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DOSE-ESCALATION OF ALLOPURINOL VERSUS BENZBROMARONE IN GOUT PATIENTS: A RANDOMISED CONTROLLED TRIAL

M.K. Reinders[1], C. Haagsma[2], E.N. Van Roon[1], J. Delsing[3], T.L.T.A. Jansen[4], M.A.F.J. Van de Laar[5], J.R.B.J. Brouwers[6]

[1]Department of Hospital Pharmacy and Clinical Pharmacology, Medisch Centrum Leeuwarden, Leeuwarden;
[2]Department of Rheumatology, Ziekenhuisgroep Twente, Almelo;
[3]Department of Rheumatology, Medisch Spectrum Twente, Enschede;
[4]Department of Rheumatology, Medisch Centrum Leeuwarden, Leeuwarden;
[5]Health Sciences, University of Twente, Enschede;
[6]Pharmacy, University of Groningen, Groningen, Netherlands

Background: The EULAR evidence based recommendations for gout advise to titrate allopurinol dosage according to attained serum urate (sUr) concentrations [1]. However, there is a lack of evidence for this approach, and for higher dosages of sUr lowering drugs in general [1]. In research and in clinical practice, a fixed dosage of allopurinol 300 mg/day is often used.
Objectives: To investigate efficacy to attain sUr ≤0.30 mmol/l, and tolerability of allopurinol 300-600 mg/day versus benzbromarone 100-200 mg/day.

Methods: A prospective, randomised, open-label trial was performed in patients recently diagnosed with crystal-proven gout. Patients were given 300 mg allopurinol or 100 mg benzbromarone s.d.d. (stage 1). Efficacy of therapy was defined as stable sUr ≤0.30 mmol/l, as advised by the British guideline for gout management [2]. When this target was not attained after 2 months, dosage was increased to allopurinol 300 mg b.i.d. or benzbromarone 200 mg s.d.d. (stage 2).

Primary endpoint was treatment success in either of both stages, defined as tolerability and attainment of target serum urate concentration. Power calculation was based on expected success rates of allopurinol 600 mg/day of 55% [3] and benzbromarone 200 mg/day of 90% [4] rendering 22 evaluable patients in each study arm.

Results: 65 patients met the inclusion criteria and were enrolled in stage 1, 36 patients received allopurinol and 29 benzbromarone. 55 patients (85%) were evaluated for analysis of stage 1.

Treatment target was reached in 8 out of 30 (27%) applying allopurinol 300 mg/day; after increase of dosage, treatment success with allopurinol 300-600 mg/day was 21 out of 27 (78%). With benzbromarone 100 mg/day, treatment target was reached in 13 out of 25 (52%); after increase of dosage, overall treatment target with benzbromarone 100-200 mg/day was reached in 18 out of 23 (78%).

Two patients stopped allopurinol and 3 patients stopped benzbromarone because of adverse drug reactions (ADR). No additional ADR were reported after increase of dosages.

No significant difference in treatment success between allopurinol and benzbromarone was found after stage 1+2, using Fischer's exact test. After stage 1, benzbromarone 100 mg/day gave significant more treatment success than allopurinol 300 mg/day (p=0.05).

Reduction of serum urate levels were: 33% [±13%] using allopurinol 300 mg/day, 49% [±14%] allopurinol 600 mg/day, 42% [±15%] using benzbromarone 100 mg/day, 46% [±8%] benzbromarone 200 mg/day.

Conclusion: In patients with gout and normal renal function, no significant differences in treatment success were found between allopurinol and benzbromarone after dosage escalation based on attained serum urate. Increase of dosage was well tolerated as well as effective for both drugs (controlled-trials.com number ISRCTN49563848).

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