The possible Role of TCI in ICU

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The pharmacokinetics of propofol have been comprehensively studied in the past.[1–5] Propofol has a suitable pharmacokinetic profile for use by infusion or target-controlled infusion (TCI).[6–12] TCIs have been used in research and clinical practice for more than 2 decades.[13–15] A widely used pharmacokinetic model of propofol TCI was developed by Marsh and colleagues,[16] and it was found to have good delivery performance. It was chosen for the commercially avail- able Diprifusor[16,17] system. Barr et al[11] found that plasma propofol concentrations corresponding to Ramsay sedation scores of 2, 3, 4, and 5 were 0.25, 0.6, 1.0, and 2.0 μg/mL. Frolich et al[10] found little systematic bias but poor precision using a lower mean propofol TCI predicted dose than ours. McMurray et al[12] found that the measurement of blood propofol concentrations showed a tendency of Diprifusor TCI to underpredict measured values (measured values higher than indicated, positive bias) in postcardiac surgery patients. Moreover, they demonstrated the tendency of the system to overpredict (negative bias) in general ICU patients. Recently, TCI has also been applied in the intensive care unit (ICU).[18–20] However, when applied in clinical care, TCI systems may not be as accurate as previously suggested,[11–13] leading various investigators to refine the infusion model.[21–29] We recently hypothesized that when propofol TCI with the pharmacokinetic model reported by Marsh is used for prolonged time, it can lose precision and accuracy.[16] The aim of our retrospective study was to determine the relationship, precision, and bias of the Diprifusor in combination with remifentanil patients undergoing neurosurgery under general anesthesia and in need of postoperative ICU sedation. We

retrospectively included patients undergoing general anesthesia for elective neurosurgical removal of brain tumors and postoperative sedation in the intensive care unit over a period of 3 months. TCI of propofol (Diprifusor – Marsh model) and remifentanil were used for general anesthesia and sedation. We compared propofol blood concentration (C_{meas}) measured by liquid chromatography–mass spectroscopy with predicted concentrations (C_{pred}) by the TCI system at 40 minutes (T0),2 hours (T1),and 4 hours (T2) and every 8 hours after starting the drug infusion and at the time of emergence from sedation. Ninety-four paired determinations of C_{meas} and C_{pred} from 15 adult ASA I patients (8 men and 7 women 54.9 ± 13 years old; BMI, 24 ± 3.2 kg/m^2) were analyzed. Mean duration of drug administration was 31 ± 6 hours. The coefficient of determination (R^2) of the linear regression model for the relationship of C_{meas} and C_{pred} was 0.43. At the time of emergence, C_{meas} was 0.5 ± 0.18 μg/mL. The bias of the TCI system (median performance error) was -34.7%, and the precision (median absolute performance error) was 36%. Wobble and divergence were 0.3% and 12.3%, respectively. This study found bias of the system out of the range of tolerability and showed a high tendency toward overestimation. These findings may lead to undersedation when propofol TCI is used for prolonged infusion In conclusion the main finding of our study was that the bias of the propofol TCI system (Marsh model) was out of the range of tolerability, showing a high tendency toward overestimation. However, if anesthesia and sedation are carefully monitored, Propofol TCI seems to be a safe option in the ASA I neurosurgical population. This altered pharmacokinetic behavior should be taken into consideration to allow a more individualized dosing of propofol TCI and remifentanil when given in prolonged infusion in this patient population. Future pharma- cokinetic propofol models should take into account real patients' data to optimize precision and bias

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