OFFICIAL ABSTRACT and CERTIFICATION

Comfortable Breathing Duration (CBD) of Fentanyl Using a Three-Compartment Model

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Opioid pharmacokinetics is important for the understanding of pain control and the opioid epidemic. The purpose of this project is to address the confortable breathing duration, or the optimal 'sweet spot' where a patient is both able to breathe and feel pain relief. This research project's procedure began with developing mathematical derivations of several opioids given published pharmacokinetic parameters (Miller 2015). The apnea time (t1), analgesia time (t2), and the comfortable breathing duration (CBD) were estimated for fentanyl, sufentanil, remifentanil, and alfentanil using Excel and Python. A tri-exponential equation that served as a piece-wise model of three curves (alpha, beta, and gamma) as well as two intersection points (alpha-eta and beta-gamma) formed the foundation for the development of my three-compartment model to estimate CBD. Data analysis suggests that at lower doses, apnea time is determined more by alpha decay and analgesia time is determined more by beta decay. At higher doses, apnea time is determined more by beta decay and analgesia time is determined more by gamma decay. To avoid longer apnea times, one should use a smaller dose, but repeat the dose more frequently to maintain analgesia. Thus, the three-compartment model demonstrated that increasing dose not only prolonged apnea time, and analgesic time, but also the comfortable breathing duration. This concept is more consistent with published clinical experience.

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