Hyperuricemia and Gout: State-of-the-Art (November 13, 2006)

Hyperuricemia associated medical problems

Significant improvement of renal impairment in crystal-confirmed chronic gout after 10 years maintenance of serum uric acid level at less than mean 5 mg%.

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Extended ABSTRACT.
Introduction. The prevalence rates of gout range from 0.3% in the Han Chinese to 13.9% in the genetically predisposed New Zealand Polynesian males. The different prevalence and incidence rates of gout reported are due to the absence of a standard case definition of gout such as self-reported and physician-diagnosed ones (crystal identification of synovial fluid and tophi in population survey is impractical), different methods of calculation of prevalence and incidence rates, and different races surveyed. Although The American College of Rheumatology Classification Criteria is used in most surveys in different races and regions, it has not been well-validated in the various populations studied.
Over the past 40 years prevalence and incidence of gout have increased significantly worldwide due to classical risk factors of male sex, increased in high red meat and alcohol consumption, and recently identified multiple genetic risk factors, increased prevalence of hypertension, metabolic syndrome, increased use of low dose aspirin, diuretics, trend from Oriental to Western diet, increased longevity, change in demographics, increased prevalence of end-stage renal disease, increased organ transplantation, and long-term cyclosporine administration. Metabolic syndrome consists of hypertension, diabetes, dyslipidemia, truncal obesity, and increased cardiovascular disease risk. Atypical presentations of gout in the elderly can mimic osteoarthritis and rheumatoid arthritis. Therefore, confirmation of crystal in atypical gout in the elderly is mandatory. Hyperuricemia as an independent and potentially modifiable moderate cardiovascular risk factor, deserves our attention.
The risk of developing gout is dependent on the level of hyperuricemia. In an at risk sample population, serum uric acid (SU) level of < 7 mg%, the annual incidence of gout is 0.1%, 0.5% for SU of 7.0-8.9%, 4.9% for SU of > 9.0 mg%[1]. The 5 year prevalence of gout is 0.6% with SU level of < 7 mg%, but 30% with SU of > 10 mg%[2].
Hyperuricemia associated medical problems are dependent on the duration and level of SU. This implies that the higher SU levels and the longer its duration, the more prevalent the manifestations of associated medical problems such as renal impairment, chronic renal failure, hypertension, metabolic syndrome[3], cardiovascular disease[4], etc.
Maintaining SU level of mean < 4.5 mg/dl is the optimal range to avoid a flare of acute arthritis[5]. This also induces reduction of the number and size of tophi and improvement of renal function in renal impairment[6] and chronic renal failure. Hypertension itself can induce hyperuricemia[7] and the former can be reduced by lowering SU level with allopurinol[8]. Chronic gout with chronic renal failure has reversed to normal renal function in several patients when SU level is maintained below 5 mg% with allopurinol over a period of 10 years[9].
After the uricosuric Benzbromarone was withdrawn from the market in 2003, the uricostatic allopurinol was still the mainstay for hypouricemic therapy. When allopurinol mono therapy fails, the addition of probenecid achieves the desired level of SU of < 5 mg%[9]. Urate is extensively reabsorbed from the glomerular ultrafiltrate in the proximal tubule via the brush-border urate-anion exchanger URAT1. The urate-anion exchanger URAT1 (urate transporter-1) is a specific target of action for both antiuricosuric and uricosuric drugs.
The development of recombinant uricase and pegylated recombinant uricase, which are very effective for severe tophaceous gout is promising, but very expensive[10]. Febuxostat is significantly more efficacious than 300 mg of allopurinol in lowering serum urate levels and more significantly reduces tophi size[11]. Among a small subset of patients with impaired renal function, there was reasonably good safety with febuxostat with consistent reduction in serum urate[12].

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Abstract

AIMS. To assess outcome of renal function in crystal-confirmed chronic gout with renal impairment by long-term maintenance of serum uric acid level at mean < 5 mg%.

METHODS. After 1patients with creatinine clearance of < 5 CC and another 1 with chronic gout with co-existing Ankylosing Spondylitis were excluded, 51 Malayo-Polynesian males, mean age 35.9+/-14.3 years, with selfmedication-induced chronic gout because of intermittent ingestion of NSAIDs and/or corticosteroids without urate-lowering drugs, were included in a prospective observational study. When inflammation had settled after treatment with NSAIDs and/or corticosteroids, Allopurinol was instituted for long-term combined with low dosage of NSAID or Colchicine for at least 6 months to 2 years to prevent flare during lowering of SU level. Urate levels were maintained for 10 years at mean < 5 mg% with concomitant treatment of co-motbidity and associated conditions.

RESULTS. Due to withdrawal of previous NSAID and/or corticosteroid and maintenance of uric acid below 5 mg%, serum creatinine dropped from mean 3.8+/-1.7 to 0.9+/-0.4 mg% in 45 cases. There were 1 death due to myocardial infarction (42 years) and 1 because of stroke (46 years) in the 6 dropouts and none in the cases. Creatinine Clearance with a range of 8 to 63 CC and median of 35 CC, improved from mean 49+/-14 to 76+/-35 CC. Number and size of tophi were significantly reduced, but beyond expectation urolithiasis was increased in 2%. Unadjusted p values from paired t tests of comparison of variables between baseline and final figures in the cases and dropouts were < 0.0001 to < 0.0005.

Conclusion. Long-term control of hyperuricemia and suppression of flare of acute gouty arthritis with concomitant therapy of co-morbidity and associated conditions have significantly improved renal function from chronic renal failure to renal insufficient, loss of renal reserve clearance, and to normal creatinine clearance with significantly improved prognosis of chronic gout, co-morbidity, and zero mortality over a period of 10 years.

Keywords: Chronic Gout Hyperuricemia Self-medication Associated Medical Conditions