Pre-operative intravenous fluid therapy with crystalloids or colloids on post-operative nausea & vomiting

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**Background & objectives:** Post-operative nausea and vomiting (PONV) is a frequent complication and may be a reason for increased morbidity and cost of treatment. Following elective surgery, it is believed to result from gut ischaemia consequent to hypovolemia from overnight fasting. This study was carried out to study the effects of pre-operative intravenous fluid supplementation, either crystalloids or colloids, on PONV.

**Methods:** In this prospective randomized clinical trial, 60 female patients undergoing elective open cholecystectomy were randomly allocated to three equal groups A, B and C. All patients received pre-operative fluid supplementation. Group A patients received 2 ml/kg Ringer lactate iv (intravenously) and served as control, Group B patients received 12 ml/kg Ringer lactate iv whereas Group C patients received 12 ml/kg of 4.5 per cent hydroxyethylstarch (Hetastarch) iv. All patients underwent cholecystectomy under standard anaesthesia technique with intraoperative fluid replacement by Ringer’s lactate (6 ml/kg/h). An independent blinded observer assessed PONV during first 24 h following surgery using visual analogue scale (VAS) score (0 = no nausea, 10 = worst imaginable nausea or vomiting). Rescue antiemetic was given whenever VAS was > 5.

**Results:** The three groups were comparable in terms of age, body weight and duration of surgery. VAS scores in Groups B and C patients were less than that of Group A patients at all time intervals post-operatively and became significantly different at 4 h post-operatively. The VAS scores of Groups B and C patients were comparable throughout. A significantly large number (90%) of Group A patients required rescue antiemetic as compared to 50 and 55 per cent patients in Group B and Group C, respectively.

**Interpretation & conclusions:** Pre-operative intravenous fluid supplementation using crystalloids and colloids results in significantly decreased incidence of PONV. Both, crystalloids as well as colloids were found to be equally effective in preventing PONV.

**Key words** Colloid - crystalloid - fluid supplementation - PONV - prophylaxis

Post-operative nausea and vomiting (PONV) is a common complication. It has often been referred to as the big “little problem”\(^1\). It can manifest as nausea, retching and vomiting that may last from minutes to days. A number of risk factors have been identified for PONV. These include factors related to patient, anaesthesia, surgical procedure, and post-operative factors\(^2\). If not controlled, it may lead to dehydration,
electrolyte imbalance, tension on sutures, bleeding, evisceration, aspiration pneumonia, increased cost of treatment, delayed discharge and unplanned re-admissions. It is a routine practice to keep patient fasting overnight before surgery. This combined with anaesthetic and surgical losses results in state of transient and relative gut ischaemia through mesenteric hypoperfusion, perioperatively. Gut hypoperfusion has been identified as one of the many factors responsible for PONV. Hence, preloading (intravenous fluid therapy in large volume before induction of anaesthesia) is likely to prevent PONV by improving mesenteric perfusion. Crystalloids and colloids are two clear options for preloading, but it is not known which of these is better for prevention of PONV. This study was planned to find the fluid of choice for prevention of PONV.

**Material & Methods**

This prospective randomized controlled clinical trial was conducted in the Department of Anaesthesiology at University College of Medical Sciences and associated Guru Teg Bahadur Hospital, Delhi from May to December 2004 after approval from the hospital ethical committee. Sixty female patients, between 18-60 yr of age, belonging to ASA Grade I-II and undergoing elective open cholecystectomy were included. Written informed consent was taken from all the patients prior to their inclusion. All patients were non smokers. Patients taking antiemetic drugs, those with history of motion sickness, those who experienced nausea and vomiting on the morning of surgery or any patient with documented disease of renal, cardiac, hepatic, nervous or gastrointestinal system (other than gallstones) were excluded from the study. If cholecystectomy lasted for more than 2 h, the patient was excluded.

