ABSTRACT:

Background: Famotidine is a histamine-type 2 (H2) receptor antagonist commonly used for the treatment of peptic ulcers and hyperacidity. By serendipity, administration of famotidine as a sole medication to a patient with schizophrenia and coincidental peptic ulcer disease was found to be associated with a dramatic resolution of positive and negative symptoms. Histaminergic projections in the brain have been implicated in the pathophysiology of schizophrenia. Modulation of the central histaminergic tone by famotidine, with possible indirect effect on glutamatergic neurotransmission at the level of the N-methyl-D-aspartate (NMDA) receptor complex, could theoretically be involved in the beneficial therapeutic effects of famotidine in schizophrenia. There were two case reports and five open trials suggested that famotidine possessed adjuvant therapeutic effects when combined with antipsychotic medications for the treatment of patients with schizophrenia. So far (up to August, 2002), no randomized double blind placebo-controlled study on this theme has been available in literature and no data exists for the use of famotidine adjuvant therapy for schizophrenia in the Chinese population. A randomized double blind placebo-controlled study on the efficacy of famotidine adjuvant therapy in the treatment of schizophrenia is thus desirable.

Objective: To study the efficacy of famotidine adjuvant therapy in the treatment of schizophrenia.

Method: Forty Chinese subjects with treatment-resistant schizophrenia

participated in a randomized double blind, placebo-controlled, 5-week study with either famotidine (40 mg/ day) or placebo added to their ongoing antipsychotic medications from week 1 to week 4. Subjects were rated on baseline, weekly thereafter, and 1 week after famotidine/ placebo discontinuation by using the Brief Psychiatric Rating Scale (BPRS), the Scale for the Assessment of Negative Symptoms (SANS) and the Clinical Global Impression-Severity Scale (CGI).

Results: This randomized double blind placebo-controlled study was reported according to the CONSORT (Consolidated Standards of Reporting Trials) guidelines. Famotidine adjuvant therapy (famotidine combined with original antipsychotic medications) was well tolerated. Repeated-measures ANOVA was performed with between-subject factors of treatment phase (famotidine/ placebo) and week within treatment phase (week 1, 2, 3, 4 and 5). Statistically significant effects were observed for BPRS scores ($F = 7.0$, $d.f. = 1,38$, $P < 0.05$), SANS scores ($F = 8.88$, $d.f. = 1,38$, $P < 0.01$) and CGI scores ($F = 15.0$, $d.f. = 1,38$, $P < 0.001$) from week 1 to week 5. Famotidine adjuvant therapy led to a statistically significant decline in all outcome measures (BPRS, SANS and CGI scores) and it resulted in:

(1) 14.4% (95% confidence interval 9.1% to 19.7%) reduction in negative symptoms, as measured by SANS. Statistically significant improvement was noted in affective flattening, avolition-apathy and anhedonia-asociality domains of SANS.

(2) 20.9% (95% confidence interval 16.0% to 25.7%) improvement in the BPRS scores and

(3) 20.3% (95% confidence interval 15.4% to 25.1%) improvement in the CGI scores.

Statistically significant ($P<0.05$) difference in improvement on BPRS scores was evident from week 3 onwards while that for SANS scores and CGI scores was evident from week 2 onwards. There was no statistically significant difference in the outcome measure scores between the last week of famotidine adjuvant therapy (week 4) and the follow-up (week 5) ratings, suggesting that the benefit achieved during famotidine adjuvant therapy persisted over the first week after discontinuation of famotidine.

Conclusions: The findings suggest that adjuvant therapy with famotidine, an H2 receptor antagonist, is probably efficacious in the treatment of schizophrenia and further support a role of histamine in the pathophysiology of schizophrenia. Famotidine adjuvant therapy may be considered as a potential treatment option for schizophrenia.