The Pathophysiology and Pharmaceutical Treatment of Gout

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Program Overview:

To provide pharmacists and nurses with an understanding of the pathophysiology and pharmaceutical treatment of gout.

OBJECTIVES:

After completing this program, participants will be able to:

- Understand the prevalence and incidence of gout,
- List pathophysiology, primary symptoms and main risk factors,
- Identify the most commonly used pharmaceuticals and their potential side effects.
The Pathophysiology of Gout

Gout is considered the most common type of inflammatory arthritis and is typically associated with a reduction in quality of life for those who suffer from it. High levels of serum uric acid, termed hyperuricemia, are a necessary prerequisite for the development of gout. As uric acid levels in the blood serum rise and the saturation threshold is exceeded within bodily fluids, monosodium urate crystals precipitate out of solution and become deposited in and around joints, especially peripherally located synovial joints. Urate crystals are sharp, needle-like structures that become lodged within joint capsules, cartilage, ligaments and tendons. The most commonly affected area is the first metatarsophalangeal joint, often referred to as the first knuckle of the big toe.

Symptoms

Clinical symptoms of gout include severe pain (often described as “excruciating”), acute inflammation, redness, fever as high as 102°F with or without chills, long-term joint damage with successive bouts, and deposits of the urate crystals (called tophi) on or under the surface of the skin, most notably within or on the ears. Due to the inflammation and pain, affected joints typically lose significant range of motion and stability. Weight-bearing becomes difficult or impossible. Light pressure, such as the weight of a single bed sheet, can be too painful to bear for some sufferers during acute episodes. Modifications in physical activity, posture, sleeping and footwear are often needed during acute gout attacks.

Gouty arthritis can develop very quickly, with the first episode often occurring in the middle of the night. Gout attacks are characterized by a rapid onset and buildup of pain (usually within 2-4 hours). In men, the initial gout attack is usually monoarticular, involving only one joint, although later attacks may be polyarticular and involve multiple joints. In postmenopausal women, the attacks are commonly oligo- or polyarticular and involve the proximal joint of the big toe and (in decreasing order of frequency) the heels, knees, wrists, fingers and elbows. The natural course of untreated acute gout varies from several hours to several weeks, although it typically subsides after 5-10 days only to come back weeks or months later depending on lifestyle and dietary habits. In subsequent attacks, tophi lumps develop and might be seen just under the skin in the outer ear, hands, feet, elbows or knees. Gout usually affects overweight men beyond the age of 40 and with a family history of gout, but it can occur at any age of adulthood and within women, especially those who are postmenopausal.

Prevalence and Incidence

Epidemiological evidence from the United States, United Kingdom, China and other countries suggests that gouty arthritis is becoming more prevalent, especially in aged men. For example, research conducted in the United States indicates that the prevalence of gout increased from 2.9 diagnosed cases per 1,000 people in 1990 to 5.2 diagnosed cases per 1,000 people ten years later in 1999. The group most notably affected by gout in the United States is men older than 75 years. The incidence of self-reported gouty arthritis also increased in the United States from the 1960s and was noted to be 8.4 cases per 1,000 people in 1992.

Epidemiological surveys conducted in the United Kingdom also suggest an increase in gout prevalence, with 9.5 cases per 1,000 people reported in 1993. Subsequent studies conducted in the United Kingdom from 2000 to 2005 found the prevalence of self-reported gout to be as high as 14 cases per 1,000 people. Random population surveys conducted in China suggest an increase in self-reported gout prevalence from 3.6 cases per 1,000 people in 2002 to 5.3 cases per 1,000 in 2004.
It should be noted that most of the research conducted on the prevalence of gout was based upon clinical assessments, self-reports and medical record or database reviews. However, these are not as sensitive or as specific as microscopic identification of monosodium urate crystals within inflamed joints which is considered the “gold standard” for gout diagnosis. Identification of intracellular urate crystals in the synovial fluid or tophus substantiates the diagnosis of gout, but it does not exclude other causes of joint inflammation such as acute pseudogout, active rheumatoid arthritis, or in rare cases, septic arthritis. Crystal-induced arthritis can mimic septic arthritis in terms of severe pain, fever, high synovial white blood cell count and other constitutional symptoms. Septic arthritis should be suspected in patients with worsening synovitis despite treatment of suspected acute gout. Synovial fluid gram stain and culture are critical in aiding with the diagnosis in such patients.