During pre-operative visit all patients were familiarized with visual analogue scale (VAS) of 0-10 cm for post-operative nausea and vomiting (PONV). On this scale, score 0 meant no nausea while score 10 meant worst imaginable nausea. Occurrence of vomiting was scored as 10. They were also familiarized with the VAS for pain. Pain was scored at regular intervals post-operatively using the VAS scale with VAS - 0 as no pain and 10 as worst imaginable pain. The baseline heart rate and blood pressure readings were recorded. All patients were kept nil per orally from 2200 h on night before surgery and were premedicated with tablet diazepam 0.2 mg/kg in the night and on the morning of surgery.

In the operation theatre, an 18-G iv cannula was inserted and monitoring for heart rate, blood pressure, ECG, end-tidal CO₂ and SpO₂ were initiated. The patients were randomly allocated to one of the three groups using computer-generated random table. Thereafter, intravenous fluids were administered to the patients over a period of 15 min prior to the induction of anaesthesia in accordance with the groups, as shown below:

- **Group A**: Ringer lactate (crystalloid), 2-ml/kg body wt (control group)
- **Group B**: Ringer lactate (crystalloid), 12-ml/kg body wt
- **Group C**: 4.5% hydroxyethylstarch (Hetastarch) (colloid), 12-ml/kg body wt

The observer (CA) was not present in the operation theatre at the time of preloading or during conduct of the case under general anaesthesia. Anaesthesia was induced only after infusing full amount of calculated intravenous fluid. After fluid administration, injection morphine 0.1 mg/kg iv was given to all patients. Anaesthesia was induced using thiopentone sodium iv (3-5 mg/kg) and tracheal intubation was facilitated using pancuronium iv (0.07-0.08 mg/kg). Anaesthesia was maintained using halothane 0.5-1 per cent and nitrous oxide 66 per cent in 33 per cent oxygen. Nasogastric tube was inserted and left on continuous drainage in all the cases. Intraoperatively, Ringer lactate iv was given to all the patients at the rate of 6 ml/kg/h. In addition, the blood losses were replaced with Ringer lactate three times the loss. Intraoperative haemodynamic monitoring included heart rate and mean blood pressure monitoring and was carried out throughout the surgery at 5 min intervals. Post-operatively it was monitored at 0,1,4 h and then every 4 h till 24 h. At the end of surgery, muscle relaxation was antagonized using injection Neostigmine 0.05 mg/kg and atropine 0.02 mg/kg. Nasogastric tube was aspirated and then removed prior to extubation of the trachea. The surgical wounds of all patients were infiltrated with 0.25 per cent bupivacaine for post-operative analgesia. Additionally, intramuscularly injection of diclofenac 1.5 mg/kg was given 8 hourly. However, no prophylactic antiemetic was given to any patient.

Duration of anaesthesia was defined as the time from induction of anaesthesia till extubation of the trachea. Duration of surgery was defined as the time...
from surgical incision to closure of skin. All patients received oxygen supplementation (30-40%) using facemask for 4 h post-operatively. Intravenous fluids were continued in the form of Ringer’s lactate (2 ml/kg/h) for 24 h post-operatively.

Blinded observer made all the observations in the post-operative period. The VAS scores for PONV were recorded postoperatively at 0, 1 and 4 h, and then 4 hourly for 24 h. Incidence of PONV from 0-4 h post-operatively was labeled as ‘early PONV’ and that from 4-24 h was labeled as ‘late PONV’. Injection ondansetron 4 mg iv was used as rescue antiemetic whenever VAS score (for PONV) became > 5 or the patient vomited. Post-operatively, VAS (for Pain) was also recorded at all these time intervals. Injection tramadol 50 mg slow iv was used as rescue analgesic whenever VAS score (for pain) became > 3.

**Statistical analysis:** The data were analyzed using SPSS version 10.0. *P* value < 0.05 was considered significant. Demographic variables were analyzed by one-way analysis of variance with Tukey’s test. Intergroup comparison of VAS scores (for PONV and pain) was done using repeated measure of ANOVA.

