Promethazine in the treatment of postoperative nausea and vomiting: a systematic review

JOSKO MARKIC • ANNA LOUISE RIDGE

ABSTRACT
Postoperative nausea and vomiting (PONV) is among the most important concerns of patients undergoing surgery. The incidence ranges from 30% to 70%. The incidence of PONV correlates with a number of risk factors a patient possesses. Patient-related risk factors in adults are: female gender, history of PONV, duration of surgery > 60 min, nonsmoking status, history of motion sickness, and postoperative use of opioids. Risk factors in children are: duration of surgery ≥ 30 minutes, age ≥ 3 years, strabismus surgery, and a history of PONV in the patient, parent or sibling. Treatment of PONV includes various classes of medications and none of them is entirely effective. If it is necessary to use combination therapy, then medicines with different sites of activity should be used. Promethazine is a phenothiazine derivate available as a medicine since its introduction in 1946. In this article, a search was performed to identify all published papers and reports evaluating the effectiveness of promethazine for the management of postoperative nausea and vomiting in adults and children. The results of this review support the finding that promethazine is not recommended as a first-line agent in the treatment of PONV, but can be considered for use as a rescue antiemetic.

Key words: promethazine, postoperative nausea and vomiting, treatment

Introduction
Postoperative nausea and vomiting (PONV), together with pain, is among the most important concerns of patients undergoing surgery. Nausea, vomiting and retching can occur with all types of anesthesia (general, regional or local). (1) The incidence ranges from 30% to 50%, with numbers reported as high as 70% in higher-risk patients. (2) Consequences of PONV are numerous and include rupture of stitches, bleeding, electrolyte imbalances, dehydration, and aspiration of gastric contents. (3, 4) Patients who experience PONV also require additional health care. All of this may delay discharge from the post-anesthesia care unit (PACU) or require additional medical interventions, resulting in increased health care costs.

This article will review the therapeutic efficacy of promethazine in the treatment of postoperative nausea and vomiting.

Evaluation and management of PONV
Current strategies for the prevention of PONV include: (a) proactive risk assessment, (b) avoiding PONV “triggers”, and (c) administration of prophylactic antiemetic medications. (1) Apfel et al. created a risk assessment scoring system and included four patient-related risk factors in it: female gender, nonsmoking status, history of PONV or motion sickness, and postoperative use of opioids. (5) Koivuranta et al. created a similar scoring system, but with five factors: female gender, history of PONV, duration of surgery > 60 min, nonsmoking status, and history of motion sickness. (6) The incidence of PONV correlates with the number of risk factors a patient possesses. A pediatric scoring system has been designed by Eberhart et al. (7) Risk factors associated with increased frequency of PONV in children are: duration of surgery ≥ 30 minutes, age ≥ 3 years, strabismus surgery, and a history of PONV in the patient, parent or sibling. Consensus panel guidelines, developed under the auspices of the Society of Ambulatory Anesthesia, recommended the prophylactic use of antiemetic therapy only for patients who are at moderate to high risk for developing PONV.

A modified and simplified treatment algorithm for the management of PONV is shown in figure 1. As shown in figure 1, treatment of PONV includes various classes of medications. None of the available antiemetics is entirely effective. If it is necessary to
Promethazine is a phenothiazine derivative available as a medicine since its introduction in 1946. It acts as a histamine H1-receptor antagonist with moderate muscarinic and dopamine (D2) receptor blocking activities. (11) Promethazine is available worldwide, in some countries as over the counter medication, and in some only by prescription. It is available in the form of an injection, oral liquid and tablet. Indications for use are: treatment of allergies, adjunct to anesthesia, motion sickness, nausea and vomiting from any cause, adjunct to management of post-operative pain, general sedation, and obstetric sedation. It is contraindicated in patients with known hypersensitivity to promethazine (cross reactivity with other phenothiazines may also occur), in patients with severe toxic central nervous system (CNS) depression or coma, and in children < 2 years of age. (12) Promethazine should be used with extreme caution in children, due to the potentially severe risk of respiratory depression. Sudden deaths in children have been associated with excessively high doses of promethazine. Therefore, the lowest effective doses are recommended in children and concomitant use of other medications having respiratory depressant effects should be avoided.

