



AMERICAN COLLEGE OF
OCCUPATIONAL AND
ENVIRONMENTAL MEDICINE

Antiemetics

Effective Date: March 27, 2020

Contributors

Editor-in-Chief:

Kurt T. Hegmann, MD, MPH, FACOEM, FACP

Evidence-based Practice Hip Panel Co-Chairs:

Carlos A. Guanche, MD

Atul F. Kamath, MD

Judith Green McKenzie, MD, MPH, FACOEM

Evidence-based Practice Hip Panel Members:

Joshua D. Harris, MD

Laura Rachel Kaufman, MD, PhD

Cameron W. MacDonald, PT, DPT, GCS, OCS, FAAOMPT

Jamie Stark, MS, PhD, MSN (cand.)

Richard E. Strain, Jr., MD

Eric M. Wood, MD, MPH, FACOEM

These panel members represent expertise in occupational medicine, orthopedic surgery, physical therapy, sports medicine, family medicine, internal medicine, physiology, exercise kinesiology, and nursing. As required for quality guidelines – Institute of Medicine’s (IOM’s) Standards for Developing Trustworthy Clinical Practice Guidelines and Appraisal of Guidelines for Research and Evaluation (AGREE) – a detailed application process captured conflicts of interest. The above Panel has none to declare relevant to this guideline.

Methodology Committee Consultant:

Kurt T. Hegmann, MD, MPH, FACOEM, FACP

Research Conducted By:

Kurt T. Hegmann, MD, MPH, FACOEM, FACP

Kristine Hegmann, MSPH, CIC

Matthew S. Thiese, PhD, MSPH

Emilee Eden, MPH

Jenna L. Praggastis, BS

Harkomal Kaur, BS

Michael L. Northrup, BS

Skyler D. Walker, BS
Chapman B. Cox
Weijun Yu, BM, BA, MS
Vivian Nguyen
Matthew Houston, BS
Patrick Bittenbender
Jenny Dang, BS
Melissa Gonzalez
Amrinder K. Thind
Helena Tremblay
Uchenna Ogbonnaya, MS

Specialty Society and Society Representative Listing:

ACOEM acknowledges the following organizations and their representatives who served as reviewers of the “Hip and Groin Disorders” Guideline from which this guidance for antiemetics was extracted. Their contributions are greatly appreciated. By listing the following individuals or organizations, it does not infer that these individuals or organizations support or endorse the treatment guidelines developed by ACOEM.

American Association of Hip and Knee Surgeons
American Association of Occupational Health Nurses
Nicole Shaffer, DNP, CRNP-BC, COHN-S, FAAOHN
Carol I. Tobias, MBA, BSN, RN, COHN-S, FAAOHN
Stephanie Weinsier, DNP, ANP-BC, COHN-S, FAAOHN

American Occupational Therapy Association

Michelle L. Bradshaw, DC, OTR/L

American Society of Anesthesiologists

Other Reviewers

James W. Butler, MD, MPH, FACOEM
Seth Gemme, MD
Richard D. Shih, MD, FACEP

Introduction

Nausea and vomiting are common complications of anesthesia. Other sources of nausea include:

- Visceral pain,
- Severe headaches,
- Traumatic brain injury,
- Eye pain,
- Heart attack,
- Infections,
- Food poisoning,
- Adverse effects of medications,
- Motion sickness,
- Severe anxiety, and
- Severe pain.

A wide variety of antiemetic agents are administered by various routes to prevent and treat perioperative and other nausea and vomiting [1-9], including:

- Serotonin receptor antagonists (5HT3 and H1) [7],
- Dopamine receptor antagonists,
- Substance P antagonists [10],
- Antihistamines, and
- Anticholinergics [11].

Uncommonly used agents have included:

- Dexamethasone [12],
- Anticonvulsants [13-20],
- Dimenhydrinate [5], and
- Neurokinin-1 receptor antagonists [21].

The specific antiemetic agents most commonly used are reportedly:

- Droperidol,
- Metoclopramide [2], and
- Ondansetron [9].

Some prior systematic reviews have suggested no clear superiority of any single antiemetic [8, 14].

Treatment Recommendation

Antiemetics

Recommended.

Antiemetics are moderately recommended for peri-operative nausea and vomiting and in cases of severe pain causing nausea and vomiting.