**Results**

Age, body weight, duration of surgery, duration of anaesthesia and the total blood loss were recorded for every patient. The mean age and body weight among the three groups were comparable. Mean duration of surgery, mean duration of anaesthesia and the mean total blood loss during surgery were also comparable (Table I).

In Group A the mean VAS ranged from 0.45 to 4.30. In Group B it ranged from 0.25 to 3.90. In Group C it ranged from 0.40 to 3.65. Mean VAS scores increased up to 4 h (early PONV) in group A patients and then decreased gradually. The VAS scores increased up to 8 h in groups B and C and then decreased gradually. Mean VAS scores in Groups B and C patients were significantly lower (*P* < 0.001) than that of Group A patients at 4 h (early PONV) post-operatively. The VAS scores of Group C patients were not significantly different than that of Group B patients during the early or late post-operative period (Table II).

Eighteen patients in Group A (90%), 10 in Group B (50%) and 11 in Group C (55%) required rescue antiemetics (Table III). This difference was statistically significant for Group A but not so for Groups B and C.

### Table I. Demographic profile of the study groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (yr)</th>
<th>Weight (kg)</th>
<th>Blood loss (ml)</th>
<th>Duration of surgery (min)</th>
<th>Duration of anaesthesia (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>41.40 ± 11.06</td>
<td>51.35 ± 9.73</td>
<td>81.84 ± 33.13</td>
<td>89.50 ± 13.37</td>
<td>103.75 ± 12.45</td>
</tr>
<tr>
<td>B</td>
<td>42.65 ± 11.14</td>
<td>50.45 ± 7.92</td>
<td>81.25 ± 40.16</td>
<td>87.50 ± 18.67</td>
<td>101.50 ± 18.43</td>
</tr>
<tr>
<td>C</td>
<td>38.85 ± 8.70</td>
<td>53.25 ± 8.66</td>
<td>83.75 ± 39.95</td>
<td>82.50 ± 18.81</td>
<td>97.00 ± 17.95</td>
</tr>
</tbody>
</table>

Values are mean ± SD (n=20)

### Table II. VAS scores for post-operative nausea and vomiting (PONV) at different time intervals in the 3 groups

<table>
<thead>
<tr>
<th>Time Intervals (h)</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.45 ± 0.89</td>
<td>0.25 ± 0.55</td>
<td>0.60 ± 0.82</td>
</tr>
<tr>
<td>1</td>
<td>1.80 ± 1.96</td>
<td>1.05 ± 1.19</td>
<td>1.15 ± 1.46</td>
</tr>
<tr>
<td>4</td>
<td>4.30 ± 3.29</td>
<td>2.40 ± 2.37*</td>
<td>2.00 ± 2.53*</td>
</tr>
<tr>
<td>8</td>
<td>4.10 ± 4.23</td>
<td>3.90 ± 3.78</td>
<td>3.65 ± 3.27</td>
</tr>
<tr>
<td>12</td>
<td>3.30 ± 3.31</td>
<td>1.40 ± 2.44</td>
<td>2.90 ± 3.52</td>
</tr>
<tr>
<td>18</td>
<td>2.40 ± 2.84</td>
<td>1.60 ± 1.70</td>
<td>1.35 ± 2.28</td>
</tr>
<tr>
<td>24</td>
<td>0.90 ± 1.65</td>
<td>0.50 ± 0.83</td>
<td>0.40 ± 0.68</td>
</tr>
</tbody>
</table>

Values are mean ± SD (n=20) *P*<0.01 compared to group A

### Table III. Patients receiving rescue antiemetics

<table>
<thead>
<tr>
<th>No. of Patients</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
</tr>
</thead>
<tbody>
<tr>
<td>With vomiting</td>
<td>13</td>
<td>6</td>
<td>8</td>
</tr>
<tr>
<td>With VAS &gt; 5 (but no vomiting)</td>
<td>5</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Total number</td>
<td>18</td>
<td>10*</td>
<td>11*</td>
</tr>
</tbody>
</table>

*P*<0.05

VAS for pain was similar at varying time intervals in the groups postoperatively and was always < 3. There was no statistically significant difference between the groups.

