## PK/PD of Morphine for Postoperative Analgesia after Coronary Artery Bypass Grafting. Intrathecal Morphine Significantly Reduces Drug Consumption

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SUMMARY. The aim of the present study was to evaluate intrathecal morphine outcome on postoperative pain and apply pharmacokinetic/pharmacodynamic model to justify morphine consumption, plasma concentration and pain intensity during coronary artery bypass grafting surgery. Thirty six patients were prospectively randomized for general anesthesia and allocated in the control or morphine (400  $\mu$ g intrathecal) group. At postoperative period, all patients received a loading dose of morphine (1 mg bolus), and then patient-controlled analgesia device was installed and delivered until 36 h. Blood samples was collected from venous catheter, morphine plasma concentrations were determined by liquid chromatography and pain intensity evaluated by visual analogue scale. Drug dose requirements and pain intensity at rest were different between groups. No kinetic parameters difference was obtained. Maximum effect model and hysteresis curve were proposed to correlate drug plasma concentration versus time, drug consumption and pain intensity. Intrathecal morphine reduces at rest morphine consumption and pain intensity postoperatively; the best fit pharmacokinetic/pharmacodynamic models were maximum effect and hysteresis curve.

*KEY WORDS:* Analgesia, Intrathecal morphine, Pharmacokinetic/pharmacodynamic modeling, Postoperative patient-controlled analgesia device.

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