Trazodone and Dothiepin Poisoning

Dear Editor:

This letter is in reference to an article by Lambert et al. (1), which dealt with the topic of trazodone poisoning. Because we are the manufacturer of trazodone, we would like to make some comments on the conclusions of the article. We believe the trazodone profile may be misunderstood by some readers.

Although suicides by overdose of antidepressant drugs are very common, the data in the literature of the past 10 years have shown that the new generation of antidepressants like trazodone appear to be much safer in overdose than tricyclics. Tricyclics can cause cardiovascular complications due to the combination of direct cardiotoxicity and anticholinergic effects, central nervous system sedation, and respiratory suppression.

Tricyclic antidepressant-related deaths have occurred even at doses of 2000 mg, and serious intoxication may be expected at doses greater than 1000 mg. However, death due to overdose of trazodone administered alone is rare, and attribution to the drug is uncertain (2).

In 1984, Root and Ohlson (3) reported the case of a patient with trazodone blood concentrations of 25.7 mg/L (thus comparable with those found in the case in question and corresponding to the ingestion of approximately 8 g of the drug); the patient was lethargic and had mild hypotension upon admission to the hospital. Two days later, the patient was discharged from the hospital after a complete recovery. In another case, the ingestion of 6 g trazodone produced only drowsiness. Plasma concentrations of 15 and 19 mg/L (corresponding to the ingestion of approximately 4–5 g trazodone) produced toxic manifestations consisting only of drowsiness and ataxia (4).

The absence of direct cardiotoxicity and the absence of the affinity for muscarinic acetylcholine receptors (5) explain the often unsuccessful suicide attempts by trazodone overdose. The greater safety and minor incidence of lethal effects of trazodone in overdose, as compared with tricyclics, have been reported in the literature (6).

Nevertheless, trazodone should be used with caution in patients with cardiovascular disease (7) or when associated with other substances, including alcohol (4,8,9).

We are partially in agreement with the authors of the article in question; in fact, we would like to note that the blood concentrations of the tricyclic dothiepin found in the patient postmortem (approximately 40 times higher than therapeutic doses) could warrant the death of the patient.

In a study by the American Association of Poison Control Centers in 1989–90, desipramine, nortriptyline, amitriptyline, and imipramine have a relative risk of death from overdose of 16.88, 8.63, 6.06, and 7.53%, respectively, whereas the risk for trazodone is indicated as being only 1.00% (6).

In light of these facts, the final statement, “This case confirms the increased toxicity and the high mortality rate of a trazodone overdose, especially when concomitant administration of alcohol and other drugs is involved” (1) appears to penalize a drug that has been proven to be one of the safest in cases of overdose.

We think the words “high” and “especially” in particular may induce some misunderstanding.

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References

**The Authors Reply:**

We are fully aware of the greater safety and the minor incidence of fatalities in trazodone overdose cases as compared with intoxications with the established tricyclics. This is already stated in the Introduction of our original paper. We are also convinced that concomitant administration of other drugs seriously increases the risk of mortality in a trazodone intoxication case.

The respondent has a valid point in stating that the reported concentration of dothiepin in the postmortem sample (2.1 μg/mL) is very high. However, dothiepin overdose patients have recovered from much higher dothiepin concentrations in the blood (up to 3.8 μg/mL) (1). The contribution of each compound (dothiepin and trazodone) in terms of percentage to the fatal outcome in this particular patient is difficult—if not impossible—to evaluate.

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**Reference**