Strength of Evidence – Moderately Recommended, Evidence (B)

Level of Confidence – High

Indications:

Pre-, peri- and post-operative nausea and emesis. Often used prophylactically either pre-operatively or at the end of the operative procedure when emesis is potentially anticipated and/or has significant impacts on the type of surgical procedure/wound. Also, may be provided post-operatively where there is ongoing nausea and/or vomiting either present or anticipated to potentially occur. In infrequent cases, severe pain without surgery may be associated with nausea and warrant treatment.

Benefits:

Reduced, prevented, or resolved nausea and vomiting

Harms:

Adverse effects vary based on type of medication. Common adverse effects include drowsiness, dry mouth, urinary retention, blurred vision, sedation, tremor.

Frequency/Dose/Duration:

Per manufacturer recommendation. Most studies administered intravenous (I.V.) medication at close of surgery with some studies administering medication immediately pre-operatively. Routes used besides I.V. have included oral, PCA pump, and intramuscular. The rectal route is used typically as a tertiary strategy after common routes and/or combinations of medications have failed, although supportive quality studies were not found for rectal (PR) administration. Medications and doses used in quality studies include (most given I.V.):

- a. Aprepitant 40, 80, 125mg and 40mg P.O.
- b. Cyclizine 50mg
- c. Dimenhydrinate 50mg and 1mg/kg
- d. Dolasetron mesylate 12.5, 25, 50, 100 mg
- e. Droperidol 0.625, 1.25, 2.5, 5, 10, 15, 50mg and 0.014 micrograms/kg
- f. Granisetron 0.1, 1, 3mg and 20, 40 micrograms/kg
- g. Metoclopramide 10,20mg and 0.25mg/kg and 10mg P.O.
- h. Ondansetron 1, 2, 4, 8mg and 100 micrograms/kg and 4, 8mg P.O.
- i. Palonosetron 0.025, 0.05, 0.075mg
- j. Perphenazine 5mg
- k. Prochlorperazine 0.1,10mg
- l. Ramosetron 0.15, 0.3, 0.6mg and 4 micrograms/kg and 0.1mg P.O.
- m. Rolapitant 20, 70, 200mg
- n. Tropisetron 2.5mg and 0.1mg/kg

Various combinations of agents have been used and generally suggest superiority of multiple agents over single agent approaches, thus providing potential tertiary treatment strategies for more difficult cases. Quality evidence supports combinations including Dolasetron and Droperidol; Droperidol and Ondansetron, and Dimenhydrinate and Droperidol [2].

Indications for Discontinuation: Resolution of symptoms

Rationale: There are multiple anti-emetic agents with demonstrated efficacy, although not all studies report efficacy. Anti-emetic agents are either non-invasive or minimally invasive depending on administration route, have low adverse effects, are mostly low cost, have demonstrated efficacy and are thus recommended.

Evidence: A comprehensive literature search was conducted using PubMed, Scopus, CINAHL, Cochrane Library, and Google Scholar without date limits using the following terms: Antiemetics, Antiemetic Agents; Hip Osteoarthritis, Hip Degenerative Joint Disease, Hip Osteoarthritis, Hip Degenerative Arthritis; controlled clinical trial, controlled trials, randomized controlled trial, randomized controlled trials, random allocation, random*, randomized, randomization, randomly; systematic, systematic review, retrospective, and prospective studies. We found and reviewed 1119 articles in PubMed, 279 in Scopus, 14 in CINAHL, 38 in Cochrane Library, 497 in Google Scholar (Went through first 100), and 50 from other sources. We considered for inclusion 36 from PubMed, 0 from Scopus, 0 from CINAHL, 0 from Cochrane Library, 0 from Google Scholar, and 83 from other sources. Of the 119 articles considered for inclusion, 86 were randomized controlled trials and 33 systematics reviews.

Guideline/Condition Applicability

Ankle and Foot Disorders

- Achilles Bursitis or Tendinopathy
- Achilles Tendon Rupture
- Bunion
- Charcot Arthropathy
- Chronic Ulcer, Lower Limb (Including Toes, Foot, Ankle, Calf)
- Fracture, Ankle
- Fracture, Calcaneus
- Fracture, Forefoot (Sesamoid, Phalanges)
- Fracture, Metatarsal Bones
- Fracture, Midfoot (Cuboid, Cuneiform, Navicular)
- Fracture, Talus
- Fracture, Tibia or Fibula
- Hammertoe
- Morton Neuroma
- Paronychia

