

## Role of dextrose on reducing postoperative nausea and vomiting following endoscopic middle ear surgery: a randomized, double-blind, controlled study

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### Abstract

**Context:** Despite of prophylaxis, nausea or vomiting is most common in the postoperative period, may leads to unanticipated readmission, prolonged hospital stay and patient's frustration. Earlier studies have reported conflicting results of dextrose on postoperative nausea and vomiting hence we designed this study.

**Aim:** Testing the role of intravenous 5% dextrose on reducing the frequency of postoperative nausea and vomiting.

**Study design:** A prospective, randomized, double-blind, placebo-controlled study.

**Methods:** In this study, we allocated 90 healthy patients scheduled for tympanoplasty under general anesthesia. The participants were randomized into two groups ( $n=45$ ) to receive either Ringer's lactate solution (group C) or 5% dextrose in Ringer's lactate solution (group D) intravenously following surgery. A standard technique was applied for general anesthesia in all patients and single dose of ondansetron 4 mg was given intravenously half-hour before recovery from anesthesia. Postoperative nausea and vomiting scores, antiemetic doses were recorded at 0, 30, 60, 90, 120 min and 24 hours. The duration of stay in post-anesthesia care unit was also noted. The data recorded were analyzed using student t-test and chi-square test. A value of  $P < 0.05$  was considered as significant and 0.0001 was considered as extremely significant.

**Results:** Postoperative nausea and vomiting scores were not different between the groups and non-significant statistically ( $P > 0.05$ ). Conversely, patients in group D consumed less antiemetic doses ( $P = 0.004$ ), and had a short duration of stay in the post-anesthesia care unit ( $P < 0.0001$ ) when compared with patients in group C.

**Conclusion:** In this study, postoperative dextrose 5% intravenous infusion resulted in improved postoperative emesis management as explained by decrease in rescue antiemetic consumption and post-anesthesia care unit duration of stay.

**Keywords:** Dextrose, Nausea, Postoperative, Prevention, Vomiting.

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### Introduction

Middle ear surgery (mastoidectomy and tympanoplasty) performed under local or general anesthesia is complicated with high incidence of nausea and vomiting in the postsurgical period. The reported incidence is 62% to 80% when no prophylactic antiemetic was given.<sup>1</sup> Postoperative nausea and vomiting (PONV) is the second most common complication of surgery and anesthesia, may results in tardy oral intake, dehydration, electrolyte imbalance, unforeseen readmissions,<sup>2,3</sup> delayed discharge, increased rates of gastric aspiration and wound dehiscence.<sup>4</sup> Therefore prevention of PONV is vital, economical, improves outcomes and augments patient's satisfaction.

The pharmacologic remedies targeting blockade of emetogenic receptors have shown a decrease in the

incidence of PONV by about 20%.<sup>5</sup> Recently proposed two other therapies include perioperative carbohydrate (dextrose) loading and fluid administration. Many studies have reported the use of perioperative intravenous (IV) fluid therapy and its effect on the frequency and severity of PONV even though results are conflicting.<sup>6,7,8,9</sup> The data that indicate the use of IV dextrose solution following surgery to reduce nausea and vomiting are limited and shown mixed results.<sup>10,11</sup> We hypothesis that dextrose 5% administration during emergence from general anesthesia could reduce the incidence of PONV. Therefore this study was designed to evaluate relationship of postoperative IV administration of dextrose on PONV in patients undergoing endoscopic middle ear surgery (tympanoplasty) under general anesthesia (GA).

### Material and Method

Ninety, American Society of Anesthesiologists physical status I and II, non-diabetic patients of both sex, between 20 to 50 years of age, scheduled for middle ear endoscopic surgery (tympanoplasty) requiring GA were enrolled to participate in this prospective, randomized, placebo-controlled, double-blind study. Subsequent to approval of the study by the institutional ethical committee, written informed consent was obtained from each participant and

appropriate investigations were completed. Patients were randomized (using computer generated randomization numbers) in to two groups of 45 each to receive either Ringer lactate (RL) solution (control group C) or 5% dextrose liquid in Ringer's lactate solution (study group D). Patients with body weight more than 80 kg, a history of epilepsy, diabetes, jaundice, coagulopathy, hypertension, heart disease, asthma, renal failure, currently receiving steroid or antiemetic, and women with pregnancy were excluded from the study. Patients who suffered from severe perioperative hypotension requiring treatment with large volumes of IV fluid or blood transfusion were disqualified for analysis.