Several studies have also examined the incidence of gouty arthritis. For example, the Framingham Heart Study, which followed over 5,000 people for almost three decades, discovered that the incidence of gout per 1,000 people was 1.4 women and 4.0 men, indicating that gout is almost three-times more common in men. In other studies, gout incidence was also higher in men than in women and the rates increased with advancing age.

Risk Factors

Several risk factors have been identified for the development of gout including hyperuricemia. Hyperuricemia, or high levels of uric acid in the blood serum, is considered the most essential factor in the pathogenesis of gout. In a Taiwanese study, the prevalence of gout was over four times higher in men who had been previously diagnosed with asymptomatic hyperuricemia. Uric acid precipitates out of solution and forms urate crystals when it reaches a saturation threshold that is partially dependent on pH levels and other biochemical factors.

Genetic factors are also fairly evident in gout, but gene expression is quite variable, which accounts for the differences in an individual’s genotype and phenotype. Because the kidneys excrete the majority of uric acid from the body, families with genetic conditions limiting kidney clearance often have a higher incidence of gout. For example, a certain gene codes for human “urate transporter-1,” which is important for controlling reabsorption of uric acid from the proximal tubules of the kidneys. As such, urate transporter-1 is targeted by many drugs that influence serum uric acid levels in efforts to reduce the prevalence of gout.

A direct link between gout and diet has been recognized for centuries, which is why gout has been labeled the “rich man’s arthritis” for many years. In general, diets high in purines, which are found in abundance in organ meats, cured meats, seafood, some vegetables, aged cheese, and red wine and beer, significantly increase the risk of gout because the purines are metabolized into uric acid within the body. In scientific studies, dietary consumption of meats and seafood was found to be associated with the highest risks of gout, whereas consumption of certain dairy products such as milk appeared to offer protection. Other identified risk factors include consumption of sugar-sweetened soft drinks, candy, and sugary carbohydrates such as donuts, whereas other protective factors include consumption of caffeinated coffee and high doses (greater than 1,500 mg daily) of vitamin C. Excessive alcohol consumption (seven or more drinks within 48 hours) is a well-established trigger of acute gout attacks.

Specific purine-rich foods to avoid or minimize in order to reduce the risk of acute gout attacks include beef, liver, kidney, game meats, goose, pork, sweetbreads, anchovies, herring, sardines, mackerel, mussels, crab, shrimp, lobster, caviar, mussels, mushrooms, yeast, asparagus, spinach, cauliflower, peas, beans, lentils, most nuts and seeds, wheat, rye and essentially any form of alcohol.
Sluggish metabolism, obesity, hypertension and diabetes are also associated with gout. Amongst people with gout, the prevalence of metabolic syndrome is about 2.5 times more common compared to those without gout.\textsuperscript{18} The Framingham Heart Study identified obesity and high blood pressure as risk factors for developing gout.\textsuperscript{11} Diuretic use is a significant risk factor for gout, but the relationship is somewhat confounded because diuretic therapy is often recommended for hypertension, renal disease and cardiac failure, which are also linked with gout. As such, there is uncertainty whether the diuretics or the disease conditions contribute more to the pathophysiology of gout. Gout can also result from blood disorders or cancers such as leukemia.

Gout and osteoarthritis often affect the same joints, such as the first metatarsophalangeal joints, the tarsal joints of the ankle and the synovial joints of the knees, elbows and wrists.\textsuperscript{19} These findings suggest that osteoarthritis may predispose one to urate crystal deposition and gout, but more research is needed to explore this association before conclusions can be drawn.

**Differential Diagnosis**

Generalist physicians are often the first to see patients with gout and therefore they play a critical role in the diagnosis and management of gouty arthritis. In a recent study, only 0.02 percent of gout was diagnosed, treated and managed by rheumatologists (joint specialists), whereas family physicians accounted for 77 percent of cases, subspecialists other than rheumatologists accounted for 18 percent and general internists about 4 percent.\textsuperscript{20}

In addition to other forms of arthritis, differential diagnoses for gout must include acute trauma. Fractures of the big toe or other joints can be ruled out via radiographs, although sprains and strains can be more problematic. “Turf toe” (hyperextension sprain of the ligaments surrounding the first metatarsophalangeal joint) occurs from excessive running on artificial turf or walking on other substrates with inappropriate shoes such as flip-flops. Turf toe mimics much of the symptomatology of gout in terms of pain and joint dysfunction, but it does not involve fever or urate crystal deposits. Further, turf toe does not usually exhibit the degree of inflammation and redness that a gouty toe does.