Plantar Fasciitis
Sprains and Strains, Ankle
Tarsal Tunnel Syndrome

Cervical and Thoracic Spine Disorders

Cervical Disc Disorder with Myelopathy
Fracture, Cervical Spine (Without Spinal Cord Injury)
Myelopathy
Neck Pain
Radicular Pain Syndrome, Cervical Spine
Sprains and Strains, Cervical Spine (Neck)
Thoracic Spine Pain

Chronic Pain

Chronic Neuropathic Pain
Complex Regional Pain Syndrome
Pain, Chronic

Elbow Disorders

Biceps Tendinitis
Dislocation, Elbow
Epicondylitis, Medial and Lateral
Fracture, Humerus, Distal
Fracture, Humerus, Proximal
Fracture, Radius, Proximal
Neuropathy of Radial Nerve (Entrapment)
Neuropathy of Ulnar Nerve (Entrapment)
Olecranon Bursitis
Osteoarthritis, Elbow
Osteonecrosis, Elbow
Pronator Syndrome
Sprains and Strains, Elbow

Eye Disorders

Foreign Body, Cornea
Pterygium

Hand, Wrist, and Forearm Disorders

Carpal Tunnel Syndrome
Compartment Syndrome
Crush Injury
Dupuytren's Contracture
Fracture, Carpal Bones
Fracture, Fingers and Thumb
Fracture, Metacarpal Bones
Fracture, Radius and Ulna, Distal

Kienböck's Disease
Laceration, Upper Extremity
Osteoarthritis, Hand and Finger
Pain in Limb
Puncture Wound
Sprains and Strains, Hand or Fingers
Sprains and Strains, Wrist
Synovial Cyst
Tenosynovitis
Tenosynovitis, Radial Styloid
Triangular Fibrocartilage Complex (TFCC) Tears
Trigger Finger or Thumb

Hip and Groin Disorders

Epididymitis
Femoral Acetabular Impingement
Fracture, Femoral Neck
Gluteus Medius Tear
Greater Trochanteric Pain Syndrome
Groin Pain, Adductor-Related
Groin Strain
Hip Dysplasia
Labral Tear, Hip
Ligamentum Teres Rupture
Meralgia Paresthetica
Orchitis
Osteoarthritis, Hip
Osteonecrosis, Hip
Pain, Hip
Sciatica
Strains, Hamstring
Strains, Hip Flexor
Strains, Lower Abdominal
Tendinosis, Gluteus Medius

Knee Disorders

Iliotibial Band Syndrome
Meniscus Disorders, Knee
Osteoarthritis, Knee
Osteonecrosis, Knee
Pain, Knee
Patellar Tendinopathy
Patellofemoral Joint Syndrome

Sprains and Strains, Knee
Strains, Quadriceps and Calf

Low Back Disorders

Ankylosing Spondylitis
Facet Degenerative Joint Disease
Fracture, Lumbosacral Spine (Without Spinal Cord Injury)
Fracture, Vertebra
Low Back Pain
Radicular Pain Syndrome, Lumbar Spine
Spinal Stenosis
Spondylolisthesis

Opioids

Opioid use may cause nausea and vomiting

Shoulder Disorders

Adhesive Capsulitis of Shoulder
Brachial Plexus Injuries
Calcific Tendinitis, Shoulder
Dislocation, Acromioclavicular Joint
Dislocation, Glenohumeral
Fracture, Clavicle
Impingement Syndrome
Labral Tear, Shoulder
Osteoarthritis, Shoulder
Osteonecrosis, Shoulder
Pain, Shoulder
Rotator Cuff Syndrome
Rotator Cuff Tear
Sprains and Strains, Shoulder and Upper Arm
Thoracic Outlet Syndrome

