A randomized-controlled trial of high- or low-volume intravenous Plasma-Lyte[®] to prevent hypotension during sedation for colonoscopy

Une étude randomisée contrôlée de la capacité du Plasma-Lyte[®] intraveineux en volume élevé ou faible pour prévenir l'hypotension pendant la sédation pour colonoscopie

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Abstract

Purpose The purpose of this study was to compare the incidence of hypotension during sedation in adults presenting for elective colonoscopy and randomized to intravenous Plasma-Lyte 148[®] at either 2 mL·kg⁻¹ (low volume) or 20 mL·kg⁻¹ (high volume).

Methods Patients aged ≥ 18 yr presenting for elective colonoscopy, with or without gastroscopy, after oral bowel preparation were randomized to receive the intervention immediately before the start of the procedure. Hypotension

was defined as a ≥ 25% decrease in systolic blood pressure (SBP) from baseline during the procedure. Secondary outcomes included SBP < 90 mmHg, lowest SBP during sedation, duration of hypotension, use of vasopressors, postoperative outcomes, and cost.

Results Seventy-five patients were randomly allocated to either the low-volume or high-volume group, respectively (total n = 150). The incidence of hypotension was similar in the two groups (59% vs 56%, respectively; odds ratio, 0.90; 95% confidence interval, 0.47 to 1.71; P = 0.74). The incidence of SBP < 90 mmHg, the lowest SBP during sedation, the duration of hypotension, the use of vasopressors, and postoperative outcomes were also similar in the two groups.

Conclusions This study does not support the routine use of 20 mL·kg⁻¹ of intravenous Plasma-Lyte 148 to prevent hypotension and other complications during sedation for elective colonoscopy in adult patients. Clinical Trials Registry (ANZCTR 12615001288516).

Trial registry number: Registered on 25 November 2015 at the Australian and New Zealand Clinical Trials Registry (ANZCTR12615001288516).

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Résumé

Objectif L'objectif de cette étude était de comparer l'incidence d'hypotension pendant la sédation chez des adultes se présentant pour une colonoscopie non urgente et randomisés à recevoir du Plasma-Lyte 148[®] en solution intraveineuse à des concentrations de 2 mL·kg⁻¹ (volume faible) ou de 20 mL·kg⁻¹ (volume élevé).

Méthode Des patients âgés ≥ 18 ans se présentant pour une colonoscopie non urgente, avec ou sans gastroscopie, après une préparation intestinale par voie buccale, ont été randomisés à recevoir l'intervention à l'étude immédiatement avant le début de la procédure. L'hypotension était définie en tant qu'une réduction ≥ 25 % de la tension artérielle systolique (TAS) depuis la valeur de

base pendant la procédure. Les critères d'évaluation secondaires comprenaient une TAS < 90 mmHg, la TAS la plus basse pendant la sédation, la durée de l'hypotension, l'utilisation de vasopresseurs, les devenir postopératoires et le coût.

Résultats Soixante-quinze patients ont été alloués de façon aléatoire aux groupes à faible volume ou à volume élevé, respectivement (n total = 150). L'incidence d'hypotension était semblable dans les deux groupes (59 % vs 56 %, respectivement; rapport de cotes, 0,90; intervalle de confiance 95%, 0,47 à 1,71; $P = 0,74$). L'incidence de TAS < 90 mmHg, la TAS la plus basse pendant la sédation, la durée de l'hypotension, l'utilisation de vasopresseurs et les devenir postopératoires étaient également semblables dans les deux groupes.

Conclusion Cette étude n'appuie pas l'utilisation de routine de 20 mL·kg⁻¹ de Plasma-Lyte 148 en intraveineuse pour prévenir l'hypotension et les autres complications pendant la sédation pour colonoscopie non urgente chez des patients adultes. Registre d'études cliniques (ANZCTR 12615001288516).

Colonoscopy is a procedure most commonly performed under sedation, and therefore, strategies to improve safety and quality, as well as to reduce its cost, are important. Patients having a colonoscopy report a range of unwanted symptoms associated with the fasting and bowel preparation incumbent with the procedure, including nausea, headache, and dizziness.¹ In addition, dehydration and sedative drugs may precipitate hypotension during the procedure, which, although usually mild and transient, may require treatment.² In an attempt to ameliorate these symptoms and signs, many anesthesiologists commonly administer prophylactic intravenous fluids during sedation for colonoscopy.^{3,4} Nevertheless, this practice is not supported by the currently available evidence^{1,5} and may increase the cost of care.

