



Late-Onset Respiratory Depression Following Preoperative Intrathecal Morphine

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Learning Objectives:

- Intrathecal morphine-induced respiratory depression can occur early (within first 1 hour following administration) and late (up to 24 hours, highest at 3-12 hours) following administration. Risk peaks at 6 hours post-injection.
- Contributing factors to respiratory depression following neuraxial opioid administration include age >65, high dose (>500 mcg) ITM, use of additional opioids, opioid-naïve patient, slowing of CSF dynamics with increased age, hypobaricity of ITM, Trendelenburg position, increased intra-abdominal pressure, positive pressure ventilation, and co-existing lung disease.

Case Report:

- 70-year-old Caucasian female presenting for distal pancreatectomy and splenectomy.
- PMH of pancreatic cyst/neoplasm, peripheral arterial disease, HTN, GERD w/ Barrett's Esophagus, Osteoarthritis, and former smoker (>10-year smoking history).
- 150 mcg intrathecal morphine administered preoperatively to reduce postoperative pain and opioid consumption.
- Patient also received 2 mg midazolam preop, low-dose IV ketamine infusion at 10 mg/hr, and 100 mcg IV fentanyl on induction.
- Intraop, EtCO₂ increased to 61 mmHg, ABG 6.99/88.9/133/21.8.
- MV increased through changes in PPV settings and intraabdominal pressures decreased by surgical team.
- EtCO₂ levels greatly improved, and patient was extubated successfully and without complication.
- Prior to extubation, 4/4 twitches on TOF documented and patient reversed with 2 mg/kg Sugammadex (130 mg).
- Upon arrival to PACU, patient would awaken to voice and was oriented to name, but not place or time. Pt was oxygenating well requiring only minimal O₂ via NC. There was some hypotensive requiring IV phenylephrine infusion.
- Postoperative CMP, CBC, and perioperative medication review were unremarkable.
- 30 minutes into PACU stay, patient became drowsier.
- IV ketamine infusion was turned off 1 hour into PACU stay.
- ABG at this time resulted as: 7.129/61.1/95/20.3.
- Trial of IV naloxone given up to 200 mcg in divided doses with dramatic clinical improvement..
- Patient was placed on IV naloxone infusion for 24 hours and admitted to the ICU.