Traumatic Brain Injury

Fracture, Skull (Closed)
Headache
Traumatic Brain Injury

Workplace Mental Health

Posttraumatic Stress Disorder

References

1. Gralla, R.J., et al.
Recommendations for the use of antiemetics: evidence-based, clinical practice guidelines. *Journal of Clinical Oncology*, 1999. 17(9): p. 2971-2971.
2. Eberhart, L., et al.
Droperidol and dimenhydrinate alone or in combination for the prevention of post-operative nausea and vomiting after nasal surgery in male patients. *European journal of anaesthesiology*, 1999. 16(11): p. 790-795.
3. Bailey, P.L., et al.
Transdermal scopolamine reduces nausea and vomiting after outpatient laparoscopy. *Anesthesiology*, 1990. 72(6): p. 977-980.
4. Lee, D., et al.
The effect of oral and I.V. ramosetron on postoperative nausea and vomiting in patients undergoing gynecological laparoscopy with total intravenous anesthesia. *Journal of anesthesia*, 2009. 23(1): p. 46-50.
5. Kranke, P., et al.
Dimenhydrinate for prophylaxis of postoperative nausea and vomiting: a meta-analysis of randomized controlled trials. *Acta anaesthesiologica Scandinavica*, 2002. 46(3): p. 238-244.
6. Rawlinson, A., et al.
Mechanisms of reducing postoperative pain, nausea and vomiting: a systematic review of current techniques. *Evid Based Med*, 2012. 17(3): p. 75-80.
7. Barrett, T.W., et al.
A randomized, placebo-controlled trial of ondansetron, metoclopramide, and promethazine in adults. *The American journal of emergency medicine*, 2011. 29(3): p. 247-255.
8. Furyk, J.S., R.A. Meek, and D. Egerton-Warburton
Drugs for the treatment of nausea and vomiting in adults in the emergency department setting. *The Cochrane Library*, 2015.
9. Gupta, A., et al.
Does the routine prophylactic use of antiemetics affect the incidence of postdischarge nausea and vomiting following ambulatory surgery?: A systematic review of randomized controlled trials. *ANESTHESIOLOGY-PHILADELPHIA THEN HAGERSTOWN-*, 2003. 99(2): p. 488-495.
10. Diemunsch, P., et al.
Single-dose aprepitant vs ondansetron for the prevention of postoperative nausea and vomiting: a randomized, double-blind phase III trial in patients undergoing open abdominal surgery. *British journal of anaesthesia*, 2007. 99(2): p. 202-211.
11. De Oliveira, G., et al.
Systemic metoclopramide to prevent postoperative nausea and vomiting: a meta-analysis without Fujii's studies. *British journal of anaesthesia*, 2012. 109(5): p. 688-697.

12. Ahn, E., et al. Palonosetron and ramosetron compared for effectiveness in preventing postoperative nausea and vomiting: a systematic review and meta-analysis. *PloS one*, 2016. 11(12): p. e0168509.
13. Grant, M.C., et al. The effect of preoperative gabapentin on postoperative nausea and vomiting: a meta-analysis. *Anesthesia & Analgesia*, 2016. 122(4): p. 976-985.
14. Kazemi-Kjellberg, F., I. Henzi, and M.R. Tramèr Treatment of established postoperative nausea and vomiting: a quantitative systematic review. *BMC anesthesiology*, 2001. 1(1): p. 2.
15. Kim, W.O., et al. Ramosetron for the prevention of postoperative nausea and vomiting (PONV): a meta-analysis. *Korean journal of anesthesiology*, 2011. 61(5): p. 405-412.
16. Fujii, Y., et al. Ramosetron for preventing postoperative nausea and vomiting in women undergoing gynecological surgery. *Anesthesia & Analgesia*, 2000. 90(2): p. 472-475.
17. Joo, J., et al. Ramosetron versus ondansetron for postoperative nausea and vomiting in strabismus surgery patients. *BMC anesthesiology*, 2015. 16(1): p. 41.
18. Kim, S., et al. Comparison of ramosetron with ondansetron for prevention of postoperative nausea and vomiting in patients undergoing gynaecological surgery. *British journal of anaesthesia*, 2009. 103(4): p. 549-553.
19. Mihara, T., et al. Reevaluation of the effectiveness of ramosetron for preventing postoperative nausea and vomiting: a systematic review and meta-analysis. *Anesthesia & Analgesia*, 2013. 117(2): p. 329-339.
20. Yokoi, A., et al. Comparative efficacy of ramosetron and ondansetron in preventing postoperative nausea and vomiting: An updated systematic review and meta-analysis with trial sequential analysis. *PloS one*, 2017. 12(10): p. e0186006.
21. Liu, M., et al. Neurokinin-1 receptor antagonists in preventing postoperative nausea and vomiting: a systematic review and meta-analysis. *Medicine*, 2015. 94(19).
22. Alexander, R. and M. Fennelly Comparison of ondansetron, metoclopramide and placebo as premedicants to reduce nausea and vomiting after major surgery. *Anaesthesia*, 1997. 52(7): p. 695-698.
23. Alexander, R., et al. Comparison of ondansetron and droperidol in reducing postoperative nausea and vomiting associated with patient-controlled analgesia." *Anaesthesia*, 1995. 50(12): p. 1086-1088.

