

Effect of intraoperative intravenous crystalloid infusion on postoperative nausea and vomiting after gynaecological laparoscopy: comparison of 30 and 10 ml kg⁻¹

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Background. I.V. fluid administration has been shown to reduce postoperative nausea and vomiting (PONV). The optimum dose is unknown. We tested the hypothesis that administration of i.v. crystalloid of 30 ml kg⁻¹ would reduce the incidence of PONV compared with 10 ml kg⁻¹ of the same fluid.

Methods. A total of 141 ASA I female patients undergoing elective gynaecological laparoscopy were randomized, in double-blind fashion, to receive either 10 ml kg⁻¹ ($n=71$; CSL-10 group) or 30 ml kg⁻¹ ($n=70$; CSL-30 group) of i.v. compound sodium lactate (CSL).

Results. In the first 48 h after anaesthesia, the incidence of vomiting was lower in the CSL-30 group than in the CSL-10 group (8.6% vs 25.7%, $P=0.01$). Anti-emetic use was less in the CSL-30 group at 0.5 h (2.9% vs 14.3%, $P=0.04$). The incidence of severe nausea was significantly reduced in the treatment group at awakening (2.9% vs 15.7%, $P=0.02$), 2 h (0.0% vs 8.6%, $P=0.04$) and cumulatively (5.7% vs 27.1%, $P=0.001$). The numbers needed to treat to prevent vomiting, severe nausea and antiemetic use in the first 48 h were 6, 5 and 6, respectively.

Conclusion. I.V. administration of CSL 30 ml kg⁻¹ to healthy women undergoing day-case gynaecological laparoscopy reduced the incidence of vomiting, nausea and anti-emetic use when compared with CSL 10 ml kg⁻¹.

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Postoperative nausea and vomiting (PONV) remains one of the most common postoperative complications and is experienced by up to 70% of patients. Hofer and colleagues¹ used psychometric and stress assessment to evaluate patient satisfaction and feeling of wellbeing after general anaesthesia, and suggested that a significant improvement could be achieved by reduction of PONV. They also stressed the importance of cost of therapies for improving patient satisfaction and outcome. Other symptoms, including headache, sore throat, dizziness and thirst, are frequently reported even after relatively minor short procedures. In addition to subjective discomfort, these symptoms may result in patient dissatisfaction, multiple pharmacological interventions,

delayed discharge or unanticipated admission and additional costs of care.^{1–4}

Patients incur a fluid deficit by mandatory preoperative fasting. Guided i.v. fluid therapy improves outcomes in major surgery.^{5,6} It has been suggested that relative hypovolaemia may be a factor in such adverse outcomes after surgery and that perioperative administration of i.v. fluids reduces their incidence.⁷ Our group has demonstrated a small reduction in PONV by intra-operative replacement of the pre-operative volume deficit.⁸ The present study aimed to determine whether a relationship exists for perioperative i.v. fluid administration and PONV. Gan and colleagues⁹ showed an earlier return to bowel function, decreased length of hospital

stay and a reduction in PONV by using oesophageal Doppler with goal-directed therapy aimed at maintaining stroke volume. While they studied a major surgery group with expected blood loss in excess of 500 ml, their work supports our hypothesis that reduced bowel mucosal perfusion may be a factor in PONV.

We therefore tested the hypothesis that infusion of balanced salt solution at 30 ml kg⁻¹ compared with 10 ml kg⁻¹ would reduce the incidence of PONV in healthy women undergoing ambulatory gynaecological laparoscopy.

