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Contributors: See bmj.com

Funding: No participating centre directly received funds for involvement in TREC. GH undertook TREC as part of her work funded by the Ministry of Health, Brazil. TREC was jointly funded by Fundação Oswaldo Cruz, the Cochrane Schizophrenia Group, the British Council, CAPES (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior), and FAPERJ (Fundação de Amparo à Pesquisa do Estado do Rio de Janeiro). All salary funding was intramural. Drugs used in the trial were supplied by the local government through Secretaria Municipal de Saúde do Rio de Janeiro. A computer was given by the Resource Centre for Randomised Controlled Trials (www.rcrt.ox.ac.uk/).

Competing interests: None declared.

Ethical approval: TREC was approved by ethics committees from Escola Nacional de Saúde Pública Fundação Oswaldo Cruz, Instituto Philippe Pinel, and Hospital Municipal Jurandyr Manfredini, Instituto Municipal de Assistência à Saúde Nise da Silveira and by the members of the Consumer Advocate Group of Rio de Janeiro (SOSINTRA—Society of family and friends of

the mentally ill in Rio de Janeiro). TREC was also approved by the National Council of Ethics in Research.

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(Accepted 10 July 2003)

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 μ kat/l (normal range 0.18-0.58 μ kat/l), serum alanine aminotransferase 2.68 (0.08-0.72) μ kat/l, total bilirubin 215.46 (1.71-22.23) μ mol/l, amylase 9.35 (0-1.67) μ kat/l, lipase 57.58 (1.9-4.77) μ kat/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 hyperlacticaemia.³⁻⁴ But we believe that tenofovir was central to the onset of hyperlacticaemia 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 hyperlacticaemia.⁵ Patients who take tenofovir and didanosine should be closely monitored. Doses of didanosine should allow for simultaneous use of tenofovir.

Funding: None.

Competing interests: None declared.

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(Accepted 4 June 2003)

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BMJ 2003;327:711