In the operation theater pulse oxymetry, noninvasive blood pressure, capnography and standard 5 leads electrocardiography (ECG) were attached and baseline hemodynamic parameters were recorded. An IV line established in non-dominant hand with 18 G IV cannula, premedicated with glycopyrrolate 4 $\mu$ g/kg, midazolam 30 $\mu$ g/kg and Ringer's lactate solution started for fasting requirement as calculated by 1, 2, 3 formula. All participants underwent a uniform standard technique for GA using IV thiopentone 5 mg/kg for induction, IV vecuronium 0.1 mg/kg to facilitate tracheal intubation and IV fentanyl 2 $\mu$ g/kg to attenuate stress response to intubation and analgesia. Anesthesia was maintained with halothane 0.5 to 1% in a mixture of oxygen and nitrous oxide (33%:66% and nitrous oxide was replaced with air before closure of the cavity of middle ear). No antiemetic medication was administered intra-operatively. Hypotension (a decrease in mean arterial pressure (MAP) by >20% from baseline value or systolic arterial pressure less than 90 mm Hg) was treated with additional IV crystalloid given as needed at the discretion of attending anesthesia provider. Every patient received 4 mg of ondansetron 30 min before emergence from general anesthesia. Neostigmine 50 $\mu$ g/kg and glycopyrrolate 8 $\mu$ g/kg IV was used to reverse residual muscle relaxation. No narcotic was given at conclusion of surgery and in the post-anesthesia care unit (PACU), however aceclofenac 1 mg/kg IV was given to maintain postoperative analgesia.

On arrival to the PACU the intra-operative fluid was discontinued and an interventional fluid was started, all patients received 500 ml of this fluid for 60 min. The bottles of the study fluid were placed in the sequentially numbered, black opaque plastic bags and sealed to conceal group assignment to the patient, attending anesthetist, and PACU care provider. Anesthesiology resident not involved in the study prepared all this bags. PONV scores were assessed at 0, 30, 60, 90, 120 min in the PACU and 24 hours postoperatively in the ward by verbal descriptive scale (VDS)<sup>12</sup> consists of score 0 = no PONV: no complaint of nausea and vomiting; score 1 = mild PONV:

complains of nausea but refuse antiemetic treatment; score 2 = moderate PONV: patient has nausea and allow treatment with antiemetic; and score 3 = severe PONV: patient has nausea with episode of emesis (retching or vomiting) requiring antiemetic treatment.

Rescue antiemetic (Ondansetron 4 mg IV) was given when the VDS scores were three or more, only after excluding other causes of PONV such as hypovolemia, hypotension, hypoxia, etc. Intra-operative narcotic analgesic medications and their doses were noted. Anesthesia duration was considered as the time from induction of GA till tracheal extubation and the time from surgical skin incision to skin closure was considered as duration of surgery All patients received supplemental oxygen (5L/min) using a well fitted facemask for 4 hours and IV Ringer's lactate (2 ml/kg/h) postoperatively for 24 hours.

### **Statistical analysis**

The primary goal of the study was to compare the PONV incidence (by yes or No) in between the groups. To arrive at a power of 0.8 ( $\alpha=0.05$ ), to find out a 20% intergroup difference in the incidence of PONV assuming a prevalence of 72% during endoscopic middle ear surgery,<sup>1</sup> a power analysis revealed a sample size of 43 per group. Accordingly we extended to include 45 patients per group.

The secondary outcome measures included assessment of vomiting scores, rescue antiemetic consumption and duration of stay in PACU. Consumption of antiemetic was defined as all rescue antiemetic medication classes and doses consumed by every patient for the whole period of stay in PACU. The data were analyzed statistically by using the chi-square test and t-test. Statistically a value of  $P < 0.05$  significant,  $P < 0.001$  highly significant and  $P < 0.0001$  extremely significant was considered.

### **Results**

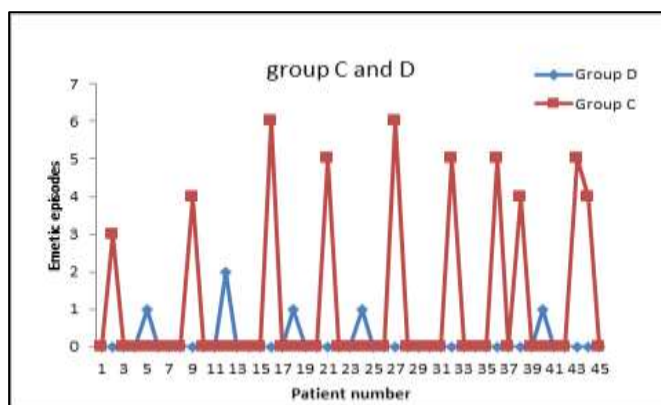
Totally 90 patients participated and completed the study. The study groups were comparable with respect to demographic profile of participants including age, sex, height, weight, ASA grade and body mass index (BMI). The mean period of nil by mouth (NBM) in group D was 653.33 $\pm$ 40.17 min and in group C it was 658.22 $\pm$ 39.83 min, the difference in the time was statistically non-significant ( $P=0.5653$ ). Preoperative blood glucose levels, intra-operative narcotic use, and IV fluid administered were comparable between the groups (Table 1). The mean time of anesthesia, mean time of surgery, and mean blood loss were similar between the groups and non-significant statistically [Table 1]. Thus, by minimizing the effects of variables on the treatment outcomes the randomization in our study was successful.