Patients and methods

Following institutional ethics board approval and informed written consent, 141 ASA I female patients undergoing elective gynaecological laparoscopy for investigation of infertility were randomized by computer-generated random number sequence into two groups: the CSL-10 group ($n=70$) received compound sodium lactate (CSL) 10 ml kg⁻¹; the CSL-30 group ($n=70$) received CSL 30 ml kg⁻¹. CSL contains sodium 131 mmol litre⁻¹, potassium 5 mmol litre⁻¹, calcium 2 mmol litre⁻¹, chloride 111 mmol litre⁻¹ and lactate 29 mmol litre⁻¹. To maintain patient and investigator blinding, i.v. fluid administration was initiated in the preoperative area by the investigator, who sited a 16G i.v. cannula (after application of topical lidocaine 1%, 1 ml) and attached CSL 500 ml. The investigator did not see the patient again until they went to the Post Anaesthesia Care Unit (PACU). In all patients, fluid was given in the preoperative area and operating theatre and completed by the end of surgery. Patients returned to the PACU without fluids attached. Neither the patient nor investigator was aware of the volume given or the group allocation.⁷

Patients were excluded if there was a history of congestive cardiac failure, hypertension, valvular heart disease, diabetes mellitus, epilepsy or relevant drug allergy. Those with established gastrointestinal disease or who had received anti-emetic medication in the 24 h before the procedure were excluded also. Patients were also excluded if they developed intra-operative hypotension, excessive blood loss or if the surgery involved more than a diagnostic laparoscopy.

After application of routine monitoring, standardized induction of anaesthesia was performed in which all patients were given fentanyl 2 µg kg⁻¹. Propofol 2–4 mg kg⁻¹ was titrated to induce anaesthesia, and atracurium 0.35 mg kg⁻¹ was administered to facilitate tracheal intubation. In all patients, the lungs were mechanically ventilated via a tracheal tube to maintain isocapnia for the duration of the procedure. Anaesthesia was maintained with sevoflurane (1–3%) in a mixture of nitrous oxide and oxygen in a 70/30 ratio. Muscle relaxation was antagonized with neostigmine 2.5 mg and glycopyrrolate 0.5 mg. Before discontinuation of anaesthesia, each patient received rectal diclofenac 100 mg and the laparoscopic puncture site was

infiltrated with bupivacaine 0.25%. Prophylactic anti-emetics were not administered at any time.

Postoperative care was standardized. Rescue anti-emetics were administered to patients on demand: ondansetron 4 mg i.v. in the PACU and prochlorperazine 12.5 mg i.m. in the ward area. Analgesia was given to patients complaining of pain. This comprised of fentanyl 50 µg i.v. in the PACU, meperidine 50 mg i.m. or simple oral analgesics (acetaminophen/codeine 500–1000 mg/8–16 mg) every 6 h in the ward area. Mefenamic acid 500 mg every 8 h or acetaminophen/codeine 500–1000 mg/8–16 mg every 6 h, or both, were available at home. Data collection was performed by a single assessor 30 min after emergence from anaesthesia and at 2 h after surgery, before discharge. Patients were telephoned at home by the same investigator for symptoms 24 and 48 h after surgery. Using a standardized questionnaire, patients were asked if they experienced vomiting/dry retching or nausea (severe/moderate/mild/none), and about sore throat, dizziness, thirst and analgesic use. Vomiting/dry retching was scored yes/no; nausea was scored none, mild, moderate or severe on a verbal patient-rated scale. Anti-emetic and analgesic use were taken from pharmacy records while in hospital, and direct questioning after discharge.

Statistics

Data were analysed using a standard statistical program (Sigma Stat[®], Version 2.0 Jandel Scientific, Chicago, Illinois, USA). $P<0.05$ was considered significant. Data for categorical variables are presented as proportions and percentages. Data for continuous variables are presented as mean (SD). Statistical analysis utilized independent samples *t*-test for continuous variables, and χ^2 and Fisher's exact tests for categorical variables. Quantitative analysis of the effect was assessed by calculation of the number needed to treat (NNT). We calculated a sample size of 70 patients would be required in each group ($\alpha=0.05$, $\beta=0.2$), projecting a 42% incidence of vomiting and accepting a 25% reduction in this incidence as clinically meaningful.¹⁰ Multiple comparisons were not corrected for as each time point was analysed individually, and cumulative data were for each patient and not each episode of nausea/vomiting/anti-emetic use.

