Cardiac arrest from tramadol and fentanyl combination

Sir,

Tramadol is a centrally acting atypical opioid analgesic commonly used in the treatment of moderate to severe pain. It has a low affinity to μ opioid receptors and also inhibits the reuptake of serotonin and norepinephrine. Fentanyl is a potent, synthetic opioid with a rapid onset of action and strong affinity to μ receptor. Both the drugs are considered to have a high safety profile and used widely in anaesthesia. Fentanyl and tramadol impair presynaptic reuptake of serotonin and in combination with other serotonergic medications can cause serotonin syndrome. We report a case where premedication with the two drugs in therapeutic doses led to serotonin syndrome with severe life-threatening cardiac arrhythmia.

A 43-year-old male American Society of Anaesthesiologists physical status1 patient, with radicular pain was scheduled for C5–6 anterior cervical discectomy. He was on gabapentin 150 mg tid and ibuprofen 200 mg bid for pain relief since 1 month. Preanaesthetic evaluation had been insignificant, and and so was the examination prior to shifting into the theatre. After connecting standard monitors and preoxygenation, intravenous (i.v.) fentanyl 50 μg (0.83 μg/kg, in dilution of 1 ml = 50 μg) was administered. Patient was agitating, and pain was thought to be the cause of his agitation. For the fear of developing chest wall, rigidity another agent was considered instead of higher doses of fentanyl. I.v. tramadol 75 mg (1.25 mg/kg, in dilution of 1 ml = 20 mg) was administered slowly over 2–3 min. Immediately a supraventricular rhythm (SVT) with a rate of 180/min and ventricular ectopics were noted on the monitor. It soon deteriorated to ventricular tachycardia (VT) and then into ventricular fibrillation (VF).

Cardiopulmonary resuscitation (CPR) was initiated, and airway was secured with endotracheal intubation. Defibrillation with biphasic mode (200 J) was administered thrice during the CPR cycle without sustained sinus rhythm. Injection amiodarone 300 mg bolus was administered after 3rd shock after which sustained sinus rhythm was achieved. After initiating maintenance amiodarone infusion (0.5 mg/kg/h for 24 h) and vasoactive support (noradrenaline and adrenaline infusion at 20 mcg/min) patient was shifted to the intensive care unit (ICU).

In the ICU, ventilation was continued for a day with midazolam and morphine for sedation and analgesia. A bedside echocardiogram revealed a good cardiac contractility and output. Induced hypothermia at 34°C was maintained for the day. The next day vasoactive drugs were weaned off, and the patient was awake and successfully extubated. Amiodarone was changed to oral mode of administration and patient was discharged to the ward on 2nd day.

The combination of tramadol and fentanyl for premedication is seldom used. The combination has improved tolerance for awake endotracheal intubation[1] and has reduced the incidence of supraventricular arrhythmia in patients undergoing pulmonary resection.[2]

Fentanyl associated fatalities have been primarily due to respiratory depression as even low concentrations lead to it.[3] Life-threatening central nervous system (CNS)

and cardiac complications are generally found after tramadol ingestion at high doses with unintentional or intentional suicidal attempts. Ahmadi *et al*., after analysing the cases of tramadol intoxication found mortality rate of 0.97%. Most of the cases have been reported in conjunction with other drugs such as CNS depressants.[4] However, Shadnia *et al*., reported two fatalities with tramadol intoxication without any co-ingestions.[5]

In therapeutic doses, both tramadol and fentanyl have been implicated in serotonin toxicity though tramadol is more notorious for severe toxicity.[6] Serotonin toxicity is marked by the triad of neuromuscular excitation, autonomic stimulation and changes in mental state. Based on the clinical profile we suspected serotonin syndrome to be causative for the complication in our patient. The features of toxicity from drug combination develop rapidly after onset of effective blood levels of the second drug. The autonomic features such as tachycardia and tachypnea are not usually severe.[6]

In our patient, the administration of i.v. fentanyl initiated the toxicity features (agitation) which became more pronounced with tramadol dose. However, the cardiac signs erstwhile considered not to be of serious consequence, in our patient caused near fatal arrhythmia. The rhythm quickly transformed from SVT to VT and then to VF [Figure 1].No role of use of gabapentin preoperatively in this peroperative drug interaction between fentanyl and tramadol could be explained.

To our knowledge and belief, this is the first report of serotonin toxicity with tramadol and fentanyl combination, in therapeutic doses without any other serotonergic medication. The inability to monitor serum drug level has been a limitation, but the absence of any other drug administered prior to fentanyl and tramadol effectively establishes the aetiology.

This case report highlights the dangers of combining two drugs with potential of serotonin toxicity and the severity of cardiac complication that can even be near fatal.

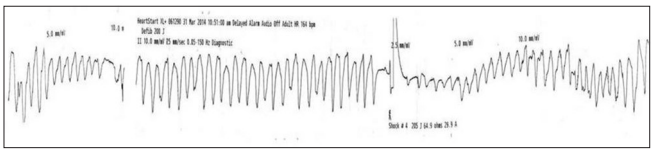

Figure 1: Electrocardiogram tracing of the rhythm during cardiopulmonary resuscitation

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