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INTRODUCTION

- Medetomidine is a potent alpha-2 adrenergic agonist approved for veterinary use possessing both sedative and pain-relieving properties.
- Medetomidine is a racemic mixture with two enantiomers: dexmedetomidine, the active form, and levomedetomidine and exerts its effect by binding to a G protein coupled receptor (GPCR) found in the central and peripheral nervous systems.
- The emergence of medetomidine as a novel adulterant in the U.S. illicit drug supply signals a troubling development in the escalating polysubstance crisis.
- Synergistic effects with opioids pose significant concerns for acute pain physicians and anesthesiologists due to its profound sedative, and cardiorespiratory effects.
- Medetomidine has been linked to overdose, and hospitalizations in Maryland, Missouri, Colorado, Pennsylvania, and California, and more recently fatalities have surged in cities like Philadelphia, Pittsburgh, and Chicago.
- Medetomidine can exacerbate cardiopulmonary conditions in patients with preexisting diseases such as obstructive lung disease, coronary artery disease and heart failure.

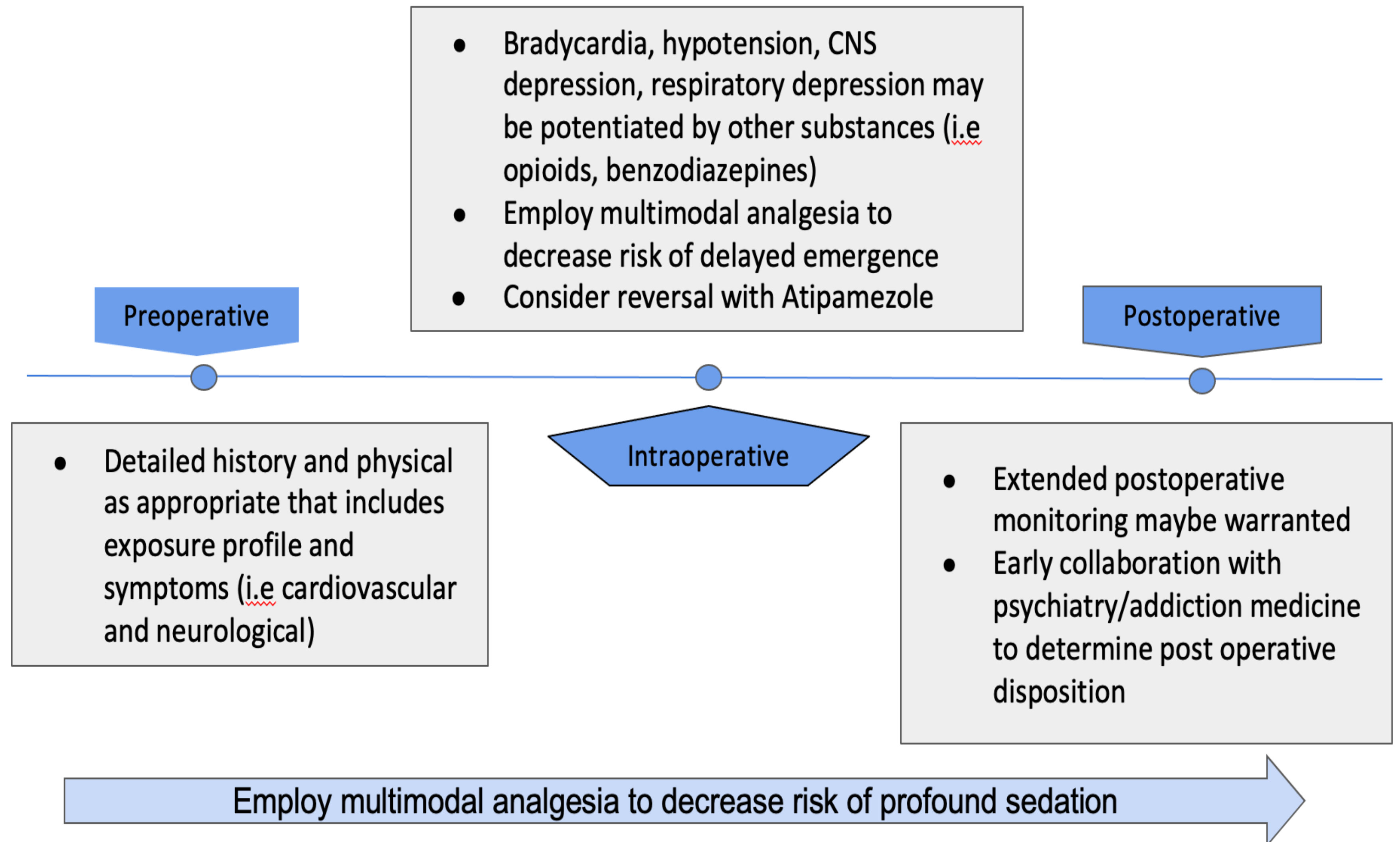
CLINICAL MANAGEMENT

- Perioperative management strategies include:
 - Hemodynamic support with vasopressors (epinephrine, norepinephrine) for profound hypotension.
 - Anticholinergics (atropine, glycopyrrolate) for refractory bradycardia.
 - Ventilator support in life-threatening respiratory depression.
 - Some patients may require arterial cannulation, central venous access, and large-bore IVs for hemodynamic monitoring and vasoactive agent administration in extreme cases.
- Multi-modal approaches for analgesia, including ketamine, IV acetaminophen, and NSAIDs, while avoiding dexmedetomidine and opioids to prevent further exacerbation of the effects of Medetomidine.
- Atipamezole, an alpha-2 antagonist, has shown effectiveness in reversing medetomidine in animal studies and human trials, but its lack of FDA approval and limited human data restrict its clinical applicability.

Table 1 Table summarizing pharmacologic properties, and effects of medetomidine

	Medetomidine
Potency	~200-fold more potent. higher potency leads to greater effects at lower doses, increasing overdose risk
Duration of action	Longer duration, approximately 1 to 1.5 hours
Cardiovascular effects with overdose	Profound bradycardia, hypertension ± hypotension
Respiratory depression	More severe, especially in combination with other depressants (e.g., opioids)
CNS effects	ataxia, disorientation, seizures (in overdose cases)
Reversal agent	Atipamezole (not FDA-approved for humans)

Figure 1 Summary of perioperative considerations



DISCUSSION/CONCLUSION

- Medetomidine's role in illicit drug use presents significant anesthetic and acute pain management challenges.
- Its potent analgesic effects, combined with profound cardiovascular and respiratory depression, necessitate careful perioperative planning
- Supportive care, vigilant monitoring, and avoidance of potentiating agents are critical.
- Given the limited human data, management strategies rely on extrapolation from veterinary medicine and related alpha-2 agonists.
- In severe cases, administering atipamezole might be a worthy consideration.
- Further research and public health initiatives are needed to enhance understanding and improve patient outcomes.

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