24. Ali-Melkkilä, T., et al. Tropisetron and metoclopramide in the prevention of postoperative nausea and vomiting: A comparative, placebo-controlled study in patients undergoing ophthalmic surgery. *Anaesthesia*, 1996. 51(3): p. 232-235.
25. Alon, E., et al. Tropisetron for treating established postoperative nausea and vomiting: a randomized, doubleblind, placebo-controlled study. *Anesthesia & Analgesia*, 1998. 86(3): p. 617-623.
26. Bestas, A., et al. Effects of ondansetron and granisetron on postoperative nausea and vomiting in adult patients undergoing laparoscopic cholecystectomy: a randomized, double-blind, placebo-controlled clinical trial. *Current therapeutic research*, 2007. 68(5): p. 303-312.
27. Bilgin, T. E., et al. A comparative study of the antiemetic efficacy of dexamethasone, ondansetron, and metoclopramide in patients undergoing gynecological surgery. *Medical Science Monitor*, 2010. 16(7): p. CR336-CR341.
28. Bodner, M. and P. F. White. Antiemetic efficacy of ondansetron after outpatient laparoscopy. *Anesthesia and analgesia*, 1991. 73(3): p. 250-254.
29. Candiotti, K. A., et al. A randomized, double-blind study to evaluate the efficacy and safety of three different doses of palonosetron versus placebo for preventing postoperative nausea and vomiting. *Anesthesia & Analgesia*, 2008. 107(2): p. 445-451.
30. Chen, J. J., et al. Efficacy of ondansetron and prochlorperazine for the prevention of postoperative nausea and vomiting after total hip replacement or total knee replacement procedures: a randomized, double-blind, comparative trial. *Archives of internal medicine*, 1998. 158(19): p. 2124-2128.
31. Choi, D., et al. Prophylactic control of post-operative nausea and vomiting using ondansetron and ramosetron after cardiac surgery. *Acta anaesthesiologica scandinavica*, 2010. 54(8): p. 962-969.
32. Cholwill, J., et al. Comparison of ondansetron and cyclizine for prevention of nausea and vomiting after day-case gynaecological laparoscopy. *British journal of anaesthesia*, 1999. 83(4): p. 611-614.
33. Chun, H., et al. Efficacy of palonosetron for the prevention of postoperative nausea and vomiting: a randomized, double-blinded, placebo-controlled trial. *British journal of anaesthesia*, 2014. 112(3): p. 485-490.
34. Claybon, L. Single dose intravenous ondansetron for the 24-hour treatment of postoperative nausea and vomiting. *Anaesthesia*, 1994. 49: p. 24-29.

35. Cozanitis, D., et al.
A comparison of ranitidine, droperidol or placebo in the prevention of nausea and vomiting after hysterectomy. Canadian journal of anaesthesia, 1996. 43(2): p. 106.
36. Culebras, X., et al.
The antiemetic efficacy of droperidol added to morphine patient-controlled analgesia: a randomized, controlled, multicenter dose-finding study. Anesthesia & Analgesia, 2003. 97(3): p. 816-821.
37. Davidson, E. D., et al.
The effects of metoclopramide on postoperative ileus. A randomized double-blind study. Annals of surgery, 1979. 190(1): p. 27.
38. Desilva, P., et al.
The efficacy of prophylactic ondansetron, droperidol, perphenazine, and metoclopramide in the prevention of nausea and vomiting after major gynecologic surgery. Anesthesia & Analgesia, 1995. 81(1): p. 139-143.
39. Diemunsch, P., et al.
Intravenous dolasetron mesilate ameliorates postoperative nausea and vomiting. Canadian journal of anaesthesia, 1997. 44(2): p. 173.
40. Dobkin, A. B., et al.
Double-blind evaluation of Metoclopramide (MK 745, Sinemet®), Trimethobenzamide (Tigan®), and a placebo as postanaesthetic anti-emetics following Methoxyflurane anaesthesia. Canadian Anaesthetists' Society Journal, 1968. 15(1): p. 80-91.
41. Du, S. P., et al.
Ondansetron in the treatment of postoperative nausea and vomiting in ambulatory outpatients: a dose-comparative, stratified, multicentre study. European journal of anaesthesiology. Supplement, 1992. 6: p. 55-62.
42. Eberhart, L., et al.
Dimenhydrinate and metoclopramide alone or in combination for prophylaxis of PONV. Canadian Journal of Anesthesia, 2000. 47(8): p. 780.
43. Eberhart, L. H., et al.
Droperidol and dolasetron alone or in combination for prevention of postoperative nausea and vomiting after vitrectomy. Ophthalmology, 2004. 111(8): p. 1569-1575.
44. Egerton-Warburton, D., et al.
Antiemetic use for nausea and vomiting in adult emergency department patients: randomized controlled trial comparing ondansetron, metoclopramide, and placebo. Annals of emergency medicine, 2014. 64(5): p. 526-532. e521.
45. Fortney, J. T., et al.
A comparison of the efficacy, safety, and patient satisfaction of ondansetron versus droperidol as antiemetics for elective outpatient surgical procedures. Anesthesia & Analgesia, 1998. 86(4): p. 731-738.

