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Intrapartum intravenous fluids for caesarean delivery and newborn weight loss

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ABSTRACT

Objective: To examine weight loss (WL) and excess weight loss (EWL) among newborns of caesarean delivery, comparing colloids plus crystalloids versus crystalloids only. Also, to examine different doses of intrapartum intravenous fluids (IVF) on WL and EWL.

Design: Comparative safety retrospective cohort study.

Setting: University teaching hospital, Moncton, Canada.

Patients: Mothers exposed to IVF with caesarean delivery between 2008 and 2016.

Interventions: Exposure to colloids plus crystalloids was compared to crystalloids only, and dose-response analyses were performed for colloids, crystalloids and total IVF doses. Linear and logistic regression models were used, adjusting for potential confounders.

Main outcome measures: Infants' WL was measured at days 1, 2 and 3 postpartum, and EWL defined as loss of > 7% of birth weight.

Results: From 801 mother-infant pairs, 176 were exposed to colloids plus crystalloids and 625 were exposed to crystalloids only (overall mean birth weight = 3416 g, EWL = 2%, 41.4% and 55.5% on days 1, 2 and 3 respectively). No significant difference in newborns' WL was observed on any of the days assessed. Adjusted odds ratio (95% CI) of EWL was 1.0 (0.3–3.3) at 24 hours, 1.0 (0.7–1.5) at 48 hours and 1.4 (0.9–2.2) at 72 hours. No dose-response relationship was detected with type-specific and total IVF exposures.

Conclusions: The risk of EWL was similar with colloids plus crystalloids and crystalloids only, suggesting that both therapeutic options can be considered during

caesarean delivery. The absence of dose-response relationships adds confirmatory evidence to the IVF safety profiles.

Keywords: Birth weight, Weight loss, Colloids, Crystalloids, Caesarean section.

INTRODUCTION

Hypotension is the most significant adverse effect in women undergoing spinal anesthesia for caesarean delivery, affecting on average 70% of pregnant women.[1,2] The administration of intravenous (IV) fluids (i.e. crystalloids and colloids) prior to and/or during anesthesia represents one of the most common strategies to prevent maternal hypotension.[1] Among the IV fluids, crystalloid solutions are the most frequently used, with normal saline (NS) and Ringer's lactate (RL) as the most common choices.[3] Systematic reviews and meta-analyses indicate that pre- or co-loading with colloids – specifically hydroxyethyl starches (HES) – is superior to crystalloids alone, with volumes larger than 500 ml offering no significant additional benefits.[1–5] Current practice advocate combining colloids and crystalloids solutions rather than colloids alone.[2]

While colloids are becoming an increasingly used choice as IV fluid in pregnant women undergoing caesarean section, no study has examined the impact of colloids – or colloids plus crystalloids combination – on excess weight loss (EWL) among newborns. Although normal physiological weight loss occurs after delivery,[6,7] EWL (i.e. loss of more than 7-10% of birth weight) is considered a complication which increases the risk of hyperbilirubinemia, hypernatremic dehydration, hospitalizations and long-term

morbidities.[8–10] Recent literature reports growing evidence of positive association between IV fluids – specifically crystalloids – and EWL (between 7% to 10%),[11–14] and it remains unclear whether different IV fluid combinations present similar safety profiles. The primary objective of the current study was to examine amount of weight loss and EWL among newborns of caesarean delivery, comparing colloids plus crystalloids intrapartum IV fluids versus crystalloids only. The secondary objective was to examine the association between different doses of intrapartum IV fluids and newborn weight loss, as well as EWL.

METHODS

Study Design

A population-based retrospective cohort design was used. The cohort was selected from mothers hospitalized at the Dr. George-L.-Dumont University Hospital Centre (New Brunswick, Canada) between April 2008 and June 2016. Trained medical staff extracted the information from the hospital medical records of mothers undergoing caesarean deliveries and their linked newborns' files. Data collection was performed on two periods for logistical and sample size reasons; (1) records from all (n = 320) caesarean deliveries between April 2008 and January 2010 and (2) a random sample of 500 caesarean deliveries between February 2010 and June 2016 were retained. Performing separate primary analysis for the two periods did not show major differences in results.

Cohort Selection

The cohort inclusion criteria were: (1) a pregnancy with a recorded caesarean delivery between April 1, 2008 and June 31, 2016; (2) recorded singleton live birth; (3) maternal

age at the beginning of pregnancy of 15-45 years; (4) gestational duration of 20-45 weeks; and (5) exposure to colloids or crystalloids IV fluids before caesarean delivery. The exclusion criteria were: (1) missing data on IV fluids administration and other potential variables and (2) infants with feeding difficulties leading to unsuccessful oral feeding (neither breastfeeding nor formula) during the hospitalization period (i.e nil per os [NPO]).

