

Serotonin Syndrome after Concomitant Treatment with Linezolid and Citalopram

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Linezolid, a new synthetic antimicrobial, is an important weapon against methicillin-resistant *Staphylococcus aureus* (MRSA). Although there are reports of serotonin syndrome developing after concomitant use of linezolid and the selective serotonin reuptake inhibitor paroxetine, this report concerns a patient receiving citalopram who developed thrombocytopenia, serotonin syndrome, and lactic acidosis and died following long-term linezolid therapy.

Linezolid (Pharmacia & Upjohn), a new synthetic antimicrobial, is an important weapon against methicillin-resistant *Staphylococcus aureus* (MRSA). This report concerns a patient who developed thrombocytopenia, serotonin syndrome, and lactic acidosis and died following linezolid therapy.

An 81-year-old man, afebrile and of normal mental status, underwent surgical debridement of ankle osteomyelitis due to MRSA. He had been receiving citalopram, 20 mg b.i.d., for 3 weeks prior to admission to the hospital. His other medications included low doses of prednisone and methotrexate, digoxin, trinitras transdermic patch, torasemid, insulin, and oxazepam. Following surgery the patient began linezolid therapy at a dosage of 600 mg b.i.d. The evolution of the infection was good, but after 1 week of linezolid therapy changes in the patient's mental status became apparent, and at week 3 the patient developed fever, high blood pressure, tachycardia, confusion, and tremors without localizable neurologic signs. Blood study results were as follows: alanine amino transferase, 66 U/L; total creatine phosphokinase, 766 U/L (mixed blood, 2.2%; platelet count, 96×10^9 cells/L; serum lactate level, 17.5 μ M; and total

CO₂ concentration, 9 mM. The findings of a CT scan of the brain were normal. During needle introduction for lumbar puncture the patient experienced a cardiac arrest. Following rapid intubation and ventilation, resuscitation without drugs was successful. The patient's serum lactate level rose to 29.1 μ M, and, in addition to severe lactic acidosis (pH, 6.9), the hepatic failure worsened. Cardiac ultrasonography showed major ventricular dysfunction. The patient died following 3 additional cardiac arrest episodes. An autopsy revealed drug encephalopathy and myocardial infarction; the latter probably occurred after cardiac arrest since the patient's cardiac isoenzyme and troponin levels were normal prior to the arrest. The results of bacterial cultures were negative, and no other abnormalities were noted.

An increasing number of reports have documented adverse reactions to linezolid, including thrombocytopenia [1–4] and liver toxicity [4]. Serotonin syndrome (fever, agitation with mental status changes, and tremors [5]) has been noted in 2 recent reports of concomitant use of the selective serotonin reuptake inhibitor (SSRI) paroxetine and oxazolidinone therapy [6, 7].

Linezolid therapy may not be a long-term treatment option for a number of patients, particularly elderly patients. If no other choice is available and linezolid must be administered to a patient receiving an SSRI, such as citalopram, treatment with the SSRI should be discontinued at least 2 weeks prior to starting linezolid therapy. In addition, one must be aware of the risks of lactic acidosis and serious liver damage, and close monitoring of the patient's blood count, hepatic function, and lactate level is mandatory.

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