46. Gan, T., et al. Double-blind comparison of ondansetron, droperidol and saline in the prevention of postoperative nausea and vomiting. *BJA: British Journal of Anaesthesia*, 1994. 72(5): p. 544-547.
47. Gan, T. J., et al. Rolapitant for the prevention of postoperative nausea and vomiting: a prospective, double-blinded, placebo-controlled randomized trial. *Anesthesia & Analgesia*, 2011. 112(4): p. 804-812.
48. Graczyk, S. G., et al. Intravenous dolasetron for the prevention of postoperative nausea and vomiting after outpatient laparoscopic gynecologic surgery. *Anesthesia & Analgesia*, 1997. 84(2): p. 325-330.
49. Grover, V., et al. Efficacy of orally disintegrating ondansetron in preventing postoperative nausea and vomiting after laparoscopic cholecystectomy: a randomised, double-blind placebo controlled study. *Anaesthesia*, 2009. 64(6): p. 595-600.
50. Helmy, S. Prophylactic anti-emetic efficacy of ondansetron in laparoscopic cholecystectomy under total intravenous anaesthesiaA randomised, double-blind comparison with droperidol, metoclopramide and placebo. *Anaesthesia*, 1999. 54(3): p. 266-271.
51. Hüseyinoğlu, Ü. and K. Ülker Preoperative use of 10-mg metoclopramide and 50-mg dimenhydrinate in the prophylaxis of postoperative nausea and vomiting in elective caesarean births: a prospective randomized clinical study. *The Journal of Obstetrics and Gynecology of India*, 2016. 66(4): p. 252-258.
52. Jellish, W. S., et al. Ondansetron versus droperidol or placebo to prevent nausea and vomiting after otologic surgery. *Otolaryngology—Head and Neck Surgery*, 1998. 118(6): p. 785-789.
53. Jellish, W. S., et al. Ondansetron versus droperidol or placebo when given prophylactically for the prevention of postoperative nausea and vomiting in patients undergoing middle ear procedures. *Journal of clinical anesthesia*, 1997. 9(6): p. 451-456.
54. Jung, W. S., et al. Oral administration of aprepitant to prevent postoperative nausea in highly susceptible patients after gynecological laparoscopy. *Journal of anesthesia*, 2013. 27(3): p. 396-401.
55. Kaufmann, M. A., et al. Prophylactic antiemetic therapy with patient-controlled analgesia: a double-blind, placebo-controlled comparison of droperidol, metoclopramide, and tropisetron. *Anesthesia and analgesia*, 1994. 78(5): p. 988-994.
56. Khalil, S. N., et al. Ondansetron prevents postoperative nausea and vomiting in women outpatients. *Anesthesia and analgesia*, 1994. 79(5): p. 845-851.

