

Marked effect of milnacipran combined with olanzapine for a delusional depressive patient

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Abstract: This report is the first to describe the use of milnacipran and olanzapine in combination in the treatment of delusional depression. The patient was a 55-year-old woman, and the combination treatment brought her marked amelioration of delusional depression without significant side effects. This suggests that the combination therapy of milnacipran and olanzapine is efficacious and safe in the treatment of delusional depression.

Keywords: combination therapy, delusional depression, milnacipran, olanzapine

Introduction

Depression with psychotic features responds poorly to treatment with a tricyclic antidepressant or a conventional antipsychotic alone, but their combination shows a clearly preferable therapeutic effect (Spiker et al 1985). Recently, Rothschild et al (2004) reported that the combination therapy of a selective serotonin reuptake inhibitor (SSRI) (fluoxetine) and an atypical antipsychotic (olanzapine) showed a significantly higher response rate than placebo or olanzapine monotherapy and exhibited extrapyramidal symptoms comparable with placebo. The combination therapy of newer drugs is preferable from the point of view of side effects.

Milnacipran is a novel antidepressant that selectively inhibits the reuptake of serotonin and noradrenaline without directly affecting the postsynaptic receptor sites, and its response and remission rate has been reported to be higher than SSRIs (Montgomery et al 1996). The combination therapy of milnacipran and a newer antipsychotic drug may therefore exhibit better therapeutic effects on depression with psychotic features than that of an SSRI and a newer antipsychotic drug. To our knowledge, this is the first report on the marked effect of milnacipran combined with olanzapine for treating a delusional depressive patient.

Case report

The patient was a 55-year-old homemaker who had no past history of psychiatric disorders. She worked hard looking after her bedridden mother-in-law. In 1998, she suffered from depression accompanied by a delusion of poverty. She was treated with 5 mg/d of haloperidol and 150 mg/d of trazodone. Almost one month after the therapy was started, her symptoms of depression with delusion remitted. Although she was informed about the disadvantage of long-term treatment with a conventional antipsychotic drug, she wished to continue this medication because of fear of relapse. Her medication regime continued unchanged for 3 years.

In April 2001, she was diagnosed with drug-induced parkinsonism and her haloperidol was stopped. Two months later, she again suffered from depression accompanied by irritation and loss of appetite and activity. She also suffered from

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persecutory delusion. The patient was diagnosed with major depression with psychotic features (DSM-IV). On July 3rd, 2001, she was hospitalized and started on 2 mg/d of risperidone in addition to 100 mg/d of trazodone. She developed severe akathisia, so administration of risperidone was stopped and treatment with 10 mg/d of olanzapine was started on July 6th, 2001. Her akathisia did not reappear and her anxiety gradually decreased. Five days later, trazodone was stopped and milnacipran 50 mg/day was started because her anorexia and hypobulia still persisted. Later that month, her facial expression was not depressive and her anorexia had remitted; however, the delusions that caused her to refer to herself as a "pig" and a "fool" still remained. On August 8th, 2001, the tendency to make delusional remarks disappeared and her loss of both volition and activity remitted. The dosage of milnacipran was increased to 100 mg/d because this dosage was reported to be effective in the reduction of recurrences (Rouillon et al 2000). The combination therapy of both olanzapine and milnacipran caused no adverse events.

The patient was discharged a month later and her medication was continued without change. In February 2002, her appetite increased and the olanzapine was reduced to 5 mg/d. In March 2002, the milnacipran was reduced to 50 mg/d because her increased appetite persisted. She stopped visiting our hospital by her own decision in February 2003. In October 2003, she again suffered from depression, persecutory delusion, and anorexia and revisited our hospital. She was started on 100 mg/d of milnacipran and 5 mg/d of olanzapine. Milnacipran 100 mg/d was prescribed because this dosage was reported to be optimal (Montgomery et al 1996). Four weeks after the therapy was started, the patient's depressive mood and delusions disappeared completely. About two years have passed since

the last episode remitted. Her medication has continued unchanged and her depressive symptoms have not returned.

Discussion

In this case, risperidone induced severe akathisia and replacing it with olanzapine produced good results. Both SSRIs and serotonin-noradrenaline reuptake inhibitors (SNRIs) would be candidates for combination with olanzapine in the treatment of depression with psychotic features as they have fewer side effects. Milnacipran has much lower interindividual variation in plasma levels than SSRIs: it does not induce/inhibit hepatic P450 enzymes and therefore has a very low potential for drug-drug interactions (Puozzo et al 2002). These characteristics of milnacipran make it preferable for use in the drug combination therapy of depression with psychotic features.

This case suggests that the combination therapy of milnacipran and olanzapine is effective and safe compared with the traditional combination therapy of tricyclic antidepressants and typical antipsychotics for the treatment of delusional depression.

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