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Management Of Acute Gout: A Review Article

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Abstract

Gout is the most common cause of inflammatory arthritis in men aged over 40 years and is frequently encountered in clinical practice. Gout is currently the most common form of inflammatory arthritis in men. The overall incidence of gout has increased rapidly in the past 20 years. Some of the risk factors for the development of gout include: increased ethanol intake, high dietary purine consumption, obesity and the use of certain drugs, such as diuretics. Another important risk factor for the development of gout is hyperuricaemia. Acute gout can be diagnosed on the basis of detection of monosodium urate crystals in the synovial fluid of affected joint. The management of acute gouty arthritis includes use of colchicine and other anti-inflammatory drugs. Now a days NSAIDs are commonly prescribed in acute gouty arthritis because colchicine exert side effects.

INTRODUCTION

Gout is an acute inflammatory disease that 1 in 100 people in Pakistan. Gout is caused by increased level of uric acid in blood. Gout affected persons are increasing day by day due to dietary factors and life style changes(Huang et al, 2005). Gout may be inherited in nature. Gout affected persons have a family history of gouty arthritis. Other causes of gout include the increased production of uric acid, the decreased excretion of uric acid by the kidneys and the decreased breakdown of uric acid in the body. Acute gouty arthritis occurs in men 95% of the time, and the first attack usually takes place between the ages of 40 and 50 (Beutler et al,1994). This disease occurs in woman after menopause and is uncommon before menopause. Gout cases are increasing due to ingestion of drugs especially aspirin that increases serum uric acid level. It may be due to ingestion of food that has high content of purine. When purine breaks the formation of uric acid occurs. Most mammals have an enzyme called uricase, which breaks down uric acid so it can be easily removed from the body. Because humans lack uricase, uric acid is not as easily removed, and can build up in body tissues. Uric Acid is synthesized in liver from the catabolism of purine. Uric acid is excreted through kidney if kidney is not working properly serum uric acid level increases. If concentrations of uric acid reach 7 mg/dL and above, uric acid begins to deposit in joints and inflammatory process starts in joints leading to painful gouty arthritis.

Phagocytosis of MSU crystals is the inciting factor of acute gouty arthritis. The urate crystals are recognized as foreign and taken up by macrophages, inciting an inflammatory response (activation of the NLRP3 inflammasome). This activation triggers a cascade that results in the release of interleukin (IL)-1 and other inflammatory cytokines. The release of the cytokines rapidly ignites a broader inflammatory response and the infamous redness, pain, and swelling of an acute gout flare. The joint becomes warm, swollen, red, and extremely tender. The skin is tense, hot, shiny and sometimes has a dusky red discoloration. The pain increases in intensity within the first 24 hours and will gradually subside after two or 3 days. Acute gouty arthritis typically presents as monoarthritis in 85-90% cases with first metatarsophalangeal (MTP) involvement at presentation in more than 50% cases. A gouty arthritis attack can occur in other areas besides the great toe joint, including the ankle joint, the arch and toes. Occasionally several joints will be involved. Gouty arthritis is often less severe in the elderly than in younger patients (Campbell et al, 1988) and is often mistaken for osteoarthritis. This is further complicated by the coexistence of gout and osteoarthritis in the same joints, especially Heberden's nodes (Lally et al, 1989). Acute gouty arthritis typically presents with a sudden and severe exquisitely painful joint, most classically in the first metatarsophalangeal joint (toe). Demonstrating the presence of monosodium urate (MSU) crystals in the joint fluid or tophus has been the gold standard for the diagnosis of gout.

The diagnosis is made clinically and confirmed by the analysis of the joint fluid or synovial fluid. A sample of the joint fluid microscopically will show a characteristic needle shaped crystal found only in gout. A blood test to measure the uric acid level may also be helpful (Yu et 1997). Non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids and colchicine are used for the treatment of acute gout attacks.

TREATMENT OF ACUTE GOUT

Treatment options for acute gout include nonsteroidal anti-inflammatory drugs (NSAIDs), colchicine, systemic corticosteroids and intra-articular aspiration and injection of long acting corticosteroid (Zhang et al, 2006) although the evidence for these options is of varying strength. Serum uric acid concentrations may be lowered with dietary changes that include weight reduction, restriction of alcohol consumption and avoidance of foods that have high content of purine. Management includes reduction of serum uric acid levels to normal, which is the treatment goal for the prevention of acute gout attacks. Symptomatic hyperuricemia usually requires medication.

