J Forensic Sci, September 2009, Vol. 54, No. 5
doi: 10.1111/j.1556-4029.2009.01141.x
Available online at: www.blackwell-synergy.com

Authors' Response

Sir,

We are appreciative of the letter from Zvosec and Smith, in identifying similarities between the case we reported (1) and some other GHB deaths recently reported by them (2). In their letter, the authors raise a number of issues about the safety of GHB and ask some specific questions about our reported case.

In our case, an autopsy was indeed performed, and we consider an autopsy to be critical in the investigation of all presumed drug-caused deaths. The decedent in our case weighed 105 pounds and was 5 foot, 2 inches tall. The GHB dose she was prescribed (7.5 g total nightly dose, divided into two doses of 3.75 g each) translates to 0.078 g/kg per dose. Medications prescribed to her (Xyrem, tramadol, gabapentin, Zyrtec, Provigil, and carisoprodol) were by five different doctors, which may well have led to the fatal outcome. Gabapentin was tested for but not detected.

Zvosec et al. are concerned that the manufacturer of Xyrem does not adequately warn patients about the risk of combined use of the drug with other sedative hypnotics; however, the package insert they cite (3) states "Sodium oxybate is contraindicated in patients being treated with sedative hypnotic agents," and the package insert we reviewed in our paper states "The combined use of alcohol (ethanol) with sodium oxybate may result in the potentiation of the central nervous system-depressant effects of sodium oxybate and alcohol. Therefore, patients should be warned strongly against the use of any alcoholic beverages in conjunction with sodium oxybate. Sodium oxybate should not be used in combination with sedative hypnotics or other CNS depressants."

Zvosec et al. also question whether there is adequate warning to patients with medical conditions which might interact with the drug, such as obstructive sleep apnea. The package insert we reviewed in our paper (4) states that sodium oxybate is a CNS depressant with the potential to impair respiratory drive, especially in patients with already-compromised respiratory function. It goes on to describe two patients seen during the clinical studies who discontinued use of sodium oxybate because of an increase in obstructive sleep apnea, and concludes that caution should be observed if Xyrem is prescribed to patients with compromised respiratory function. The decedent in our case had a dental appliance designed to reduce snoring and help maintain her airway at night, a treatment for sleep apnea. It is unknown when in the sequence of her sleep apnea treatment she was started on Xyrem.

Zvosec et al. also express concern that the patient's history of sarcoidosis was excluded as a contributory cause without an autopsy being performed. In fact as noted above an autopsy was performed, and while some contribution from that condition was noted, the death was found to be secondary to the intoxicating effects of the drugs. We agree that there is significant variability in the ways in which medical examiners evaluate and certify drug deaths, and support the need for an autopsy, a review of the patient's medical history, and comprehensive toxicology in all potential drug deaths.

References

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