**Table 1: The demographic characteristics of the participants**

Variables	Group C (n=45)	Group D (n=45)	P value
Age (years)	29.04±9.32	29.11±9.69	0.9729
Sex ratio-male: female (n)	23:22	21:24	0.5500
ASA Grade I& II (n)	35:10	34:11	0.7286
Height (cm)	160.2±11.19	161.69±7.79	0.4237
Body weight (kg)	58.76±7.9	59.22±5.53	0.7497
Body mass index (kg/metre <sup>2</sup> )	22.83±1.51	22.38±1.66	0.1820
Duration of nil by mouth (min)	658.22±39.83	653.33±40.17	0.5653
Preoperative blood glucose mg/dl	102.67±7.2	103.6±7.21	0.5419
IV fluid received (ml/kg/h)	2.49±0.06	2.44±0.3	0.2759
Duration of surgery (min)	105.3±7.63	104.86±7.71	0.7862
Duration of anaesthesia (min)	119.33±7.22	119.13±7.85	0.9002
Intra-operative narcotic used (mg)	118.76±13.92	117.93±11.86	0.7615
Intra-operative blood loss (ml)	16.71±1.62	17.06±1.6	0.3053

Results are mean ± standard deviation, group C: control group; group D: 5% dextrose group; n: number, ASA: American Society of Anaesthesiologists; mg: milligram, cm: Centimetre, kg: Kilograms, dl: decilitre, IV: intravenous; min: minutes, ml: millilitre, h: hour. P value calculated using t-test and chi-square test.

The incidence of PONV was more in group C (62.2% i.e. 28/45) than in Group D (46.7% i.e. 21/45). This difference in frequency was statistically not significant ( $P=0.1434$ ). The average number of emetic episodes per participant in group C was  $1.045±0.42$  and in group D it was  $0.1333±0.41$  (Fig. 1). This variation was statistically significant ( $P=0.0039$ ), 25 out of 45 patients (55.56%) in group C received antiemetic whereas 15 out of 45 patients (33.33%) in group D received antiemetic postoperatively, this dissimilarity was statistically significant ( $P=0.0366$ ). The mean dose of antiemetic used in group C was  $3.55±4.19$  mg and it was  $1.51±1.96$  mg in group D, this disparity was significant statistically ( $P=0.0040$ ). The Mean duration of PACU admission of patients in group D was  $139.67±14.2$  min, which was shorter when compared with  $185.18±13.39$  min of group C patients. Statistically, this difference was extremely significant ( $P < 0.0001$ , Table 2).



**Fig. 1: Showing the severity of vomiting episodes in group C and D**

**Table 2: Emetic episodes and rescue medications**

Variables	Group C (n=45)	Group D (n=45)	P value
Patients with PONV, yes	28(62.2%)	21(46.7%)	0.1434>0.05
Patients with vomiting, yes	10(22.22%)	5(11.1%)	0.5319>0.05
Average emetic episodes per participant	1.045±2.022	0.133±0.41	0.0039<0.05
Patients received Antiemetic	25(55.56%)	15(33.33%)	0.0366<0.05
Mean dose of antiemetic used per individual (mg)	3.55±4.19	1.51±1.96	0.0040<0.05
Mean duration of stay in PACU (min)	185.18±13.39	139.67±14.2	0.0001<0.05

Values are number, percentage and mean ± standard deviation, calculated using Statpac, version 4.0, 1997-2016 applying t-test, West Indies. Group C: control group, group D: 5%

dextrose group; PONV: postoperative nausea and vomiting; mg: milligram; min: minutes; PACU: Post-anesthesia care unit, n: number.

## Discussion

PONV have several momentous effects on both final cost and therapeutic outcome of a given procedure. Moreover, the most routinely used preventive measures are based on managing the patients with extra-medications is an additional burden and expose them to more risky side effects. On the contrary, management of emesis with oral glucose is a well-known modality associated with minimum or no hazard for non-diabetic patients.<sup>13</sup>

This study shows a new effect of postoperative infusion of 5% dextrose in decreasing the number of rescue antiemetic doses by 43.75% in the non-diabetic patients after endoscopic middle ear surgical (tympanoplasty) procedures. The only difference between the group C and group D in our study was the inclusion of 5% dextrose 500 ml in the postoperative fluid management.

