

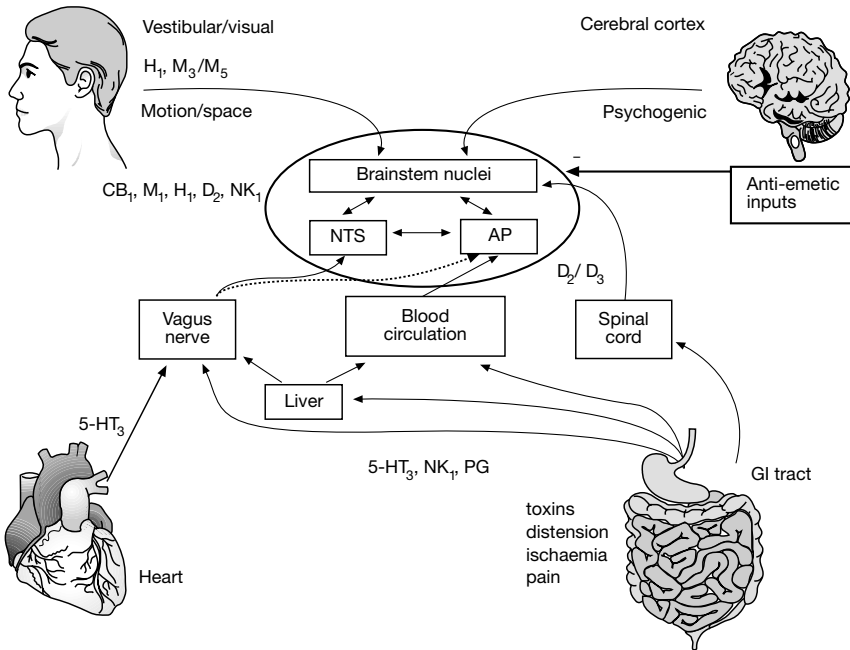
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AP, area postrema; CB₁, Cannabinoid₁ receptor; D₂/D₃, dopamine_{2/3} receptors; H₁, histamine₁ receptor; 5-HT₃, 5-Hydroxytryptamine₃ receptors; M_{3/5}, muscarinic_{3/5} acetylcholine receptor; NK₁, neurokinin₁ (tachykinin) receptor; NTS, nucleus tractus solitarius.

Figure 1.4 Summary of aspects of the pharmacology of emesis and anti-emetics showing the major inputs by which emesis can be activated together with the major transmitter receptor systems involved. Redrawn and modified from Sanger and Andrews 2001

5-HT₃ receptor antagonists (Andrews 1994). These agents are very efficacious in the acute phase of anti-cancer chemotherapy-induced emesis because their primary site of action is to block the activation by 5-HT (released from the intestinal enterochromaffin cells by the chemotherapeutic agent) of the 5-HT₃ receptors located on the peripheral terminals of the vagal afferents. Any emetic stimulus acting via this pathway will have its effect reduced or blocked by a 5-HT₃ receptor antagonist. However, emetic stimuli acting via other mechanisms (e.g. motion, dopamine and opiate receptor agonists acting via the AP/NTS) will not be affected. 5-HT₃ receptors are present in the NTS but there is little preclinical evidence to implicate them in the anti-emetic effect of 5-HT₃ receptor antagonists. The reduced efficacy of 5-HT₃ receptor antagonists in PONV, as compared to the acute phase of chemotherapy-induced emesis, suggests that activation of a pathway containing 5-HT₃ receptors plays a less significant role in PONV. Based upon an understanding of the role of 5-HT and 5-HT₃ receptors in emesis (see above), it would be predicted that 5-HT₃ receptor antagonists would have

and ondansetron groups, respectively. Similarly, the combination of droperidol 1.25 mg and ondansetron 4 mg resulted in significant reduction of the incidence of PONV in the first 24 hours in patients undergoing gynaecological laparoscopy (Wu *et al.* 2000)

The comparative efficacy of combinations of droperidol and ondansetron has been compared when given as a mixture within a patient-controlled analgesia (PCA) syringe. Wrench and colleagues investigated 60 patients undergoing gynaecological surgery and post-operative PCA (morphine 1 mg/ml) (Wrench *et al.* 1996). Patients were randomised to receive three anti-emetic regimens: (i) ondansetron 4 mg bolus plus ondansetron 8 mg per 60-ml syringe; (ii) droperidol 1.25 mg plus droperidol 3 mg per 60-ml syringe; (iii) a combination of both drugs as a bolus plus both drugs added to the syringe. There was a relatively low incidence of PONV in all groups in this study but at 12 h post-operatively the incidence of nausea in the combination group was 5% compared with 20 and 25% in the droperidol and ondansetron groups, respectively ($p < 0.05$).

Several studies have shown not only efficacy of dexamethasone for the prevention of PONV but also increased efficacy when used in combination with ondansetron, granisetron, tropisetron and droperidol (Table 5.7). For example, Splinter and Rhine (1998) gave children undergoing squint surgery one of two anti-emetic regimens in a randomised double-blind manner: ondansetron 150 µg/kg (maximum 8 mg) or ondansetron 50 µg/kg plus dexamethasone 150 µg/kg (maximum 8 mg). The design of this study was not ideal as discussed above but the incidence of vomiting at 24 h was 28% in the ondansetron group compared with 9% in the combination group. Furthermore, no children in the combination group vomited on the way home.

Table 5.7 Ondansetron–dexamethasone, granisetron–dexamethasone and tropisetron–dexamethasone combinations

<i>Reference</i>	<i>Combinations</i>	<i>Surgery</i>	<i>Results</i>
McKenzie <i>et al.</i> (1994)	Ondan Ondan + Dexameth	Major gynaecological	Improved
Lopezolaondo <i>et al.</i> (1996)	Ondan, Dexameth Ondan + Dexameth	Major gynaecological	Improved
Splinter & Rhine (1998)	Ondan Ondan + Dexameth	Paediatric Strabismus	Improved
Fujii <i>et al.</i> (2000)	Gran Gran + Dexameth	Laparoscopic cholecystectomy	Improved
Fujii <i>et al.</i> (1998)	Gran, Dexameth Gran + Dexameth	Middle ear surgery	Improved
Holt <i>et al.</i> (2000)	Tropis Tropis + Dexameth	Paediatric tonsillectomy	Improved

Ondan, ondansetron; Gran, granisetron; Dexameth, dexamethasone; Tropis, tropisetron.

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