57. Koivuranta, M., et al.
Comparison of ondansetron and droperidol in the prevention of postoperative nausea and vomiting after laparoscopic surgery in women. *Acta anaesthesiologica scandinavica*, 1997 41(10): 1273-1279.
58. Korttila, K., et al.
Intravenous dolasetron and ondansetron in prevention of postoperative nausea and vomiting: a multicenter, double-blind, placebo-controlled study. *Acta anaesthesiologica scandinavica*, 1997. 41(7): p. 914-922.
59. Kovac, A., et al.
Prophylactic intravenous ondansetron in female outpatients undergoing gynaecological surgery: a multicentre dose-comparison study. *European journal of anaesthesiology. Supplement*, 1992. 6: p. 37-47.
60. Kovac, A. L., et al.
A randomized, double-blind study to evaluate the efficacy and safety of three different doses of palonosetron versus placebo in preventing postoperative nausea and vomiting over a 72-hour period. *Anesthesia & Analgesia*, 2008. 107(2): p. 439-444.
61. Kovac, A. L., et al.
Efficacy of repeat intravenous dosing of ondansetron in controlling postoperative nausea and vomiting: a randomized, double-blind, placebo-controlled multicenter trial. *Journal of Clinical Anesthesia*, 1999. 11(6): p. 453-459.
62. Kovac, A. L., et al.
Ondansetron prevents postoperative emesis in male outpatients. *Journal of clinical anesthesia*, 1996. 8(8): p. 644-651.
63. Kovac, A. L., et al.
Treatment of postoperative nausea and vomiting with single intravenous doses of dolasetron mesylate: a multicenter trial. *Anesthesia & Analgesia*, 1997. 85(3): p. 546-552.
64. Kreisler, N. S., et al.
Small-dose droperidol effectively reduces nausea in a general surgical adult patient population. *Anesthesia & Analgesia*, 2000. 91(5): p. 1256-1261.
65. Lee, S., et al.
Prophylactic antiemetic efficacy of granisetron or ramosetron in patients undergoing thyroidectomy. *Asian journal of surgery*, 2002. 25(4): p. 309-314.
66. Madej, T. and K. Simpson
Comparison of the use of domperidone, droperidol and metoclopramide in the prevention of nausea and vomiting following major gynaecological surgery. *BJA: British Journal of Anaesthesia*, 1986. 58(8): p. 884-887.
67. Madenoglu, H., et al.
Randomized, double-blinded comparison of tropisetron and placebo for prevention of postoperative nausea and vomiting after supratentorial craniotomy. *Journal of neurosurgical anesthesiology*, 2003. 15(2): p. 82-86.

68. Maestre, J., et al.
Prevention of postoperative nausea and vomiting with metoclopramide, droperidol and ondansetron: a randomized, double-blind comparison with placebo in ambulatory surgery. *Ambulatory Surgery*, 1997. 5(4): p. 153-159.
69. Malins, A., et al.
Nausea and vomiting after gynaecological laparoscopy: comparison of premedication with oral ondansetron, metoclopramide and placebo. *BJA: British Journal of Anaesthesia*, 1994. 72(2): p. 231-233.
70. McKenzie, R., et al.
Comparison of ondansetron versus placebo to prevent postoperative nausea and vomiting in women undergoing ambulatory gynecologic surgery. *Anesthesiology*, 1993. 78(1): p. 21-28.
71. McKenzie, R., et al.
A randomized, double-blind pilot study examining the use of intravenous ondansetron in the prevention of postoperative nausea and vomiting in female inpatients. *Journal of clinical anesthesia*, 1993. 5(1): p. 30-36.
72. Metaxari, M., et al.
Antiemetic prophylaxis in thyroid surgery: a randomized, double-blind comparison of three 5-HT 3 agents. *Journal of anesthesia*, 2011. 25(3): p. 356-362.
73. Moens, P., et al.
Single I.V. bolus dose of ondansetron in the prevention of postoperative nausea and emesis. *Acta anaesthesiologica Belgica*, 1997. 48(4): p. 245-250.
74. Morris, R., et al.
International, multicentre, placebo-controlled study to evaluate the effectiveness of ondansetron vs. metoclopramide in the prevention of post-operative nausea and vomiting. *European journal of anaesthesiology*, 1998. 15(1): p. 69-79.
75. Naguib, M., et al.
Prophylactic antiemetic therapy with ondansetron, tropisetron, granisetron and metoclopramide in patients undergoing laparoscopic cholecystectomy: a randomized, double-blind comparison with placebo. *Canadian Journal of Anaesthesia*, 1996. 43(3): p. 226-231.
76. Paech, M., et al.
Single-dose prophylaxis for postoperative nausea and vomiting after major abdominal surgery: ondansetron versus droperidol. *Anaesthesia and intensive care*, 1995. 23(5): p. 548-554.
77. Paxton, L., et al.
Prevention of nausea and vomiting after day case gynaecological laparoscopy: a comparison of ondansetron, droperidol, metoclopramide and placebo. *Anaesthesia*, 1995. 50(5): p. 403-406.
78. Polati, E., et al.
Ondansetron versus metoclopramide in the treatment of postoperative nausea and vomiting. *Anesthesia & Analgesia*, 1997. 85(2): p. 395-399.
79. Purhonen, S., et al.
Comparison of tropisetron, droperidol, and saline in the prevention of postoperative nausea and vomiting after gynecologic surgery. *Anesthesia & Analgesia*, 1997. 84(3): 662-667.

