Correspondence

In vitro Stability of Endogenous Gamma-hydroxybutyrate in Postmortem Blood

Sir:

We and others (1, 2) have previously described the nearly ubiquitous presence of apparent "endogenous" GHB (gamma-hydroxybutyrate) in postmortem blood at levels that encompass those sometimes attributed to GHB overdosage (3–6). We have now completed a brief study to determine the importance of storage conditions on the stability of GHB in postmortem blood.

Blood (and urine, when available) was collected from the inferior vena cava during the autopsies of 26 adults who died during August-September, 1997 of circumstances unrelated to GHB usage. The specimens were stored in glass containers with or without the presence of 10 mg/mL sodium fluoride at either room (25°C) or refrigerator (4°C) temperature. GHB concentrations were measured within 2 months by gas chromatography-mass spectrometry (7). The results are shown in Table 1.

It is apparent that room temperature storage had little or no effect on "endogenous" GHB concentrations in fluoride-preserved blood compared to refrigerated storage. However, the absence of fluoride resulted in a 50% higher average GHB value in refrigerated postmortem blood specimens, and the additional factor of room temperature storage of such specimens caused nearly a doubling of the already-elevated GHB content.

Our analysis of nonfluoridated urine for GHB from 17 of the 26 autopsies in this series (14 were undetectable, 3 had 5.1–9.5 mg/L) confirmed our previous experience (1) that postmortem urine does not appear susceptible to the mechanisms that produce such a dramatic rise in GHB levels in postmortem blood. Other investigators (8) have demonstrated a spontaneous postmortem increase of GHB in brain tissue, and have postulated that GHB is formed from GABA or succinic semialdelhyde during conditions of anoxia. We continue to suggest that postmortem urine is a better specimen than blood for the investigation of GHB-involved death.

TABLE 1—*GHB Concentrations in Postmortem Blood.*

n	NaF	Interval (days)*	Temp.	GHB (mg/L)†
6	yes	60	4°C	19 (<5–76)
			25°C	20 (9–65)
20	no	40	4°C	32 (<5–77)
			25°C	57 (9–433)

* Average duration from specimen collection to analysis.
† GHB concentration expressed as average and range (parentheses).

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Commentary on McIntyre IM, King CV, Staikos V, Gall J, Drummer OH. A fatality involving moclobemide, sertraline and pimozide. J Forensic Sci 1997;42:951–53

Sir:

We read with interest the case report by McIntyre et al. describing the death of a 22-year-old male who took moclobemide, sertraline and pimozide (1). Although the authors propose that serotonin syndrome was the cause of death, we believe that arrhythmia due to pimozide is a second possibility that should be seriously considered. Serotonin syndrome is characterized by neurologic manifestations and an occasionally fatal clinical picture including circulatory collapse, malignant hyperthermia, convulsions and rhabdomyolysis. Although we understand that legal restrictions may have limited the data available for publication, there is little evidence

of this symptom complex in the case history presented. Cases of moclobemide and sertraline induced serotonin syndrome have been described in the literature, but both drugs are rare causes of it.

On the other hand, pimozide cardiotoxicity is common and has been of great concern since its early development. This is because of the ability of pimozide to prolong the electrocardiographic QT interval in a concentration dependent manner (2). QT interval prolongation is associated with life-threatening arrhythmias of the torsade de pointes types and sudden unexpected cardiac death. In 1971, the Australian Adverse Drug Reaction Advisory Committee reported three cases of fatal cardiac disorders in patients younger than 37 years old who had taken pimozide (3). In 1995, the Committee on Safety of Medicines in the United Kingdom notified their physicians of an association between pimozide and serious arrhythmia, stating that they have received a total of 40 reports with 16 deaths since 1971 (4). Due to these safety concerns, pimozide is restricted in the USA to the treatment of Tourette's syndrome and the US Food and Drug Administration recommends an EKG before beginning treatment and periodically there after.

We have recently described a fatal case of pimozide toxicity that was associated with QT interval prolongation and sudden cardiac death (2). The concentration of pimozide measured from venous blood samples drawn during the resuscitative effort in this patient was 50 ng/mL (2). The concentrations of pimozide reported by McIntyre et al. (60 ng/mL antepartum and 130 ng/mL postpartum) are very likely to be cardiotoxic. The peak plasma concentration may actually have been higher than those reported as the time of ingestion is not known. Lastly, it is notable that hallucination and drowsiness noted in the patient are characteristics of pimozide toxicity. The possibility of sudden cardiac death due to pimozide should be considered in this case and when toxicity is observed in patients taking the drug.

References

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