Gout arthritis. As a result, the study shows the effectiveness of all pharmacological treatment types, the selection of the treatment depends on the co morbidities of the patients and there was no best treatment as a monotherapy.

Shekelle et al (8) reported in their systematic review, the effectiveness of colchicine in the management of acute gout even when they used in small dose compared to high dose. However, the high dose group had reported diarrhea as complication. The study reported the effectiveness of steroid over indomethacin. However, there was no comparison of NSAID as the studies collected were small and ineffective. The Authors reached their conclusion based on moderate level studies and stated that all NSAID, Cortisones and Colchicine were effective treatment for acute inflammatory gout. The limitation of this study was the placebo control trials not included in their studies. Moreover, there were a large crossover rate, the studies which considered to be of high quality were unclear with the criteria used, as the sample number of each study was small and the statistical methods were not clearly identified and many factors that might be significant as the patient's past medical history, the type and severity of the Inflammation

Seth et al (9) in their systematic review suggested using the urate lowering agent in combination with low dose NSAID, Colchicine and Corticosteroid in the treatment in acute gout flares. The Authors suggested lowering the uric acid concentration will lead to better outcome. The dose of Colchicine has been effective in the management of acute attacks. The limitation of this study was the possible bias and the NSAID which has been used in the study has been withdrawn, so it would be a difficulty to draw a conclusion from this study. Li et al. (10) demonstrated in their systematic review a high quality validity. The authors described the previous systematic reviews which concerned the management of acute Gout. They stated the importance of using uric acid

lowering agent in order to control hyperuricemia as first line with other medications which used to manage acute attacks. The studies which were involved in this systematic review have wide varies to use different types of medications as colchicines, NSAID, and Intra articular Corticosteroids. However, the study did not reach a conclusion to specify the superior medication as there was lack of level I evidence and studies that evaluate the effectiveness of the Acute Gout therapy. Furthermore, they criticized the methodology used in most studies which used their study.

Van Durme et al (5) another systematic review of high quality and relatively low risk of bias according to the AMSTAR score of systematic review. The Cochrane database considered to be a well known level one evidence database for systematic reviews and meta-analysis. the review included 23 trials of 2200 patients. However, they reported the limitation of most of the studies which supported the NSAID. Furthermore, they downgraded most of the moderate quality studies due to their evaluation of bias risk. The majority of the reports showed equality outcome of the NSAID drugs. No clear limitation has been found to discuss in Van Durme systematic review.

Colchicine in low dose used to be beneficial in acute attack. The study found that statically significantly useful proportion of the patient in low dose approximately (38%) and high dose approximately (33%) colchicine groups achieved 50% reduced pain compared to the control group about (16%) (1). Colchicine has been recommended 1.2 mg for acute attacks followed by 0.6mg in 1 h , to a maximum of 1.8 mg .However, colchicine use is limited because of its multiple potential side effects as gastrointestinal problems, neuromuscular toxicity , rhabdomyolysis , and renal failure. However, these side effect could be resolved within days to months after cessation of Colchicine (7)

## **Conclusion**

There is no best drug and no optimal dose identified in treating acute Gout attacks. Doctors should be careful in selecting the treatment considering the side effect of each medication and deal with each patient individually to provide the best health care.

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