Promethazine should not be given subcutaneously or intra-arterially due to severe local reactions including necrosis. Intravenous (I.V.) administration may also cause serious tissue reactions and it should be used only in emergency situations or when intramuscular or oral administration is contraindicated. Veins should be large and patent. Promethazine should be used with caution in patients with cardiovascular disease, narrow-angle glaucoma, prostatic hypertrophy, bone marrow depression, impaired liver function, asthma, peptic ulcer disease, sleep apnea, and hypertensive crisis. Promethazine may lower the seizure threshold so it should be used with caution in patients with seizure disorders or if they are receiving other medications which may also lower the seizure threshold. Adverse effects of promethazine are numerous and they include cardiovascular symptoms (tachycardia, bradycardia, hypotension, hypertension), CNS symptoms (sedation, excitation, extrapyramidal reactions, dystonia, neuroleptic malignant syndrome, hallucinations, insomnia), dermatologic symptoms (photosensitivity, rash), gastrointestinal symptoms (xerostomia, abdominal pain, diarrhea), hematomatologic symptoms (thrombocytopenia, agranulocytosis), and other such as cholestatic jaundice, hepatitis, thrombophlebitis, blurred vision, and tinnitus. (12)

When administered for the treatment of nausea and vomiting, promethazine dosage regimen in adults should be 25 mg orally at night, increased to 50–75 mg at night or 25 mg 2–3 times daily if necessary (maximum, 100 mg in 24 hours), or by deep intramuscular injection or by slow intravenous injection 12.5–25 mg, repeated at intervals of not less than 4 hours (usual maximum, 100 mg in 24 hours). (13)

The review of promethazine effectiveness in treatment of PONV

Medline, Cochrane Database of Systematic Reviews, and Cochrane Central Register of Controlled Trials (1970 – June 2010) were searched to identify all published papers and reports evaluating the effectiveness of promethazine for the management of postoperative nausea and vomiting in adults and children. Search terms were promethazine, and postoperative nausea and vomiting. Studies in languages other than English were excluded. Titles and abstracts of retrieved papers were reviewed. Studies were included if they were systematic reviews or randomized controlled trials (RCTs). Non-randomized clinical trials were also included if the data published in them was considered relevant for this review. The reference lists of included studies were hand searched to identify any additional studies. The studies in which promethazine was used as part of a combination of medicines (for example, lytic cocktails) were excluded. Different medicines, doses, and regimens have been used in these studies and the findings cannot be used to conclude which agent is most effective for preventing PONV.

After analysis of retrieved papers, 19 relevant clinical trials and 4 systematic reviews were identified evaluating the effectiveness of promethazine for the management of PONV. Data relevant for evaluation of promethazine effectiveness was extracted and tabulated (table 1, table 2).

The majority of 19 clinical trials (12/19: 63.2%) were double-blind RCTs, 3 were RCTs, and 4 articles presented nonran-
Table 1. Clinical trials evaluating the effectiveness of promethazine for the management of PONV.