80. Rodrigo, M., et al. Ondansetron for prevention of postoperative nausea and vomiting following minor oral surgery: a double-blind randomized study. *Anaesthesia and intensive care*, 1994. 22(5): p. 576-579.
81. Ryu, J., et al. Rameisetron versus ondansetron for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. *Surgical endoscopy*, 2010. 24(4): p. 812-817.
82. Sandhu, H. S., et al. Comparison of ondansetron, dimenhydrinate versus placebo as PONV prophylaxis for outpatient gynecological laparoscopy. *Ambulatory Surgery*, 1999. 7(4): p. 187-191.
83. Shirdashtzadeh, N., et al. Comparison of parenteral promethazine versus midazolam effect as a preoperative medication on postoperative nausea and vomiting after appendectomy. *Caspian journal of internal medicine*, 2011. 2(3): p. 270.
84. Singla, N. K., et al. Phase II study to evaluate the safety and efficacy of the oral neurokinin-1 receptor antagonist casopitant (GW679769) administered with ondansetron for the prevention of postoperative and postdischarge nausea and vomiting in high-risk patients. *Anesthesiology: The Journal of the American Society of Anesthesiologists*, 2010. 113(1): p. 74-82.
85. Sinha, A. C., et al. Aprepitant's prophylactic efficacy in decreasing postoperative nausea and vomiting in morbidly obese patients undergoing bariatric surgery. *Obesity surgery*, 2014. 24(2): p. 225-231.
86. Suen, T., et al. Ondansetron 4 mg for the prevention of nausea and vomiting after minor laparoscopic gynaecological surgery. *Anaesthesia and intensive care*, 1994. 22(2): p. 142-146.
87. Sung, Y.-F., et al. A double-blind, placebo-controlled pilot study examining the effectiveness of intravenous ondansetron in the prevention of postoperative nausea and emesis. *Journal of clinical anesthesia*, 1993. 5(1): p. 22-29.
88. Tang, J., et al. The effect of timing of ondansetron administration on its efficacy, cost-effectiveness, and cost-benefit as a prophylactic antiemetic in the ambulatory setting. *Anesthesia & Analgesia*, 1998. 86(2): p. 274-282.
89. Tang, J., et al. A comparison of costs and efficacy of ondansetron and droperidol as prophylactic antiemetic therapy for elective outpatient gynecologic procedures. *Anesthesia & Analgesia*, 1996. 83(2): 304-313.
90. Taylor, A. M., et al. A double-blind, parallel-group, placebo-controlled, dose-ranging, multicenter study of intravenous granisetron in the treatment of postoperative nausea and vomiting in patients undergoing surgery with general anesthesia. *Journal of clinical anesthesia*, 1997. 9(8): p. 658-663.

91. Valanne, J. and K. Korttila
Effect of a small dose of droperidol on nausea, vomiting and recovery after outpatient enflurane anaesthesia. *Acta anaesthesiologica scandinavica*, 1985. 29(4): p. 359-362.
92. Vallejo, M. C., et al.
Aprepitant plus ondansetron compared with ondansetron alone in reducing postoperative nausea and vomiting in ambulatory patients undergoing plastic surgery. *Plastic and reconstructive surgery*, 2012. 129(2): p. 519-526.
93. Van den Berg, A.
A comparison of ondansetron and prochlorperazine for the prevention of nausea and vomiting after tympanoplasty. *Canadian journal of anaesthesia*, 1996. 43(9): p. 939-945.
94. Wallenborn, J., et al.
Prevention of postoperative nausea and vomiting by metoclopramide combined with dexamethasone: randomised double blind multicentre trial. *Bmj*, 2006. 333(7563): p. 324.
95. Wilson, A., et al.
Single-dose I.V. granisetron in the prevention of postoperative nausea and vomiting. *British journal of anaesthesia*, 1996. 76(4): p. 515-518.
96. Wilson, E. B., et al.
Metoclopramide versus ondansetron in prophylaxis of nausea and vomiting for laparoscopic cholecystectomy. *The American journal of surgery*, 2001. 181(2): p. 138-141.
97. Wu, O., et al.
Additive anti-emetic efficacy of prophylactic ondansetron with droperidol in out-patient gynecological laparoscopy. *Canadian Journal of Anesthesia*, 2000. 47(6): p. 529-536.