**Complications**

Properly treated, gout rarely poses a long-term health threat. Left untreated, gout can develop into a painful and disabling chronic disorder. Chronic gout attacks can destroy cartilage and bone, causing irreversible joint dysfunction and disability. A gout survey conducted in 2006 suggested that 66 percent of people with gout considered the pain to be the worst they ever experienced, while an estimated 75 percent claimed that flare-ups made walking very difficult and about 70 percent reported trouble playing sports or even putting on socks and shoes.\textsuperscript{18} If gout is not treated, tophi (chalky clumps of urate crystals) can grow to the size of golf balls and cause a variety of problems in joints and organs. Kidney stones occur in 10-40 percent of gout patients and about 25 percent of those with chronic hyperuricemia develop kidney disease, which sometimes culminates in kidney failure.\textsuperscript{13} Although, it should be noted that in most cases the kidney disease comes first and causes high concentrations of uric acid secondarily due to reduced filtering. Other conditions that are associated with long-term gout include cataracts, dry eye syndrome and lung complications.

**Alternative Therapies**

Non-pharmaceutical or “alternative” therapies for gout are not well investigated, but their popularity over the years suggests some efficacy. However, herbs, supplements and tinctures that may be beneficial for some people may be harmful for others. Common alternative strategies to combat gout include...
consumption of antioxidant-rich foods or strong antioxidant supplements such as vitamins C and E in efforts to minimize joint tissue damage, eating sour cherries and cranberries or drinking their juices in attempts to dissolve the urate crystals, avoiding purine-rich foods, reducing alcohol consumption, and increasing purified water consumption to dilute the crystals and help flush them out of the body. To combat pain and inflammation, non-pharmacological compounds commonly used include methylsulfonylmethane (MSM), Harpagophytum procumbens (Devil’s claw), Uncaria tomentosa (Cat's claw), Ananus comosus (bromelain) and Curcuma longa (turmeric). Acupuncture and homeopathic tinctures are also utilized for pain and inflammation control, although no scientific studies have examined their effectiveness for acute gout attacks. Alternating hot and cold compresses is a simple inflammation control method that is backed by some research in regards to acute gouty arthritis.

In conclusion, gout is the most common form of inflammatory arthritis and its prevalence and incidence have risen in recent decades. Numerous risk factors for the development of gout in both men and women have been established and include hyperuricemia, genetic factors, age, purine-rich diet, alcohol consumption, sluggish metabolism, obesity, diuretic use, renal disease, hypertension and possibly osteoarthritis. Gout can mimic other types of arthritis and joint injuries, so urate crystals from joint fluid must be identified for accurate diagnosis. Alternative therapies have been used to combat gout for centuries, although pharmaceutical treatment is the best researched and most utilized by modern medicine. Untreated, gout can cause significant short-term and long-term disability.

The Pharmaceutical Treatment of Gout

The majority of patients who experience gout are cared for by their family physicians. Although both the physician and patient may easily recognize that they are dealing with an acute gout attack, errors in selecting the most appropriate medication and proper dose are common. The clinical stages of gout are divided into the asymptomatic hyperuricemia stage, the intermittent acute flare-up stage and the chronic tophi-forming stage. Treatment of gout usually commences after the first acute attack, especially if podagra is involved. The aims of treatment are threefold: to alleviate the pain and inflammation associated with acute attacks, to prevent future attacks and to decrease uric acid levels in the serum. As such, anti-inflammatorories, analgesics and urate-lowering drugs are typically deployed in combination to combat gout.

The critical issues when starting drug therapy for acute gout are rapid initiation of the therapy, adequate drug dosing and appropriate duration of therapy. The options available for the treatment of gout are nonsteroidal anti-inflammatory drugs (NSAIDs), systemic and intra-articular corticosteroids, colchicine and xanthine oxidase inhibitors.