We previously reported that 15 mL·kg⁻¹ of intravenous lactated Ringer's solution offered no advantages over 1.5 mL·kg⁻¹ of the same solution in elective colonoscopy patients.¹ The primary outcome of that study (i.e., a $\geq 25\%$ decrease in systolic blood pressure [SBP] from baseline before fluid administration during sedation), the incidence of SBP < 100 mmHg, and all other secondary outcomes were similar in the two groups. There is a lack of further randomized trials, although an observational study⁵ did report no association between the volume of fluid administered and hypotension during the procedure. Nevertheless, 64% of anesthesiologists who responded to a recent survey still routinely administer prophylactic intravenous fluids.⁴

Barriers to the implementation of evidence include lack of confidence in the quality of evidence, lack of generalizability of the results, and lack of information about the cost of non-compliance.⁶ We therefore repeated our previous study using a higher volume of intravenous fluid to increase the likelihood that any dehydration was reversed. We used a different fluid formulation (Plasma-Lyte 148[®]) than in our previous report (lactated Ringer's) because it has an osmolarity and sodium and chloride content closer to that of plasma than lactated Ringer's solution. We also included patients having combined colonoscopy and gastroscopy as well as patients having colonoscopy alone. Furthermore, we followed a protocol for sedation rather than allowing the anesthesiologists to use their discretion, and we calculated the costs of fluid infusion in the different groups.

Our hypothesis was that the incidence of hypotension (defined as a $\geq 25\%$ decrease in SBP from baseline) during sedation would be lower in adults presenting for elective colonoscopy who received 20 mL·kg⁻¹ vs 2 mL·kg⁻¹ of Plasma-Lyte 148 just prior to their procedure.

Methods

This study was a single-centre parallel-group double-blind randomized trial. The study was prospectively approved by the Melbourne Health Research Ethics Committee on December 16, 2014 (approval number 2014.219).

Eligibility criteria

The study was conducted in the endoscopy suite of the Royal Melbourne Hospital, an academic tertiary referral and trauma centre in Melbourne, Australia. Enrolment criteria included patients aged ≥ 18 yr presenting for elective colonoscopy (with or without gastroscopy) under intravenous sedation following successful completion of oral bowel preparation. Exclusion criteria included patients with inadequate English language comprehension due to a language barrier, cognitive deficit or disability, a contraindication to intravenous fluid infusion (e.g., uncontrolled congestive heart failure or end-stage renal failure), or those scheduled for an intravenous fluid infusion for any reason. The patients provided written consent before randomization and data collection.

Randomization and bias control

Patients were randomized to 2 mL·kg⁻¹ (low volume) or 20 mL·kg⁻¹ (high volume) of intravenous Plasma-Lyte 148 (Baxter Healthcare, Australia). The randomization schedule was generated before the study commenced (via

www.randomisation.org), and group allocation was concealed in numbered opaque envelopes. Patients, anesthesiologists, and study observers were blinded to group assignment. Blinding of patients was facilitated by the use of a low-volume intravenous infusion (rather than no infusion) in the control group. Blinding of anesthesiologists and study observers was facilitated by having a dedicated researcher administer the randomized intervention before patient care was transferred to the procedural team.

Primary and secondary outcomes

The primary outcome was the occurrence of hypotension (defined as a $\geq 25\%$ decrease in SBP from baseline measurement before fluid administration) during sedation for colonoscopy.¹ Secondary outcomes were SBP < 90 mmHg, lowest SBP during sedation, duration of hypotension, use of vasopressors, thirst, as well as post-procedure effects (i.e., nausea, vomiting, headache, drowsiness, dizziness, recall, dreaming), quality of recovery, patient satisfaction, post-discharge hospital stay, and the cost of intravenous fluid infusion.

