



### **K30 Gabapentin, A Novel Adjunctive Agent: Case Review of Twenty-Two Postmortem Toxicology Investigations**

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This presentation will discuss the clinical uses and role of gabapentin in postmortem forensic toxicology.

Gabapentin (Neurontin) is indicated as an adjunctive antiepileptic drug (AED). It has been in clinical use since 1993 for the treatment of complex partial seizures. Although conventional AEDs such as carbamazepine, phenytoin and valproic acid continue to be the mainstay of clinical management, new generation therapeutics like gabapentin have emerged as useful adjuncts with low interaction potentials and improved tolerability. Gabapentin is not metabolized and does not bind to plasma proteins. Elimination of unmetabolized drug occurs via the renal route which likely accounts for the lack of hepatic drug interactions that are common to some of the other new anticonvulsant drugs (felbamate, lamotrigine and topiramate).

Gabapentin is a novel antiepileptic agent that binds to voltage-dependent calcium channels. However, the exact mechanism of action is somewhat elusive. Gabapentin was originally indicated for the treatment of partial epilepsy, but recent investigations into the adjunctive potential of gabapentin have resulted in more widespread use for other disorders including pain management, psychiatric illness and bipolar disorder. A review of the literature indicates potential uses for movement disorders, migraine prophylaxis and cocaine dependence.

Since the 1990s, gabapentin emerged as an alternative chronic pain treatment. It is used for the management of diverse symptoms associated with neuropathic pain in combination with other therapeutic agents. In particular, gabapentin is reported to increase the analgesic effect of morphine, indicating a pharmacodynamic interaction. Morphine pharmacokinetics are apparently unaffected, but gabapentin concentrations are reported to increase when used in combination with the opiate, indicating a pharmacokinetic effect.

The pharmacodynamics of gabapentin are not well understood, but studies have shown that in combination with morphine, it blocks dopamine release from the nucleus accumbens, and as a result, may have some clinical utility for the treatment of opioid dependence. There have been relatively few reports of drug interactions or toxicities associated with gabapentin. However, the correlation between blood concentration and clinical efficacy is unclear. This, in combination with the increased use of the drug as an adjunct for the treatment of nonepileptic disorders warrants further pharmacological investigation.

A total of twenty-two medical examiner cases involving gabapentin were reviewed. Postmortem blood concentrations ranged from 3 – 130 mg/L and all but one case involved multiple drug use. Case histories and toxicology results were consistent with adjunctive therapy for seizure and pain management. Common combinations included concomitant use of gabapentin with opiates (n=14), selective and nonselective serotonin reuptake inhibitors (n=13) and benzodiazepines (n=11). The majority of cases were attributed to accidental death. Case histories and toxicological findings are reviewed.

#### **Gabapentin, Postmortem Toxicology, Blood**