Weight Loss and EWL

From the infants' medical records, we extracted information on birth weight and infants' weight at 24, 48 and 72 hours. EWL was defined as loss of > 7% of birth weight, calculated at 24, 48 and 72 hours postpartum.[6,7,15]

IV Fluids Exposure

Colloids (Voluven®, Pentaspan® and others/non specified) plus crystalloids (RL, NS and others/non specified) use was defined as the maternal intrapartum exposure to both colloids and crystalloids IV fluids for caesarean delivery. Crystalloids use (RL, NS and others/non specified) was defined as the maternal intrapartum exposure to crystalloids only. The doses of colloids were categorized as: 0, > 0-500, > 500 ml and doses of crystalloids were categorized as: 0, > 0-1000, > 1000-2000, > 2000 ml. We calculated the total doses of IV fluids; categorized into: 0-1000, > 1000-2000, > 2000-3000, > 3000ml.

Confounding Variables

Two classes of potential risk factors were included in the analysis. First, gestational and maternal variables, including: maternal age in years at delivery, number of pregnancies, number of viable births, number of lost pregnancies, gestational diabetes (yes/no), hypertension during pregnancy (yes/no), pre-eclampsia (yes/no), cigarette smoking

during pregnancy (yes/no), alcohol drinking during pregnancy (yes/no), drug use during pregnancy (yes/no), epidural before caesarean section (yes/no), and elective caesarean section (yes/no). Second, infant related variables, including: gestational age in weeks, Apgar score, fever during hospitalization (yes/no), breastfeeding during hospitalization (yes/no), phototherapy on days 1 (yes/no), 2 (yes/no) and 3 (yes/no), number of urine on each of day 1, 2 and 3, and number of stools on each of day 1, 2 and 3.

Statistical Analysis

The descriptive statistics for the characteristics of the mothers-infants pairs were calculated and compared between groups. We compared the amount of weight lost by infants in both groups at 24, 48 and 72 hours postpartum using crude and adjusted linear regressions, with crystalloids only users as reference group. Three regression models were constructed: *Model 1* (crude), *Model 2* (adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, and elective caesarean section) and *Model 3* (adjusted for the variables in Model 2, in addition to Apgar score, breastfeeding, number of stools, number of urine, presence of fever and phototherapy). The purpose of this methodology is that the additional variables in Model 3 were measured during the postpartum period and not at baseline, and through them, the effect of IV fluids on weight loss could be mediated.

Additional regression models for colloids and crystalloids doses were used to examine trends and dose-response relationships with newborn weight loss, similarly with the total IV fluid doses. Logistic regression models were used to estimate crude and adjusted odds

ratios (ORs) and 95% confidence intervals (CIs) for EWL, with adjustment for potential confounders as listed above. Firth penalized maximum likelihood estimation method was used whenever quasi-complete separation in data was detected in logistic regression models.[16]

Sensitivity Analysis

First, the maximum physiological limits of weight loss for newborns are controversial,[17,18] thus, we reanalyzed our data using EWL defined as (1) loss of > 5% and (2) loss of > 10% of birth weight. Second, suboptimal breastfeeding and delayed onset of lactogenesis can lead to EWL.[11,15] Therefore, we tested its potential effect using 2 different techniques; (1) performed all analyses among the subgroup of breastfed newborns only and (2) excluded breastfeeding as potential confounder from Model 3. Using a type I error of 0.05 and 80% power, a sample size of 818 mother-infants pairs was estimated to be sufficient to detect a between-group weight loss difference of 10%. All statistical analyses were conducted using SAS software, version 9.3 (SAS Institute Inc., Cary, NC). This study was approved by the Research Ethics Committee of the Vitalité Health Network.

RESULTS

A total of 801 mother-infant pairs fulfilled our inclusion and exclusion criteria (see Figure 1 for the selection process). From these, 176 mother-infant pairs were exposed to colloids plus crystalloids intrapartum and 625 were exposed to crystalloids only. Among the colloids plus crystalloids group, 58.5% were exposed to Voluven®, 12.5% to Pentaspan®, and 29% to other colloids or non-specified. For crystalloids, 87.3% were

exposed to RL only, 7.1% to RL and NS, and 5.6% to other crystalloids or non-specified. The most frequently used doses of colloids and crystalloids were > 500 ml and >1000-2000 ml, respectively. Overall, the mean birth weight for the newborns was 3416 g. During the hospitalization period, EWL of > 7% was detected in 15 infants (2%) at 24 hours, 318 infants (41.4%) at 48 hours, 351 infants (55.5%) at 72 hours, and EWL of > 10% was detected in 3 infants (0.4%) at 24 hours, 17 infants (2.2%) at 48 hours and 100 infants (15.8%) at 72 hours.

In both groups, most women were ≤ 35 years of age, with approximately 1 to 4 gravidity, 0 to 1 parity and 0 to1 abortus (Table I). However, women exposed to crystalloids only were more likely to have suffered from gestational diabetes, to have been exposed to epidural before caesarean section, to report cigarette smoking and alcohol drinking. The incidence of preterm deliveries and phototherapy on day 3 were higher among infants in the colloids plus crystalloids group, while breastfeeding during hospitalization was more successful in the crystalloids only group.

