

1 mg t.i.d. and methylphenidate 5 mg t.i.d. with sustained remission (5 months) of both affective and anxiety symptoms.

The last case was a 68-year-old male with symptoms of a major depression and a past history of MDD with psychosis, in addition to alcohol dependence which had been in remission for the past 11 years. After several trials on various combinations of antidepressants, he was finally stabilized on paroxetine 20 mg b.i.d., nortriptyline 50 mg t.i.d. and methylphenidate 20 mg t.i.d. seven months later he continued to feel well and reported he was recently able to complete (and enjoy!) Homer's *Odyssey*.

The authors summarized their findings making several key points, including:

- * All patients had chronic depression only partially responsive to an SSRI.
- * Three met criteria for "double depression" (i.e., episodes of MDD superimposed on chronic dysthymia).
- * Most had failed on HCAs and/or bupropion.
- * Methylphenidate augmentation produced complete or near complete sustained remission with no increase in adverse effects.
- * No patient developed tolerance or appeared to abuse methylphenidate.

As with any small, open case series, the possibility of confounds due to various factors remains a distinct possibility. The authors note several, including:

- * Placebo expectancy.
- * Additional time on an SSRI.

- * Possible increased SSRI serum levels due to the addition of methylphenidate.
- * Direct antidepressant effects of the psychostimulant.

There is, however, a large anecdotal case report history which has found that psychostimulants can improve outcome in various groups, including:

- * Augmenting TCAs and MAOIs in partially responsive depressions.
- * The medically ill, depressed patient.
- * The elderly, depressed patient.

The second observation is that when methylphenidate is started at low doses (e.g., 2.5 to 5 mg/day) and increased slowly when clinically indicated, doses as high as 60 mg/day were well tolerated and did not lead to an abusive pattern.

Finally, while the mechanism of action is uncertain, the ability of these agents to enhance catecholamine activity (at least initially) is consistent with the literature that demonstrates combined NE and/or DA, as well as 5-HT actions, may be more beneficial than either effect alone for insufficiently responsive, depressed patients.

Reference:

Stoll AL, Pillay SS, Diamond L, et al. Methylphenidate augmentation of serotonin selective reuptake inhibitors: a case series. *J Clin Psychiatry* 1996;57:72-76.

Paroxetine Withdrawal Symptoms

Discontinuation (abrupt or gradual) of paroxetine may cause withdrawal symptoms. Withdrawal symptoms may begin at the end of tapering and even up to 14 days after

discontinuation of paroxetine. Patients experience dizziness, nausea, paresthesias, and headaches. These symptoms generally last only a few days. Careful monitoring during paroxetine (and other SSRI) discontinuation is recommended given the significant rate of occurrence and potential severity of withdrawal symptoms. Patients should be advised of potential transient adverse effects after paroxetine discontinuation. A very gradual taper of paroxetine will decrease both the incidence and severity of withdrawal symptoms. If paroxetine withdrawal symptoms are severe, administration of paroxetine or fluoxetine rapidly alleviates them.¹⁻²

A 36-year-old man developed transient behavior symptoms with severe aggressive and suicidal impulsivity following the withdrawal of paroxetine 50 mg/day. He had received paroxetine for 6 weeks as a part of a clinical study of the drug for the treatment of stuttering. Two days after paroxetine was abruptly stopped he had hypomanic-like symptoms. These abated spontaneously after 2½ weeks. Another patient in this same clinical trial, a 48-year-old man, was tapered off paroxetine over a 12-day period. Physical and behavior symptoms began in the second week, lasted about 9 days, and then remitted spontaneously.³ Some patients have experienced a "withdrawal buzz" which they have likened to a "jolt," a "rush," a "shock," or a brief moment of disorientation and dizziness.⁴⁻⁶

Shock-like sensations after discontinuation of paroxetine have been reported by some patients.⁷ Withdrawal symptoms lasting up to three weeks have been reported in some patients following paroxetine discontinuation.⁸

References:

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- Psychopharmacol* 1994;14:206-207.
2. Barr LC, Goodman WK, Price LH. Physical symptoms associated with paroxetine discontinuation (letter). *Am J Psychiatry* 1994;151:289.
3. Bloch M, Stager SV, Braun AR, et al. Severe psychiatric symptoms associated with paroxetine withdrawal. *Lancet* 1995;346:57.
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5. Koopowitz LF, Berk M. Paroxetine induced withdrawal effects. *Human Psychopharmacol* 1995;10:147-148.
6. Phillips SD. A possible paroxetine withdrawal syndrome. *Am J Psychiatry* 1995;152:645-646.
7. Frost L, Lal S. Shock-like sensations after discontinuation of selective serotonin reuptake inhibitors. *Am J Psychiatry* 1995;152:810.
8. Pyke RE. Paroxetine withdrawal syndrome. *Am J Psychiatry* 1995;152:149-150.

Tramadol Abuse Potential: A Warning

In compliance with a request from the Food and Drug Administration, Ortho-McNeil sent a letter on March 20, 1996, to Health Care professionals calling attention to the potential for abuse of tramadol (*Ultram* - Ortho-McNeil). It cited the receipt of 115 spontaneous domestic reports of adverse events described as drug abuse, dependence, withdrawal, or intentional overdose. This does not include cases of accidental overdose.

Editor's Comment: The above cited letter emphasized that patients with a past or present history of addiction or dependence on opioids accounted for the majority of the reports of abuse and dependence, etc. It advised that tramadol should not be prescribed for such patients. Since there are no reports indicating that tramadol is available illicitly, the reports of its abuse must be instances of prescription drug abuse. Hence, readers should be familiar with the clinical