Fentanyl, rather than Tramadol: A cause of respiratory depression

Sir,

We read with interest the case report “Tramadol – induced respiratory depression in a morbidly obese patient with normal renal function” by Thrivikrama P Tantry et al.[1] We agree with the authors that respiratory depression in clinical practice by Tramadol is extremely rare, for which the authors have given the references of studies of Tramadol and unchanged end tidal carbon dioxide (EtCO₂), respiratory rate and blood gases. The only study quoted by the authors of respiratory depression due to Tramadol was performed on cats, and no similar study on human beings has been reported. The possible cause of respiratory depression following Tramadol injection as discussed by the authors could be CYP₂D₆ duplication in this patient. Simultaneously, they have also admitted that the Asian population has the lowest incidence of CYP₂D₆ UM genotype compared with other continents, and the possibility of having such a genotype in this patient is rare. We could find only one case report[2] of Tramadol-induced respiratory depression in a human being, and the patient had both CYP₂D₆ genotype duplication as well as renal impairment. As this patient had normal renal functions and also the screening for CYP₂D₆ genotype duplication by polymerase chain reaction (PCR) was not done, we should look for the other possible causes of delayed respiratory depression in this patient.

There is ample evidence available in the literature regarding Fentanyl causing delayed respiratory depression in the post-operative period. The case reports published by Adams and Pybus[3] showed delayed respiratory depression due to Fentanyl up to 4 h after the surgery in the post-operative period. The study conducted by Hess et al.,[4] cited the cause of delayed respiratory depression by Fentanyl due to increase in free plasma concentration and secondary peak occurring several hours after the last dose of the drug administered due to the diffusion of drug back into the plasma from adipose tissue and skeletal muscles. Rigg and Goldsmith[5] compared the respiratory depression with different drugs using the CO₂ response curve as an index. They reported that the magnitude and duration of respiratory depression with just 1.3 mcg/kg Fentanyl was comparable to those of an equianalgesic dose of morphine and, compared with other drugs, Fentanyl had a significant respiratory depressant effect in the post-operative period. In a study on 26 patients, Becker et al.,[6] showed that fentanyl has a biphasic effect on the ventilatory response to CO₂. The maximum respiratory depression was found shortly after intravenous administration of the drug, which then decreased steadily. Continued monitoring showed that a second phase of respiratory depression occurred maximally at 160 min after the last dose of narcotic. Caspi et al.,[7] reported a sudden onset of extreme abdominal and thoracic rigidity, leading to respiratory depression in 15 patients, 2–6 h after the last dose of Fentanyl after an apparently normal recovery from anaesthesia, which was rapidly reversed with Naloxone.

We believe that instead of Tramadol, the delayed respiratory depression in the reported patient was due to Fentanyl (total 300 mcg), to which the sedative effect of injection Tramadol (total 400 mg) was added and the patient thereafter developed CO₂ narcosis and became...
unresponsive. The administration of Naloxone in the post-operative period, when the patient was found to be drowsy for the first time, could have reversed the respiratory depression due to Fentanyl and prevented the need for mechanical ventilation at the 17th hour. As the patient was found to be “increasingly drowsy”, there has to be a time period when the patient appeared drowsy for the first time. The arterial blood gas (ABG) at the 17th hour shows pH of 6.989 and pCO₂ of 121.4 mmHg. This could not have happened all of a sudden in this patient. The increase in the levels of arterial pCO₂ must have begun several hours prior to the 17th hour. Hence, serial ABG analysis in the early post-operative period could have helped to pick up the rising trend of PaCO₂ much earlier than when the patient became unresponsive, subsequently requiring mechanical ventilation.

This patient was an elderly obese male with obstructive airway disease and chronic respiratory failure. His pre-operative saturation was 90% with PaO₂ 73.2 mmHg, PaCO₂ 55.5 mmHg and pH 7.347. His pulmonary function tests showed FEF25–75 value of 33%, which is an effort independent test and indicates severe degree of obstructive airway disease. This patient was operated for thigh reduction plasty under general anaesthesia (GA). We are surprised why regional anaesthesia (RA) was not considered in this elderly obese patient of chronic obstructive pulmonary disease elderly obese patient of chronic obstructive pulmonary disease. The reason for opting for GA instead of RA by the authors in this morbidly obese patient was based on “unpublished, personal experience”.

The case report is based on “presumption”, “suspicion”, “exclusion” and “unpublished personal experience”. The fact remains that respiratory depression with Tramadol in a patient with normal renal function has never been reported. It appears that the authors have overzealously tried to publish it as the first ever case report of respiratory depression with Tramadol, without any supportive evidence.

Ghansham Biyani, Sadik Mohammed, Pradeep Bhatia
Department of Anaesthesiology and Critical Care, Dr. S N Medical College, Jodhpur, Rajasthan, India

Address for correspondence:
Dr. Pradeep Bhatia,
A 54/3, Anvind Nagar, Golf Link Road, Jodhpur - 342 011, Rajasthan, India.
E-mail: pk_bhatia@yahoo.com

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Potassium chloride: A high risk drug for medication error

Sir,

Despite the improved system of manufacturing, packaging and delivery, 44,000-98,000 patients die each year as a result of medical error. [1] Potassium chloride has been involved in many fatal incidences in the past. Between 1996 and 1998, the Joint commission for Accreditation of Healthcare Organizations (JCAHO) found 10 deaths due to wrong administration of potassium chloride, and six cases of these were due to identical labels. The Commission recommended that concentrated potassium chloride should not be made available outside the pharmacy unless appropriate specific safeguards are in place.[2,3] Recently, another near fatal report of medication error with potassium chloride has been published. [4] The 12 points recommendations [Table 1] about pharmacist’s and multidisciplinary professional’s role in preventing medication error with potassium chloride have been