NSAIDS

NSAIDs are commonly used for treatment of acute gout. The anti-inflammatory effects of these medications occur mainly through inhibition of the cyclo-oxygenase enzyme which prevents the transformation of arachidonic acid to prostaglandins, particularly prostaglandin E2. Other NSAID mechanisms include inhibition of lipooxygenase with reduced generation of leukotriene B4 and inhibition of neutrophil activation and aggregation. If the diagnosis is clear, NSAIDs are the preferred therapy for acute gout and are effective when used early in the attack. Most drugs achieve clinical efficacy within 1 to 3 days of initiation of therapy and the majority of patients experience complete resolution of an acute attack of gout within 5 to 8 days. NSAIDs are considered to be the drugs of choice to treat acute gout (Cheng et al 2004). NSAIDs are also used to prevent the occurrence of future attacks (Falasca et al, 2006). In the treatment of an acute attack, high doses of NSAIDs are prescribed during the first three to four days of an attack. Thereafter standard doses are prescribed for maintenance (Gaffo et al 2008). Treatment for acute gout is aimed at reducing the pain and inflammation that accompany acute gout attacks. Non-steroidal anti-inflammatory drugs, specifically indometacin, are the most popular treatment for acute gout in the United Kingdom (Martin U. 2006). Non steroidal anti-inflammatory drugs are affective against acute gouty arthritis and have fewer side effects as compared to colchicine.

ETORICOXIB

Etoricoxib is a selective cyclo-oxygenase (COX)-2 inhibitor, which is being prescribed in Europe for the management of acute gouty arthritis. Etoricoxib provides symptomatic relief in acute gouty arthritis as well as in osteoarthritis. This drug has fewer side effects as compared to other NSAIDS therefore it can be prescribed as a treatment option for patients requiring NSAID therapy, particularly those at risk of upper gastrointestinal disturbance and uncontrolled hypertension. Etroricoxib should be taken at the lowest effective dose for the shortest possible duration (Croom et al 2009)

CORTICOSTEROIDS

Corticosteroids can be used in acute gout. These are useful where NSAIDs or colchicine are contra-indicated. Intra-articular corticosteroid (betamethasone 5.7 mg or methylprednisolone acetate 40 mg for a knee joint) is effective and convenient when only one joint is involved and when that joint is easy to inject. In this situation it is usually possible to aspirate joint fluid to confirm the diagnosis and exclude sepsis. Provided joint fluid has been obtained and has been sent to the laboratory for culture, it is appropriate to go ahead with the corticosteroid injection. It is not safe to inject a joint in which sepsis is a possibility if it has not been possible to obtain synovial fluid. Injecting corticosteroid is likely to temporarily suppress the joint inflammation and result in a delay in recognition of the joint infection. . Systemic therapy can be used when more than 1 joint is involved or the patient is refractory to other treatments. Dosage adjustment is required in elderly patients and those with chronic renal or hepatic failure. Corticosteroids should not be given to patients with diabetes mellitus without careful monitoring.

ACTH

Synthetic adrenocorticotropic hormone (ACTH) is a steroid preparation that has been useful in acute gouty arthritis. It is administered by intramuscular or intravenous injection of 40-80 IU. ACTH induces glucocorticoid release from the adrenal cortex. If ACTH is withdrawn, then rebound attacks, mild hypokalemia, worsening of glycemic control, and fluid retention will ensure. Other features that render ACTH a less attractive option are cost, inconvenience of parenteral administration, and dependence on the sensitivity of the adrenal cortex

COLCHICINE

Colchicine has been used both in the acute setting and in the management of chronic gout. It exerts anti-inflammatory effects through several mechanisms. Colchicine binds to tubulin causing anti-proliferative effects by arresting cell growth. It also inhibits phagocytic and cytokine secretory functions of leukocytes. Chemotactic responses of neutrophils to leukotriene B4, IL-8, and other cytokines are disrupted. At high concentrations, colchicine has recently been shown to inhibit urate crystal-induced activation of NALP3 inflammasome. This protein complex cleaves caspase-1 which then activates interleukin 1-, a pro-inflammatory cytokine felt to be central in the pathogenesis of gout. Although this drug has been used to treat acute gout since the sixth century and is of proven efficacy. Colchicine prevents the inflammatory reaction. Colchicine, an extract of the Colchicum autumnale plant, has been used for over a 1000 years in the treatment of gout. The precise mechanism by which colchicines relieves the intense pain of gout is unknown. However, it is believed that the most important action resulting in pain relief involves blockade of the inflammatory response to uric acid crystals, through inhibition of crystal phagocytosis and neutrophil migration(Cronstein et al, 2006). Colchicine has been utilized for the treatment of acute gouty arthritis in past and has proven affective in acute gouty arthritis but it exerts side effects like nausea, vomiting, diarrhea, and stomach cramps when taken by mouth and severe (even fatal) blood disorders when taken intravenously. Colchicine is of proven benefit in patients with chronic gout, as prophylaxis therapy to prevent acute attacks, particularly when establishing urate-lowering therapy(Terkeltaub et al, 2003). However, long-term use of colchicine may also lead to side-effects such as myopathy and bone marrow suppression, particularly in patients with renal impairment.

