SEVERE DELIRIUM FOLLOWING SINGLE DOSE OF TRAMADOL

Sir,

Given the volume of use of analgesic preparations with approved indications for acute pain, a number of drug interactions including less well-known and potentially clinically significant drug-drug interactions are increasingly being reported.[1] A 32-yearold male on treatment for cysticercosis was receiving Tab. albendazole, phenytoin, steroids and ranitidine. Meanwhile, the patient developed allergic rhinitis, fever, body and joint pain. His general and systemic examination was normal. He was started on cetrizine for allergy and tramadol for body and joint pain. There was no concomitant use of antidepressants. The patient continued to receive Tab. albendazole and oral steroid without any change in dosage. After 6 hours he developed violent behavior and delirium. There were no myoclonic twitches or muscular rigidity. On examination he had tachycardia and excessive sweating. Pupils were bilateral 3 mm in size? and reacting to light. Bowel and bladder functions were normal. Blood investigations showed raised erythrocyte sedimentation rate, blood urea and serum creatinine were normal. Facilities for estimation were not available. The abnormal behavior could be controlled with haloperidol and both the drugs (tramadol and cetrizine) were discontinued. The Naranjo score^[2] for adverse drug reaction was 9. There was no history of any significant illness prior to cysticercosis and he was not an alcoholic. He responded well and recovered completely. Although tramadol may represent a well-established, safe therapy for pain,^[3-5] abuse and dependence on tramadol as well as tramadol-related deaths have been increasingly reported, either when the drug is ingested alone or taken in combination with other potentially interactive drugs.[5-7] Mild and transient central nervous system stimulation during therapy with tramadol has been reported in 7% of patients in clinical trials.^[7] The debilitating reaction following a single oral dose of tramadol may include ataxia, dilation of the pupils, numbness, tremulousness, and dysphoria lasting for hours and disappearing after discontinuation of the therapy.^[7] Rarely may it lead to fluctuating confusion and cognitive deficits (reversible after discontinuation of the drug).^[8] The exact mechanism of the adverse response is not known; however, based on phenotyping results, it has been suspected that it may be related to high concentrations of the active O-desmethyl metabolite of tramadol.[7]

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