Protocol

Patients followed our institutional protocol for bowel preparation and fasting, which was the same regardless of the scheduled time for the procedure. Patients received 4 L of oral bowel preparation (Glycoprep-C®, Fresenius Kabi, Australia), and unless advised otherwise by their treating doctor, they were instructed to drink the preparation on the afternoon before the procedure and fast for solids from the time they commenced bowel preparation. Patients were encouraged to drink a liberal amount of fluids until six hours before the procedure and advised to take their regular antihypertensive medications on the day of the procedure.

Patients received the intravenous fluid infusion while seated in a recliner chair or lying on a stretcher prior to colonoscopy. Intravenous access was established using a 20G cannula, and the infusion (which was warmed) was administered over 20 min via a volumetric pump. Fluid bags, infusion pumps, and warmers were covered to facilitate blinding. All infusion equipment, except for the intravenous cannula, was removed when the infusion was complete.

Patient monitoring during colonoscopy was conducted in accordance with the standards of the Australian and New Zealand College of Anaesthetists.⁷ The blood pressure cuff was placed on the arm without the intravenous cannula. Attending anesthesiologists were advised to administer fentanyl and propofol directly into the intravenous cannula without a background fluid infusion to achieve a score of 3 on the Observer's Assessment of Alertness/Sedation

(OAA/S) Scale—i.e., drowsy but still responsive to command or mild physical stimulation.⁸ Supplemental oxygen was administered during sedation. Vasopressors (either metaraminol or ephedrine) were administered at the anesthesiologist's discretion, but no intravenous fluid bolus was administered unless vasopressor treatment failed and intravenous fluids were deemed clinically necessary. At the end of the procedure, patients were transferred to the postanesthesia care unit (PACU) and then discharged from the PACU and from the hospital according to institutional criteria.

Measurements

The following baseline characteristics were recorded: age, sex, body mass index, American Society of Anesthesiologists' physical status, comorbidities, type of bowel preparation, fasting times for solids and fluids, and the planned procedure. Intraprocedural measurements included the duration of sedation (time from first administration of sedative drugs to removal of the endoscope) and sedative and vasopressor doses.

The SBP was measured noninvasively before and after intravenous fluid infusion, every 2.5 min during sedation, and in the PACU. Patients self-assessed their thirst on a 100-mm visual analogue scale (VAS) before and after intravenous fluid infusion and in the PACU (0 = not thirsty at all; 100 = extremely thirsty).⁹ They completed the Quality of Recovery-15 (QoR-15)¹⁰ questionnaire [minimum (worst) score = 0, and maximum (best) score = 150] before intravenous fluid infusion and in the PACU, and the modified Brice questionnaire¹¹ (regarding intraoperative awareness) in the PACU when fully oriented after sedation (OAA/S = 5). Before discharge, patients were asked about their experience of nausea, vomiting, headache, drowsiness, and dizziness following the procedure. Prior to hospital discharge, patients rated their satisfaction with anesthesia care on a five-point Likert scale (1 = very dissatisfied to 5 = very satisfied). Satisfaction was defined as a score of 4 or 5. Actual discharge time was recorded. No post-discharge data were collected.

Statistical analyses

Based on the 30% incidence of hypotension in the low-volume group ($1.5 \text{ mL} \cdot \text{kg}^{-1}$) from our previous study¹ and a clinically important reduction in hypotension to 10%, the required sample size was calculated to be 72 patients per group ($\alpha = 0.05$ and $\beta = 0.2$). To account for potential dropouts, 150 patients were recruited. Analyses were conducted on an intention-to-treat basis.

Continuous data were tested for normality using graphical methods; normally distributed data were summarized using mean (standard deviation [SD]), skewed data were summarized using median [interquartile range (IQR)], and categorical data were summarized using number (percent). Comparisons between groups were conducted using unpaired two-tailed Student's *t* tests (normally distributed data), rank-sum tests (skewed data), and Chi square or Fisher's exact tests (categorical data). For non-normal data, effect sizes were calculated using Somers' *d*, where the effect of being in the high-volume vs the low-volume group is reported as percentage chance (95% confidence interval [CI]). This can be interpreted as the percentage chance that a patient randomized to high vs low volume will have a higher value for the parameter (lower percentage likelihood if negative). For categorical data, the risk difference and 95% CI are reported. Repeated measurements were compared using repeated measures analysis of variance (SBP and thirst) or the signed-rank test (QoR-15). For repeated measures analysis of variance, residuals were assessed using normal Q-Q plots; variances were assessed using residual vs fitted values plots; sphericity was assessed using epsilon calculated using Greenhouse-Geisser and Huynh-Feldt; and group-by-time interactions were included. Interactions were tested first, and if not statistically significant at the $P > 0.10$ level, the interaction term was removed from the model and the remaining three assumptions were tested.