<table>
<thead>
<tr>
<th>No.</th>
<th>Article; Study Type; Study Design</th>
<th>Conclusion</th>
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<tbody>
<tr>
<td>01.</td>
<td>Conner (1977) (14) Double-blind RCT; Adults aged 18 – 70 years (N = 270) One hour before surgery, patients received morphine 5 mg or 10 mg alone or in combination with promethazine 6.25, 12.5, or 25 mg. Promethazine 25 mg alone also was studied.</td>
<td>The use of promethazine had no effect on incidence of nausea. Also, it was reported that there was no statistically significant difference between the various doses of promethazine.</td>
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<td>02.</td>
<td>Dodson (1978) (16) Double-blind RCT; Women aged 16 – 70 years (N = 124) As a premedication, 2-3 hours before surgery: 1. morphine 2.5 mg p.o.; 2. promethazine 50 mg p.o.</td>
<td>Vomiting during anesthesia, or during the 1st hour after surgery occurred in 8 patients, of whom 7 received lorazepam. There was no difference between the groups in respect to late PONV.</td>
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<td>03.</td>
<td>Vella (1985) (16) Double-blind RCT; Women in labour (N = 477).</td>
<td>Both metoclopramide and promethazine prevented the increase in nausea and vomiting associated with pethidine administration, with promethazine having a more sustained effect - by 4 hours promethazine produced a significant reduction in nausea from the level before pethidine administration.</td>
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<td>04.</td>
<td>Blanc (1991) (10) Double-blind RCT; Children aged 2 – 10 years (N = 100; 47 M + 53 F) Patients received: 1. droperidol 0.075 mg/kg i.v. + placebo i.m.; 2. promethazine 0.5 mg/kg i.v. + promethazine 0.5 mg/kg i.m. (max. 25 mg).</td>
<td>The incidence of vomiting pre-discharge in groups 1 and 2 was not significantly different. The incidence of vomiting post-discharge and overall was significantly higher with droperidol than with promethazine. Promethazine pretreatment reduced the incidence of postoperative vomiting in unpremedicated children.</td>
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<td>05.</td>
<td>Silverman (1992) (17) RCT; Women aged 18 – 60 years (N = 30) In patient care unit, patients were assigned to receive patient-controlled analgesia: 1. morphine; 2. morphine + promethazine 0.625 mg with each morphine dose (average of 17.6 mg over 24-h period).</td>
<td>Visual analogue scale (VAS) scores for nausea were not significantly different between the two groups. The addition of promethazine to morphine was associated with a significant decrease in the symptom-therapy score for nausea.</td>
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<td>06.</td>
<td>Sandhya (1994) (18) RCT; Women aged between 22.4 ± 2.5 and 25.0 ± 4.88 years (N = 32) Patients received pentazocine 0.6 mg/kg i.v. 5 minutes before induction of anaesthesia along with either: 1. isotonic saline (Control group); 2. promethazine 25 mg; 3. metoclopramide 10 mg.</td>
<td>Promethazine and metoclopramide in the doses used in this study are ineffective for antiemetic prophylaxis.</td>
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<td>07.</td>
<td>Tarkkila (1995) (19) Double-blind RCT; Adults aged 50 – 83 years (N = 60) For premedication the patients received: 1. oral diazepam 5-15 mg + placebo patch; 2. oral promethazine 10 mg + placebo patch; 3. oral promethazine 10 mg + transdermal scopolamine patch 1.5 mg.</td>
<td>The combination of oral promethazine and transdermal scopolamine was most effective in reducing PONV and also reduced the need for postoperative pain treatment.</td>
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<td>08.</td>
<td>Rodola (1995) (20) Double-blind RCT; Adults aged 18 – 40 years (N = 120; 58 M + 62 F) Premedication before surgery: 1. no treatment = Control group; 2. atropine 0.01 mg/kg i.m. + diazepam 0.2 mg/kg p.o.; 3. atropine 0.01 mg/kg i.m. + promethazine 1 mg/kg i.m.</td>
<td>The combination of promethazine and atropine was very effective in reducing occurrence of PONV. Promethazine is suggested as an effective and inexpensive medication to prevent PONV in orthopedic surgery.</td>
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<td>09.</td>
<td>Khalil (1999) (21) Double-blind RCT; Adults aged 13 -72 years (N = 87; 46 M + 41 F). At induction of anaesthesia, patients received: 1. ondansetron 4 mg; 2. promethazine 25 mg; 3. promethazine 12.5 mg + ondansetron 2 mg; 4. placebo</td>
<td>Over the 24-h period, the incidence of nausea was significantly reduced in promethazine and combination group compared with placebo group. Incidence of vomiting was significantly reduced in combination group compared with promethazine, ondansetron and placebo group. Incidence of combined nausea and vomiting was reduced in promethazine and combination group compared with placebo group. Combination of ondansetron and promethazine and promethazine alone are effective and inexpensive choices.</td>