Differences in Weight

We observed no significant difference in newborns' weight loss between women exposed to colloids plus crystalloids compared to crystalloids only intrapartum on any of the three days assessed (Table II). Moreover, none of the doses of colloids, crystalloids or total IV fluids was found to be associated with a significant difference in weight loss, nor with a trend of increased or decreased risk over time. We obtained similar estimates for Models 2 and 3 (only results from Model 3 are presented, others are available upon request).

Differences in EWL by Group

We observed no significant difference in the risk of EWL (>7%) at 24 hours (adjusted OR: 1.0; 95% CI: 0.3–3.3), 48 hours (adjusted OR: 1.0; 95% CI: 0.7–1.5) or 72 hours (adjusted OR: 1.4; 95% CI: 0.9–2.2) (Table III). Elective caesarean section was associated with a significant increased risk of EWL at 48 hours (adjusted OR: 1.7; 95% CI: 1.1–2.6) and at 72 hours (adjusted OR: 1.8; 95% CI: 1.1–2.9). Number of stools measured on each day was significantly associated with EWL (adjusted OR, 95% CI: 1.6, 1.1–2.3; 0.8, 0.7–0.9; and 0.7, 0.6–0.8 at 24, 48 and 72 hours, respectively). We obtained similar estimates for Models 2 and 3.

Differences in EWL by Dose

At 24 hours postpartum, the number of cases of EWL was too small to examine specific crystalloids doses. However, neither colloids doses nor total IV fluids doses were associated significantly with EWL (Table IV). At 48 and 72 hours postpartum, we observed no significant association between colloids, crystalloids or total IV fluids and EWL, with the exception of a marginal protective effect from EWL at 72 hours postpartum for crystalloids at doses >1000-2000 (adjusted OR: 0.2; 95% CI: <0.1–0.9). No trend or dose-response relationship was observed with the increase in doses of intrapartum IV fluids (Table IV). Results from the 3 sensitivity analyses supported the primary analyses estimates (results are available upon request).

DISCUSSION

This comparative safety study revealed two main findings. First, the newborn weight loss and the risk of EWL did not differ when colloids plus crystalloids or crystalloids only IV fluids where administered intrapartum for caesarean delivery. Second, there was no dose-response relationship between colloids, crystalloids or total IV fluids and an increased risk of EWL. The results were consistent in different models and sensitivity analyses on breastfed newborns and EWL of >5% and >10% showed similar results.

To the best of our knowledge, this study is the first to compare the risk of EWL for different types of intrapartum IV fluids for caesarean delivery. Previous studies have demonstrated comparable neonatal safety profiles of colloids versus crystalloids, specifically for neonatal acidosis (risk ratio [RR] 0.2; 95% CI 0.01-4.1) and Apgar score (meta-analysis of 3 studies with 209 women: RR: 0.2; 95% CI 0.03-2.1).[1] Similarly, no significant difference in Apgar score was found among neonates exposed to colloids plus crystalloids versus crystalloids only (meta-analysis of 2 studies with 107 women: RR: 0.1; 95% CI 0.01-1.2).[1] Still, it is noteworthy that the number of events in those studies was low and medications used in these older trials (e.g dextrans and gelatins) no longer reflect the current practice of using HES as the preferred choice.[2,4,5] Recently, the CAESAR trial compared two treatment regimens similar to the current study and reported no difference in Apgar score or umbilical pH.[2]

Of nine published studies, five reported significant positive associations between doses of intrapartum fluids and weight loss[11–14,19] whereas the other four reported no significant relationships.[20–23] However, studies with significant findings are different

from the current study since they were based on vaginal births and breastfed newborns[11,12,19] or very small sample sizes.[13,14] Our results corroborate the results of one case-control[23], two prospective cohort studies[20,22], as well as the only RCT on intrapartum IV fluids and EWL to date.[21]

Previous studies hypothesized that since fluids move freely from the mother to her fetus, newborns may become overhydrated and a consequent correction for the newborns' fluid balance is an increase in diuresis and weight loss.[20,24] This hypothesis was partially supported by recent reports[11,12], but caution must be exercised as the observed weight loss could be attributed to insufficient feeding, especially among breastfed infants. Previous studies had suggested that the intrapartum administration of crystalloids could significantly affect the onset of lactogenesis[12,15,25] through the development of breast engorgement, which in turn could negatively affect milk production[25] and increase breast edema.[26] However, our results suggest that if this is the case, it will not lead to an increased risk of EWL. Future studies are warranted to fully examine the effect of IV fluids – and their specific types – on lactogenesis and EWL. A noteworthy finding is the significant association between elective caesarean delivery and EWL. It is possible that pregnant women opting for an elective caesarean delivery could have suffered from other obstetric conditions that leave their newborns more prone to EWL.

