Comments on "Weight gain management in patients with schizophrenia during treatment with olanzapine in association with nizatidine"

Comentários sobre "Manejo do ganho de peso em pacientes portadores de esquizofrenia durante o tratamento com olanzapina em associação com nizatidina"

Dear Editor,

It is well known that, when compared with first generation antipsychotics, the second generation antipsychotics are more effective in reducing positive and negative symptoms but the use of such drugs, especially clozapine and olanzapine, is associated with substantial body weight gain in a considerable proportion of patients with schizophrenia.[1]

The mechanisms by which antipsychotic medications produce weight gain may include appetite stimulation, reduction in physical activity, and disturbance of metabolic regulation. Many drugs marketed to induce weight loss suppress appetite and hunger by enhancing the action of monoamine neurotransmitters (histamine, serotonin, and norepinephrine) in the brain. olanzapine and clozapine inhibit or reduce the activity of those neurotransmitters, thus increasing appetite and, consequently, weight gain.[2]

However, weight gain is caused by a complex array of different factors, either drug-related (e.g. receptor affinity to DA, 5HT and H) or patient related (e.g. genetic vulnerability, gender, age, weight at baseline, type of psychiatric disorder, and individual lifestyle). Moreover, weight gain is not homogeneously evaluated across research studies with different outcome variables been employed (e.g. % as mean weight gain, body mass index change) making evaluation of the results difficult to interpret.[2]

Pharmacological and nonpharmacological strategies for antipsychotic-associated weight gain and associated metabolic disturbances have been tried, such as: medication switching, medication addition to influence weight loss or prevent weight gain, or even to increase insulin sensitivity. Among these pharmacological strategies, it has been found that HT2 blocker compounds such as cimetidine were reported to reduce weight gain in patients with type 2 diabetes.[3]

Nizatidine, which is similar to cimetidine, is also a histamine H-2 receptor antagonist and has been proposed to have weight-reducing effects in patients taking olanzapine.[4] In order to test such hypothesis, Assunção et al. in a well designed, 12-week randomized controlled trail published in the last issue, compared the effect of nizatide (600 mg/day) or placebo in patients with schizophrenia treated with olanzapine (5-20 mg/day).[5]

The study showed that olanzapine was effective in reducing psychopathology severity but the hypothesis that nizatidine could be beneficial in preventing weight gain was not proved since no difference was found between groups, i.e. the concomitant use of olanzapine with nizatidine had no effect on weight when compared to the use of placebo. Actually, the nizatidine group gained more weight (1.1 kg) than the placebo group (0.7), although such difference was not statistically significant.

Despite of a well conceived hypothesis and an adequate add-on design study, the authors stated that their results did not differ from similar studies that could not find an effect either, like, for example, the 16-week trial of Cavazzoni et al. with nizatidine.[5] Moreover, factors such a relatively small sample size, which has contributed to the lack of adequate power of the study, and the fact that nizatide started to be used after patients had already gained about 7 kg may have influenced the results.

Only through good quality randomized controlled trials, as is the case of the study by Assunção et al., it is possible to obtain the adequate evidence necessary to establish reliable treatment strategies. The evidence derived from the study by Assunção et al. does not recommend the use of nizatidine as drug management for the prevention of weight gain in patients using olanzapine.

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