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Author's Response

Sir:

Thank you for the comments regarding our article *"A fatal drug interaction between oxycodone and clonazepam."* First, it should be noted that the dosages and concentrations in Table 1 are all referenced from previously published literature and are considered typical initial dosages and concentrations (1–3). There is a typographical error presented in Table 1 of our article. The maximum daily dose should have been printed as 20–320 mg/day. We appreciate the correction.

In regards to the reader's comment on the oxycodone dose ranging from 20–1360 mg, one would expect a wide variation in the dosage of oxycodone if it is titrated to the patient's subjective interpretation of pain, or lack thereof. As with any scientific investigation, there exist subjects who represent the "extrema" of a sigmoid dose-response curve. With regards to the *general* population, the mean, median, and typical ranges of therapeutic/toxic/lethal doses should be of concern. Even if oxycontin pharmacotherapy is individualized, a modest and reasonable starting dose should be used. Several investigations on the use of oxycodone for a variety of pathologies have revealed effective doses that fall within the range listed in Table 1 of our paper (4–6).

The wide range in dosage of oxycontin will obviously produce the wide range in plasma concentrations noted in the reader's references (7–9). The argument of subjects that exhibit extreme responses to therapeutic oxycontin administration also extends itself to toxic/lethal dosages and plasma concentrations. We feel that the range of plasma concentrations presented in our table encompasses the majority of patients. The reader stated that it would be impossible to determine a lethal plasma concentration. A basic principle of toxicology states that every substance can be toxic and/or fatal, it is simply a matter of dose and concentration. Typically these dosages are determined by an LD50 investigation. In *theory* it may be possible that a pure opioid agonist may not follow this principle, but *practically* and taken in context of the general population a toxic and/or fatal dose is obtainable with oxycontin. Obviously there is not a single numerical dose or plasma concentration of *any* drug that is therapeutic, toxic, or lethal in *every* individual. Hence, scientific investigations employ the use of population samples to get mean, median, and/or a range of dosages or concentrations. We feel that the dosages and plasma concentrations presented in Table 1 exhibit the *usual* dosages and blood concentrations applicable to a majority of the population.

Multiple factors are considered when determining a cause of death in a drug abuse death. The cause of death in this particular subject was not solely determined by the toxicology findings. As stated in the conclusion, the pathological findings as well as the toxicological findings suggest that the cause of death was due to anoxic conditions as a result of inadequate respiration from severe CNS depression. We agree with the reader's statement that "Multiple factors besides postmortem plasma concentrations should be considered when determining which substance or substances were the cause of a drug abuse death."

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