Letter to the Editor

Paroxetine Not to Blame

To the Editor:

In reference to a case report published in the *Journal* by Vermeulen (1), I wish to make several points that call into question the conclusion drawn about paroxetine by the author.

In all three cases cited in the report, concomitant medications and/or alcohol ingestion significantly complicated the clinical picture and likely played a major role in morbidity and mortality.

In Case 1, diphenhydramine and dextromethorphan were both collected at autopsy. Furthermore, the patient had been prescribed regular trifluoperazine. In Case 2, blood ethanol levels of 0.25% were collected upon admission to the hospital. Dilantin was also administered in the emergency department. The patient had been prescribed an amalgamation of regular medications, including fluoxetine and sertraline in addition to paroxetine. In Case 3, postmortem imipramine and desipramine levels were consistent with lethal concentrations. The patient’s regular medications included Fiorinal. Butalbital, a major component of Fiorinal, may lead to acute barbiturate poisoning and to respiratory depression and coma.

Several important points regarding the clinical presentations must also be made. In Case 2, no paroxetine was detected in admission blood samples. Also in Case 2, charcoal was not administered until 5 h after hospital admission. This certainly runs counter to the standards of immediate postoverdose supportive measures. In all three cases, paroxetine dosage information (and number of pills ingested) was sorely lacking.

Based on this information, I feel that the author’s conclusion that “paroxetine was directly involved in the cause of death” was a very spurious one indeed.

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References


The author’s reply:

I wish to respond to the Letter from Dr. Altman about my article on paroxetine (1). I am in complete agreement with Dr. Altman that alcohol and concomitant medications complicated the clinical picture: they usually do because it is rare for drug-related deaths to be attributed to one drug alone.

I would like to address each of the six points raised by Dr. Altman.

In Case 1, the diphenhydramine and dextromethorphan levels were not in the toxic range. Trifluoperazine was not detected. Noncompliance is not unusual in our cases.

In Case 2, I believe that the ethanol and fluoxetine levels were addressed at length, and the similarity between Case 2 and a published fluoxetine/ethanol overdose was stated. I explored the possibility of an adverse drug–drug interaction because fluoxetine and paroxetine both inhibit CYP11D. Sertaline was not detected.

In Case 3, that the imipramine and desipramine levels were consistent with lethal concentrations is precisely my point. I postulated that they reached that level because of a drug–drug interaction between paroxetine and imipramine/desipramine by inhibition of CYP11D6 that has been well documented (2,3).
Butalbital was not detected, which makes barbiturate poisoning completely irrelevant.

Dr. Altman's point about not finding paroxetine in antemortem admission blood from the hospital is an important one. It is possible that paroxetine was in the sample but below our level of detection (LOD). Our LOD using gas chromatography–nitrogen-phosphorus detection is in the 200-ng/mL range. The amount of admission blood was limited, leaving us with no sample to retest.

As for charcoal not being administered until 5 h after admission, yes, that is true. I stated that earlier intervention by the hospital staff may have resulted in a different outcome.

Finally, those of us involved in death investigations would like nothing better than to have information regarding dosage, prescription amounts, and especially number of pills ingested. Unfortunately, we are often stymied by a lack of information resulting from obstrusive measures taken by the decedent and alteration of death scenes by well-meaning but ill-advised friends and relatives.

It is also an a priori consideration that blood levels of a drug at 100 times the therapeutic range may well be in the toxic range. If Dr. Altman has any evidence that paroxetine levels of 4.0, 3.7, and 1.4 mg/L are not toxic, he should make it known to the forensic toxicology community.

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References