Serotonin Syndrome after Concomitant Treatment with Linezolid and Meperidine

Parbodh K. Das,1,2 Dawn I. Warkentin,2,3 Robert Hewko,3,4 and Donna L. Forrest1,2
1Leukemia/Bone Marrow Transplant Program of British Columbia, British Columbia Cancer Agency, 2Vancouver Coastal Health, and Departments of 3Pharmaceutical Sciences, 4Psychiatry, and 5Medicine, University of British Columbia, Vancouver, British Columbia, Canada

Serotonin syndrome has been reported with administration of linezolid and serotonin reuptake inhibitors. Meperidine blocks the neuronal reuptake of serotonin. Serotonin syndrome after concomitant linezolid and meperidine therapy has not been described. We describe serotonin syndrome after concomitant use of linezolid and meperidine in a 27-year-old man with acute leukemia.

Linezolid is a reversible, nonselective inhibitor of monoamine oxidase [1]. Meperidine blocks the neuronal reuptake of serotonin and is contraindicated in patients who are receiving traditional monoamine oxidase inhibitors [2]. Serotonin syndrome has been reported with administration of linezolid and serotonin reuptake inhibitors [3]. However, serotonin syndrome after concomitant linezolid and meperidine therapy has not, to our knowledge, been described.

Case report. A 27-year-old man who received a diagnosis of acute myeloid leukemia initiated therapy with high-dose cytarabine and daunorubicin. On the first day of his chemotherapy, he was noted to be febrile and neutropenic and, therefore, began treatment with broad-spectrum antibiotics (timentin and tobramycin). Empirical liposomal amphotericin B (Ambisome; Astellas Pharma) was added to the treatment regimen on day 9 for persistent fever that was unresponsive to broad-spectrum antibiotics. Premedication with meperidine (25 mg administered intravenously before and halfway through administration of daily liposomal amphotericin B) was used for amphotericin-associated rigors. Six days after starting treatment with amphotericin, the patient remained febrile, and surveillance cultures revealed vancomycin-resistant enterococcus in the stool. Vancomycin therapy was discontinued, and treatment with linezolid was started for suspected vancomycin-resistant enterococcus sepsis. Two hours after the third dose of linezolid and 0.5 h after meperidine was given, the patient appeared to have marked psychomotor agitation. He was tremulous with myoclonus and was exhibiting paranoid ideation with transient visual hallucinations. His vital signs were as follows: temperature, 40.5 °C; respiratory rate, 26 breaths/min; heart rate, 120 beats/min; and blood pressure, 125/50 mm Hg. The findings of cardiovascular and respiratory examinations were essentially normal. It was difficult to perform a CNS examination because of the patient’s acute confused state. The laboratory profile revealed normal electrolyte levels and normal renal and hepatic function, and a CT scan of the head had normal findings. Treatment with meperidine was discontinued, and methotrimeprazine hydrochloride was given for agitation. The neuropsychiatric symptoms resolved within 2 h, and the patient defervesced while receiving broad-spectrum antimicrobial therapy.

Discussion. Serotonin syndrome is a potentially severe adverse drug interaction characterized clinically by the sudden onset of altered mental status, autonomic dysfunction, and neuromuscular abnormalities. Not all of these findings are consistently present in all patients [4]. This syndrome has been reported with concomitant administration of nonselective monoamine oxidase inhibitors (such as linezolid) and serotonin reuptake inhibitors [4]. In particular, drugs that inhibit monoamine oxidase type A are strongly associated with severe cases of the syndrome, especially when these agents are used in conjunction with meperidine, dextromethorphan, and other similar drugs that are known to block the neuronal reuptake of serotonin.

Our patient received meperidine 90 min after his third dose of linezolid, and he became symptomatic 30 min later. The diagnosis was made on the basis of the sudden onset of altered mental status, myoclonus, and autonomic dysfunction in the context of normal biochemical test results and normal findings of a CT of the head. As in the case of our patient, the symptoms associated with serotonin syndrome are usually rapidly reversible when treatment with the offending drugs is discontinued.

To the best of our knowledge, this is the first report of
serotonin syndrome with concomitant use of linezolid and meperidine. This can be of major clinical significance in view of the increased use of linezolid in treating patients with leukemia who are receiving numerous other medications with serotonin reuptake inhibitor properties.

Acknowledgments

Potential conflicts of interest. All authors: no conflicts.

References