1) NSAIDs for the Treatment of Gout

In a patient without complications, NSAIDs are the preferred therapy for the treatment of acute gout attacks. Combination therapy with NSAIDs and colchicine is used by 50-64 percent of rheumatologists when treating acute gout attacks. NSAIDs reduce joint pain and improve joint function through anti-inflammatory and analgesic properties, but they do not prevent the progression of disease. NSAIDs mainly inhibit prostaglandins that are present in many cell types and responsible for the inflammation response. Common over-the-counter NSAIDs include ibuprofen (Advil, Motrin, Midol), naproxen (Aleve, Naprosyn) and aspirin. More powerful prescription NSAIDs include celecoxib (Celebrex), diclofenac (Voltaren) and indomethacin (Indocin). Due to low-cost and convenience, ibuprofen is the most commonly used NSAID for the symptoms of gout.
Ibuprofen is used to reduce inflammation, pain and fever, which are all common symptoms of acute gout attacks. Ibuprofen works by inhibiting the enzyme cyclooxygenase (COX), which converts arachidonic acid to prostaglandin H2 (PGH2). PGH2, in turn, is converted by other enzymes to several other prostaglandins, which mediate pain, inflammation and fever, and to thromboxane A2, which stimulates platelet aggregation and blood clot formation. Like most other NSAIDs, ibuprofen is considered a nonselective COX inhibitor; that is, it inhibits two isoforms of cyclooxygenase, COX-1 and COX-2. The analgesic, antipyretic, and anti-inflammatory activity of ibuprofen appears to be achieved mainly through inhibition of COX-2, whereas inhibition of COX-1 would be responsible for unwanted effects on platelet aggregation and the gastrointestinal system.27

Typical adult dosage of ibuprofen for gout (as well as for osteoarthritis and rheumatoid arthritis) is 400-800 mg orally every 6-8 hours up to a maximum daily dose of 3,200 mg based on patient response and tolerance.28 Treating physicians may decide to prescribe a higher initial dose of ibuprofen to stop an acute gout attack, followed by lower daily doses to prevent future attacks. High doses and long-term use of ibuprofen, like all NSAIDs, can cause significant side effects. Ibuprofen may cause life-threatening heart or circulation problems such as heart attack or stroke, especially with long-term use. Ibuprofen should not be administered to gout patients just before or after heart bypass surgery as it can lead to chest pain, weakness, shortness of breath, slurred speech or problems with vision or balance. Ibuprofen can also cause serious effects on the stomach or intestines, including bleeding and perforation. These conditions can be fatal and can occur without warning, especially in older adults. Risk factors for gastrointestinal complications include history of ulcer, concomitant use of glucocorticoids or anticoagulants, cardiovascular disease, dosage, and age greater than 75 years. Symptoms of gastrointestinal bleeding include black, bloody or tarry stools, and coughing up blood or vomit that looks like coffee grounds. Patients with a history of stomach ulcers or ulcerative colitis should be especially cautious with ibuprofen or other NSAID use. It should be noted that high-dose H2 blockers and proton-pump inhibitors are “gastro-protective” agents, helping decrease NSAID-associated gastrointestinal ulcerations.

Other serious side effects caused by ibuprofen and other NSAIDs include renal insufficiency and elevated liver enzymes. Renal complications are increased in patients with preexisting renal disease, congestive heart failure, coronary artery disease, cirrhosis, those receiving diuretics and the elderly. Ibuprofen and other NSAIDs are not recommended in patients with edema, congestive heart failure, nephritic syndrome, cirrhosis, or high levels of serum creatinine.

The FDA has categorized ibuprofen in category D for pregnancy. As such, taking ibuprofen during the last 3 months of pregnancy may harm the unborn baby. It is not known whether ibuprofen passes into the breast milk or if it can harm a nursing baby.

Allergic reaction to ibuprofen is not uncommon. Signs of an allergic reaction include hives, difficulty breathing, facial, tongue and throat swelling, headache and dizziness. Less serious ibuprofen side effects may include upset stomach, mild heartburn, diarrhea, constipation, bloating, nervousness, blurred vision and tinnitus (ringing in the ears).
2) Corticosteroids for the Treatment of Gout

Corticosteroids are a class of steroid hormones that are produced naturally in the adrenal cortex. Corticosteroids are involved in a wide range of physiologic actions such as stress response, immune response and regulation of inflammation, among others behaviors. Glucocorticoids are a type of corticosteroid that interact with several inflammatory processes, including antigen presentation to T-cells, reduction in prostaglandin and leukotriene synthesis, migration of monocytes, lymphocytes and neutrophils, as well as macrophage and fibroblast production of cytokines, which all combine to hamper inflammatory and autoimmune responses. Common glucocorticoids used for the treatment of gout include methylprednisolone (Medrol) and prednisone (Deltasone, Meticorten, Orasone) which are categorized as Group-A hydrocortisones based on their chemical structures. Allergic reactions to one member of a group typically indicate an intolerance of all members of the group, which is known as the “Coopman classification”. Synthetic glucocorticoids are used in the treatment of joint pain and inflammation and can be taken orally or injected directly into an arthritic joint capsule. Glucocorticoids not only display anti-inflammatory properties, but they reduce the occurrence and progression of joint damage. For example, oral prednisolone in combination with disease-modifying anti-rheumatic drugs (DMARDs) and NSAIDs significantly decreases joint erosions. Glucocorticoids as a monotherapy are generally reserved for gout sufferers who cannot take either NSAIDs or colchicine due to allergy or other contraindications.

