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New drug for gout shows early promise

Research question Is febuxostat a safe and effective alternative to allopurinol for patients with gout?

Answer Febuxostat seems better than a fixed dose of allopurinol at reducing serum concentrations of urate, but not at improving the clinical symptoms of gout.

Why did the authors do the study? Febuxostat is a new and potent xanthine oxidase inhibitor, designed to reduce the production of uric acid in people with gout. Like allopurinol, it is for preventing, not treating, acute attacks of gout. Febuxostat is the first new drug in this field for several decades. The authors wanted to compare the new drug with the current standard treatment, allopurinol. Their study was funded and analysed by a company with close links to the manufacturers of febuxostat.

What did they do? They tested two doses of the new drug against a fixed dose of allopurinol in a double blind, randomised trial lasting one year. Of the 760 US adults who participated in and contributed to the analysis, most were white men aged >50 years, all had chronic gout and hyperuricaemia (mean serum urate concentration 585 µmol/l at baseline), and 44% had already tried allopurinol. Participants took 80 mg or 120 mg febuxostat or 300 mg allopurinol daily for 52 weeks. They also took colchicine or naproxen as prophylaxis against acute flare ups of gout for the first eight weeks of the trial. The authors followed up participants regularly and compared their serum concentrations of urate, and their clinical progress by recording flare ups of gout and by measuring the size of gouty tophi in the 156 patients who had them.

What did they find? After 52 weeks' treatment, 62% (154/250) of participants taking 120 mg febuxostat, 53% (136/255) of those taking 80 mg febuxostat, and 21% (53/251) of those taking allopurinol had reached the treatment goal of a serum urate concentration of <357 µmol/l for the last three months of the trial. On this measure, both doses of febuxostat worked significantly better than allopurinol. In clinical terms, however, the three treatments were similar: tophi shrank substantially in all three groups, and about two thirds of participants in each group had at least one flare up of gout (70% (150/215) in the febuxostat 120 mg group, 64% (147/228) in the febuxostat 80 mg group, and 64% (150/234) in the allopurinol group). Side effects were also similar, although participants taking 120 mg febuxostat were significantly more likely to drop out of the trial than those taking allopurinol (98/251 *v* 66/254, P=0.003), and the commonest adverse event leading to withdrawal was abnormal liver function (7/251 of those taking 120 mg febuxostat *v* 1/254 of those taking allopurinol, P=0.04).

What does it mean? Febuxostat may prove a reasonable alternative to allopurinol for people with gout, but it's too early to say for certain. The favourable laboratory results in this trial did not translate to a better clinical outcome for patients, worries remain about febuxostat's long term safety, and it has not yet been tested against the commonest dose schedule for allopurinol (titrated against serum urate concentration rather than fixed).

Becker et al. Febuxostat compared with allopurinol in patients with hyperuricemia and gout. *New England Journal of Medicine* 2005;353:2450-61

Editor's choice

Doing things differently

The beginning of a new year is a time to think about doing things differently. The first *BMJ* of the new year has several suggestions.

If fear of precipitating acute glaucoma has prevented you from dilating a patient's pupils before checking for diabetic retinopathy, stop worrying and get out the mydriatic eye drops. Gerald Liew and colleagues (p 3) tell us that you are twice as likely to spot retinopathy through a dilated pupil and there is very little chance of precipitating acute angle closure glaucoma, though they do say you should warn the patient to seek medical attention if symptoms develop.

If you have been following guidelines on treating chronic cough with empirical treatments for gastro-oesophageal reflux disease, stop—A B Chang and colleagues' systematic review suggests you should first check that the patient has GORD (p 11). If you have ever thought of giving clarithromycin to patients with stable coronary heart disease, don't (p 14).

And if you have ever frowned on a mother whose baby sucks a dummy or pacifier, think again. De-Kun Li and colleagues' case-control study indicates that sleeping with a dummy/pacifier cuts the risk of sudden infant death by more than 90% (p 18). The authors acknowledge the limitations of their study and that only half of eligible women agreed to take part. They don't claim that dummies prevent sudden infant death, but it's a hypothesis worth testing.

Any day now we expect the UK government to announce its plans for reforming primary care, so we have asked some thoughtful people for their vision for primary care in 2015. Most are surprisingly utopian. Despite talking of patients being "utterly bemused," Peter Lapsely (p 43) sees out of hours work being made more attractive, linkage to the "by now excellent" NHS Direct telephone and internet advice service, and patients acknowledging that they have responsibilities as well as rights. Dougal Jeffries (p 44) sees recovering morale and an end to competition: "the ruinously costly 'choose and book' fiasco is a fading memory." Providers will relearn "the simple lessons of cooperation and coordination." Like others, he sees most care happening outside hospitals and lots of patients availing themselves of alternative therapies provided within the NHS. Carol Black (p 47) and Mayur Lakhani and Maureen Baker (p 41) are aspirational: strong clinical and professional leadership and medical professionalism will ensure high levels of public trust.

Alone among our visionaries, Hamish Meldrum is underwhelmed by life in 2015 (p 46): Tesco Health has taken over the failing NHS Direct; Connecting for Health finally integrates the NHS computing systems eight years late and £25bn over budget; patients have less choice because hospitals have closed and local treatment centres offer only a limited selection of treatments, and patients are charged for non-essential services including hotel care in hospital. Why is it I find Meldrum's vision the most convincing? Note to self for 2006: try to look on the bright side.

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