DISCUSSION

Gout is a common inflammatory arthritis resulting from the crystallisation of uric acid within joints. It is often, but not always, associated with hyperuricaemia. It is common, affecting around 2% of men aged over 30 years and women aged over 50 years, and its prevalence appears to be increasing (Choi et al,2005). Gout is a common disease both in primary care and hospital practice (Mikuls et al 2005). Lifestyle and dietary recommendations for gout patients should consider overall health benefits and risk, since gout is often associated with the metabolic syndrome and an increased future risk of cardiovascular disease (CVD) and mortality (Choi et al, 2007). An acute attack of gout requires immediate treatment. For this purpose anti-inflammatory drugs are commonly utilized. The usefulness of nonsteroidal anti-inflammatory drugs is limited by their side effects, but in general, the risks are greatest in elderly patients, particularly those with renal dysfunction (Unsworth J et al 1987). During acute gouty arthritis analgesic are prescribed. The link between uric acid and gout has been known for over 250 years, and colchicine has been used for the treatment of gout since the 6th century. Colchicine is frequently used for treatment of acute gout attacks and also as prophylaxis against acute gout attacks in patients with chronic disease (Borstad et al, 2004). The use of large doses of colchicine to treat acute gout is no longer appropriate, especially in older patients, because of the serious adverse effects arising from large doses. The recommended dose for colchicine in the treatment of acute gout is 1.0 mg stat, followed by 0.5 mg 6 hourly, up to a maximum dose of 2.5 mg per 24 hours (Jason et al, 2007).. Many patients do not require medications. During the period between gout attacks, patients are advised to avoid foods high in purine and to reduce weight. Patients should also avoid alcohol and reduce any stress. Drug treatments for acute attacks of gout are aimed at relieving pain and reducing inflammation. They should be started as early as possible.

AVOID CHANGING HYPOURICAEMIC THERAPY

During the treatment of acute gout any sudden change (especially fall) in the concentration of serum uric acid will exacerbate the attack. Patients taking regular hypouricaemic therapy should therefore not stop their treatment. Likewise, hypouricaemic therapy should not commence until after the attack has settled. The use of concurrent low-dose colchicines (0.5 mg twice daily) during the introductory phase of hypouricaemic therapy reduces the frequency of attacks during that relatively high-risk period.

CONCLUSION

A definitive diagnosis of acute gout is made by detection of monosodium urate crystals in the synovial fluid of an inflamed joint. However, when this is not feasible a clinical diagnosis can sometimes be made with reasonable accuracy. The mainstays of acute gout management are colchicine, NSAIDs, and systemic or intra-articular corticosteroids. Gout is the most common inflammatory arthritis. Arthrocentesis and identification of negatively birefringent monosodium urate crystals from aspirate is the gold standard for diagnosis. Gout is an increasingly prevalent condition worldwide and creates a heavy economic burden. Available

treatments are generally effective; however, they are not devoid of adverse events. The management of a patient presenting with acute gout involves exclusion of sepsis, confirmation of the diagnosis with crystal identification whenever possible and prompt treatment with an anti-inflammatory drug. Any sudden change (especially fall) in the concentration of serum uric acid will exacerbate the attack is sometimes used to reduce recurrences. Changes of hypouricaemic therapy should be avoided during an acute attack. Hypouricemic drugs should not be prescribed during an acute gouty attack. Hypouricaemic therapy for acute gout should be delayed at least until the acute attack has settled. Evaluation and management of hyperuricemia should be undertaken when all symptoms of acute gout are resolved and the patient is stable on daily prophylaxis with NSAIDs or colchicine.

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