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<td>10.</td>
<td>Parlow (1999) (22) Double-blind RCT; Women aged 35 ± 9 years (N = 95) Patients received droperidol 0.5 mg i.v. intraoperatively, and prior to transfer from post-anesthetic recovery room: 1. promethazine 0.6 mg/kg i.m.; 2. placebo</td>
<td>The incidence of nausea, vomiting, and rescue antiemetic use in the recovery room was similar between the groups. Promethazine had no effect on postdischarge nausea scores, vomiting, or rescue antiemetic requirements.</td>
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<tr>
<td>No.</td>
<td>Article; Study Type; Study Design</td>
<td>Conclusion</td>
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<td>11</td>
<td>Kreisier (2000) (23) Double-blind RCT; Adults aged between 46.7 ± 15.7 and 50.0 ± 15.3 years (N = 150;59 M+91 F)</td>
<td>Before emergence from general anesthesia, patients received PONV prophylaxis: droperidol 0.625 i.v. or placebo. If PONV occurred in the postanesthesia care unit, patients received rescue antiemetic (N = 31): 1. droperidol 0.625 i.v.; 2. ondansetron 4 mg i.v.; 3. promethazine 12.5 mg i.v.</td>
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<td>12</td>
<td>Ikechebelu (2003) (24) Retrospective study; Women aged 18 – 40 years (N = 295)</td>
<td>Premedication: 1. atropine 0.6 mg; 2. atropine 0.6 mg + diazepam 10 mg; 3. atropine 0.6 mg + promethazine 50 mg</td>
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<td>13</td>
<td>Chia (2004) (25) Double-blind RCT; Women aged between 44.0 ± 10.2 and 47.0 ± 5.2 years (N = 90)</td>
<td>1. Pre-group - received promethazine 0.1 mg/kg infusion before anesthesia induction 2. Post-group - received promethazine 0.1 mg/kg infusion at the end of surgery 3. Control group - received normal saline</td>
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<td>14</td>
<td>Moser (2006) (26) Prospective study (nonrandomized); Adults aged 27 – 81 years (N = 87)</td>
<td>1. promethazine 6.25 mg or 12.5 mg i.v.; 2. ondansetron 4 mg i.v.</td>
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<td>15</td>
<td>Habib (2005) (27) Retrospective review (not randomized); Adults aged 18 – 65 years (N = 431)</td>
<td>Rescue antiemetic in PACU: 1. ondansetron 4 mg; 2. droperidol 0.625 to 1.25 mg; 3. metoclopramide 10 mg; 4. promethazine 6.25 to 25 mg; 5. dimenhydrinate 25 to 50 mg. In the original double-blind RCT, patients (N = 2061) received PONV prophylaxis before the induction of anesthesia: ondansetron 4 mg, droperidol 0.625 or 1.25 mg, or placebo. (28)</td>
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<td>16</td>
<td>Naile (2007) (29) Double-blind RCT; Adults aged 16 – 80 years (N = 120). Oral premedication 1 hour prior surgery and subsequent at 8 hours intervals for total 24 hours: 1. shaving of fresh ginger 250 mg; 2. metoclopramide 10 mg; 3. prochlorperazine 5 mg; 4. promethazine 20 mg; 5. ondansetron 4 mg; 6. placebo.</td>
<td>The frequency and quantity of PONV was significantly lower in the ginger group than in the control group. The incidence of nausea was considerably less with promethazine than in the control group.</td>
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<td>17</td>
<td>Habib (2007) (30) Retrospective review (not randomized); Adults aged &gt; 18 years</td>
<td>Patients (N = 18209) initially received PONV prophylaxis with ondansetron 4 mg. Rescue antiemetic administered in PACU within 4 hours after PONV prophylaxis (N = 3814): 1. ondansetron 4 mg; 2. promethazine 6.25; 12.5 or 25 mg</td>
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<tr>
<td>18</td>
<td>Pellegrini (2009) (31) RCT; Adults aged between 33.98 ± 10.9 and 37.09 ± 11.0 years (N = 85)</td>
<td>IPA is as effective in treating PONV as promethazine in patients who have been identified as high risk for PONV.</td>
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<td>19</td>
<td>Gan (2009) (32) Double-blind RCT; Women aged between 32.8 ± 7.2 and 34.3 ± 8.3 years (N = 138)</td>
<td>15 min before the end of surgery i.v. and then 12 h after surgery for five oral doses, patients received: 1. granisetron 0.1 mg i.v. (1 mg oral); 2. promethazine 6.25 mg i.v. (12.5 mg oral); 3. granisetron + promethazine (combination, same doses as above)</td>
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F, females; M, males; N, number; PACU, post-anesthesia care unit; PONV, postoperative nausea and vomiting; RCT, randomized controlled trials.
The doses of promethazine were determined in 6486 patients of which 6299 were adults aged 16 or more, and 100 were children. One clinical trial included 87 patients aged 13 – 72 years, but we were unable to identify the exact number of participants that were under or over 16 years from the published data. (21) Promethazine was used in different dosages and administered using different routes of administration (oral, intramuscular, intravenous, combined intramuscular + intravenous) across the studies. The use of different dosages may have led to different effects. The doses of promethazine were determined in

