

Accidental injection of remifentanyl can cause a much more dangerous situation than the same dose of fentanyl

Takayuki Kunisawa · Michio Nagashima ·
Akihiro Suzuki · Osamu Takahata ·
Hiroshi Iwasaki

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To the Editor:

The duration of the action of remifentanyl is clearly much shorter than that of fentanyl. The distribution volume of remifentanyl is much smaller than that of fentanyl and the elimination half-life of remifentanyl is extremely short compared with that of fentanyl [1, 2]. Bolus injection of fentanyl can be used for relief from pain caused by an invasive procedure such as epidural catheterization. Two micrograms per kilogram of fentanyl is considered to be safe based on some reports [3, 4]. If that dose of fentanyl is administered to a patient (assumed to be a 50-year-old female with a height of 150 cm and weight of 50 kg) for pharmacokinetic (PK) simulation, the effect-site concentration (ESC) calculated using the pharmacokinetic model TIVA Trainer version 8 (<http://www.eurosiva.org>; calculation interval of 1 s) with Shafer's parameter [1] never reaches 2 ng/mL—which is considered to be the maximum concentration that has no effect on respiration—after bolus injection (Fig. 1). In contrast, if the same dose of remifentanyl was used instead of fentanyl, what would happen? PK with Minto's parameter [2] shows that the ESC of

remifentanyl can reach 7.08 ng/mL and remains over 2 ng/mL for 7 min and 19 s (Fig. 1). Since the above concentration of remifentanyl can easily cause respiratory depression, an accidental injection of remifentanyl may cause a critical situation.

This occurs because ke_0 (the plasma effect-site equilibrium constant) of remifentanyl is larger and the rapid distribution volume of remifentanyl is smaller than those of fentanyl. Thus, knowledge of PK is required in order to avoid risk even in a simple situation such as the above example, and the bolus injection of 2 $\mu\text{g}/\text{kg}$ of remifentanyl should not be performed.

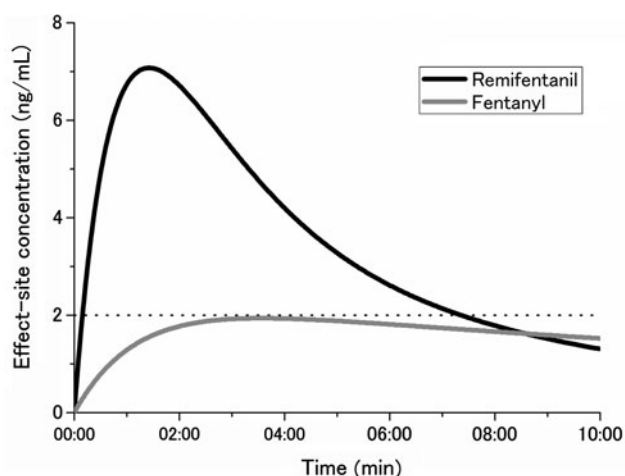


Fig. 1 ESCs of fentanyl and remifentanyl after the bolus injection of 2 $\mu\text{g}/\text{kg}$. The patient in the PK simulation is assumed to be a 50-year-old female with a height of 150 cm and a weight of 50 kg. The ESC of fentanyl never reaches 2 ng/mL after bolus injection. The ESC of remifentanyl exceeds 2 ng/mL 10 s after bolus injection, increases rapidly to 7.08 ng/mL, and remains over 2 ng/mL for 7 min and 19 s. ESC, effect-site concentration

T. Kunisawa
Surgical Operation Department, Asahikawa Medical College
Hospital, Asahikawa, Japan

M. Nagashima
Department of Anesthesia and Critical Care, Massachusetts
General Hospital and Harvard Medical School,
Boston, MA, USA

T. Kunisawa (✉) · A. Suzuki · O. Takahata · H. Iwasaki
Department of Anesthesiology and Critical Care Medicine,
Asahikawa Medical College, 2-1-1 Midorigaoka-Higashi,
Asahikawa, Hokkaido 0788510, Japan
e-mail: taka.kunisawa@nifty.ne.jp

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