Rising a Novel Weapon in the War against Gout and Hyperuricemia

Jung Soo Song
Division of Rheumatology, Department of Internal Medicine, Chung-Ang University College of Medicine, Seoul, Korea

Gout, which is caused by the deposition of monosodium urate crystals in synovial fluid and other tissues, is the most common inflammatory rheumatic disease in men, at least in the Western world and is increasing in prevalence worldwide [1-7]. In addition to extremely painful recurrent acute and chronic arthritis, gout has an impact on morbidity and premature mortality [8-13]. Effective urate-lowering treatment (ULT) that maintains uric acid below 6 mg/dL can prevent further monosodium urate crystal formation and dissolve away existing crystals. However, studies show that only a minority of gout patients receive effective treatment, the majority continuing to experience recurrent acute attacks, further joint damage and other potentially fatal complications [14,15]. Chronic management of gout must include the long-term use of urate-lowering agents after an attack is treated and prophylactic therapy has been considered.

Allopurinol, a xanthine oxidase (XO) inhibitor, is the most widely used medication for effective ULT in patients with gout and hyperuricemia since 1966. But it has various adverse effects including potentially life-threatening allopurinol hypersensitivity syndrome, Stevens-Johnson syndrome, and toxic epidermal necrolysis, more often in older patients with renal insufficiency, as well as hematologic cytopenia, hepatitis, and vasculitis [16,17]. In some patients with gout and hyperuricemia, serum uric acid could not be controlled below 6 mg/dL with 400 mg or more doses of allopurinol.

For the need of more effective and safe medication, febuxostat was developed in 1998, was approved by United States Food and Drug Administration in 2009 and approved by Korean Ministry of Food and Drug Safety in 2012. As a non-purine selective XO inhibitor, febuxostat inhibits both oxidized and reduced types of XO. It does not inhibit enzymes involved in purine or pyrimidine metabolism, as does allopurinol. Febuxostat is also structurally unrelated to allopurinol; its structure does not resemble a pyrimidine or a purine. As a result of its selectivity and structural differences, febuxostat tends to cause fewer adverse events when compared with allopurinol [18,19]. The efficacy and safety of febuxostat was demonstrated in some clinical trials [18,20]. Unfortunately, there is no well designed meta-analysis to compare the efficacy and safety of febuxostat at different doses in patients with hyperuricemia.

Song and Lee [21] demonstrated the relative urate-lowering efficacy and safety of febuxostat and allopurinol in hyperuricemic patients with or without gout by using a Bayesian network meta-analysis involving 8 randomized controlled trials comparing the urate-lowering efficacy of 5 different interventions. Bayesian network meta-analysis, stat-of-the-art technique, has strengths that synthesizes all available direct and indirect data to allow for simultaneous comparisons of different treatment options [22,23], whereas traditional meta-analyses do not rank the efficacy and safety of treatments and do not provide sufficient information to guide physicians’ decision-making.

This study aimed to compare the efficacy and safety of febuxostat 40 mg, febuxostat 80 mg, febuxostat 120 mg, and allopurinol 100/300 mg daily in hyperuricemic patients with or without gout. In this more scientific and cutting edge analysis, the authors concluded that febuxo-
stat 80 mg and febuxostat 120 mg were more efficacious than allopurinol (100 to 300 mg) and that febuxostat 40 mg and allopurinol (100 to 300 mg) were comparable. The safety of febuxostat at all doses was comparable with that of allopurinol.

This meta-analysis has a number of strengths. The number of patients in each individual study ranged from 67 to 1,768, and this analysis included a total of 4,099 patients. Network meta-analyses synthesize all available data to allow for simultaneous comparisons of different treatment options that lack direct head-to-head comparisons. In contrast with the individual studies, the authors were able to provide more accurate data by increasing the statistical power and resolution through pooling the results of independent analyses and ranking of the efficacy and safety of febuxostat at the doses tested and allopurinol. Nevertheless, there are several shortcomings stated in this article, these results can encourage the warrior in the battlefield against gout and hyperuricemia, sufficiently. Now we, rheumatologists can be armed with a novel and powerful weapon with strong evidences.

In conclusion, this article demonstrated the efficacy and safety of novel medication febuxostat compare to allopurinol at different doses for the treatment of gout and hyperuricemia using novel Bayesian network meta-analysis.

**CONFLICT OF INTEREST**

No potential conflict of interest relevant to this article was reported.

**REFERENCES**