### Table 2. Systematic reviews evaluating the effectiveness of promethazine for the management of postoperative nausea and vomiting.

<table>
<thead>
<tr>
<th>No.</th>
<th>Article; Methodology</th>
<th>Remarks / Results concerning promethazine role</th>
<th>Conclusions; Comment</th>
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<tbody>
<tr>
<td>01.</td>
<td>Tramer (1999) (33) MEDLINE (1966 – Apr 1998), EMBASE (1980 – Apr 1998), and Cochrane library search was conducted. Included one study with promethazine (17)</td>
<td>The addition of promethazine to morphine was associated with a significant decrease in the symptom-therapy score for nausea.</td>
<td>Promethazine showed promising results but the number of patients is limited and the recommendations cannot be based on the available evidences.</td>
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<td>02.</td>
<td>Fujii (2005) (34) MEDLINE and EMBASE search (Jan 1990 – Oct 2003) was conducted. Included two studies with promethazine (21), (22)</td>
<td>Over the 24-h period, the incidence of PONV was significantly reduced in promethazine group and combination group of promethazine and ondansetron compared with placebo group and ondansetron group. (21) There was no difference between the placebo and promethazine groups in the worst level of nausea reported, the incidence of nausea of any severity, moderate to severe nausea, vomiting, or the need for rescue antiemetics following discharge. (22)</td>
<td>Among traditional antiemetics (e.g., anticholinergics, antihistamines, phenothiazines, butyrophenones, and benzamides), dimehydrinate and perphenazine are highly efficacious for prophylaxis against PONV following laparoscopic cholecystectomy.</td>
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<td>03.</td>
<td>Carlisle (2006) (35) Cochrane systematic review The Cochrane Central Register of Controlled Trials (Jan 1966 - May 2004), EMBASE (Jan 1985 - May 2004), CINAHL (1982 - May 2004), ISI WOS (to May 2004), Lilac, and Ingenta searches were conducted. Included 7 clinical trials from Table 1 evaluating the effectiveness of promethazine: (21), (22), (10), (19), (15), (20), (18)</td>
<td>Compared to placebo, the risk for PONV is decreased by promethazine, but there was no evidence that the risk of postoperative vomiting is changed by promethazine. Compared to no treatment, there was no evidence that promethazine changes the risk of postoperative nausea, or the risk of postoperative vomiting.</td>
<td>Eight medicines (droperidol, metoclopramide, ondansetron, tropisetron, dolasetron, dexamethasone, cyclizine and granisetron) were identified that reliably prevented nausea or vomiting after surgery. There was no reliable evidence that one medicine was better than another.</td>
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<tr>
<td>04.</td>
<td>Fujii (2008) (36) MEDLINE and EMBASE searches from Jan 1990 to Dec 2007 were conducted. Included one study with promethazine (21)</td>
<td>Over the 24-h period, the incidence of PONV was significantly reduced in promethazine group and combination group of promethazine and ondansetron compared with placebo group. There was no difference between placebo and ondansetron groups.</td>
<td>Combination of antiemetic therapy with an antiserotonin (ondansetron, granisetron) or dexamethasone is highly effective for the prophylaxis against PONV.</td>
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</table>

PONV, postoperative nausea and vomiting.
In seven clinical trials different groups were identified: reported by the intervention used. Six clinical trials presented in Table 1 are effect of promethazine as precisely as no common or unique outcome could to pool the data in a meta-analysis as ved clinical trials, it was not possible 24-h period.

Due to the heterogeneity of the retrieved clinical trials, it was not possible to pool the data in a meta-analysis as no common or unique outcome could be determined. In order to analyze the effect of promethazine as precisely as possible, the outcomes of retrieved clinical trials presented in Table 1 are reported by the intervention used. Six different groups were identified:

1) Promethazine vs. placebo
In seven clinical trials (16, 18, 20-22, 24, 25), promethazine was compared to placebo. In 5 of them women only participated (N = 989; aged 18 – 55 years), one trial was with adults (N = 120) aged 18 – 40 years, and one trial included 87 patients aged 13 – 72 years. Promethazine was found effective in reducing the occurrence of PONV in 5 articles, while 2 studies found it ineffective for antiemetic prophylaxis.

2) Promethazine vs. another antiemetic medicine
In three clinical trials (13, 26, 29), promethazine was compared to another antiemetic medicine. One study with children (N = 100), aged 2 – 10 years, reported that promethazine reduced the incidence of postoperative vomiting when compared to droperidol, and the other with adults (N = 87) aged 27 – 81 years, found promethazine as effective as ondansetron. The third study, with patients aged 16 – 80 years (N = 120), found that shavings of fresh ginger decreased the incidence of PONV significantly when compared to placebo. The same study also evaluated the effect of promethazine and found that the incidence of nausea was considerably less with promethazine than in the control group.

