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Fulminant liver failure in a patient on carbamazepine and levetiracetam treatment

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AIM: A 22-year old female with a history of developmental delay and seizures successfully treated with carbamazepine and levetiracetam developed fulminant hepatic failure, and subsequently died. She was admitted to the hospital following secondary generalized seizures of 35-min duration. Intoxication was taken into consideration during the clinical course. Therefore, a LC-MS/MS method was enlarged to simultaneously determine levetiracetam besides carbamazepine in body fluids and tissues collected at autopsy.

METHOD: Postmortem specimens were screened for drugs and volatiles. Carbamazepine and levetiracetam concentrations were determined from blood and tissues such as liver, lungs, muscle and kidneys by LC-MS/MS following addition of lamotrigine as an internal standard and liquid-liquid extraction (pH 4.6, ethyl acetate). The method was fully validated (recovery from blood and tissue homogenate, linearity of response, intra- and interassay variation, ionsuppression/-enhancement).

RESULTS: The analytical method allows rapid and precise measurement of levetiracetam and carbamazepine even in difficult specimens. Both drugs were present in blood at concentrations within or below the therapeutic range. Moreover, tissue concentrations suggested long-term administration of carbamazepine and levetiracetam, which is in accordance with the medical history. Autopsy failed to determine a cause of death. The most significant finding on microscopic examination was a hyperacute liver damage with evidence of almost complete hepatocyte necrosis.

CONCLUSION: After excessive drug concentrations could be ruled out, death may have occurred as a result from the metabolic consequences of the prolonged seizure to cause severe hepatic injury. A mechanism of injury to the hepatocyte may be membrane damage by either an increased production of free radicals and/or a decreased free radical scavenging capacity.

KEYWORDS: *Fulminant liver failure, Carbamazepine, Levetiracetam*

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