

Studies examine treatment for gout and the condition's protective effects

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The goal in treating patients with gout is to reduce acute attacks by lowering serum urate levels, which are usually high in this disease. At the same time, high serum urate levels have been shown to lower the risk of developing Parkinson's disease (PD). A new study compared the safety and efficacy of febuxostat, a new drug being developed for gout that was recently approved for use in Europe, and a commonly used drug that has been around for years. Another study examined the link between gout and PD in individuals 65 years and older. The studies were published in the November issue of *Arthritis Care & Research* (<http://www3.interscience.wiley.com/journal/77005015/home>).

For many years, the most common drug used to treat gout was allopurinol, which is generally safe and effective, but has been known to cause life-threatening rashes in rare cases. Its dosage often has to be reduced in patients with impaired kidney function, but previous clinical trials have shown that febuxostat is effective at lowering urate levels and that its dosage may not need to be adjusted.

A Phase III, randomized, double-blind multi-center trial, known as the APEX (Allopurinol- and Placebo-Controlled, Efficacy Study of Febuxostat) trial, was conducted to compare the safety and efficacy of febuxostat with allopurinol and a placebo in patients with high urate levels (uricemia) and gout, some of whom had impaired renal function. It was the largest randomized controlled clinical trial to date comparing the two drugs. Led by H. Ralph Schumacher of the University of Pennsylvania, the 28-week trial involved 1,072 patients at 167 sites in

the U.S. who had serum urate levels of at least 8 mg/dl and gout, with normal or impaired renal function. Patients were randomized to receive one of three dosage levels of febuxostat once daily; allopurinol; or a placebo. The allopurinol dose given was based on kidney function; those with normal function received half the normal dose.

The results showed that a significantly greater proportion of patients receiving febuxostat at any dose achieved serum urate levels below 6 mg/dl for the last three months in which they participated in the trial. In those with impaired kidney function, about half in the febuxostat groups reached this level, while none of the patients with renal impairment who received the lower dose of allopurinol reached it. During the first eight weeks, more patients receiving febuxostat needed treatment for flares compared with the other groups. This may have been due to a more abrupt lowering of urate levels that caused crystal mobilization. Adverse events, mostly mild to moderate, occurred with similar frequency across the treatment groups.

The authors conclude that febuxostat's effects at these dosage levels "are significantly greater than those produced by the commonly used doses of up to 300 mg of allupurinol or by placebo," adding that "The efficacy of febuxostat in subjects with renal impairment is promising and warrants further study."

In another study published in the same issue, researchers led by Hyon Choi of the Arthritis Research Centre of Canada in Vancouver, identified 11,258 patients aged 65 or older with gout and 56,199 age and sex matched controls. They divided the gout patients according to those who were being treated with at least one prescription (72 percent) and those who did not receive any prescriptions for anti-gout medication during the study period, which was 1991 to 2004. They also included data on other medical conditions and medication use, such as diuretics and nonsteroidal anti-inflammatory drugs (NSAIDs) known to be

associated with gout or PD risk.

During the follow-up period, which averaged about eight years, they identified 1,182 new cases of PD. They found a 30 percent reduction in the risk of PD among those with a history of gout, independent of age, sex, prior medical conditions and use of diuretics and NSAIDs.

"These findings lend further support to the purported protective role of uric acid against PD," the authors state, adding a potential caution that lowering urate levels too much too long might also have harmful neurodegenerative consequences such as PD.

Source: Wiley

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