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Antiemetics for Nausea & Vomiting

Introduction

1. Nausea is a protective mechanism to warn the body of potential toxin ingestion; it may occur with or without emesis.
2. A common presenting complaint in emergency departments.
3. No widely accepted evidence-based guideline to optimize the use of antiemetic medications for N/V in the adult ED setting.
4. A broad list of possible causes; unique etiologies include cannabinoid hyperemesis and hyperemesis gravidarum of pregnancy.
5. Complex pathophysiology involving CNS, ANS, gastric dysrhythmias, and the endocrine system.

Pharmacology

	Ondansetron (5HT-3)	Metoclopramide (D2, 5HT-3)	Prochlorperazine (D2, M1, H1)	Promethazine (D2, M1, H1)	Haloperidol (D2)	Droperidol (D2)
Dose	Oral, IM, IV: 4-8 mg as a single dose	IV: 10-20 mg as a single dose PO: 10 mg as a single dose	PO: 5-10 mg IM: 5-10 mg; IV: 2.5-10 mg PR: 25 mg	Oral, IM, IV, rectal: 12.5 – 25 mg	IV/IM, PO: 0.5-2 mg	IV/IM: 1.25-2.5 mg
Administration	• via IV push	• IV: ≤10 mg can be given IVP over 1-2 min; give doses >10 mg over at least 10 min	• IV: max rate 5mg/min • IV can cause hypotension • Do not give SC	• Avoid SubQ formulations due to risk of severe tissue damage (ISMP 2018) • IM =preferred parenteral route	• Can give the lactate injectable formulation IM or IV • Consider ECG monitoring prior and during IV administration for high-risk patients	• IM, IV via slow IV push administration • Consider ECG monitoring prior and during IV administration for high-risk patients
PK/PD	Onset:PO ~30 min Peak: PO: ~2 hrs ODT: ~ 1 hr	Onset: PO: 30-60 min IV: 1-3 min IM: 10-15 min Peak: 1-2 hrs	Onset: 30-40 min IM: 10-20 min PR: ~ 60 min Peak: IV: 30-60 min	Onset: PO, IM: ~20 min; IV: ~5 min Peak: Oral: ~2.5 h PR: ~ 8 hr	Onset: IM: ~28 min; IV: 3-20 min; PO: 60-90 min Peak: IM: 20 min IV: ~30 min PO: 2-6 hrs	Onset: Peak: IV/IM: up to 30 min
Adverse Effects	QTc prolongation, HA, constipation	QTc prolongation, EPS, diarrhea, somnolence	QTc prolongation, EPS	QTc prolongation, EPS, sedation, phlebitis	QTc prolongation, EPS, somnolence	QTc prolongation (box warning), EPS, orthostatic hypotension

Overview of Evidence

Author, year	Design/ sample size	Intervention & Comparison	Outcome
April, 2018	RCT (n=122)	Inhaled isopropyl alcohol + ondansetron PO inhaled isopropyl alcohol + placebo PO inhaled placebo + ondansetron PO	• Mean decrease in nausea VAS score was 30 mm (95% CI 22-37 mm) for group A, 32 mm (95% CI 25-39 mm) for group B, and 9 mm (95% CI 5-14 mm) for group C • No adverse events were reported in either arm • **Aromatherapy with or without PO ondansetron provided greater relief than PO ondansetron alone**
Meek, 2018	RCT (n=215)	Efficacy of droperidol (1.25 mg IV) vs ondansetron (8 mg IV) vs 0.9% saline placebo for adult ED nausea	• **Symptom improvement occurred in 75% (95% CI 64-85%) of droperidol participants, 80% (95% CI 69-89%) for ondansetron, and 76% (95% CI 64-85%) for placebo** • Mean VAS score changes were -29 mm (95% CI -36 to -23mm) in droperidol, -34 mm (95% CI -41 to -28 mm) in ondansetron, and -24 mm (95% CI -29 to -19 mm) in placebo • Superiority was not demonstrated for droperidol or ondansetron vs placebo
Parker, 2018	Retrospective review (n=35,824)	Review of ondansetron use in first-trimester nausea and vomiting of pregnancy and incidence of major birth defects	• **No association found with ondansetron use and increased risk of birth defects for most of the 51 defects groups** • Modest increase in risk of cleft palate (adjusted OR 1.6, 95% CI 1.1-2.3) observed in NBDPS and renal agenesis-dysgenesis (adjusted OR 1.8, 95% CI 1.1-3.0) observed in BDS (adjusted OR 1.8, 95% CI 1.1–3.0) – though these findings may be due to chance
Culver, 2017	RCT (n=133)	Ondansetron + IV opioid vs IV opioid to prevent opioid-induced nausea	• **No significant difference in nausea 5 min post opioid administration between ondansetron + opioid vs opioid monotherapy (7.2% vs. 12.5%; p=0.308)** • No statistical difference in emesis, rescue antiemetic use, or nausea severity between treatment groups
Egerton-Warburton, 2014	RCT (n=270)	Efficacy of ondansetron (4 mg IV) vs metoclopramide (20 mg IV) vs placebo in nausea and vomiting reduction in the ED	• Mean decrease in VAS score was 27 mm (95% CI 22-33 mm), 28 mm (95% CI 22-34 mm), 23 mm (95% CI 16-30 mm) for ondansetron, metoclopramide, and placebo, respectively • **Differences in VAS score reduction of antiemetics vs placebo were not significant**
Braude, 2008	RCT (n=120)	Promethazine (25 mg IV) vs ondansetron (4 mg IV) to treat undifferentiated nausea in the ED	• **Similar nausea reduction in visual analog scale (VAS) score (difference -2 mm; 95% CI = -13 to 8 mm**) • Similar anxiety reduction in both groups (difference -1 mm; 95% CI=-10 to 10 mm) • Promethazine was associated with significantly more sedation than ondansetron (difference 14 mm; 95% CI= 5 to 24mm)

Conclusions

- Antiemetic agents studied in the ED setting include ondansetron, promethazine, prochlorperazine, metoclopramide, and droperidol.
- Clinicians should Optimize therapy based on efficacy, side effect profile, patient's preference, and cost in selection of agent.
- May utilize IV Benadryl for EPS prevention of agents.

References

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