Treatment of acute gout in patients with coronary artery disease

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Case Scenario

Mr. L, aged 63 years, was recently diagnosed to have with acute gouty arthritis. He had an acute gout flare last month and was given diclofenac injection by a private general practitioner. He comes to you for advice whether he should take the injection if he has another flare. Mr. L has been on treatment for his chronic essential hypertension and dyslipidaemia for the past 10 years. He also had two previous episodes of myocardial infarction in year 2005 and 2010, and he had angioplasty done twice. He stopped smoking and consuming alcohol three months ago.

In patients with pre-existing coronary artery disease, what is the first-line therapy for acute gouty arthritis?

Search Strategy

In order to answer the clinical query above, we need to address two sub-questions: "Are NSAIDs harmful in patients with coronary artery disease?" and "What are the treatment options other than NSAIDs?". To answer the first question, a search was conducted on PubMed using the following combination keywords of: NSAID, cardiovascular safety and meta-analysis. For the second question, the following combination keywords were used to conduct a search on PuBMed: acute pain, gout arthritis, treatment, corticosteroid and colchicine were used to conduct a search on PubMed. The most updated systematic reviews with or without meta-analysis and well-conducted randomizsed controlled trials were selected to answer the questions.

Evidence Summary

Many patients with gout have co-morbidities including hypertension, renal impairment, and coronary heart disease. Anti-inflammatory therapies (colchicine, NSAIDs and corticosteroids) are used to treat acute gout flares. Use of these agents may be limited by contraindications that are commonly presented in patients with gout. The goals when treating gout are no different in these patients, but the choice and dosage of drugs may need to be modified.

Rest and prompt treatment with NSAIDs are recommended as first-line treatments for acute gout flare, provided there are no contraindications. Examples of NSAIDs used are diclofenac, indomethacin, ketoprofen, celecoxib (COX-2 inhibitor) and etoricoxib. These NSAIDs are effective in relieving pain and reducing inflammation. However, there is growing concern about the adverse effect profile of NSAIDs.

Are NSAIDs harmful in patients with coronary artery disease?

In a recent published meta-analysis, the use of NSAIDs have been associated with increased risk of non-fatal myocardial infarction (MI).[1] The results of four cohort studies, two nested case control studies and nine randomized control trials (RCT) were selected for analysis. Among the six observational studies, two included individuals with prior coronary artery disease (CAD) and another four included individuals with either no prior history of CAD or a percentage of individuals with

prior history below 25%. In six observational studies, the pooled relative risk of NSAIDs for non-fatal MI was 1.30 (95% CI, 1.20 to 1.41). In nine RCTs investigating coxibs, the pooled relative risk for non-fatal MI was 1.61 (95% CI, 1.04 to 2.50).[1]

What are the treatment options for patients with acute gout and coronary artery disease other than NSAIDs?

Low-dose colchicine remains an option in patients in whom NSAIDs are contraindicated. Single-ingredient oral colchicine is effective in reduction of pain and clinical symptoms in patients experiencing acute attacks of gout.[2] Conventional high doses of colchicine are known to have considerable GI adverse effects (diarrhoea, nausea, vomiting and abdominal pain) and thus its use is limited at those doses;. The rate of GI adverse events was higher in patients taking high-dose colchicine (76.9%) compared to low-dose colchicine (25.7%) (OR 9.6; 95% CI,: 4.2 to -22.1).[3] Wertheimer et al.[4] compared the safety and efficacy of colchicine with NSAIDs for the treatment of gout and showed that hospitalizsation for GI complications (1.8%) and heart failure (1.9%) is more common with NSAIDs. The author concluded that despite higher cost per dose, colchicine could be more cost effective for the management of gout flares than NSAIDs.

The safety and efficacy of colchicine, especially in the presence of co-morbidity and potential contraindications, has not been extensively investigated compared to NSAIDs. Further research is required to directly compare the efficacy and cardiovascular risk of NSAIDs andwith those of colchicine.

A short course of corticosteroids is a reasonable option when use of NSAIDs or colchicine is contraindicated. Prednisolone is as effective as NSAIDs based on two randomised sed trials. First, Janssens et al.[5] conducted a double-blind, randomised controlled trial of 120 patients with gout to test the effectiveness of prednisolone and naproxen forin the treatment of monoarticular gout. After 90 hours, there was 44.7mm and 46.0 mm reduction in the pain score for prednisolone and naproxen, respectively (difference 1.3 mm; 95% CI,: -9.8 to 7.1), suggesting equivalence. Based on another randomizsed trial by Man et al., [6], prednisolone is as effective as NSAIDs (intramuscular diclofenac plus oral indomethacin) in acute gout and has fewer adverse effects. In both the studies, patients receiving oral corticosteroids experienced no significant side effects. This finding is consistent with other studies that have investigated short-term oral steroid use in the treatment of asthma and rheumatoid arthritis.[7, 8]

Conclusion

Patients with gout frequently have contraindications to acute and chronic gout medications. Clinicians must make therapeutic decisions based on possible risks versus benefits of the individual treatment. In conclusion, NSAIDs would be the recommended first-line treatment for patients not otherwise contraindicated. However, colchicine (if patients are able to tolerate) or corticosteroids (in the absence of sepsis) should be prescribed instead of NSAIDs to patients at high cardiovascular risk.

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