3) Promethazine + another antiemetic vs. placebo or the same antiemetic alone
In three clinical trials (19, 21, 32), combination of promethazine with another antiemetic was compared to placebo or to those same antiemetics administered alone. The study with 87 patients, aged 13 – 72 years, reported that a combination of promethazine with ondansetron reduced the incidence of nausea, vomiting and combination of nausea and vomiting when compared with placebo. The same study also reported the combination of promethazine and ondansetron to be more effective in reducing the incidence of vomiting and combined nausea and vomiting than promethazine or ondansetron alone. The second study with women (N = 138), aged 32.8 ± 7.2 and 34.3 ± 8.3 years, reported the combination of promethazine and granisetron with promethazine monotherapy. The third study, with adults (N = 60) aged 50 – 83 years, also reported a combination of medicines to be the most effective. In this study, oral promethazine was combined with a transdermal scopolamine patch, and it was found that this combination is more effective in reducing incidence of PONV than promethazine monotherapy.

4) Promethazine in combination with morphine
In two clinical trials (14, 17), the effect of promethazine and morphine combination on incidence of nausea was tested. Both studies, one with adults (N = 270) aged 18 – 70 years and the other with women (N = 30) aged 18 – 60 years found that the use of promethazine had no effect on the incidence of nausea. However, the later study reported that the use of promethazine, as an adjunct to morphine, was associated with a decrease in the symptom-therapy score for nausea.

5) Promethazine as a rescue antiemetic (2nd line treatment) vs. other antiemetics
In four clinical trials (23, 27, 30, 31), promethazine was used as a rescue antiemetic and was compared to other antiemetics. Adults (N = 4361) participated in these trials. In two studies (N = 116) the difference between promethazine and other used medicine was not revealed. Other two studies (N = 4245) found promethazine to be more efficient in reducing PONV than the repeated dose of the same antiemetic used for prophylaxis.

6) Promethazine vs. lorazepam
One clinical trial (15), with women (N = 124) aged 16 – 70 years, compared promethazine to the sedative lorazepam. The primary outcome of this trial was their effect as premedicants. However, no difference among them was found in respect to late PONV.

Four systematic reviews published between 1999 and 2008 were identified. Two systematic reviews (33, 36) included only one clinical trial evaluating the efficacy of promethazine in management of PONV. In one of them, it is stated that promethazine showed promising results in preventing nausea but due to limited number of patients a conclusion could not be made. The second review recommended a combination of an antiserotonin plus traditional antiemetics (this included promethazine) as highly effective for prophylaxis against PONV. The third review (34) included two clinical trials with promethazine. Among the conclusions in this review promethazine was not explicitly stated. The review which included the most clinical trials evaluating the effectiveness of promethazine was a Cochrane systematic review.

(35) The objective of that review was to assess the prevention of postoperative nausea and vomiting by different medicines and to compare their efficacies. In order to achieve that, 737 randomized controlled trials involving 103 237 people that compared a medicine with placebo or another medicine were included. Out of that, 7 clinical trials involving 618 people evaluated the effectiveness of promethazine. It was found that eight medicines reliably prevented nausea or vomiting after surgery: droperidol, metoclopramide, ondansetron, tropisetron, dolasetron, dexamethasone, scopolamine patch, and it was found that this combination is more effective in reducing incidence of PONV than promethazine monotherapy.
cyclizine and granisetron. Those medicines prevented nausea or vomiting in three or four people out of every 10 who would have vomited or felt nauseated with a placebo. The authors did not find reliable evidence that one medicine was better than another. Side effects were mild. In regard to promethazine, there was no evidence that the risk of postoperative vomiting was affected by promethazine. Also, compared to no treatment, there was no evidence that promethazine changed the risk of postoperative nausea or the risk of postoperative vomiting.

**Conclusions**

It is evident from tables 1 and 2 that despite its widespread use, little data evaluating the therapeutic efficacy of promethazine is available. There are more articles evaluating efficacy of other antiemetics, but evaluation of these treatments was beyond the scope of this review. Current guidelines do not recommend the use of promethazine and metoclopramide in the treatment of PONV, nor as a part of pharmacologic combination for adults and children, nor as a single agent in children. (8) A recent Cochrane Database Systematic Review found that, compared to placebo, the risk for PONV is decreased by promethazine, but there was no evidence that the risk of postoperative vomiting is changed by promethazine. Also, compared to no treatment, there was no evidence that promethazine changes the risk of postoperative vomiting and postoperative nausea.(35) The results of this review support the finding that promethazine is not recommended as a first-line medicine in the treatment of PONV, but can be considered for use as a rescue antiemetic.

**ACKNOWLEDGMENT**

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**REFERENCES**