## **Methadone in Ambulatory Surgery: Clinical Effectiveness**

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**Background:** More than 50 million Americans undergo outpatient surgery annually. Surveys state that many patients (>80%) report inadequate postop pain relief. Opioids are the primary systemic pharmacotherapy for surgical pain. Clinical research shows that a single intraoperative dose of a long-duration opioid (i.e. methadone) produces better analgesia than repeated doses of short-duration opioids, in inpatient surgery. Nevertheless, in ambulatory surgery, methadone has never been evaluated. Our study tested the innovative hypothesis that in ambulatory surgery, intraoperative use of methadone, compared with conventional short-duration opioids, reduces postoperative pain and opioid consumption, with similar or diminished side effects.

**Methods:** Patients undergoing short-stay (<24 hr) ambulatory surgical procedures (i.e. laparoscopy) (n=59), were randomized 2:1 to receive either single-dose methadone (0.1 mg/kg IV N=18 or 0.2 mg/kg IV, N=22 based on ideal body weight, in a dose-escalation cohort design) at anesthesia induction or short-duration opioid (fentanyl, hydromorphone, N=19) throughout the operation per usual practice. Intraoperative and postoperative opioid consumption until discharge was recorded (and converted to morphine equivalents). Patients were assessed for pain intensity at rest, with coughing and with activity at 15, 30, 45 min, 1, 2, 3, 4 h after admission in the PACU, at bedtime and at discharge. Pain relief and level of sedation were assessed at the same times. Opioid side effects assessed included ventilatory depression (respiratory rate, oxygen saturation) and Opioid-Related Symptom Distress Scale (ORSDS). After discharge, patients recorded daily their pain self-assessments, home opioid use, and side effects in a written diary, until 30day postop clinic visit.

**Results:** Average doses of intraoperative methadone were  $6\pm1$ mg (0.1 mg/kg cohort) and  $11\pm1$ mg (0.2 mg/kg cohort). Average intraoperative total nonmethadone morphine equivalents given in short-duration opioid, 0.1mg/kg methadone and 0.2mg/kg methadone group were  $30.4\pm3$ ,  $2.0\pm0.4$  and  $1.4\pm0.3$  mg respectively. Patients receiving a single 0.2 mg/kg methadone dose required significantly less opioids intraoperatively and postoperatively during their hospital stay, compared to short-duration opioid group ( $23\pm3$  vs  $48\pm4$  mg morphine equivalents; p<0.05). Patients receiving intraoperative methadone used less takehome opioid (total 30d opioid averaged 16, 12 and 4 pills in short-duration opioid, 0.1 mg/kg methadone, and 0.2 mg/kg methadone groups), and stopped taking opioids earlier. Methadone did not cause any greater postop sedation or other adverse effects.

**Conclusion:** A single intraoperative methadone dose (0.2mg/kg ideal body weight) decreases intraoperative and postoperative opioid requirements, decreases post-discharge home opioid use for up to 30days postoperatively, with similar side effects.