K14 Serum and Blood Concentrations of the Oxcarbazepine (Trileptal®) Metabolite, 10-Hydroxy-Carbazepine

Lee M. Blum, PhD, Erica L. Horak, BS, and Robert W. Dalrymple, BA, National Medical Services, Inc., 3701 Welsh Road, Willow Grove, PA 19090*

After attending this presentation, attendees will learn about the observed serum/plasma and blood concentrations of 10-hydroxycarbazepine, the active metabolite of oxcarbazepine (Trileptal®), in a patient population.

This presentation will impact the forensic community and/or humanity by providing a review of such a population is important as either an elevated or a sub-therapeutic circulating level of anticonvulsant drugs such as oxcarbazepine can be a significant finding in a forensic investigation.

Serum and blood concentrations from over 53,000 specimens were reviewed for the 10-hydroxy-carbazepine metabolite of oxcarbazepine (Trileptal®). Oxcarbazepine is an anticonvulsant drug used for the treatment of partial seizures alone or as adjunct therapy in adults and as add-on therapy in children ages 4 to 16 with epilepsy. Although it is chemically similar to carbamazepine, its metabolism is different. Following administration, oxcarbazepine is rapidly reduced to 10-hydroxy-carbazepine which is primarily responsible for the anticonvulsant activity of the drug. It is available as 150 mg, 300 mg and 600 mg filmed capsules for oral administration. In adults, 1200 mg/day and 2400 mg/day are typically administered for adjunct therapy and monotherapy, respectively. In children, depending on their weight up to 1800 mg/day can be given. It's recommended that all doses be given in a twice a day regimen. Peak concentrations following a single dose are within 1-3 hours for oxcarbazepine and 4-12 hours for the metabolite. Steady state plasma concentrations of 10-hydroxy-carbazepine are usually achieved in 2 to 3 days. The half-life of the parent is approximately 2 hours while that of the metabolite is about 9 hours. The suggested target concentrations for therapeutic monitoring of 10-hydroxy-carbazepine have been reported to be approximately 13 – 35 mcg/mL. Common adverse effects related to oxcarbazepine therapy included dizziness, somnolence, diplopia, fatigue, nausea, vomiting and ataxia among others. A review of patient samples was performed to determine the observed ranges of serum/plasma (n=53,485) or blood (n=174) concentrations in a patient population. Because samples were received from other testing facilities, no histories or dosing regimens were provided. The analyses were performed by HPLC with a reporting limit of 0.5 mcg/mL. In the serum/plasma population, 2154 samples had no 10hydroxy-carbazepine detected. Of those patients with oxcarbazepine metabolite found, the concentration ranged from 0.5 to 110 mcg/mL with a mean = 16.9 ± 9.6 mcg/mL and a median = 16.0 mcg/mL. In those samples where blood was tested, 32 were none detected and the remaining patient samples had a mean = 18.9 ± 21.9 mcg/mL (range 0.5 – 140 mcg/mL) and a median = 14.5 mcg/mL. Approximately 60% of the serum/plasma samples, where 10-hydroxy-carbazepine was reported, were within the targeted therapeutic range of 13 – 35 mcg/mL, while about 45% of the blood samples were within this range. The percentage of samples greater than 35 mcg/mL was 4.2% for the serum/plasma samples and 9.9% for the blood samples. The serum/plasma concentrations with the highest frequencies of samples ranged between 9 and 18 mcg/mL. Although many factors may have influenced the concentrations observed, a review of such a population is important as either an elevated or a sub-therapeutic circulating level of anticonvulsant drugs such as oxcarbazepine can be a significant finding in a forensic investigation.

Oxcarbazepine, 10-Hydroxycarbazepine, Serum/Blood Concentrations

 ** Presenting Author*