

024P A CLINICAL TRIAL OF ADJUNCTIVE ALLOPURINOL TREATMENT IN PATIENTS WITH CHRONIC SCHIZOPHRENIA: A DOUBLE BLIND AND PLACEBO CONTROLLED TRIAL

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Schizophrenia is a chronic progressive disease and it affects more than 1% of the population. The etiology of schizophrenia remains unknown in a majority of cases (Mohammadi and Akhondzadeh, 2001). There is a large amount of data showing that adenosine plays a role opposite to dopamine in the brain. Adenosine agonists and antagonists produce behavioral effects similar to dopamine antagonists and dopamine agonists, respectively (Akhondzadeh et al., 2000). Allopurinol, a well-known hypouricemic drug that inhibits xanthine oxidase, has been used with controversial results as an add-on drug in the treatment of poorly responsive schizophrenic patients (Lara et al., 2001). Therefore, the purpose of the present investigation was to assess the efficacy of allopurinol as an adjuvant agent in the treatment of chronic schizophrenia in an eight-week double blind and placebo controlled trial.

Eligible participations in the study were 46 patients with schizophrenia. All patients were inpatients and were in the active phase of the illness, and met DSM-IV criteria for chronic schizophrenia. Patients were allocated in a random fashion, 23 to haloperidol 15 mg/day plus allopurinol 300 mg/day and 23 to haloperidol 15 mg/day plus placebo. Patients were assessed by a psychiatrist at baseline and after 2, 4, 6 and 8 weeks after the medication started. The mean decrease in PANSS score from baseline was used as the main outcome measure of schizophrenia to treatment. A two-way repeated measures analysis of variance (time- treatment interaction) was used. The two groups as a between-subjects factor (group) and the five measurements during treatment as the within-subjects factor (time) were considered. In addition, a one-way repeated measures analysis of variance with a two-tailed post-hoc Tukey mean comparison test were performed in the change from baseline in each group. To compare the two groups at baseline and the outcome of two groups at the end of the trial, an unpaired Student's t-test with a two-sided P value was used. To compare the demographic data, Fisher's exact test was performed.

Although both protocols significantly decreased the score of the positive, negative and general psychopathological symptoms over the trial period, the combination of haloperidol and allopurinol showed a significant superiority over haloperidol alone in the treatment of positive symptoms and PANSS total scores (Greenhouse-Geisser corrected:  $F=7.04$ ,  $d.f.=1$ ,  $P=0.01$  and  $F=5.06$ ,  $d.f.=1$ ,  $P=0.01$  respectively). No significant differences were observed between the two protocols on the negative scores ( $F=0.23$ ,  $d.f.=1$ ,  $P=0.62$ ).

The results of this study suggest that allopurinol may be an effective adjuvant agent in the management of patients with chronic schizophrenia. Nevertheless, results of larger controlled trials are needed, before recommendations for a broad clinical application can be made.

Akhondzadeh S. *et al.* (2000). *Journal of Clinical Pharmacy and Therapeutics* 25, 131-137.

Lara D.R. *et al.* (2001). *Journal of Clinical Psychopharmacology* 18, 235, 237

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