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Drug points

Fatal lactic acidosis associated with tenofovir

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Recently introduced, tenofovir disoproxil is the first nucleotide analogue for treating HIV-1 infection.[1] We report a fatal case of lactic acidosis during treatment with tenofovir.

A 45 year old woman presented with vomiting, abdominal pain, and obtundation. She was HIV positive and had been recently treated with a combination of didanosine, stavudine, and nevirapine and had chronic hepatitis C. Because concentrations of liver enzymes had increased eight weeks before admission, nevirapine was stopped; concentrations then returned to initial values. Admitting doctors prescribed enteric coated didanosine (250 mg a day), stavudine (30 mg twice a day), and tenofovir (300 mg a day).

Three days before admission she had developed vomiting, abdominal pain, and then confusion and obtundation. On admission she was jaundiced and disoriented, and we felt tender hepatomegaly. Laboratory values were serum aspartate aminotransferase 2.35 µkat/l (normal range 0.18-0.58 µkat/l), serum alanine aminotransferase 2.68 (0.08-0.72) µkat/l, total bilirubin 215.46 (1.71-22.23) µmol/l, amylase 9.35 (0-1.67) µkat/l, lipase 57.58 (1.9-4.77) µkat/l, international normalised ratio for prothrombin time 2.12, blood pH 7.24, P_{CO_2} 2.38 (4.66-5.99) kPa, sodium bicarbonate 11.4 (22-26) mmol/l, and lactic acid 16.38 (0.6-1.7) mmol/l. Computed tomography showed fatty infiltration of the liver and slight enlargement of pancreas.

We discontinued antiretrovirals and gave her bicarbonate, vitamin K, thiamin, and riboflavin. Unfortunately, lactic acidosis worsened; she developed severe bleeding and died 36 hours later.

Tenofovir is being increasingly used even though its safety is not certain.[2] Because of its low affinity for mitochondrial DNA polymerase γ, tenofovir may be less toxic to mitochondria than nucleoside analogues and less likely to cause hyperlacticacidaemia.[3 4] But we believe that tenofovir was central to the onset of hyperlacticacidaemia because the woman died soon after taking the drug.

The woman had taken stavudine and didanosine without side effects. Tenofovir may have directly caused lactic acidosis or may have affected the toxicity of the other drugs. Taking tenofovir and didanosine together can increase didanosine concentrations by 60%, leading to hyperlacticacidaemia.[5] Patients who take tenofovir and didanosine should be closely monitored. Doses of didanosine should allow for simultaneous use of tenofovir.

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