Logistic regression was used to generate odds ratios (OR) and CI for the primary outcome and to identify risk factors for the primary outcome. As only one of the five patients with a body mass index $< 18.5 \text{ kg}\cdot\text{m}^{-2}$ coded positive for the primary outcome, this group was amalgamated with the $18.5\text{--}24.9 \text{ kg}\cdot\text{m}^{-2}$ group. We included pre-sedation variables only, because post-sedation variables, such as propofol dose and duration of sedation, could vary as a result of hypotension as well as being a potential risk factor for hypotension. All variables were included in a multivariable model.

The intravenous administration set used in the study cost A\$7.12, with each litre of Plasma-Lyte 148 costing A\$1.95. These costs are uniform across the state of Victoria, Australia under its collective purchasing agreement for public health services. As unused intravenous fluid was discarded, volumes were rounded up to the next litre. The number of patients having elective colonoscopy in Australian public hospitals was estimated using Australian-refined diagnosis-related group codes G46C (complex endoscopy, same day [used for combined gastroscopy and colonoscopy]) and G48C (colonoscopy, same day) (version 7.0; 2013–2014).¹² The number of patients having elective colonoscopy in Australian private hospitals was

estimated using Medicare Australia data for codes 32090 and 32093 (colonoscopy without and with polypectomy) (2013–2014).¹³ All costs are expressed in Australian dollars.

Stata® 14 (Stata Corporation, College Station, TX, USA) was used for statistical analyses. Two-tailed *P* values are reported, and $P < 0.05$ was considered statistically significant.

Results

Patients were recruited from March to August 2015. All randomized patients completed the study in accordance with the approved protocol, and no patient received any additional intravenous fluid apart from the allocated intervention (Fig. 1).

Patients in the two groups were similar at baseline ($n = 75$ per group; Table 1). Median [IQR] fasting times for fluids were longer than was required by institutional protocol (9 [7–13] hr), and 18% of patients received low-volume hyperosmotic bowel preparation instead of 4 L of iso-osmotic Glycoprep-C. Forty-two (28%) patients were scheduled for gastroscopy in addition to colonoscopy.

Allocated mean (SD) fluid administration was 159 (33) mL in the low-volume group and 1,478 (288) mL in the high-volume group (Table 1). Median [IQR] duration of sedation was 26 [18–36] min, and median [IQR] propofol dose was 0.20 [0.14–0.27] $\text{mg}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$, and both were similar between the two groups (Table 2).

The incidence of the primary outcome (i.e., hypotension, defined by a SBP $\geq 25\%$ from baseline measurement before fluid administration) did not differ significantly between the low- and high-volume groups (59% vs 56%, respectively; OR, 0.90; 95% CI, 0.47 to 1.71; $P = 0.74$) (Table 3). The incidence of SBP < 90 mmHg, the lowest SBP during sedation, the duration of hypotension, and the use of vasopressors were also not significantly different between the two groups (Table 3). Thirst after infusion was the only significant predictor of the primary outcome in the multivariable logistic regression model (OR, 0.84; 95% CI, 0.72 to 0.99; $P = 0.04$) (Table 4).

There was no significant interaction between the effects of group and time on SBP ($P = 0.17$). Main effects analysis showed that SBP was significantly different over time (within-group $P < 0.001$), but there was no difference between the two groups (between-group $P = 0.55$) (Fig. 2). Assumptions of the model were met (residuals normally distributed, equal variances, sphericity confirmed). There was no significant interaction between the effects of group and time on SBP ($P = 0.58$). Main effects analysis showed that SBP was significantly different over time (within-group $P < 0.001$), but there was no difference between the

Fig. 1 Study flow diagram

two groups (between-group $P = 0.07$) (Fig. 2). Assumptions of the model were met (residuals normally distributed, equal variances, sphericity confirmed).