In addition, time spent in the PACU is both costly and burdensome to the patient as well as to the caring institute. This study shows a 33% decrease in length of stay in the PACU in group D patients compared with group C patients. But, whether this decrease can be applicable to other major surgical procedures is also an indebted worthy research.

The mechanism of vomiting may be central and peripheral, surgery of the inner ear stimulates the receptors in the vestibular labyrinth, and from here impulses are transmitted mostly through the brain stem vestibular nuclei to the cerebellum, then to the chemoreceptor trigger zone (CTZ), area postrema, solitary tract nucleus and finally to the vomiting center to cause vomiting. The CTZ contains emetogenic dopamine (D<sub>2</sub>) and opioid receptors, hence administration of opioids increases the incidence of PONV.<sup>14</sup> Junger *et al.*, reported an increased risk of PONV more than twice with use of nitrous oxide.<sup>15</sup> Apfel *et al.*,<sup>16</sup> in a study demonstrated similar PONV incidence (30%) with other volatile anesthetic agents. Muscle relaxants have no effect on the incidence of PONV,<sup>17</sup> but reversal of residual muscle relaxation with atropine and neostigmine has an increased emesis episodes in spite of the antiemetic effect of atropine.<sup>18</sup>

Operative procedure, anesthetic technique, and postoperative pain, are considered to affect the incidence of PONV. Surgical factors during middle ear surgery include an increased middle ear pressure generated by diffusion of nitrous oxide.<sup>19</sup> In our study, however, these effects were well equilibrated between the groups, and the pressure raise in the middle ear was prevented by replacing the nitrous oxide with air before closure of tympanic membrane. Therefore, the difference in the frequency of PONV between the groups can be credited to the effect drugs studied.

A totality of 90 patients was included in our study. The control group C had 62.2% incidence of PONV while the dextrose group D had 46.7% incidence only. This difference in incidence was not significant statistically ( $P=0.1434$ ). Our result is in accordance with report of Dabu-Bondoc *et al.*,<sup>20</sup> who studied 62 ASA I and II gynecologic outpatients with 50 grams of IV dextrose. In their study, dextrose containing liquid in Ringers' lactate solution was administered IV following recovery in PACU was associated with alike nausea scores but a reduced doses of rescue antiemetic use compared with control group. Despite prophylactic antiemetic administration 30 minutes before recovery from general anesthesia to all their patients, nausea occurred in 46.7% of their participants, almost alike to what we observed in our study. The dose and rate of dextrose infused IV was higher than our patients received, and comparison was not done between post-infusion and baseline blood glucose levels as this study. Patel *et al.*,<sup>12</sup> in his study found an incidence of 52.9% in dextrose group and 46.7% in control group. This may be because of administration less dextrose for a prolonged period (5% dextrose 250 ml for 2 hours), so we administered 500 ml of 5% dextrose in 60 minutes. Our dose of dextrose and duration of administration is in-between the doses and time of Dabu-Bondoc *et al.*, and Patel *et al.*, study.

## Limitations of study

Firstly we enrolled only healthy, nonsmoking and non-diabetic patients undergoing middle ear endoscopic (tympanoplasty) surgery. Extrapolating the findings of this study to patients with major health co-morbidities, requiring major thoracic or abdominal surgeries is questionable. Surely, the execution of this treatment modality in patients with diabetes would be problematic. So as to say, that these data imply a further study to assess the effects of IV dextrose solution in other non-diabetics undergoing major surgical procedures is appealing.

Secondly, several studies have reported that the incidence of PONV is higher during childhood and early adulthood.<sup>21</sup> The limitation of our study is that we could not analyzed the effect of age on PONV, as all patients we selected were adults. Kovac *et al.*, in their study proven that the BMI is not an established risk factor for PONV and total body weight (TBW) was not a considerable risk factor in their study.<sup>22</sup>

A third limitation of our study is participant's blood glucose levels were measured only before operation and not after the administration of IV dextrose solution. Further investigation is required to clarify whether the positive effect of dextrose-containing fluid on PONV was correlated exclusively to

simple caloric supplementation, or else to a more complex mechanism that such therapy provides.

## Conclusion

We attempted to evaluate the relationship of dextrose administration to PONV during emergence from general anesthesia. Dextrose-containing fluid infusion during emergence and in the beginning of recovery from general anesthesia was not accompanied with differences in the severity or frequency exceeding 20% of PONV. The relationship of PONV to the timing of infusion and optimal dose of dextrose required remains mystery and may deserve further investigation.

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