Results

A total of 141 patients were randomized to take part in this study. One patient was excluded because of anti-emetic administration intra-operatively. Pre-operative patient characteristics and intra-operative data were similar between groups (Table 1).

The total number of patients experiencing vomiting in the first 48 h after anaesthesia was reduced in the CSL-30 group (Table 2). The greatest difference between the groups was seen at 0.5–2 h. Anti-emetic use was less in the CSL-30 group at 0.5 h. The total incidence of nausea was similar in both

Table 1 Patient characteristics and medication. CSL, compound sodium lactate; LMP, last menstrual period; VAS, visual analogue scale. Continuous data are presented as mean (range) for age, or mean (SD). Categorical data are presented as number (%)

Group	CSL 10 ml kg ⁻¹ (n=71)	CSL 30 ml kg ⁻¹ (n=70)	P-value
Age (yr)	33.5 (21–42)	33.0 (21–44)	0.574
Weight (kg)	65.6 (12.0)	62.5 (10.2)	0.103
Fasting duration (h)	13.2 (2.5)	12.8 (2.8)	0.429
Procedure duration (min)	22.0 (12.2)	19.4 (9.7)	0.172
Previous PONV or motion sickness, n (%)	22 (32.9)	20 (28.6)	0.714
Smoker, n (%)	22 (31.4)	23 (32.8)	1.0
Menstrual (LMP days 1–8) n (%)	17 (23.%)	26 (37.1)	0.129
CSL (ml kg ⁻¹)	9.7 (1.0)	27.5 (5.8)	0.001
Nausea VAS (preoperative)	0.0 (0.0)	0.0 (0.0)	0.886
Fentanyl (µg kg ⁻¹)	1.7 (0.4)	1.7 (0.4)	0.685
Propofol (mg kg ⁻¹)	2.9 (0.4)	3.0 (0.4)	0.19
Neostigmine (µg kg ⁻¹)	39.2 (6.5)	41.0 (6.3)	0.113
Glycopyrrolate (µg kg ⁻¹)	7.8 (1.3)	8.2 (1.3)	0.113
Atracurium (mg kg ⁻¹)	0.39 (0.1)	0.41 (0.1)	0.113

Table 2 Postoperative nausea, vomiting and anti-emetic use. Categorical data presented as number (%). Cumulative refers to number of patients affected or treated, not number of episodes. CSL, compound sodium lactate

	CSL 10 ml kg ⁻¹	CSL 30 ml kg ⁻¹	P-value
Vomiting			
Preoperative	0 (0.0)	0 (0.0)	0.886
0.5 h	9 (12.9)	2 (2.9)	0.06
2 h	7 (10.0)	1 (1.4)	0.07
24 h	6 (8.6)	3 (4.4)	0.52
48 h	1 (1.5)	1 (1.5)	0.49
Cumulative	18 (25.7)	6 (8.6)	0.01
Nausea: severe only			
Preoperative	0 (0.0)	0 (0.0)	0.886
0.5 h	11 (15.7)	2 (2.9)	0.02
2 h	6 (8.6)	0 (0.0)	0.04
24 h	5 (7.1)	2 (2.9)	0.46
48 h	0 (0.0)	1 (1.5)	0.99
Cumulative	19 (27.1)	4 (5.7)	0.001
Nausea: severe with anti-emetic given			
Preoperative	0 (0.0)	0 (0.0)	0.886
0.5 h	10 (14.3)	2 (2.9)	0.04
2 h	6 (8.6)	0 (0.0)	0.04
24 h	3 (4.5)	1 (1.4)	0.58
48 h	0 (0.0)	1 (1.5)	0.99
Cumulative	16 (22.3)	4 (5.7)	0.008
Nausea: total			
Preoperative	0 (0.0)	0 (0.0)	0.886
0.5 h	17 (24.3)	19 (27.1)	0.85
2 h	11 (15.7)	8 (11.4)	0.62
24 h	8 (11.4)	3 (4.4)	0.23
48 h	3 (4.3)	2 (3.0)	0.97
Cumulative	26 (37.1)	26 (37.1)	0.86
Anti-emetic use			
Preoperative	0 (0.0)	0 (0.0)	0.886
0.5 h	10 (14.3)	2 (2.9)	0.035
2 h	7 (10.0)	2 (2.9)	0.168
24 h	3 (4.29)	1 (1.47)	0.63
48 h	0 (0)	1 (1.5)	0.98
Cumulative	16 (22.9)	8 (11.9)	0.146