The present study has some important strengths. Our objective was to compare newborn weight loss and EWL after two widely used prevention and treatment options for hypotension during caesarean delivery. Through comparing similar IV fluid regimens,

and accounting for numerous potentially confounding variables, we minimized the potential bias of confounding by indication, in this case hypotension itself. Indeed, maternal hypotension itself – and the associated reduction in utero-placental blood supply – can lead to fetal acidosis, which cause weak rooting and sucking reflexes. The later factors can severely compromise lactogenesis, leading to significant newborn weight loss that can be erroneously attributed to IV fluids exposure.[1,27–29] In addition, we used a large set of statistical models and sensitivity analyses to confirm the validity of our observed estimates. However, the results should be interpreted with consideration of the following limitations. We were unable to distinguish between pre- and co-loading of IV fluids administered. We did not have data on intrapartum oral fluids nor the exact onset of successful breastfeeding (day 1, 2, or 3). Given that this is a comparative safety study with an active treatment regimen as a reference group, we cannot exclude the possibility that both IV fluid regimens have a deleterious effect on newborn weight loss. Nevertheless, such comparisons (use versus no use) are less clinically relevant because not treating a woman who requires IV fluids for prevention of hypotension is not an option.

In summary, in the current comparative safety study, the difference in weight loss and the risk of EWL were similar with colloids plus crystalloids and crystalloids intrapartum IV fluids among women undergoing caesarean delivery. The absence of dose-response relationships between both IV fluids types and EWL adds confirmatory evidence to their safety profiles. Combined with previous studies, these results suggest that both therapeutic options can be considered as safe during caesarean sections.

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Competing interests None declared.

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Data sharing statement Data are available after discussion with the Oracle Study Investigators in accordance with our data-sharing policy.

Contribution to Authorship SE, ABa, BS, SD, AM, WH, ABl and MB have contributed to the concept and design of the study. SE and MB performed the analysis and drafted the first draft. SE, ABa, BS, SD, AM, WH, ABl and MB participated in the interpretation of the data. SE, ABa, BS, SD, AM, WH, ABl and MB contributed in drafting and revising of the full manuscript, and have approved the manuscript as submitted. SE, ABa, BS, SD, AM, WH, ABl and MB have met the criteria of authorship, and take public responsibility for the study contents.

Ethics Approval This research project was approved by the Research Ethics Committee of the Vitalité Health Network (first approval 23-12-2009, amendment approved on 26-5-2016).

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What is already known on this topic?

- Use of intravenous fluids (i.e. crystalloids and colloids) prior to and/or during anesthesia is a common strategy to prevent maternal hypotension during caesarean sections.
- No study has examined the impact of colloids – or colloids plus crystalloids combination – on excess weight loss (EWL) among newborns.
- Published literature provides conflicting evidence of association between IV fluids – specifically crystalloids – and EWL.

What this study adds?

- Weight loss difference and the risk of EWL were similar with colloids plus crystalloids and crystalloids only among women undergoing caesarean delivery.
- No dose-response relationship observed between colloids, crystalloids or total IV fluids and an increased risk of EWL.
- Primary and sensitivity analyses suggest that both therapeutic options can be considered as safe during caesarean sections.

References

1 Cyna AM, Andrew M, Emmett RS, *et al.* Techniques for preventing hypotension during spinal anaesthesia for caesarean section. In: *Cochrane Database of Systematic Reviews*. John Wiley & Sons, Ltd 2006. doi:10.1002/14651858.CD002251.pub2

2 Mercier FJ, Diemunsch P, Ducloy-Bouthors AS, *et al.* 6% Hydroxyethyl starch (130/0.4) vs Ringer's lactate preloading before spinal anaesthesia for Caesarean delivery: The randomized, double-blind, multicentre CAESAR trial. *Br J Anaesth* 2014;**113**:459–67. doi:10.1093/bja/aeu103

3 Teoh WHL, Westphal M, Kampmeier TG. Update on volume therapy in obstetrics. *Best Pract Res Clin Anaesthesiol* 2014;**28**:297–303. doi:10.1016/j.bpa.2014.07.004

4 Mercier FJ. Cesarean delivery fluid management. *Curr Opin Anaesthesiol* 2012;**25**:286–91. doi:10.1097/ACO.0b013e3283530dab

5 Ripolles Melchor J, Espinosa, Martinez Hurtado E, *et al.* Colloids versus crystalloids in the prevention of hypotension induced by spinal anesthesia in elective cesarean section. A systematic review and meta-analysis. Minerva Anestesiol. 2015;**81**:1019–30.

