INTRODUCTION

Obsessive-compulsive disorder (OCD) is a chronic disorder which may frequently be seen with major depression and which may also be resistant to pharmacotherapy (1). Fluoxetine has the advantage of carrying both antidepressant and antiobsessive effects. Antipsychotics may be added, if the patient is resistant (2). Sulpiride is a well-known antipsychotic with less side effects below 400 mg/day (3). There are limited studies about the antidepressant effect of sulpiride but recent data suggests that it is effective in depression and is well tolerated at 200-1200 mg. Whether this effect is antidepressant or antipsychotic, it is unknown. In a study of depressive patients, a single low dose of sulpiride was given and the side effects were moderate sedation, constipation and dry mouth (4). In another double-blind comparative study of bipolar depression, sulpiride was combined with lithium. Depression and anxiety recovered very well and there were no side effects (5).

Case report

The case was a 53 years old, female. She had severe extrapyramidal symptoms during a combination treatment with fluoxetine and sulpiride.

ABSTRACT:

SEVERE EXTRAPYRAMIDAL SYMPTOMS DUE TO SULPIRIDE AND FLUOXETINE COMBINATION IN A CASE OF OCD

Sulpiride is an antipsychotic agent which has an antidepressant effect in low doses. The combination of antipsychotics in lower dosages with antidepressants in obsessive-compulsive disorder (OCD) patients has also been reported to be useful. The case reported was a 53 years old female patient with OCD and major depression according to the DSM-IV diagnostic criteria. OCD diagnosis was present for six years and she had been depressed for the last six months. She was accepted as having resistant OCD according to the patient’s history. After she was hospitalized, the treatment began with fluoxetine 20 mg/day. In the second week fluoxetine dosage was raised to 40 mg/day and 200 mg/day sulpiride was added. On the third day of combination treatment, severe extrapyramidal symptoms emerged and this prompted us to quit the use of sulpiride. Biperiden 3 mg/day was ordered in order to relieve those side effects. As these precautions were not efficacious, fluoxetine dosage was lowered to 20 mg/day, and then it was quitted. Diphenhidramine 100 mg/day, propranolol 40 mg/day and diazepam 10 mg/day were ordered. Except chewing movements extrapyramidal symptoms lasted for a week.

Key words: obsessive-compulsive disorders, extrapyramidal symptoms, sulpiride, fluoxetine, drug interaction

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contamination obsession and washing compulsion, she could not get out of the bathroom for many hours. She had fatigue, weakness, depressive moods, diminished pleasure, feeling of hopelessness, suicidal thought and weight loss. Her complaints began 6 years ago. She has been taking a bath too often and she has been spending more than 9 hours in the bathroom everyday. She thought that all liquid accumulations were urine, and contaminating her. She had been treated with clomipramine, haloperidol, and diazepam combinations but they were not effective. She had quitted therapy herself. During the previous 6 months she could not get out of the bathroom, she could not find time and energy for her routines. She had thoughts of death because she was afraid that she could never improve. Her weight loss was about 15 kgs in 6 months.

Her psychological examination revealed that her physical development was well, she was walking slowly and appeared ashamed. She had depressive and anxious moods. She had contamination obsession and washing compulsion. She had hopelessness due to her illness and she had suicidal thoughts. She knew she was ill but she thought that it was not a psychological problem.

Her physical examination and laboratory tests including complete blood counting, biochemical analyzes, electrocardiogram and radiological examinations were as usual.

She was diagnosed as OCD with major depression according to DSM IV diagnostic criteria. She was accepted as having resistant OCD according to the patient's history. After she was hospitalized, the treatment was fluoxetine 20 mg/day in the first week. In the second week fluoxetine the dosage was raised to 40 mg/day and 200 mg/day sulpiride was added. In the third day of combination therapy, severe extrapyramidal symptoms emerged and that prompted us to quit sulpiride. Biperiden 3 mg/day was ordered. As these were not efficacious, fluoxetine dosage was lowered to 20 mg/day, and then quitted. Diphenhydramine 100 mg/day, propranolol 40 mg/day and diazepam 10 mg/day were ordered. Except chewing movements, extrapyramidal symptoms lasted for a week.

DISCUSSION

The case is a chronic and resistant case which was not treated sufficiently. We planned to begin with fluoxetine and increase the dosage quickly. Sulpiride was added at a dose of 200 mg/day to accelerate the response to treatment. We had to quit sulpiride on the third day of treatment because of the severe extrapyramidal side effects. The Fluoxetine dosage was lowered to 20 mg/day and then quitted, because severe EPS were continuing.

In this case, the cause of extrapyramidal side effects was unclear. It may be because of fluoxetine or sulpiride or both of them. There are reports of extrapyramidal side effects of fluoxetine and sulpiride (6,7). SSRI's are well-known causes for akathisia. Tremors and dystonic reactions due to SSRI's are also reported. Such events may either be caused by the combined use of D2 antagonists or asymptomatic parkinson disorder (8).

Nevertheless the combination of antidepressants with antipsychotics (especially fluoxetine-haloperidol combination) may also cause extrapyramidal symptoms (EPS) (7). It is also reported that the combination of SSRI's with low a dose of D2 antagonists may cause a more apparent increase in production and secretion of dopamine in prefrontal dopaminergic projection areas (9).

Drug interactions are very important and should be considered during combination treatments. Cytokrom P450 and other cytokrom enzyme systems have an important role in the therapeutics, effectiveness, interactions, side effects and these mechanisms are not yet clear (10).

Fluoxetine and sulpiride combination may potentize each other or may cause elevation in blood levels which may increase the risk for EPS. But there are no reports to verify this theory. On the contrary in an experimental study with rats, fluoxetine was given with a non-competetitive NMDA receptor antagonist, MK-801, and the combination inhibited the leukomotor hyperactivity (11). EPS in fluoxetine treatment is rare but in sulpiride treatment it is more frequent, although sulpiride is associated with less EPS than phenothiazines (12).

In the case presented, the treatment period was very short and the dosages were low but extrapyramidal side effects were severe. We could not find any organic or pathological sign to explain the EPS. Fluoxetine is a cytokrom P-450 2D6 and 3A4 inhibitor (10). The inhibitor effect of sulpiride on cytokrom P-450 enzyme system has not been described yet. Severe extrapyramidal side effects in the case we report may either be related to cytokrom
P-450 enzyme system or may just be hypersensitivity reaction to sulpiride. There are no reports about interaction of fluoxetine and sulpiride.

We suggest that extrapyramidal side effects in this case are related with both sulpiride and fluoxetine effects on cytokrom P-450 enzyme system or potentiation between them by increasing blood levels.

Combinations of SSRI’s, especially of fluoxetine with antipsychotics, especially with sulpiride may cause severe EPS, and this may complicate the treat-ment.

References:


