P03-113

LIVER FAILURE UNDER VALPROIC ACID

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Valproic acid (VPA, 2-propylvaleric acid) is originally an antiepileptic drug, which has been in use for more than 30 years in over 100 countries. The clinical application of VPA has expanded in the last years. Approval has been granted by the FDA for treatment of migraine and cluster headache in 1996, and for treatment of mania and long-term prophylaxis of bipolar affective disorder in 1995. In ongoing studies, VPA has been reported to inhibit growth of several types of cancer cells; in addition, effects on neurodegeneration, and on virus replication in HIV infection have been demonstrated potentially expanding the application of VPA in the future. Despite a good tolerability of the drug, reports of hepatotoxicty even in patients without risk factors become more frequent. We analysed all cases of VPA induced severe hepatic side effects reported to the german Federal Institute for Pharmaceuticals & Medical Products (BfArM) between 1993 and 2009. A special intention was to detect correlations with present co-medication as a crucial factor in the break-down of hepatic function. As frequent co-medications in VPA-induced hepatic side effects benzodiazepines, and antiepileptics, especially carbamazepine, lamotrigine and topiramate were found. In addition, propofol as a co-medication was found in 4 lethal cases. Different pathomechanisms of VPA hepatotoxicity and a therapeutic approach with carnitine are discussed. Current international guidelines for prevention of VPA-induced liver failure are contrasted. Weekly control of liver enzymes in the first treatment weeks might help to detect VPA-induced hepatic side effects earlier.

https://doi.org/10.1016/S0924-9338(11)72987-X Published online by Cambridge University Press