Tramadol-induced respiratory depression in a morbidly obese patient with normal renal function

Sir,

Among opioids, tramadol hydrochloride is considered safer than other opioids with respect to its respiratory effects. Dose of tramadol in post-operative patient is up to 250 mg intravenous (i.v.) in initial hour and 600 mg in 24 h.[1] The metabolite of tramadol, O-desmethyl tramadol, (+ODT) has been shown to have an affinity for μ opioid receptors (200 times) than that of parent drug and is responsible for analgesia. Tramadol-induced respiratory depression was reported previously in patients with altered renal function.[2] We report such an event in a morbidly obese patient but with normal renal and hepatic functions who received tramadol in clinical doses.

A 50-year male, weighing 143 kg (BMI: 50.7 kg/m^2), ASA 2 classification, was without any co-morbidity was scheduled for surgery for thigh reduction-plasty [Figure 1]. Nonsmoker nonalcoholic patient with good exercise tolerance reported two uneventful previous surgeries two years ago. He had no history suggestive of obstructive sleep apnoea (OSA) syndrome. Patient had normal renal, liver, cardiovascular function tests. Though pulmonary function tests [Figure 2] were suggestive of early minimal small air way obstruction, after consultation with pulmonologist, it was concluded as adequate. Pre-operative arterial blood gas (ABG) showed pH of 7.347, pCO_2 of 55.5 mmHg, pO_2 of 73.2 and saturation of 90%.

Operating table width was adjusted with additional supports to accommodate hugely built patient.

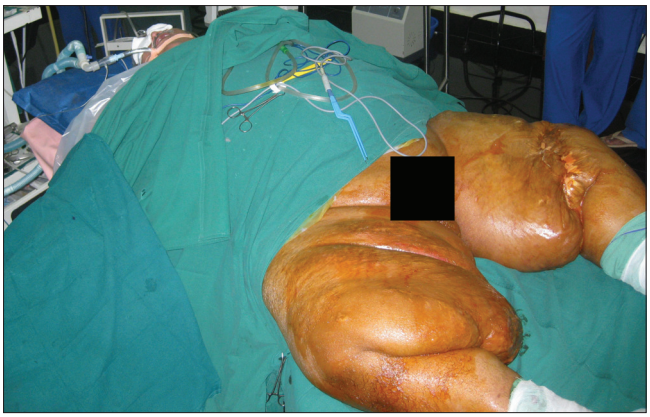

Figure 1: Morbidly obese patient under anaesthesia for thigh reduction plasty

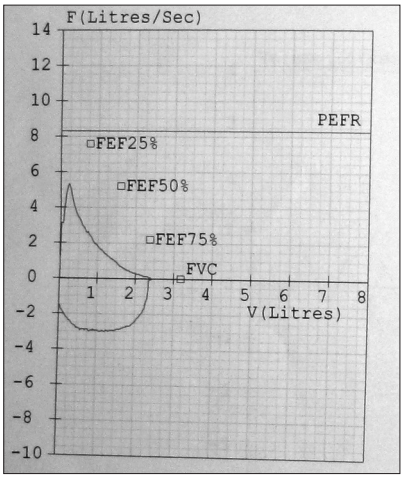

Figure 2: Preoperative pulmonary function testing curves. (FVC of 75% of predicted, FEV1 of 68% of predicted, FEF25-75 of 33% of predicted and FVV1/FVC ratio of 90% of predicted)

Anaesthesia was induced with fentanyl (150 μg i.v), inj. Propofol (2.5 mg/kg) and succynylcholine (1.5 mg/kg). Sevoflurane-vecuronium-fentanyl (150μg) was used for maintenance. During the uneventful surgery, patient received three units of whole blood, inj. diclofenac sodium 75 mg (i.m). Extubation was uneventful.

In the first hour of post-operative period, patient complained severe pain at the operating site. Inj. tramadol 200 mg i.v. was advised and ordered to repeat 8th hourly. Four hours later, patient had adequate pain relief. Second dose of tramadol was administered at 8th hour. Patient was found increasingly drowsy and further tramadol injection was omitted. Patient became unresponsive at 17th hour with sluggish low respiratory rate breathing. ABG showed pH of 6.989, pCO_2 of 121.4 mmHg, pO_2 of 57.1 mmHg, HCO_3 of 28.6 mmol/l and SpO_2 of 65%. Emergency intubation was done and mechanical ventilation was started. Inj. Naloxone 0.4 mg i.v. was administered. Subsequently, patient was conscious with adequate mechanical ventilation. ABG parameters improved further. Patient was extubated at 28th hour.

In clinical practice, respiratory depression by tramadol is extremely rare.[3] Previous studies shown unaltered end-tidal CO_2 changes or respiratory functions with tramadol usage in contrast to injection morphine[4] or pethedine[5] in spontaneously breathing patients. Further, the respiratory rate, arterial O_2 and CO_2 tensions were found normal in spontaneously breathing patients following upper abdominal surgeries who received epidural tramadol.[6] Teppema *et al.*[7] observed dose dependent respiratory depression due to tramadol in cats in doses 1-4 mg/kg and highlight the similar possibility in humans in the early postoperative period when residual anaesthetic effects still existing. However, our patient had dose of 1.5 mg/kg and the respiratory effects were observed in late post operative period where anaesthetic effects are ruled out.

Our patient had minimally altered but adequate pulmonary functions. Preoperative ABG showed minimally increased CO_2 levels, a significant increase in CO_2 level and unresponsiveness followed tramadol injections suggesting the possibility of respiratory depression by tramadol. Should the primary cause of respiratory depression be due to pulmonary insufficiency, then patient would have developed respiratory failure in the early post operative period itself when the residual anaesthetic effects still persist. Our patient had excellent recovery from anaesthesia. Conscious patient with complete cognitive and neuromuscular recovery usually need further sedation (and paralysis) for elective mechanical ventilation. Further, respiratory function was unaffected by the surgical incision. Thus, elective mechanical ventilation was not considered.

Respiratory depression following iatrogenic tramadol overuse can occur in individuals carrying CYP_2D_6 duplication (ultrarapid metabolisers, UM).[8] These patients display increased enzyme activity for tramadol, resulting highly increased transformation to active metabolite (+)ODT. However, Asian population have the lowest incidence of 0.5%-2.5% of the CYP_2D_6 UM genotype, compared to other continents, and the possibility of having such a genotype in our patient could be rare. Routine screening tests for UM genotyping (by polymerase chain reaction) may

not be economically feasible, which is a limiting factor to investigate further in our clinical settings.

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