General Anesthesia

Intravenous fluid loading with or without supplementary dextrose does not prevent nausea, vomiting and pain after laparoscopy

[Une charge liquidienne avec ou sans dextrose supplémentaire ne prévient pas les nausées, les vomissements et la douleur après une laparoscopie]

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Purpose: To examine the effects of *iv* compound sodium lactate (CSL) with and without caloric supplementation with dextrose on nausea, vomiting and pain following general anesthesia for laparoscopy.

Methods: We compared *iv* fluid loading with and without supplementary dextrose for the prevention of postoperative nausea and vomiting (PONV). In a prospective double-blinded controlled trial, 120 ASA I female patients undergoing elective gynecological laparoscopy were randomized to one of three groups, and received either: (a) CSL 1.5 mL·kg⁻¹ per hour fasting duration; (b) CSL, 1.5 mL·kg⁻¹ per hour fasting duration with 0.5 g·kg⁻¹ dextrose added in 50% formulation (CSL/dextrose); or (c) no *iv* fluid (control).

Results: Compared with control the percentage of patients who had no PONV within 24 hr of anesthesia in the CSL and CSL/dextrose groups was 78% vs 83% and 71%, $P = 0.81$ and $P = 0.683$ respectively. The numbers needed-to-harm for causing PONV episodes in CSL/dextrose vs CSL or control groups were 5.7 [95% confidence interval (CI), 5.57–5.91] and 8.2 (95% CI, 8.01–8.37) respectively. The number needed-to-treat for prevention of PONV episodes in CSL vs control was 19.2 (95% CI, 19.08–19.37). A greater proportion of patients in the CSL/dextrose group required narcotic analgesia in the postanesthetic care unit compared to those in the control group (16/35 vs 7/37, $P = 0.03$). The CSL/dextrose group also demonstrated hyperglycemia (serum glucose 14.0 ± 3.94 vs 5.0 ± 1.01 vs 5.2 ± 0.9 mmol·L⁻¹, $P < 0.0001$) in the postanesthetic care unit compared to the CSL and control groups. The CSL/dextrose group also reported increased thirst at 24 hr compared to control (20/35 vs 11/37, $P = 0.035$).

Conclusion: These findings suggest that: 1) administration of dextrose is associated with nausea, increased opioid requirement and late thirst after elective gynecological laparoscopy; 2) *iv* fluids did not decrease PONV.

Objectif: Vérifier les effets d'un lactate de sodium composé *iv* (LSC), avec et sans apport calorique complémentaire avec du dextrose, sur les nausées, les vomissements et la douleur après une anesthésie générale pour laparoscopie.

Méthode : Nous avons comparé une charge liquidienne avec et sans dextrose supplémentaire comme prévention des nausées et vomissements postopératoires (NVPO). Une étude prospective, contrôlée et à double insu a été réalisée auprès de 120 femmes d'état physique ASA I devant subir une laparoscopie gynécologique réglée. Les patientes, réparties en trois groupes, ont reçu : (a) 1,5 mL·kg⁻¹ de LSC par heure de jeûne ; (b) 1,5 mL·kg⁻¹ de LSC par heure de jeûne avec 0,5 g·kg⁻¹ de dextrose ajouté dans une préparation à 50 % (LSC/dextrose) ou (c) aucun soluté (témoin).

Résultats : Comparé à celui des témoins, le pourcentage de patientes sans NVPO pendant les 24 h qui ont suivi l'anesthésie dans les groupes LSC et LSC/dextrose a été respectivement de 78 % vs 83 % et 71 %, $P = 0,81$ et $P = 0,683$. Le nombre de patientes lésées, nécessaire pour causer des NVPO dans le groupe LSC/dextrose vs les groupes LSC ou témoin a été respectivement de 5,7 [intervalle de confiance de 95 % (IC), 5,57–5,91] et 8,2 (IC de 95 %, 8,01–8,37). Le nombre néces-

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Accepted for publication August 12, 2002.

Revision accepted February 12, 2003.

saire à traiter pour prévenir les NVPO dans le groupe LSC vs le groupe témoin a été de 19,2 (IC de 95 %, 19,08–19,37). Plus de patientes du groupe LSC/dextrose ont eu besoin d'analgésique narcotique en salle de réveil, comparées aux patientes témoins (16/35 vs 7/37, $P = 0,03$). À la salle de réveil, on a aussi trouvé de l'hyperglycémie dans le groupe LSC/dextrose (glucose sérique de $14,0 \pm 3,94$ vs $5,0 \pm 1,01$ vs $5,2 \pm 0,9$ mmol·L⁻¹, $P < 0,0001$), comparé aux groupes LSC et témoin. À 24 h, le groupe LSC/dextrose, comparé aux témoins, a aussi présenté une augmentation de la soif, (20/35 vs 11/37, $P = 0,035$).