High doses of oral steroids, such as prednisone and methylprednisolone, are commonly prescribed to suppress acute gout flare-ups. Daily doses less than 7.5 mg are well tolerated to control pain long-term, but ACR guidelines recommend daily doses below 5 mg due to glucocorticoid side effects. Prednisone can be given at high doses of 35 mg for 1-3 days and then tapered over 1-2 weeks, which reduces the likelihood of side effects. In a randomized controlled trial, 35 mg of prednisolone daily for 5 days was found to be as effective as 500 mg twice daily of naproxen in patients with acute gout. Further, the patients with gout did not report any serious adverse effects from the short-term use of systemic corticosteroids. Intramuscular, intravenous and intra-articular injections may also be used, although joints should not be injected more than 3 times yearly.

The long-term side effect profile for corticosteroids includes osteoporosis, suppression of the hypothalamus, pituitary and adrenal glands, Cushing’s syndrome, weight gain, emotional instability, depression, hypertension, erectile dysfunction, myopathy, impaired wound healing, reduced infection fighting ability, gastritis, colitis, glucose intolerance, diabetes mellitus and skin atrophy. Clinical and experimental evidence indicates that corticosteroids can cause permanent eye damage by inducing central serous retinopathy, which can also manifest as cataracts and glaucoma. Calcium and vitamin D supplementation is recommended in the prevention for those on corticosteroids. In regards to pregnancy, corticosteroids display a small but significant teratogenic effect, causing a few birth defects per 1,000 pregnant women treated.

3) Colchicine for the Treatment of Gout

Colchicine is a very common generic drug used to treat gout and it was originally extracted from the Colchicum autumnale plant (meadow saffron). Oral colchicine has been used for over 40 years as an unapproved drug with no prescribing information, dosage recommendations, or drug interaction warnings approved by the U.S. Food and Drug Administration until July of 2009. Colchicine in combination with probenecid (which improves the kidneys’ ability to remove uric acid from the body) was approved by the FDA prior to 1982, but it wasn’t until 2009 that it was approved as a monotherapy for the treatment and prophylaxis of acute gout flares. Despite its relatively high toxicity, many physicians still use colchicine
at dosages of 0.6 mg every 1-2 hours for acute gout attacks until the patient is pain-free or diarrhea ensues. The FDA-approved dose of oral colchicine (Colcrys) for the treatment of acute gout is a single 1.2 mg dose followed by a 0.6 mg dose (for a total of 1.8 mg) within 12 hours from the onset of symptoms.\textsuperscript{35} Research suggests that low-dose colchicine is effective for acute gout if started within 12 hours of symptoms, although there is a need to avoid colchicine or adjust the dose in patients with renal or hepatic impairment and/or those who are taking drugs that interact with colchicine.\textsuperscript{36}

Colchicine inhibits microtubule polymerization by binding to tubulin, one of the main constituents of microtubules. Availability of tubulin is essential to mitosis, thus colchicine essentially acts as a “mitotic poison.” In addition to inhibiting mitosis, colchicine also inhibits neutrophil motility and activity, leading to a net anti-inflammatory effect. Colchicine is primarily eliminated by the hepatobiliary tract, although renal excretion accounts for 10-20 percent of colchicine elimination in patients with normal kidney function.\textsuperscript{35}

Colchicine is often recommended when a patient is unable to take NSAIDs such as ibuprofen. However, the drug’s effectiveness is usually offset by intolerable side effects. Common side effects of colchicine usage include gastrointestinal upset, nausea, vomiting, diarrhea and neutropenia, although high doses can also damage bone marrow and lead to anemia, which is related to the hyper-inhibition of mitosis. Primary side effects associated with all mitotic inhibitors are muscle damage and peripheral neuropathy, or numbness and tingling in the hands and feet due to peripheral nerve damage.