There were no significant changes in the heart rate or mean blood pressure within the groups either in the intra-operative or the post-operative period. The three groups were found to be comparable in terms of heart rate and blood pressure intra- and post-operatively.

**Discussion**

This prospective, randomized, controlled trial has shown a reduced incidence of PONV using rapid fluid supplementation (12 ml/kg) with crystalloid (Ringer’s lactate) or colloid (4.5% Hetastarch) as compared to conservative fluid therapy (2ml/kg) in ASA grade I and II females undergoing open cholecystectomy. The reduction in the incidence of PONV was more evident.
in the early (0–4 h) post-operative period. Number of patients requiring rescue antiemetic was significantly greater in conservative fluid therapy group (Group A). However, the incidence of PONV was same in the test groups, whether receiving Ringer lactate (Group B) or 4.5 per cent Hetastarch (Group C).

Various reviews have found the incidence of ‘early PONV’ to be as high as 34 per cent and the incidence of ‘late PONV’ to be 50 per cent.8 Earlier studies have also demonstrated the beneficial effect (reduction in PONV) of fluid supplementation, varying from minor to significant.9–12 Some authors have documented the reduction in PONV with fluid therapy in early as well as late post-operative period12, while others observed it only in late post-operative period13. We observed a reduction in PONV only during early post-operative period. It is worth mentioning here that we could demonstrate the beneficial effect of fluid therapy by using only 12 ml/kg of crystalloid or colloid, in comparison to 30 ml/kg of crystalloids used by Magner et al12. Ali et al7 also demonstrated a significant reduction (68%) in PONV in patients with only small amount (15 ml/kg of Hartmann’s solution) of fluid supplementation. While it is generally agreed that the fluid therapy prevents PONV, not much work has been done on choice of fluid. Literature search revealed only one earlier study comparing the effect of crystalloids and colloids14. In the study by Moretti et al14 colloid was used for intra-operative resuscitation in 90 patients undergoing elective non-cardiac surgery; they found that the incidence of nausea and vomiting, severe pain, periorbital oedema, double vision and the use of rescue antiemetics was significantly reduced in patients receiving colloids. However, they had used 6 per cent hydroxyethyl starch (HES). We used 4.5 per cent HES. It stays in the intravascular compartment for approximately 12 to 14 h. It is isotonic with saline having an osmolarity of 308 mosm/l. Our study and that of Moretti et al14 provide evidence in support of HES solutions having a beneficial effect of PONV.

Crystalloids are distributed extracellularly and have a transient haemodynamic effect, which is achieved with large amounts. Colloids are made up of larger molecules and are primarily distributed intravascularly. They have a rapid and sustained effect and a lesser amount is required for the same.

As a routine, during elective surgery, patients are advised to fast overnight. This combined with intra-operative anaesthetic and surgical losses that are often inadequately replaced, results in hypovolemia with resultant reduced blood flow to the gut. Gut ischaemia if not corrected, is associated with excessive release of serotonin. This is said to be the main cause of PONV. Mythen & Webb6 provided direct evidence to this effect; they observed that peri-operative plasma volume expansion with colloids during cardiac surgery, guided by oesophageal Doppler monitoring of stroke volume, reduced the incidence of gut mucosal hypoperfusion. Thus, fluid supplementation reduces the incidence of PONV, most probably, by improving the mesenteric perfusion and preventing gut ischaemia and resultant serotonin release.

Through selection of patients and standardization of anaesthesia technique, we eliminated most of the risk factors for PONV and focused on the effect of only one variable, i.e. fluid replacement.

Based on the results of our study we conclude that pre-operative fluid supplementation (Ringer lactate 12 ml/kg) decreases the incidence of PONV. Crystalloids and colloids were found to be equally effective in reduction of PONV.

References

5. Gan TJ, Mythen MG, Glass PS. Intraoperative gut hypoperfusion may be a risk factor for postoperative nausea and vomiting. Br J Anaesth 1997; 78: 476.

