

Brief Commentary

A Costly Lesson: Fatal Respiratory Depression Induced by Clindamycin during Postoperative Patient Controlled Analgesia

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Many drugs can cause neuromuscular blockade. Clindamycin-related neuromuscular blockade is commonly reported, but fatal clindamycin-induced neuromuscular blockade is rarely reported. We describe a 47-year-old woman who initially presented with endometrial carcinoma. She underwent a laparoscopic-assisted vaginal hysterectomy (LAVH) and bilateral adnexectomy under general anesthesia, secondary to antibiotic treatment with clindamycin 1.2g in 250 mL for about 30 minutes through the peripheral intravenous route during postoperative patient controlled analgesia (PCA). She became unconscious near the end of the infusion, then, despite resuscitation attempts, she died. Clindamycin appeared to have triggered delayed respiratory depression during PCA. A combination of clindamycin and fentanyl led to her respiratory depression in the fatal case.

Key words: Respiratory depression, clindamycin, fatal case, postoperative patient controlled analgesia

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In addition to having antibacterial effects, clindamycin blocks neuromuscular conduction and enhances the effects of non-depolarizing agents (1,2). For this reason, anesthesiologists are very concerned about the clindamycin-related neuromuscular blockade. However, after leaving the post anesthetic care unit (PACU), the clinician may ignore interaction between clindamycin and other drugs (for example opioids). Delayed respiratory depression triggered by clindamycin during postoperative patient controlled analgesia (PCA) is not reported in the literature. The purpose of this brief commentary is to record such a fatal respiratory depression associated with clindamycin.

A 47-year-old woman (weight: 37.0 kg; height: 150 cm) with endometrial carcinoma was scheduled for a laparoscopic-assisted vaginal hysterectomy (LAVH) and bilateral adnexectomy under general anesthesia. She had no history of known drug allergies but did have a history of cholecystectomy under general anesthesia.

On the patient's arrival in the operating room, standard monitoring were applied. Her vital signs were normal. After breathing oxygen from a face mask, induction of anesthesia was carried out with midazolam 2 mg, fentanyl 150 µg, and etomidate 20 mg. Three minutes later, succinylcholine 100 mg was given, and tracheal intubation (rapid sequence) was applied. Anesthesia was maintained with nitrous oxide, 60 – 65% in oxygen supplemented with sevoflurane, and by administration of propofol 200 mg and cis-atracurium 8 mg iv. During the operation, more fentanyl (100 µg) was given in divided doses. At the end of surgery, which took about half an hour, atropine 0.5 mg and neostigmine 1 mg were given. The patient received PCA with a total dose of fentanyl 300 µg and tramadol 500 mg in a 100 mL solution in 24 hours in the PACU. The PCA machine was programmed to continuous infusion of 2mL·h⁻¹, a bolus dose of 4 mL, and a lockout interval of 30 minutes. Thirty minutes later, the patient's condi-

tion remained satisfactory while she was in the PACU, with a train of 4 (TOF) > 0.8. Later she returned to the ward, where she talked to visitors coherently. The patient's heart rate was 76 beats/min, and the rhythm was sinus. The blood pressure was 118/70 mmHg. The respiratory rate was 17 breaths/min. The temperature was 37.3°C. Vital signs was stable until cefotiam (2 g) and pantoprazole (40 mg) were be given intravenously, respectively. Subsequently clindamycin (Clindamycin Hydrochloride, 1.2 g in 250 mL 0.9% sodium chloride solution) was infused for about 30 minutes through the peripheral intravenous route. Within 5 minutes after the clindamycin was almost totally infused, the patient felt nausea and fell asleep. Approximately 3 minutes later, she cyanosed with a deep respiratory depression followed by a fatal cardiac arrest. Immediately, cardiopulmonary resuscitation was performed, but was not able to revive her.

Our patient developed fatal respiratory depression associated with the use of intravenous clindamycin and PCA. This may be due either to peripheral clindamycin-related neuromuscular blockade or central depression produced by opiates or postoperative residual neuromuscular blockade.

Fentanyl is widely regarded as a short-acting opiate, but fentanyl has a significant respiratory depressant effect in the postoperative period (3,4). Fentanyl was administered in the surgical sedation and postoperative analgesia in the case. However the patient was still speaking with her family members and her respiratory rate was 17 breaths/min a few minutes before the fatal incident. In addition, the patient, who underwent the same routine general anesthesia and PCA in another surgery a few years ago, did not develop respiratory depression. For that reason, the clinicians didn't monitor the patient in the postoperative period. Therefore, interpretation of the fatal event was completely not based on establishing a causal relationship between the fentanyl and the fatal respiratory depression.

The main risk factor known to be associated with development of a respiratory arrest secondary to fentanyl is clindamycin. Clindamycin triggers muscular relaxation and creates a prolonged blockade of non-de-

polarizing muscle relaxants, irrespective of the presence of neostigmine (5,6). Neuromuscular blockade is associated with many antimicrobial agents, including aminoglycosides and the polymyxins, etc. There are reports that these drugs may cause respiratory depression. But the mechanism of clindamycin-induced neuromuscular block is different from other antibiotics (7). Clindamycin appears to cause muscle relaxation predominantly by a direct action of contractility rather than by inhibition of neuromuscular transmission. This may be the reason that clindamycin had fewer reports of respiratory depression compared with other neuromuscular blocking antibiotics. There is a report of a profound neuromuscular block from clindamycin that was given to a patient who fully recovered (TOF of 1.0) (8). So neuromuscular blockade would appear in our patient when clindamycin was infused. This supports the assumption that clindamycin enhances the postoperative residual neuromuscular block in the patient when the fatal event took place, even if it is very small. A further factor contributing to the fatal outcome was the very high clindamycin dosing and rapid infusions. According to previous experience, the recommended maximum dose is no more than 1.2 g one hour and 30 mg/min (9). Therefore, the intravenous dosage of clindamycin 1.2 g for about 30 minutes to a patient who weighed only 37 kg was undoubtedly inappropriately high. We speculate that clindamycin peripheral ganglia muscle inhibition may trigger delayed respiratory depression induced fentanyl and synergistic effect of clindamycin and fentanyl led to her respiratory depression in the fatal case, which suggests that the combined use of clindamycin and PCA should be prudent in order to avoid Respiratory depression in the immediate postoperative periods. Even though anesthesiologists might have mastered the knowledge, other physicians should also be fully aware of the actions and side effects of the antibiotics. It is imperative that all health care professionals who either prescribe or care for patients receiving clindamycin and PCA in immediate postoperative periods be aware of this potentially fatal complication and remain vigilant at all times in monitoring the patients.

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