6 Flaherman VJ, Schaefer EW, Kuzniewicz MW, *et al.* Early weight loss nomograms for exclusively breastfed newborns. *Pediatrics* 2015;**135**:16–23. doi:10.1542/peds.2014-1532

7 Miller JR, Flaherman VJ, Schaefer EW, *et al.* Early weight loss nomograms for formula fed newborns. *Hosp Pediatr* 2015;**5**:263–8. doi:10.1542/hpeds.2014-0143

8 Moritz ML, Manole MD, Bogen DL, *et al.* Breastfeeding-associated

hypernatremia: are we missing the diagnosis? *Pediatrics* 2005;**116**:e343–7. doi:10.1542/peds.2004-2647

9 Escobar GJ, V.M G, Armstrong MA, *et al.* Rehospitalization for neonatal dehydration: A nested case-control study. *Arch Pediatr Adolesc Med* 2002;**156**:155–61. doi:poa10396 [pii]

10 Van Amerongen RH, Moretta AC, Gaeta TJ. Severe hypernatremic dehydration and death in a breast-fed infant. *Pediatr Emerg Care* 2001;**17**:175–80. doi:10.1097/00006565-200106000-00006

11 Chantry CJ, Nommsen-Rivers LA, Peerson JM, *et al.* Excess Weight Loss in First-Born Breastfed Newborns Relates to Maternal Intrapartum Fluid Balance. *Pediatrics* 2011;**127**:e171–9. doi:10.1542/peds.2009-2663

12 Noel-Weiss J, Woodend a K, Peterson WE, *et al.* An observational study of associations among maternal fluids during parturition, neonatal output, and breastfed newborn weight loss. *Int Breastfeed J* 2011;**6**:9. doi:10.1186/1746-4358-6-9

13 Hirth R, Weitkamp T, Dwivedi A. Maternal Intravenous Fluids and infant weight. *Clin Lact* 2012;:59–63.

14 Sheehan K FB. The Role of Intrapartum Intravenous Therapy and Newborn Weight Loss: Challenging the 7% Rule. *Clin Mother Child Heal* 2015;**12**:8–12. doi:10.4172/2090-7214.1000181

15 Dewey KG, Nommsen-rivers LA, Heinig MJ, *et al.* Risk Factors for Suboptimal Infant Breastfeeding Behavior, Delayed Onset of Lactation, and Excess Neonatal Weight Loss. *Pediatrics* 2003;**112**.

16 Firth D. Bias Reduction of Maximum-Likelihood-Estimates. *Biometrika* 1993;**80**:27–38. doi:10.1093/biomet/80.1.27

17 Tawia S, Mcguire L. Early weight loss and weight gain in healthy , full-term , exclusively-breastfed infants. *Breastfeed Rev* 2014;**22**:31–42.

18 Mezzacappa MA, Ferreira BG. Excessive weight loss in exclusively breastfed full-term newborns in a Baby-Friendly Hospital. *Rev Paul Pediatr (English Ed* 2016;**34**:281–6. doi:10.1016/j.rppede.2016.03.003

19 Moen V, Brudin L, Rundgren M, *et al.* Hyponatremia complicating labour--rare or unrecognised? A prospective observational study. *BJOG* 2009;**116**:552–61. doi:10.1111/j.1471-0528.2008.02063.x

20 Lamp JM, Macke JK. Relationships among intrapartum maternal fluid intake, birth type, neonatal output, and neonatal weight loss during the first 48 hours after birth. *J Obstet Gynecol Neonatal Nurs* 2010;**39**:169–77. doi:10.1111/j.1552-6909.2010.01106.x

21 Watson J, Hodnett E, Armson BA, *et al.* A randomized controlled trial of the effect of intrapartum intravenous fluid management on breastfed newborn weight loss. *J Obstet Gynecol Neonatal Nurs* 2012;**41**:24–32. doi:10.1111/j.1552-6909.2011.01321.x

22 Grossman X, Chaudhuri JH, Feldman-Winter L, *et al.* Neonatal Weight Loss at a US Baby-Friendly Hospital. *J Acad Nutr Diet* 2012;**112**:410–3. doi:10.1016/j.jada.2011.10.024

23 Thulier DJ. Maternal hydration and infant weight: A case-control study in breastfeeding infants delivered by cesarean section. *ProQuest Diss Theses*

2013;:126.http://digitalcommons.uri.edu/oa_diss

24 Zetterström R. Excessive fluid intake before and during delivery causing water intoxication in the mother and her offspring. *Acta Paediatr* 2007;**91**:867–8. doi:10.1111/j.1651-2227.2002.tb02846.x

25 Cotterman KJ. Reverse Pressure Softening: A Simple Tool to Prepare Areola for Easier Latching During Engorgement. *J Hum Lact* 2004;**20**:227–37. doi:10.1177/0890334404264224

26 Kujawa-Myles S, Noel-Weiss J, Dunn S, *et al.* Maternal intravenous fluids and postpartum breast changes: a pilot observational study. *Int Breastfeed J* 2015;**10**:18. doi:10.1186/s13006-015-0043-8

27 Lyons G. Epidural is an outmoded form of regional anaesthesia for elective caesarean section. Proposer. *Int J Obstet Anesth* 1995;**4**:34–6.