Postoperatively, the incidence of nausea, headache, drowsiness, dizziness, recall, and dreaming were similar in the two groups (Table 3). No patient reported vomiting. The QoR-15 scores increased significantly from baseline in both groups ($P < 0.001$) with no significant difference between the two groups ($P = 0.44$). There were no significant differences in the percentage of patients who were satisfied with their care or in the length of post-procedure hospital stay between the two groups.

All patients in the low-volume group received < 1 L of intravenous fluid (A\$9.07 per patient). In the high-volume group, three patients received < 1 L, 69 patients received 1–2 L (A\$11.02), and three patients received 2–3 L (A\$12.97). The average additional cost per patient in the high-volume group over the low-volume group was \$1.95.

Discussion

This study does not support the routine use of $20 \text{ mL} \cdot \text{kg}^{-1}$ of Plasma-Lyte 148 to prevent hypotension during sedation for elective colonoscopy in adult patients. Quality of recovery, patient satisfaction, and discharge times were similar in the two groups, but high-volume fluid infusion increased the cost of care.

Our results are consistent with the findings of our previous study comparing $1.5 \text{ mL} \cdot \text{kg}^{-1}$ and $15 \text{ mL} \cdot \text{kg}^{-1}$ of intravenous lactated Ringer's solution.¹ Patients in our two studies were similar in terms of baseline characteristics, bowel preparation, and fasting, but the patients in our current study had longer procedures, received more propofol per minute, and had a higher incidence of hypotension than patients in our previous study. Our results are also consistent with Weinberg *et al.*'s observational study,⁵ although the median volume of fluid infused in that study was only 325 (range 0–1,000) mL.

Table 1 Baseline characteristics

Characteristic	Low volume (n = 75)	High volume (n = 75)
Age (yr)	49 (14)	51 (17)
< 45	26 (35)	30 (40)
45-64	39 (52)	28 (37)
≥ 65	10 (13)	17 (23)
Sex (male)	41 (55)	43 (57)
Body mass index (kg·m ⁻²)	27 (5)	26 (5)
< 18.5	2 (3)	3 (4)
18.5-24.9	25 (33)	32 (43)
25-29.9	28 (37)	28 (37)
≥ 30	20 (27)	12 (16)
ASA physical status		
I-II	64 (85)	59 (79)
III	11 (15)	16 (21)
Comorbidities		
Cardiac arrhythmias	3 (4)	2 (3)
Ischemic heart disease	3 (4)	3 (4)
Hypertension	19 (25)	11 (15)
Planned procedure		
Colonoscopy alone	56 (75)	52 (69)
Colonoscopy plus gastroscopy	19 (25)	23 (31)
Fasting		
Solids (hr)	25.5 [21.5-31]	24.5 [20.5-27.5]
Liquids (hr)	8.5 [7-11]	10.5 [7.5-15]
Bowel preparation		
Isotonic	67 (89)	65 (87)
Hypertonic	8 (11)	10 (13)
QoR-15 score pre-infusion	126 [117-139]	130 [119-140]
Allocated fluid administration (mL)	159 (33)	1,478 (288)

Data are presented as mean (standard deviation), median [interquartile range], or number (%) as indicated. Low volume = 2 mL·kg⁻¹ Plasma-Lyte 148 intravenously; high volume = 20 mL·kg⁻¹ Plasma-Lyte 148 intravenously; ASA = American Society of Anesthesiologists; QoR-15 = Quality of Recovery 15 score.; SBP = systolic blood pressure

There are a number of potential explanations for our results. First, our patients may not have been significantly dehydrated. Osmotically balanced preparations like Glycoprep-C do not encourage the movement of water from the extracellular fluid to the bowel lumen and have not been shown to change patient weight or blood chemistry.¹⁴ Although our patients had relatively long fasting times, they were encouraged to drink liberal amounts of fluids during bowel preparation, and perhaps this prevented significant dehydration.¹⁵ The VAS scores for thirst that we recorded before fluid infusion did not show extreme thirst and supports this assumption.