Table 3 Minor postoperative morbidities and analgesia. Data are number (%)

	CSL 10 ml kg ⁻¹	CSL 30 ml kg ⁻¹	P-value
0.5 h			
Sore throat	32 (45.7)	48 (68.6)	0.01
Dizziness	19 (27.0)	23 (32.9)	0.58
Thirst	43 (61.4)	43 (61.4)	0.86
Simple analgesia	0 (0)	2 (2.9)	0.476
Opiate analgesia	12 (17.1)	9 (12.9)	0.636
2 h			
Sore throat	32 (45.7)	41 (58.6)	0.176
Dizziness	8 (11.4)	5 (7.1)	0.56
Thirst	59 (84.3)	57 (81.4)	0.82
Simple analgesia	1 (0.1)	6 (8.6)	0.121
Opiate analgesia	10 (14)	12 (17.1)	0.816
24 h			
Sore throat	22 (31.4)	32 (47.0)	0.09
Dizziness	6 (8.5)	3 (4.3)	0.49
Thirst	25 (35.7)	34 (48.6)	0.17
Simple analgesia	36 (51.4)	41 (58.6)	0.38
Opiate analgesia	1 (1.4)	1 (1.4)	0.489
48 h			
Sore throat	14 (20.0)	24 (35.8)	0.068
Dizziness	2 (2.9)	1 (1.5)	0.979
Thirst	17 (24.6)	17 (25.3)	0.957
Simple analgesia	29 (41.4)	26 (37.1)	0.835

groups. However, the total incidence of severe nausea was less in the CSL-30 group, the greatest difference between the groups occurring at 0.5–2 h after anaesthesia.

The NNT for prevention of vomiting, severe nausea and anti-emetic use in the first 48 h were 6, 5 and 6, respectively.

The incidence of sore throat was higher in the CSL-30 group on awakening but not at any other time. There was no significant difference between the groups with regard to thirst, dizziness and opioid analgesic consumption (Table 3).

Discussion

This prospective, randomized, double-blind clinical investigation has shown a beneficial effect of rapid infusion of 30 ml kg⁻¹ compared with 10 ml kg⁻¹ of crystalloid solution in reducing the incidence of PONV after gynaecological laparoscopy in ASA 1 female patients. However, there were no significant differences in the subjective symptoms of dizziness, thirst or opioid consumption at any time. Sore throat was transiently increased in the CSL-30 group on emergence from anaesthesia.

Differences exist between our study and those of previous investigators who had comparable study groups. The use of propofol infusions,⁷ heterogeneous surgical approaches,⁷ different volumes of fluid administration,¹¹ opioid administration¹² and variations in blinding methods may account for the variability of previously reported effects. The current study utilized standardized anaesthesia and postoperative care in a relatively homogenous surgical population. The volumes of fluid administered in the current study differ substantially from those administered by previous investigators, in which lower volumes (e.g. 1–2 ml kg⁻¹) appear to have

been administered for the purpose of maintaining blinding. We did not exclude smokers from our study even though smoking has been shown to have anti-emetic effects.¹³ It should be noted that there was no significant difference between the groups in this regard. Menstruation (as well as gender) has been shown to be an important risk factor.¹⁴ The difference in incidence of PONV in males and females has been attributed to fluctuations in female sex hormones.¹⁵ Variation in the incidence of PONV across the menstrual cycle^{16–17} has previously been documented. Linblang and colleagues¹⁸ describe how a hormone-related threshold for PONV is altered by general anaesthesia. We found that there was a slightly higher number of menstrual patients in the study group; this was not statistically significant, and would be expected to increase the number of nauseous patients in this group¹⁹ thus lessening the difference between groups.