28 Robson SC, Boys RJ, Rodeck C, *et al.* Maternal and fetal haemodynamic effects of spinal and extradural anaesthesia for elective caesarean section. *Br J Anaesth* 1992;**68**:54–9.

29 Roberts SW, Leveno KJ, Sidawi JE, *et al.* Fetal acidemia associated with regional anesthesia for elective cesarean delivery. *Obstet Gynecol* 1995;**85**:79–83.

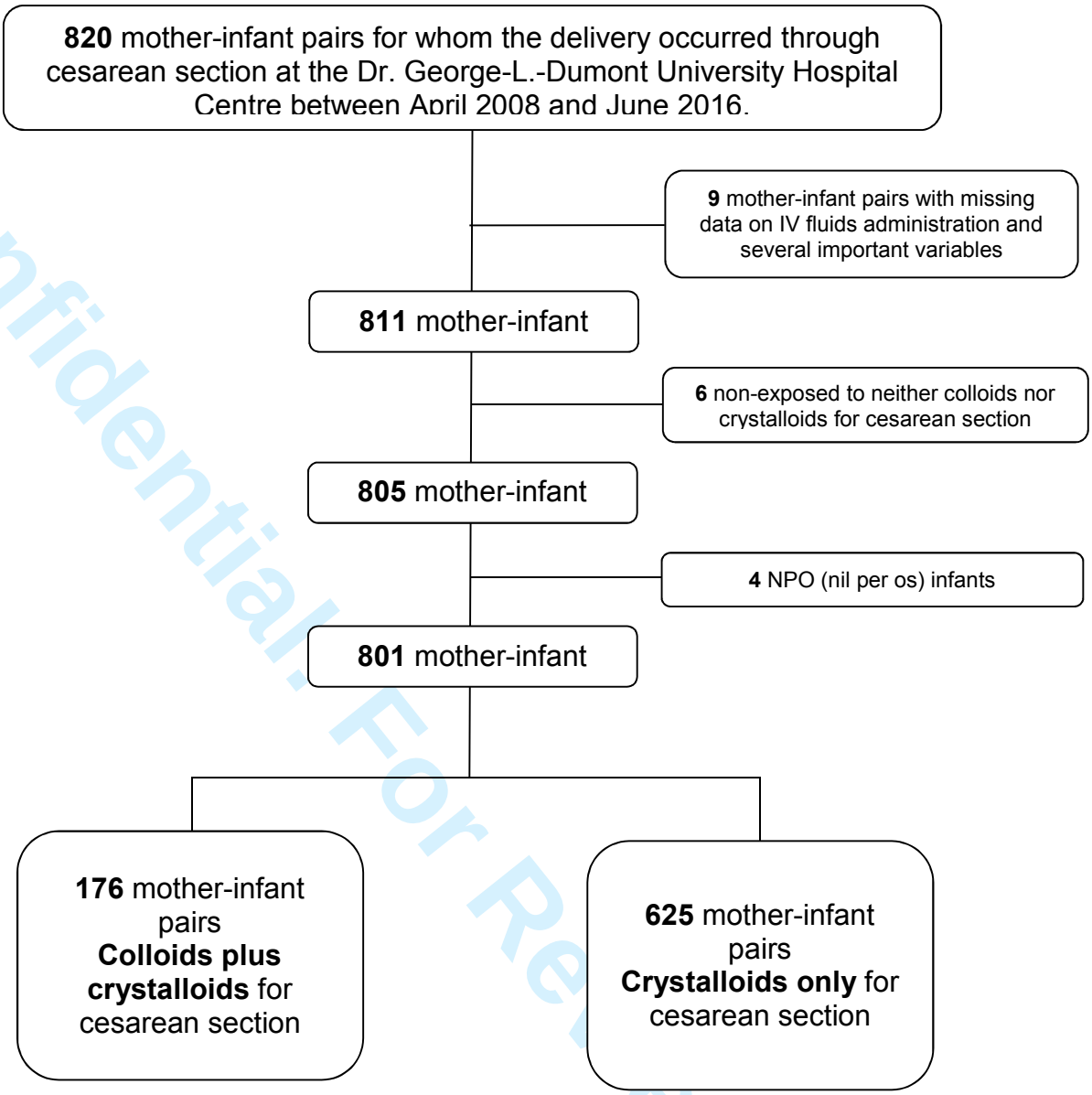

Figure 1. Cohort selection flow diagram

Table I. Characteristics of Mothers-Infants Pairs According to Intrapartum Colloids and Crystalloids Exposure for Caesarean Section

