

021P A CLINICAL TRIAL OF ADJUNCTIVE ESTROGEN TREATMENT IN WOMEN WITH CHRONIC SCHIZOPHRENIA: A DOUBLE BLIND AND PLACEBO CONTROLLED STUDY

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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). The estrogen hypothesis of schizophrenia postulates that estrogen exerts a protective effect against schizophrenia and that has partly explained the observed sex differences in premorbid adjustment, onset age, treatment response and illness course. It has been suggested that estrogen supplementation can augment the treatment effects of antipsychotics (Grigoriadis and Seeman, 2002). The purpose of the present investigation was to access the efficacy of ethinylestradiol as an adjuvant agent in the treatment of premenopausal women with chronic schizophrenia in a 8 week double blind and placebo controlled trial.

Eligible participations in the study were 32 women of child-bearing age with acute schizophrenia. All patients were inpatients and were Caucasian, in the active phase of illness, and met DSM-IV criteria for chronic schizophrenia. The minimum score of 60 on positive and negative syndrome scale (PANSS) was required for entry into the study. Patients were allocated in a random fashion, 16 to haloperidol 15 mg/day plus ethinylestradiol 0.05 mg/day and 16 to haloperidol 15 mg/day plus placebo for a 8-week, double-blind, placebo-controlled study. 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 ethinylestradiol showed a significant superiority over haloperidol alone in the treatment of positive symptoms, general psychopathology symptoms as well as PANSS total scores (Greenhouse-Geisser corrected: $F=6.17$, $d.f.=1$, $P=0.019$; $F=4.27$, $d.f.=1$, $P=0.047$ and $F=6.72$, $d.f.=1$, $P=0.015$ respectively). No significant differences were observed between the two protocols on the negative scores ($F=0.088$, $d.f.=1$, $P=0.76$). The results of this study suggest that estrogen may be an effective adjuvant agent in the management of women of child-bearing age with acute schizophrenia. Nevertheless, results of larger controlled trials are needed, before recommendation for a broad clinical application can be made.

Grigoriadis, S. & Seeman, M.V. (2002). *Can. J. Psychiatry* 47, 437-442.

Mohammadi, M.R. & Akhondzadeh, S. (2001). *IDrugs* 4, 1167-1172.