Conclusion : Ces résultats suggèrent que : 1) l'administration de dextrose est associée aux nausées, à des besoins accrus d'opioïde et une soif tardive à la suite d'une laparoscopie gynécologique ; 2) les liquides iv ne diminuent pas les NVPO.

POSTOPERATIVE nausea and vomiting (PONV) remains one of the most common postoperative complications,¹ causing discomfort, patient dissatisfaction, delayed discharge and increased costs.

We examined the hypothesis that: (a) supplementary dextrose would reduce the incidence of PONV, and (b) administration of balanced salt solution would also reduce such symptoms.

Methods

Following ethical approval and informed consent female patients undergoing elective diagnostic laparoscopy were recruited. Patients were subsequently excluded if they developed excessive blood loss or if the surgery progressed to additional procedures. Patients were randomized drawing unmarked envelopes containing assignment information and were blinded to their group allocation. The fluid volume to be administered was calculated on the basis of the interval since last oral intake ($1.5 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{hr}^{-1}$ fasting time).² The control group received no perioperative *iv* fluids; group compound sodium lactate (CSL)/dextrose received CSL with dextrose $0.5 \text{ g} \cdot \text{kg}^{-1}$ added to the infused solution as a 50% formulation; group CSL received compound sodium lactate alone. CSL contains Na^+131 , K^+5 , $\text{Ca}^{2+}2$, Cl^-111 , lactate $29 \text{ mmol} \cdot \text{L}^{-1}$, pH 6.5. Fluid was administered following induction of anesthesia over approximately 20 min. Standardized general anesthesia was administered (Table I). The lungs were mechanically ventilated and anesthesia was maintained with sevoflurane in $\text{O}_2/\text{N}_2\text{O}$ in a 1:2 ratio. All patients received neostigmine/glycopyrrolate, rectal diclofenac and wound infiltration with bupivacaine. Pharmacological antiemetic prophylaxis was not given. Standardized antiemetic and analgesic rescue medications were avail-

able. Patients were assessed by a blinded interviewer using a standardized questionnaire in the postanesthesia care unit (PACU), two hours later in the ward; and on the first postoperative morning. An adverse outcome was defined as the occurrence nausea, vomiting, antiemetic use, thirst, dizziness or sore throat.

Sample size estimation

Projecting an incidence of 70% in controls and a 50% reduction with treatment we estimated 31 patients per group, ($\alpha = 0.05$, $\beta = 0.8$). To allow for dropouts we randomized a total of 120 patients.

Statistical analysis

Statistics were performed using Sigma Stat®, (version 2.0 Jandel Scientific, Chicago, IL, USA). $P < 0.05$ was considered significant. ANOVA, Student's *t* test and Chi-square were used as appropriate. Quantitative analyses of effect was assessed by calculation of the numbers needed-to-treat (NNT), numbers needed-to-harm (NNH) and 95% confidence intervals (CI).

Results

After exclusions, data from 108 patients were analyzed. On hypothesis testing there was no statistically significant difference in PONV episodes between groups. Compared with control the percentage of patients who had no PONV within 24 hr of anesthesia in the CSL and CSL/dextrose was 78% *vs* 83% and 71%, $P = 0.81$, χ^2 and $P = 0.683$, χ^2 respectively. The NNH for PONV episodes in CSL/dextrose *vs* CSL or control were 5.7 (95% CI, 5.57–5.91) and 8.2 (95% CI, 8.01–8.37) respectively. The NNT for PONV episodes in CSL *vs* control was 19.2 (95% CI, 19.08–19.37). The CSL/dextrose group was more hyperglycemic than control or CSL groups ($P < 0.0001$, χ^2) in the PACU. More CSL/dextrose patients received fentanyl in the PACU than the control group (46.7% *vs* 8.9%, $P = 0.03$, χ^2). Thirst was increased in the CSL/dextrose group at 24 hr compared to control ($P = 0.035$, χ^2).

Discussion

Perioperative rehydration and caloric supplementation may reduce PONV³ but important methodological issues confound previous studies. The present study aimed to retest these hypotheses in a group considered at high risk of PONV. We were unable to prove that administration of CSL or CSL with dextrose decreases PONV. Our study shows that administration of CSL/dextrose is associated with PONV in 17.5% of patients and with early hyperglycemia and late thirst. The NNT for PONV in patients receiving CSL was 19.2 suggesting that clinical benefit if any, is small.