Second, 20 mL·kg⁻¹ of Plasma-Lyte 148 may not have been sufficient to overcome potential dehydration

effectively. This explanation seems unlikely as 20 mL·kg⁻¹ is greater than or equal to volumes that have proved effective in clinical studies on fluid resuscitation in ambulatory surgery patients.¹⁶⁻¹⁸ Our high-volume infusion was greater than is routinely administered clinically⁵ and is at the upper end of volumes that are practical in an ambulatory setting. Third, the low-volume infusion, which was designed to improve blinding, may have been as effective as the high-volume infusion in preventing hypotension. This seems unlikely as a preoperative fast is thought to result in fluid deficits of > 1 L.¹⁹ We therefore do not advocate investigating a greater fluid volume in the intervention group or a lesser fluid volume in the control group in future studies.

Finally, we may not have measured the most appropriate outcomes. Hypotension was chosen as the primary outcome because it is a common and significant event that often requires treatment.²⁰ Nevertheless, hypotension during elective colonoscopy rarely translates into adverse post-procedure outcomes. We measured a range of unwanted postoperative symptoms in the PACU and showed incidences similar to previous studies.²¹ We did not collect any post-discharge data, however, and it is possible that high-volume infusion results in better post-discharge quality of recovery than low-volume infusion.

The incidence of the primary outcome (57%) and SBP < 90 mmHg (41%) were relatively high in this study.¹ Nevertheless, the median duration of hypotension was short (2.5 min), and few patients were treated with vasopressors (12%). These observations are consistent with studies using similar sedation regimens.²² We did not identify significant modifiable predictors of hypotension in this study. While we found that lower VAS scores for thirst after infusion were associated with greater odds of hypotension, given the multiple factors tested, this could be a random relationship.

Strengths and limitations

Strengths of our study included that we randomized patients to a substantial volume of fluid in an attempt to understand more conclusively whether prophylactic intravenous fluids prevent hypotension and postoperative complications in colonoscopy patients. We chose a definition of hypotension (i.e., a ≥ 25% decrease in SBP from baseline during sedation) that was individualized to each patient's pre-procedure SBP, but we also assessed other common definitions of hypotension (i.e., SBP < 90 mmHg and the need for vasopressors).^{1,23,24}

We also quantified the costs of intravenous fluid administration in our study. Given the number of these procedures performed worldwide, cessation of this practice could significantly reduce cost. For example, the numbers

Table 2 Intra- and post-procedure characteristics

Characteristic	Low volume (<i>n</i> = 75)	High volume (<i>n</i> = 75)	<i>P</i> value
Sedation duration (min)			
Colonoscopy	24 [16–33]	25 [17–32]	0.63
Colonoscopy plus gastroscopy	33 [25–50]	33 [25–43]	0.64
Propofol			
mg	400 [260–549]	400 [250–560]	0.88
mg·kg ⁻¹ ·min ⁻¹	0.20 [0.15–0.27]	0.21 [0.14–0.27]	0.48
Fentanyl			
µg	50 [50–75]	50 [50–75]	0.62
µg·kg ⁻¹	0.71 [0.49–1.09]	0.82 [0.59–1.11]	0.46
QoR-15 score post-procedure	138 [125–147]	140 [133–149]	0.17

Data are presented as median [interquartile range]. Low volume = 2 mL·kg⁻¹ Plasma-Lyte 148 intravenously; high volume = 20 mL·kg⁻¹ Plasma-Lyte 148 intravenously; QoR-15 = Quality of Recovery 15 score; SBP = systolic blood pressure

Table 3 Study outcomes

Outcome	Low volume (<i>n</i> = 75)	High volume (<i>n</i> = 75)	Effect size (95% CI)	<i>P</i> value
Decrease in SBP ≥ 25% from baseline during sedation (primary outcome)	44 (59)	42 (56)	−3 (−18 to 13)	0.74
SBP < 90 mmHg during sedation	26 (35)	36 (48)	13 (−2 to 28)	0.10
Lowest SBP during sedation (mmHg)	95 (15)	94 (15)	0 (−4 to 4)	0.74
Duration of hypotension (min)	2.5 [0–10]	2.5 [0–15]	3 (−15 to 21)	0.76
Vasopressor administered	10 (13)	9 (12)	−1 (−12 to 9)	0.81
Nausea	6 (8)	2 (3)	−5 (−13 to 2)	0.15
Headache	19 (25)	12 (16)	−9 (−22 to 4)	0.16
Drowsy	46 (61)	51 (68)	7 (−9 to 21)	0.39
Dizzy	16 (21)	18 (24)	3 (−11 to 16)	0.70
Recall	5 (7)	7 (9)	2 (−6 to 12)	0.55
Dreaming	17 (23)	15 (20)	−3 (−16 to 10)	0.69
QoR-15 (change from baseline)	8 (1–20)	11 (2–19)	7 (−12 to 26)	0.44
Satisfied with care*	73 (97)	74 (99)	2 (−4 to 7)	0.56
Post-procedure hospital stay (hr)	1.4 [1.0–2.0]	1.2 [1.0–1.5]	−16 (−35 to 3)	0.10
Plasma-Lyte 148 infusion cost per patient (A\$)	9.07 [9.07–9.07]	11.02 [9.07–12.97]	195 (137 to 252)	< 0.0001