	Missing data	Colloids plus Crystalloids	Crystalloids only
	No. (%)	*No. of deliveries (%)*	
		176 (22.0)	625 (78.0)
Gestational and maternal variables			
Maternal age in years (Mean ± SD)	0 (0)	29.7 ±4.9	29.2 ±5.2
≤35		155 (88.1)	547 (87.5)
>35		21 (11.9)	78 (12.5)
Gravida	2 (0.2)		
1		89 (50.9)	285 (45.7)
2-4		79 (45.1)	311 (49.8)
≥5		7 (4.0)	28 (4.5)
Para	2 (0.2)		
0		104 (59.4)	363 (58.2)
1		55 (31.4)	200 (32.0)
≥2		16 (9.2)	61 (9.8)
Abortus	2 (0.2)		
0		135 (77.1)	439 (70.4)
1		33 (18.9)	128 (20.5)
≥2		7 (4.0)	57 (9.1)
Cigarette smoking	2 (0.2)	21 (11.9)	105 (16.9)
Alcohol drinking	4 (0.5)	14 (8.0)	85 (13.7)
Drug use	4 (0.5)	6 (3.4)	24 (3.9)
Gestational diabetes	0 (0)	5 (2.8)	38 (6.1)
Hypertension during pregnancy	0 (0)	9 (5.1)	41 (6.6)
Pre-eclampsia	0 (0)	11 (6.3)	29 (4.6)
Epidural before caesarean section	0 (0)	53 (30.1)	272 (43.5)
Elective caesarean section	4 (0.5)	73 (41.7)	233 (37.5)
Infant related variables			
Birth weight in grams (Mean ± SD)	12 (1.5)	3383 (±572)	3449 (±544)
Gestational age in weeks (Mean ± SD)	12 (1.5)	38.6 (±1.4)	39.0 (±1.6)
Preterm delivery	12 (1.5)	19 (11.1)	43 (7.0)
Low Apgar score (< 7) at 1 min	14 (1.7)	8 (4.7)	34 (5.5)
Fever during hospitalization	14 (1.7)	4 (2.3)	11 (1.8)
Phototherapy on day 1	13 (1.6)	5 (2.9)	9 (1.5)
Phototherapy on day 2	13 (1.6)	9 (5.2)	21 (3.4)
Phototherapy on day 3	14 (1.7)	18 (10.5)	36 (5.9)
Breastfeeding during hospitalization	15 (1.9)	46 (26.9)	290 (47.2)
Urine during day 1	15 (1.9)		
0		29 (17.0)	56 (9.1)
1-2		64 (37.4)	239 (38.9)

3-5		66 (38.6)	274 (44.5)
≥6		12 (7.0)	46 (7.5)
Urine during day 2	17 (2.1)		
0		1 (0.6)	5 (0.8)
1-2		28 (16.5)	150 (24.4)
3-5		112 (65.9)	355 (57.8)
≥6		29 (17.0)	104 (17.0)
Urine during day 3	73 (9.1)		
0		0 (0.0)	3 (0.5)
1-2		32 (19.5)	115 (20.4)
3-5		93 (56.7)	326 (57.8)
≥6		39 (23.8)	120 (21.3)
Stools during day 1	15 (1.9)		
0		21 (12.3)	62 (10.1)
1-2		65 (38.0)	238 (38.7)
3-5		81 (47.4)	292 (47.5)
≥6		4 (2.3)	23 (3.7)
Stools during day 2	17 (2.1)		
0		5 (2.9)	23 (3.7)
1-2		44 (25.9)	218 (35.5)
3-5		102 (60.0)	334 (54.4)
≥6		19 (11.2)	39 (6.4)
Stools during day 3	73 (9.1)		
0		5 (3.1)	21 (3.7)
1-2		63 (38.4)	193 (34.2)
3-5		84 (51.2)	312 (55.3)
≥6		12 (7.3)	38 (6.8)
Colloids doses in ml*	1 (0.1)		
0		0 (0)	625 (78.1)
>0-500		47 (5.9)	-
>500		128 (16.0)	-
Crystalloids doses in ml	26 (3.2)		
0		16 (2.1)*	0 (0)
>0-1000		54 (7.0)	168 (21.7)
>1000-2000		84 (10.8)	320 (41.3)
>2000		18 (2.3)	115 (14.8)
Total IV fluid doses in ml	26 (3.2)		
>0-1000		22 (2.8)	168 (21.7)
>1000-2000		102 (13.2)	320 (41.3)
>2000-3000		42 (5.4)	108 (13.9)
>3000		6 (0.8)	7 (0.9)

*Deliveries with missing data on crystalloids doses but available data on colloids doses (16 patients' records) were included in the Colloids plus Crystalloids group in the statistical analysis.