TABLE I Patient characteristics and medication

Groups	Control <i>n</i> = 37	CSL* <i>n</i> = 36	CSL*/dextrose <i>n</i> = 35
Age (yr)	33.0 ± 5.1	32.3 ± 4.96	33.2 ± 4.9
Weight (kg)	63.6 ± 15.6	62.0 ± 9.3	64.2 ± 9.7
Fasting time (hr)	11.4 ± 2.3	11.63 ± 2.36	11.65 ± 1.5
CSL volume (mL)	0	1,115 ± 363‡	1,148 ± 210‡
Dextrose (g)	0	0	32 ± 5.8‡
Duration of anesthesia (min)	23 ± 7	22 ± 6	23 ± 7
Fentanyl: PACU (<i>n</i>)	7/37 (18.9%)	9/36 (25%)	16/35‡ (46.7%)

Categorical variables are presented as number and proportion, continuous variables are presented as mean and standard deviation. CSL* = compound sodium lactate; PACU = postanesthesia care unit. †*P* = 0.03 (CSL/dextrose *vs* control); ‡*P* < 0.0001, (CSL/dextrose and CSL *vs* control).

TABLE II Symptoms and therapy

	Control <i>n</i> = 37	CSL <i>n</i> = 36	CSL/dextrose <i>n</i> = 35
PACU			
<i>Patients reporting</i>			
Nausea	5	4	6
Vomiting	1	1	1
<i>Patients requiring</i>			
Antiemetic	4	4	6
Total episodes	10	9	13
Patients with nausea, vomiting or antiemetic	5	5	6
Two hours			
<i>Patients reporting</i>			
Nausea	5	3	9
Vomiting	0	1	2
<i>Patients requiring</i>			
Antiemetic	0	1	2
Total episodes	5	5	13
Patients with nausea, vomiting or antiemetic	5	3	9
24 hr			
<i>Patients reporting</i>			
Nausea	1	0	1
Vomiting	1	0	1
<i>Patients requiring</i>			
Antiemetic	1	0	1
Total episodes	3	0	3
Patients with nausea, vomiting or antiemetic	1	0	1

CSL = compound sodium lactate; PACU = postanesthesia care unit.

Differences exist between our study and those of previous investigators. Yogendran *et al.* did not allow for fasting duration and the anesthetic technique had important confounding variability.⁴ Reduced dizziness, headache and sore throat were demonstrated by Cook *et al.*³ in patients given dextrose. The higher incidence of nausea in our study in the CSL/dextrose group (NNH 5.7) may be explained by our earlier patient assessment. The immediate postoperative period was associated with hyperglycemia in our patients in the CSL/dextrose group. Hyperglycemia is known

to reduce gastric emptying and increase sensation of gastric fullness⁵ and is associated with adverse neurological,⁶ cardiovascular,⁷ gastrointestinal⁵ and immunological⁸ effects. The previously demonstrated small benefit in subjective postoperative recovery symptoms may be insufficient to justify administration of solutions that cause hyperglycemia.

Opioids may reduce postoperative nausea by reducing pain, indicating a complex interaction between nociception, emesis and analgesia. The relationship between dextrose administration and pain has not to

FIGURE Thirst. * $P = 0.035$.

our knowledge been previously described. Glucose loading has been shown to elevate plasma cholecystokinin⁹ which is involved in modulating pain and altering acute tolerance to opiates.¹⁰ In our study, fentanyl administration in the PACU was more frequent in the CSL/dextrose than control indicating a possible relationship between hyperglycemia and opioid tolerance. Because acute hyperglycemia is also associated with increased sensitivity to gastric distension,⁵ the observed increase in fentanyl consumption in the CSL/dextrose group may indicate a hyperglycemia mediated increase in sensitivity to autonomic components of visceral nociception.

This study has potential limitations. First, this data may not be generalizable to different patient populations, lengthier or different surgical procedures, anesthetic techniques or all formulations of dextrose containing fluids. Second, individualized fluid therapy calculated to replace the deficit incurred by fasting may be impractical. Finally, the secondary hypothesis - that *iv* fluids would reduce the incidence of PONV - was not proved. However, it was not disproved, and here the issue of sample size is important. The *a priori* sample size estimates proved adequate to test the primary hypothesis. *Post hoc* sample size calculation (α 0.05, β 0.80) indicates that with nausea as low as reported in the current study over 600 patients per group would be required to demonstrate that *iv* fluid significantly decreases nausea. Expressed as NNT, this calculates as 19.2 patients treated for a single patient to benefit, which is far less than that of conventional antiemetics, suggesting that such treatment would have limited clinical usefulness.

Conclusion

The administration of either CSL or CSL with dextrose failed to significantly reduce PONV dizziness and sore throat compared to control. Dextrose administration resulted in hyperglycemia, increased analgesia requirement and late thirst. NNT and NNH analyses suggest that dextrose administration is associated with nausea whilst administration of CSL is associated with only a small clinical benefit. Further studies are needed to evaluate the finding of increased analgesic requirements and dextrose administration.

Acknowledgements

The authors would like to thank Dr. John Laffey for statistical advice and Dr. Brian Kavanagh for reviewing the manuscript.

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Sculpture ("Mother") exposed in *Copenhagen*