LETTERS TO THE EDITOR

AN OPEN-LABEL STUDY OF FAMOTIDINE AS A TREATMENT FOR SCHIZOPHRENIA

To the Editor:

Our interest in whether or not famotidine, a selective H_2 receptor antagonist, has potential as a treatment for schizophrenia was stimulated by a single case report (Kaminsky 1990). Recently, Oyewumi et al (1994) reported that seven out of 12 patients with treatment-resistant schizophrenia improved when open-label famotidine was added to their pre-existing antipsychotic medication.

Previous work by our group found that the supplementation of antipsychotics with nifedipine resulted in markedly elevated antipsychotic serum levels in some subjects (Stedmarl et al 1991). It is possible that this pharmocokinetic effect was responsible for the improved mental state observed in these subjects rather than the direct action of nifedipine. Before embarking on a double-blind controlled trial of the addition of famotidine to antipsychotic medication, it would be important to exclude a similar pharmacokinetic interaction. One aim of this study is to determine if such an interaction could occur with famotidine augmentation.

Five inpatients with research diagnostic criteria chronic schizophrenia (Spitzer et al 1978) were entered into an open-label study which was approved by the hospital ethics committee. Patients gave informed consent. Symptoms were measured by the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham 1962) and the Clinical Global Impression Scale (CGI) (Guy 1979).

Subjects were studied over a period of eight weeks during which the daily dose of their regular antipsychotic medication was kept constant. Following a two-week baseline, patients received 20 mg of famotidine twice daily in addition to their antipsychotic medication. After four weeks, famotidine was discontinued and subjects were assessed for a further two weeks. Blood samples were collected weekly to determine total plasma neuroleptic activity (Rao 1986).

Although five patients (age range 30 years to 51 years) were entered in the study, one patient was withdrawn because of an episode of aggression after receiving famotidine for 11 days. Of the remaining four patients, daily doses of antipsychotic medication in haloperidol equivalents (Hollister 1983) ranged from 15 mg to 120 mg. The mean total BPRS score (1 to 7 scoring system) at baseline for each subject ranged from 36 to 46.

One subject improved during the trial period with the BPRS total score decreasing from a baseline of 37 to 22 by the fourth week of famotidine administration. By the second week after the famotidine was discontinued, the rating increased to 28. All subscales of the BPRS, except "withdrawal-retardation", showed a similar pattern of reduction during the trial period. The CGI was rated as minimally improved by the end of the fourth week, and remained minimally improved during the post-study phase. The other three subjects showed little change in their BPRS totals, BPRS subscores or CGI ratings.

The assay of neuroleptic activity in plasma did not reveal any significant pharmacokinetic interactions between famotidine and the concurrent antipsychotic medication. This result was also true for the patient who improved during the famotidine augmentation.

Of the five patients, only one demonstrated an improvement in mental state after the addition of famotidine. The small number of subjects in this study does not allow inferences to be drawn about the efficacy of famotidine supplementation. However, the lack of a significant pharmacokinetic interaction does contribute an important item of information that should be taken into account when planning future studies. Based on our data, any effect seen with famotidine augmentation is less likely to be the result of a pharmacokinetic interaction.

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THE AUTHOR REPLIES

To the Editor:

The letter "An Open-Label Study of Famotidine as a Treatment for Schizophrenia" by Whiteford et al (1995) is a welcome addition to the ongoing accumulation of knowledge on the role of H_2 antagonists in the treatment of schizophrenia. The finding of a "lack of significant pharmacokinetic interaction" between the famotidine and the antipsychotic medications matches our report that famotidine did not significantly increase plasma clozapine levels in the only patient in our sample in whom we measured these levels (Oyewumi et al 1994). These findings, coupled with reports of high levels of H_2 receptor activity in areas of the brain associated with schizophrenia (Prell and Green 1986), suggest that H_2 receptors are implicated in schizophrenia.

Reports on the effect of famotidine in schizophrenia had emphasized improvement of the negative symptoms. Whiteford et al (1995) did not give details of the subscales of the Brief Psychiatric Rating Scale (BPRS) (Overall and Gorham 1962) they used. Only two items of the BPRS, namely blunted affect and emotional withdrawal, are included in the negative subscale of the Positive and Negative Syndrome Scale for Schizophrenia (PANSS) (Kay et al 1987). Perhaps a reanalysis of their data with a focus on these items might show improvement of the negative symptoms in a greater number of their subjects. We suggest using scales that primarily measure negative symptoms in future studies.

We believe that the stage is set for double-blind studies to clarify the therapeutic potential of famotidine as an adjunct treatment of schizophrenia, and to further elucidate the role of H_2 receptor activity in schizophrenia.

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