In the postoperative period, avoidance of nausea in particular has been given high priority by this patient population.^{2–4} The efficacy of routine use of prophylactic anti-emetics remains controversial.²⁰ Pharmacological prophylaxis has limited effect as measurable benefit is observed in only 20% of patients receiving ondansetron to prevent PONV.²¹ Prophylactic anti-emetic administration also increases the risk of adverse drug effects and side-effects, and increases the cost of care.²² Crystalloid fluid administration may be a simple, inexpensive, non-pharmacological therapy that could reduce these symptoms, avoiding drug-related side-effects. The usefulness of multimodal therapy, particularly in high-risk cases, has been emphasized recently.²³ We have shown that use of fluid bolus as a preventive therapy is effective and may form an important part of multimodal prevention, while being cost-effective.

Perioperative oxygen administration and hypotension after induction of anaesthesia has been shown to decrease PONV, suggesting that tissue hypoperfusion may be an important aetiological factor.^{24–27} Mucosal perfusion can be affected by general anaesthesia, raised intra-abdominal pressure and by surgical stimulation despite normal mean arterial pressure.^{28–31} Gynaecological laparoscopy is frequently performed in a head-down position, potentially magnifying regional hypoperfusion. Gastric mucosal hypoperfusion may occur during hypovolaemia in the absence of significant haemodynamic changes in healthy volunteers without surgical intervention.³² I.V. fluid administration reduces gut mucosal hypoperfusion during major surgery.⁶ In addition, sympathomimetics have been used to treat PONV, although measured haemodynamics did not differ between experimental groups in these studies.^{33–35} It is possible that both i.v. fluid loading and sympathomimetic administration reduce PONV by increasing mesenteric perfusion, which may occur in the absence of changes in measured haemodynamic parameters.

Whilst the effect of fluid management in maintaining cardiovascular stability and renal function in major surgery has been studied, their place in minor surgery remains to be established. Perioperative administration of large volumes

of fluids may have significant adverse effects. In ASA I–II gynaecological patients, NaCl 0.9% 30 ml kg⁻¹ was shown to induce hyperchloraemic metabolic acidosis. In a population similar to the current patient group, a bolus of Hartmann's solution of 20 ml kg⁻¹ administered before induction of general anaesthesia did not prevent hypotension after induction of general anaesthesia.²⁸ Saline administration (22 ml kg⁻¹) resulted in a 10% reduction of functional residual capacity and a 6% reduction of diffusing capacity in healthy volunteers.³⁶ Excessive intravascular volume administration may result in pulmonary oedema,²⁷ electrolyte abnormalities, cerebral oedema and death.²⁸ Children and adults with low muscle mass and heart disease are at increased risk of adverse effects.

This study has potential limitations. First, these data may not be applicable to different patient populations, lengthier or different surgical procedures, anaesthetic techniques or all formulations of i.v. fluids. Large volumes of fluid may have detrimental effects in some patients and therefore a ceiling of benefit is likely to exist.³⁷ Second, the present study was designed to determine whether a dose–response relationship exists for i.v. CSL and PONV. Thus, the failure of larger volumes of i.v. CSL to alter the incidence of thirst or dizziness when compared with lower volumes may not represent a lack of effect but rather reflects the study design in which there is no true control group. Third, tissue oxygenation, mucosal perfusion and emetogenic mediator release were not measured, thus the mechanism remains speculative.

In conclusion, we have found that a dose–response relationship for perioperative infusion of CSL exists in patients undergoing gynaecological laparoscopy. Intraoperative administration of 30 ml kg⁻¹ compared with 10 ml kg⁻¹ reduces the incidence of PONV and anti-emetic use for 48 h after anaesthesia.

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