

## Tramadol Ultra Rapid Metabolizers at Risk for Respiratory Depression

### **To the Editor:**

Re: "A Costly Lesson: Fatal Respiratory Depression Induced by Clindamycin during Postoperative Patient Controlled Analgesia" *Pain Physician* 2015; 18:E429-E431

In regards to a recent article by Gao Wu and colleagues (1), the authors fail to recognize the potential of tramadol infusion contributing to the patient's respiratory depression and cardiac arrest. Tramadol is a relatively safe centrally acting analgesic devoid of any serious adverse events associated with traditional opioids via respiratory depression and dependence. However, tramadol is a prodrug for the active metabolite O-desmethyltramadol (O-DSMT), which together with the parent compound, acts by binding mu opioid receptors and inhibiting the reuptake of serotonin and norepinephrine. In a subset population, notably patients who are P450 CYP2D6 ultra rapid-metabolizers, tramadol has been associated with near fatal respiratory depres-

sion and cardiotoxicity (2).

This patient received a basal rate of 10 mg/hour of Tramadol with 20 mg bolus dose at a lockout interval of 30 minutes. Total 24 hours PCA dose of tramadol was 500 mg. The elimination half-life of O-DSMT is near 7 hours. If patient was an ultra-rapid metabolizer, increasing the level of O-DSMT and possible blood epinephrine levels could have contributed to her demise.

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### **REFERENCES:**

1. Wu G, Wu G, Wu H. A costly lesson: Fatal respiratory depression induced by clindamycin during postoperative patient controlled analgesia. *Pain Physician* 2015; 18:E429-E431.
2. Elkalioubie A1, Allorge D, Robriquet L, Wiart JF, Garat A, Broly F, Fourrier F. Near-fatal tramadol cardiotoxicity in a CYP2D6 ultrarapid metabolizer. *Eur J Clin Pharmacol* 2011; 67:855-68. Epub 2011 Jun 21.