Data are presented as mean (standard deviation), median [interquartile range], or number (%), as indicated. Low volume = 2 mL·kg⁻¹ Plasma-Lyte 148 intravenously. High volume = 20 mL·kg⁻¹ Plasma-Lyte 148 intravenously. QoR-15 = Quality of Recovery 15 score; SBP = systolic blood pressure. *Satisfaction score of 4 or 5. For non-normal data, effect sizes were calculated using Somers' *d*, where the effect of being in the high-volume compared with the low-volume group is reported as percentage chance (95% CI). This can be interpreted as the percentage chance that a patient randomized to high vs low volume will have a higher value for the parameter (lower percentage likelihood if negative). For categorical data, the risk difference and the 95% confidence interval (CI) are reported

of patients coded as having a colonoscopy in Australian public and private hospitals from July 2013 to June 2014 were 444,784 and 568,208, respectively (total *n* = 1,012,992). If we assume that 64% of these patients received intravenous fluids⁴ (as reported previously), and that the average additional cost per patient is \$1.95 for a high-volume protocol over a low-volume protocol and \$11.02 for a high-volume protocol over no fluids, the additional cost in Australia for one recent year would have

been \$1.26 million (1,012,992 × 0.64 × \$1.95) and \$7.14 million (1,012,992 × 0.64 × \$11.02), respectively. This study provides an example of how pragmatic randomized studies can simultaneously inform clinical care and provide evidence to improve the efficiency of the allocation of resources within hospitals.

Our study did have a number of limitations. We recruited the patients to this study on the day of the procedure and relied on hospital protocols to ensure

Table 4 Odds ratios for the primary outcome (decrease in systolic blood pressure $\geq 25\%$ from baseline during sedation)

Predictor	<i>n</i> (%) with outcome	OR (95% CI) Univariate	<i>P</i> Value	OR (95% CI) Multivariate	<i>P</i> Value
Age (yr)					
< 44	30 (54)	Reference		Reference	
45-64	38 (57)	1.14 (0.56 to 2.32)	0.73	0.99 (0.43 to 2.27)	0.99
≥ 65	18 (67)	1.73 (0.67 to 4.51)	0.26	1.45 (0.45 to 4.66)	0.53
Sex					
Male	55 (65)	Reference		Reference	
Female	31 (47)	0.47 (0.24 to 0.90)	0.02	0.55 (0.26 to 1.14)	0.11
Body mass index ($\text{kg}\cdot\text{m}^{-2}$)					
< 25	37 (60)	Reference		Reference	
25-29.9	32 (57)	0.90 (0.43 to 1.88)	0.78	0.72 (0.32 to 1.59)	0.41
≥ 30	17 (53)	0.77 (0.32 to 1.81)	0.54	0.90 (0.33 to 2.47)	0.83
ASA physical status					
I-II	69 (56)	Reference		Reference	
III	17 (63)	1.33 (0.56 to 3.14)	0.51	1.39 (0.51 to 3.75)	0.52
Hypertension					
No	67 (56)	Reference		Reference	
Yes	19 (63)	1.37 (0.60 to 3.12)	0.46	1.32 (0.51 to 3.43)	0.56
Fasting (solids)					
≤ 24 hr	35 (53)	Reference		Reference	
> 24 hr	51 (61)	1.37 (0.71 to 2.63)	0.94	1.43 (0.71 to 2.89)	0.56
Fasting (fluids)					
≤ 6 hr	17 (65)	Reference		Reference	
> 6 hr	69 (56)	0.66 (0.27 to 1.60)	0.36	0.57 (0.22 to 1.52)	0.26
Bowel prep					
Hypertonic	10 (56)	Reference		Reference	
Isotonic	76 (58)	1.09 (0.40 to 2.93)	0.87	1.03 (0.33 to 3.17)	0.96
Planned procedure					
Colonoscopy	61 (56)	Reference		Reference	
Colonoscopy plus gastroscopy	25 (60)	1.13 (0.55 to 2.34)	0.74	1.41 (0.64 to 3.11)	0.39
Randomized group					
Low volume	44 (59)	Reference		Reference	
High volume	42 (56)	0.90 (0.47 to 1.71)	0.74	0.74 (0.36 to 1.51)	0.41
SBP post infusion (per 10 mmHg)	-	1.02 (0.86 to 1.20)	0.84	0.94 (0.77 to 1.15)	0.56
Thirst post infusion (per 10 mm)	-	0.84 (0.73 to 0.98)	0.02	0.84 (0.72 to 0.99)	0.04