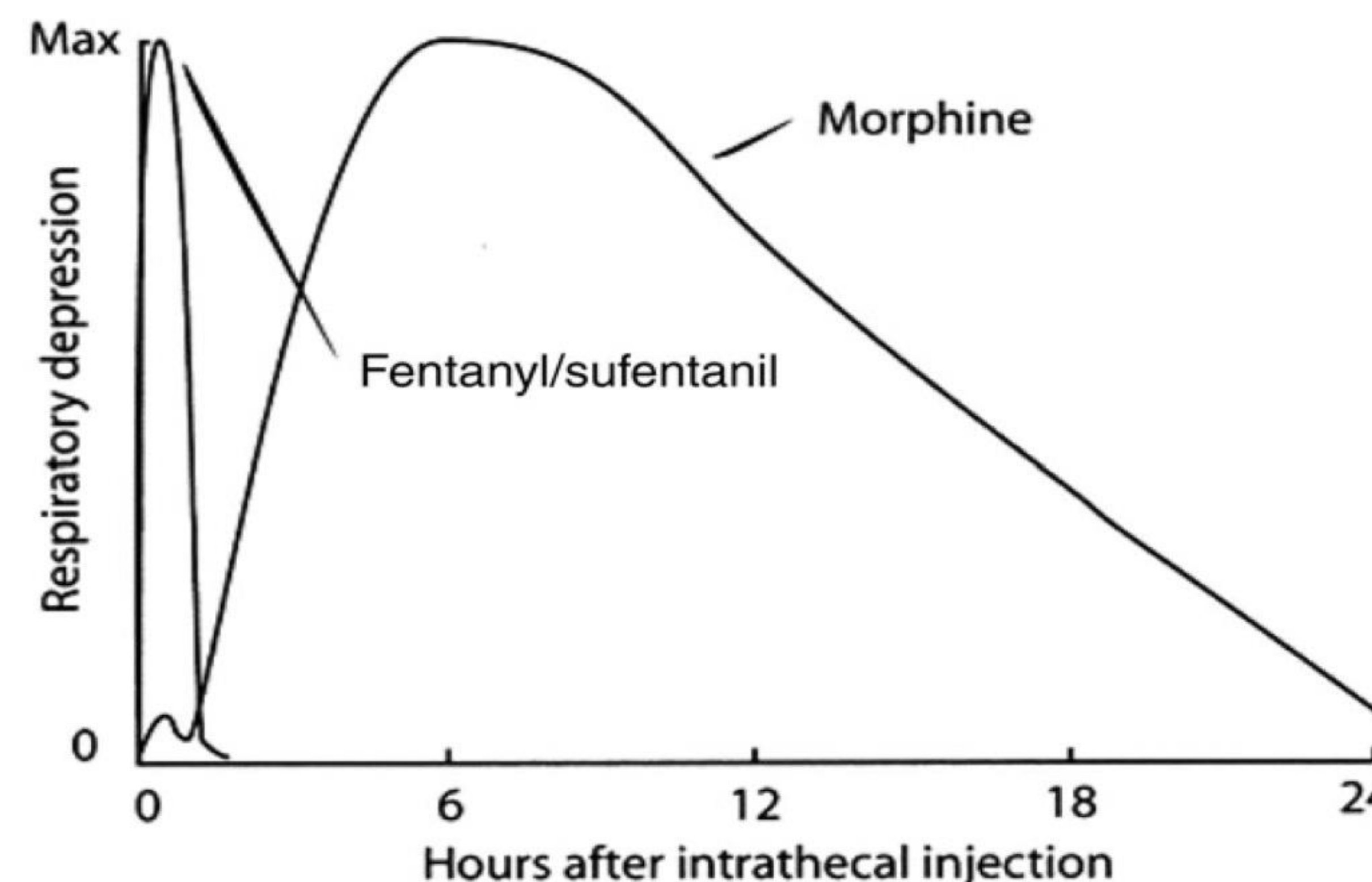


Fig 2 Time to onset of respiratory depression after fentanyl and morphine.

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Discussion:

ITM administration, while effective for postoperative pain control, is associated with risks including opioid-induced respiratory depression. The incidence is quoted as 0.03-7%. Most commonly, impaired level of consciousness is the presenting symptom. Patients receiving hydrophilic opioids intrathecally, such as morphine, have the highest likelihood of experiencing respiratory depression 20-30 min after initial administration and again at 6-12 hours following administration. The risk of intrathecal morphine-induced late-onset respiratory depression peaks at 6 hours post-injection. Risk factors that place patients at higher risk for opioid-induced respiratory depression include age >65 years old, >500 mcg morphine, use of additional opioids, and opioid-naïve patients. Other possible contributing factors include changes in CSF dynamics with age, slight hyobaricity of intrathecal morphine, and increased intra-abdominal pressure. Likely, each of these contributed to our patient's post-operative respiratory depression. As discussed earlier, the risk for late-onset intrathecal morphine-induced respiratory depression peaks at 6 hours following injection, which is when our patient's symptoms presented. CSF flow dynamics have been shown to slow with increased age, which could place patients age >65 years old at slightly increased risk of respiratory depression. This patient's age, weight, abdominal insufflation, and Trendelenburg positioning increased intra-abdominal pressure. Increased intra-abdominal pressure has been shown to cause an influx of epidural blood flow leading to compression of the dural sac, resulting in displacement of CSF rostrally. Lastly, preservative-free intrathecal morphine is slightly hypobaric in comparison with human CSF. This could allow for more rostral spread and a "high spinal." All these things could have played a role in the patient experiencing a "high spinal" consisting of 150 mcg of intrathecal morphine. Late-onset intrathecal morphine-induced respiratory depression should remain on the differential for causes of altered mental status/emergence delirium in the PACU in this patient population. This case serves as an example for why it is critical that patients receiving intrathecal morphine be monitored closely for 24 hours following injection.

