



### K3 Interpretation of Postmortem Diphenhydramine Concentrations

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The goals of this research were to determine postmortem subclavian blood therapeutic concentrations of diphenhydramine and to compare them to reported therapeutic concentrations in living individuals. Attendees will be provided additional evidence that strict reliance on data from antemortem therapeutic concentrations to interpret postmortem blood concentrations may be risky and may lead to erroneous conclusions.

Diphenhydramine is a widely used over the counter therapeutic agent, appearing in a large number of cough and cold formulations, sleep-aids and anti-allergy medications. A recent study in Maryland identified diphenhydramine as the non-prescription therapeutic drug accounting for the most drug intoxication cases in the 1990s. Diphenhydramine continues to be frequently detected as an incidental finding in cases where death is due to other causes. Nevertheless, interpretation of diphenhydramine in these cases may have forensic relevance. A previous study in this office using heart blood specimens suggested concentrations less than 1.0 mg/L might be associated with therapeutic use.

Since the drug is alkaline extractable and has a volume of distribution of 3-4 L/kg, there is a potential for postmortem redistribution of the drug. In fact, there are a number of studies in the scientific literature that indicate postmortem redistribution of diphenhydramine does occur. To reduce the interpretive problems of postmortem redistribution, it has become common to analyze a drug from a peripheral site, such as femoral or subclavian blood instead of or in addition to heart blood. As a result, the previous study was revisited to determine whether a modification of the postmortem therapeutic range is necessary if a peripheral blood specimen is used.

Heart blood and subclavian blood specimens were quantitated for diphenhydramine in 38 cases where the medical examiner ruled that the presence of diphenhydramine was an incidental finding. Diphenhydramine was quantitated by gas chromatography-nitrogen phosphorus detection following an alkaline extraction and was confirmed by full scan electron ionization gas chromatography-mass spectrometry. A single point calibrator at a concentration of 0.8 mg/L was used for quantitation. With each batch, two blood controls at concentrations of 0.2 and 1.0 mg/L were analyzed. The limit of quantitation was 0.04 mg/L and the assay was linear to 2.4 mg/L.

Thirty-four of the 38 cases had a blood concentration less than 1.0 mg/L. The average and median heart blood concentrations were 0.67 mg/L and 0.26 mg/L, respectively; the average and median peripheral blood concentrations were 0.73 mg/L and 0.25 mg/L, respectively. One case had a heart blood concentration of 9.0 mg/L and a peripheral blood concentration of 10.6 mg/L. This case was a pedestrian who died of multiple injuries. If this case is excluded, the average heart blood concentration was 0.45 mg/L and the average peripheral blood concentration was 0.46 mg/L. The average heart blood to peripheral blood diphenhydramine concentration ratio was 1.11 and the median ratio was 0.96 (range 0.27-4.34). Seventy one percent of the cases (27 of 38) had ratios between 0.7 and 1.3. The differences between the heart blood and the peripheral blood concentrations were not statistically significant. The authors conclude that the postmortem therapeutic range for diphenhydramine for a peripheral blood specimen such as subclavian blood is similar to the range established for heart blood. As a result, there are not significant interpretive differences between postmortem heart blood and subclavian blood diphenhydramine concentrations. These concentrations are slightly higher than what is reported in studies conducted in living people where concentrations up to 0.3 mg/L are reported following therapeutic use. Therefore, this study provides additional evidence that strict reliance on data from antemortem therapeutic concentrations to interpret postmortem blood concentrations may be risky and may lead to erroneous conclusions.

#### **Diphenhydramine, Postmortem, Therapeutic**