ASA = American Society of Anesthesiologists; CI = confidence interval; OR = odds ratio; SBP = systolic blood pressure

standardized preparation. We therefore could not ask patients to provide a prospective record of the amount of fluid they consumed during bowel preparation or prevent patients using products other than Glycoprep-C. Although the use of hyperosmotic bowel preparation was not a significant predictor of hypotension in our study, the number of patients receiving hyperosmotic bowel preparation was small. Our study therefore does not contribute to the evidence base about the effectiveness of

intravenous fluids in the setting of bowel preparations other than Glycoprep-C.

Another limitation was that compliance with the advice to take antihypertensive medication on the day of the procedure was not recorded. We recorded only systolic blood pressure and did not record mean blood pressure which may be a better measure of tissue perfusion. Furthermore, we measured nausea, headache, drowsiness, and dizziness only postoperatively and did not measure

Fig. 2 Systolic blood pressure (SBP) and thirst (mm on a visual analog scale; 0 = not thirsty at all; 100 = extremely thirsty) pre-infusion, post-infusion, during sedation for colonoscopy, and in the postanesthesia care unit (PACU) in patients randomized to

intravenous Plasma-Lyte 148 2 mL·kg⁻¹ or 20 mL·kg⁻¹. Results are presented as mean (standard deviation). There were no significant differences between groups

them preoperatively or immediately after fluid infusion. We assumed that the collective incidence of these symptoms was similar at baseline, but these secondary outcomes were not the basis of our sample size calculation.

We administered intravenous fluid before rather than during the procedure in order to improve blinding and ensure that the patients received the randomized intervention before sedation was administered. Nevertheless, pre-procedure administration is not typical of our clinical practice, and we did not record the time from completion of the infusion to the start of colonoscopy. Finally, although we recommended targeting moderate sedation, the propofol doses were commensurate with those recommended for general anesthesia²⁵ but consistent with the intentions of anesthesiologists practicing endoscopy sedation in our region^{3,4} and the expectations of our patients.²⁶

The generalizability of our study is potentially limited to patients with similar comorbidities who fasted according to our institution's fasting guidelines, took a single dose of high-volume isotonic bowel preparation, and received relatively deep propofol-based sedation. Nevertheless, patients with a lower risk of hypotension, a shorter fasting time, and lighter sedation seem equally unlikely as the patients in our study to benefit from high-volume prophylactic intravenous fluids. Importantly, our institution has recently moved to 2 L split-dose preparation and two hours of fasting for fluids, in line with the latest guidelines.²⁷ The generalizability of our study is also limited to health services with a similar cost base. Savings would be reduced where the cost of intravenous fluids and administration sets are lower or where an administration set with a low-volume infusion is routinely used to facilitate sedative drug administration.

In conclusion, our study adds to the evidence base on intravenous fluid administration in adult elective colonoscopy patients and can be immediately translated into clinical practice. The results apply to anesthesiologists

who administer intravenous fluids to treat suspected dehydration and prevent unwanted symptoms as well as to anesthesiologists who require only an intravenous fluid infusion for convenient drug administration. This practice is ineffective in preventing hypotension and other unwanted symptoms in adult patients presenting for elective colonoscopy and increases the costs of care.

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