Using NSAIDs with allopurinol in gout

Dear Editor.

[Re: "An update on the management of gout", BPJ 51, Mar 2013] Would you really give NSAIDs continuously while starting and titrating allopurinol? If someone starts at 50 mg and has a target dose of 300 mg, they would be on NSAID continuously for six months if we followed your suggestion of increasing 50 mg per month. It seems a long time to expose someone to the risks associated with NSAIDs. Why not just treat flare ups if they occur?

Dr Stephen Hoskin
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It is recommended that low-dose non-steroidal anti-inflammatory drugs (NSAIDs), e.g. naproxen 250 mg, twcie daily, or colchicine be co-prescribed with allopurinol to prevent rebound flares of gout while serum urate levels are being lowered. This is because urate-lowering treatment for gout is frequently associated with gout flares, and this relationship is reported to persist for the first 6 – 12 months of treatment.[1, 2] This paradoxical effect is thought to be due to rapid lowering of serum urate levels causing crystals previously precipitated in tissues to become activated. This causes activation of cyclooxygenase-2 expression (Cox-2), subsequent prostaglandin production and the classical symptoms of gout flare.[1]

Recommendations for the duration of prophylaxis differ in guidelines, ranging from one month to one year.[1] However, analysis of three randomised, placebo-controlled trials concluded that naproxen was well tolerated and that six months of prophylactic treatment was found to provide greater benefit, compared to two months of treatment, with no associated increase in adverse effects.[1]

Therefore, the consensus opinion is that a low-dose NSAID (or another suitable medicine if NSAIDs are not appropriate for an individual patient) should be continued while titrating allopurinol, for as long as it takes to achieve the target serum urate level of ≤ 0.36 mmol/L, and in some cases this may be up to six months.

Further evidence to support the use of anti-inflammatory prophylaxis during urate lowering treatment also includes the following:[3]

- A patient may be asymptomatic but there can be ongoing chronic inflammation (i.e. no flare but ongoing damage to joints)
- The use of a prophylactic medicine can reduce both the incidence and severity of flares
- If flares are not controlled, there is a risk of decreased adherence to urate-lowering treatment and consequently the potential for ongoing uncontrolled disease (e.g. development of polyarticular disease and tophi)

The patient's age and co-morbidities should be considered when choosing a prophylactic medicine, e.g. the presence of chronic kidney disease or a history of gastrointestinal bleeding. A NSAID, therefore, may not always be the appropriate choice. Low dose colchicine (0.5 mg, once or twice daily) is an alternative for some patients, although care is still required (e.g. a further reduction in dose) when it is used in patients with impaired renal function.[3]

References

1. Wortmann RL, Macdonald PA, Hunt B, Jackson RL. Effect of prophylaxis on gout flares after the initiation of urate-lowering therapy: analysis of data from three phase III trials. Clin Ther. 2010;32(14):2386–97.
2. Stamp LK, Taylor WJ, Jones PB, et al. Starting dose is a risk factor for allopurinol hypersensitivity syndrome: a proposed safe starting dose of allopurinol. Arthritis Rheum. 2012;64(8):2529–36.
3. Schlesinger N. Treatment of chronic gouty arthritis: It is not just about urate-lowering therapy. Semin Arthritis Rheum. 2012;42:155-65.

Appropriate use of antibiotics

Dear Editor

[Re: "Cold season in primary care", BPJ 52, Apr 2013] The suggestions about when to use antibiotics are very subjective. One could argue that symptoms are "significant or severe" for every patient we see, otherwise they wouldn't have bothered to spend the time and money coming to see us. How do you define "high risk"? The infection is "not resolving" by when? How do we differentiate "infection" from post infective symptoms such as a lingering cough?

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The decision whether or not to prescribe antibiotics for patients with upper respiratory tract infections (URTI) is complex and, as with any primary care decision, is likely to be based on both objective and subjective reasoning.

There has been extensive research on antibiotics in URTI, with a view to reducing inappropriate antibiotic use and, therefore, the growth of antibiotic resistance. A 2013 Cochrane systematic review concluded that antibiotics were of no benefit in patients with acute URTI, and were associated with adverse effects.[1] However, despite this research, clinical guidance cannot always be prescriptive because a guidance document will never be able to account for all the variables present in every clinical contact. Therefore, we rely on clinicians being able to interpret each individual patient-doctor interaction and come to the most appropriate decision for that patient.

We agree that whenever a patient presents, the problem they have on that day is usually regarded as "significant and severe" for them. The patient's perception of their symptoms is very relevant, however, it is the role of the clinician to objectively evaluate the significance of the patient's symptoms and signs, while also taking into consideration other factors such as patient age, relevant past history, social history and the presence of co-morbidities, when formulating a diagnosis, assessing risk and making treatment decisions. Patients with factors such as a significant past history of chronic obstructive pulmonary disease (COPD) or bronchiectasis, frail elderly people and those who are immunodeficient are considered at high risk of complications from URTI.

Clinicians will have a general idea of the usual course of a URTI, based on their experience and observation of other patients, and can judge if the infection is not resolving in the expected time, or if symptoms are increasing or worsening in severity. There is clearly a grey area between acute and chronic symptoms, as the latter always begins as the former, but again, clinical judgement is necessary. Post-infective symptoms such as lingering cough in an otherwise well person can be differentiated from infection, in which the patient's signs and symptoms are worsening in severity and they remain generally unwell.

Consensus guidance on appropriate antibiotic use for common infections seen in primary care is available in the updated Antibiotic Guide accompanying this edition of the journal. We would welcome feedback from clinicians on how they resolve the "to give an antibiotic or not" dilemma and their strategies on how to balance the benefit and risk for an individual with the wider goal of reducing inappropriate antibiotic use.

Reference

1. Kenealy T, Arroll B. Antibiotics for the common cold and acute purulent rhinitis. Cochrane Database Syst Rev 2013;6:CD000247.

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