Symptoms of colchicine poisoning start within 2-5 hours after the toxic dose has been ingested and include burning in the mouth and throat, fever, vomiting, diarrhea, abdominal pain and kidney failure. Onset of multiple-system organ failure may occur within 24-72 hours. There is no specific antidote for colchicine, although various treatments do exist and recovery may begin within 6-8 days.\textsuperscript{37}

\textbf{4) Xanthine Oxidase Inhibitors for Gout}

It is important to note that resolution of the acute attack by controlling inflammation and pain is not a cure for gout. As such, employing urate-lowering therapy in efforts to reduce serum urate levels below the threshold of super-saturation is essential in allowing the dissolution of existing urate crystals in the joints and to stop the deposition of new crystals. Medication that blocks uric acid production is classified as xanthine oxidase inhibitors, which include allopurinol (Zyloprim, Aloprim) and febuxostat (Uloric).

Xanthine oxidase inhibitors work by non-competitively blocking the molybdenum pterin center which is the active site on xanthine oxidase. Xanthine oxidase is needed to oxidize both hypoxanthine and xanthine to uric acid in the body. As such, allopurinol and febuxostat inhibit xanthine oxidase, which reduces production of uric acid.

There is evidence to suggest that if serum uric acid levels are maintained at or below 6.0 mg/dL, then gout attacks can be reduced, crystals can be depleted from joints, tophi deposits can be reduced and their recurrence prevented.\textsuperscript{38,39,40} Urate-lowering therapy is most effective when initiated about 2-4 weeks after resolution of the first acute gouty attack and should be continued long-term if not lifelong. Urate-lowering therapy should not be initiated during acute gout attacks, although it should be continued if administered for previous attacks. It is important to emphasize that urate-lowering therapy should not be stopped once initiated because intermittent usage can lead to recurrent gout attacks.\textsuperscript{41}
When starting urate-lowering therapy, or even prior to, it is important to also initiate anti-inflammatory agents such as low-dose oral colchicine, glucocorticoids or NSAIDs such as ibuprofen because xanthine oxidase inhibitors do not make a significant impact on inflammation, pain or fever.

The most commonly used urate-lowering drug is allopurinol, which was approved by the FDA in 1966 and normally used in a preventative capacity for the chronic tophi-forming stage of gout. Allopurinol is approved at daily doses of 100-800 mg daily, although the standard dose of allopurinol that achieves serum urate levels below 6.0 mg/dL is at least 300 mg daily. In the United States, 95 percent of dosing is ≤ 300 mg daily, which achieves the target urate level in less than half of cases. The main limitation for the use of allopurinol is the concern of increased toxicity in patients with renal failure. Clinicians are also concerned about the more common severe side effects of allopurinol use, such as rash formation with eosinophilia, low blood counts, systemic symptoms and Stevens–Johnson syndrome.

Febuxostat is a fairly new xanthine oxidase inhibitor that was approved by the FDA in February of 2009, and it is quickly becoming a leading choice in the treatment of chronic gout and hyperuricemia. Febuxostat is especially valuable in patients with allopurinol hypersensitivity and in patients with kidney disease. Unlike allopurinol, febuxostat inhibits oxidized as well as reduced forms of xanthine oxidase because it cannot be easily displaced from the molybdenum pterin site. Further, febuxostat is metabolized mainly by the liver with little intact drug excreted through the kidneys. As such, febuxostat is much friendlier on the kidneys compared to allopurinol.

The CONFIRMS trial presented at the 73rd Annual Scientific Meeting of the American College of Rheumatology showed that febuxostat 80 mg was superior to febuxostat 40 mg and allopurinol 300/200 mg at achieving a serum urate level < 6.0 mg/dL. Febuxostat 40 mg and allopurinol 300/200 mg were comparable in patients with normal renal function, but in patients with mild/moderate renal impairment, both febuxostat doses were more efficacious than allopurinol and equally safe.

The reported side effects of febuxostat considered relatively common included rash, nausea, diarrhea, headache, joint achiness and reduced liver function as measured by hepatic serum enzyme levels.

In conclusion, the primary aims of the treatment of gout are threefold: to alleviate the pain and inflammation associated with acute attacks, to prevent future attacks and to decrease uric acid levels in the blood serum. The mainstays of acute gout management are NSAIDs, colchicine and systemic or intra-articular corticosteroids. NSAIDs are preferable to colchicine because they cause fewer side effects. Successful treatment occurs with the prompt initiation of high-dose, short-term NSAIDs such as ibuprofen. Since many gout patients have conditions that preclude the use of NSAIDs or colchicine, systemic glucocorticoids are commonly used to treat acute gout attacks. Intra-articular injections of glucocorticoids are appropriate with mono- or oligoarticular involvement. Urate-lowering therapy with the use of xanthine oxidase inhibitors helps reduce serum urate levels and lower the risk of recurrent flare-ups and tophi formation.
References