Table II. Beta Coefficients and 95% Confidence Intervals of the Linear Regression Models for Difference in Weight at 24, 48, and 72 Hours Postpartum According to Maternal Intrapartum Colloids and Crystalloids Exposure

	Difference in weight in grams (β and 95% CI)					
	24 hours postpartum		48 hours postpartum		72 hours postpartum	
	Model 1 (crude)	*Model 3*	*Model 1 (crude)*	*Model 3*	*Model 1 (crude)*	*Model 3*
Colloids plus Crystalloids	-0.6 (-12.6, 11.4)	-5.2 (-17.5, 7.0)	-0.4 (-15.9, 15.0)	-10.8 (-26.1, 4.5)	-5.4 (-28.2, 17.4)	-9.2 (-32.0, 13.7)
Crystalloids only	Reference	Reference	Reference	Reference	Reference	Reference
Colloids doses in ml (*vs* 0)						
>0-500	-5.8 (-27.9, 16.4)	-9.3 (-31.3, 12.7)	-3.1 (-31.9, 25.7)	-9.5 (-37.3, 18.3)	-11.0 (-55.5, 33.4)	-13.1 (-56.8, 30.6)
>500	-0.4 (-14.6, 13.8)	-5.8 (-20.1, 8.5)	1.6 (-16.8, 20.1)	-9.8 (-27.8, 8.1)	-8.2 (-35.2, 18.8)	-7.9 (-34.5, 18.7)
Crystalloids doses in ml (*vs* 0)						
>0-1000	4.2 (-33.0, 41.4)	-2.6 (-40.9, 35.7)	5.0 (-43.3, 53.3)	13.9 (-34.3, 62.1)	-0.03 (-73.6, 73.5)	39.8 (-35.6, 115.1)
>1000-2000	2.9 (-33.9, 39.6)	-1.5 (-39.4, 36.4)	9.5 (-38.2, 57.2)	21.9 (-25.8, 69.6)	-7.6 (-80.1, 64.9)	39.5 (-35.1, 114.1)
>2000	-0.5 (-38.8, 37.8)	-6.8 (-46.0, 32.4)	2.8 (-46.9, 52.6)	9.8 (-39.4, 59.1)	-21.6 (-97.2, 53.9)	15.2 (-61.5, 91.9)
Total IV fluid doses in ml: (*vs* >0-1000)						
>1000-2000	-4.5 (-16.6, 7.6)	-2.9 (-15.0, 9.2)	4.3 (-11.5, 20.1)	8.1 (-7.1, 23.3)	-7.4 (-31.7, 17.0)	3.5 (-20.2, 27.3)
>2000-3000	-1.6 (-16.9, 13.7)	-2.7 (-17.8, 12.3)	0.8 (-19.1, 20.7)	-0.3 (-19.2, 18.6)	-24.8 (-54.6, 4.9)	-22.1 (-50.9, 6.6)
>3000	-26.7 (-67.7, 14.3)	-27.3 (-66.9, 12.2)	-14.4 (-38.9, 67.7)	-6.4 (-43.4, 56.2)	-3.9 (-81.1, 73.3)	-0.6 (-73.0, 71.8)

The regression coefficient represents the estimated difference in weight since birth

Model 2 adjusted results were similar to the adjusted results of Model 3 (only results from Model 3 are presented in the table; results of Model 2 are available upon request)

Model 2 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, and election to have a caesarean section.

Model 3 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, election to have a caesarean section, Apgar score, breastfeeding, number of stools, number of urine, presence of fever and phototherapy.

Table III. Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI) for Excess Weight Loss (>7%) According to Type of Intrapartum IV Fluid Received by Mothers for Caesarean Section

	24 hours postpartum		48 hours postpartum		72 hours postpartum	
	Model 1 crude OR (95% CI)	*Model 3 Adjusted OR (95% CI)**	*Model 1 crude OR (95% CI)*	*Model 3 Adjusted OR (95% CI)*	*Model 1 crude OR (95% CI)*	*Model 3 Adjusted OR (95% CI)**
Colloids plus Crystalloids	0.9 (0.2–3.2)	1.0 (0.3–3.3)	0.9 (0.6–1.3)	1.0 (0.7–1.5)	1.3 (0.9–2.0)	1.4 (0.9–2.2)
Crystalloids only	Reference	Reference	Reference	Reference	Reference	Reference
Maternal age in years	0.9 (0.8–1.0)	1.0 (0.9–1.1)	1.0 (>0.9–1.1<)	1.0 (>0.9–1.0)	1.0 (>0.9–1.1)	1.0 (>0.9–1.1)
Gravida	0.9 (0.6–1.4)	0.3 (0.1–>99)	0.9 (0.8–1.0)	0.7 (0.2–2.5)	0.8 (0.7–0.9)	8.8 (0.7–>99)
Para	0.9 (0.4–1.8)	3.8 (<0.1–24.6)	0.8 (0.7–1.0)	1.2 (0.3–4.7)	**0.7 (0.5–0.8)**	**0.1 (<0.1–0.8)**
Abortus	0.9 (0.4–1.8)	3.3 (<0.1–19.7)	0.9 (0.7–1.1)	1.3 (0.4–5.0)	0.8 (0.6–1.0)	0.1 (<0.1–1.2)
Gestational age	1.1 (0.8–1.6)	0.9 (0.6–1.4)	1.1 (1.0–1.3)	1.0 (0.9–1.2)	1.1 (1.0–1.2)	0.9 (0.8–1.1)
Cigarette smoking	2.8 (0.9–8.3)	1.9 (0.5–5.9)	0.7 (0.5–1.1)	0.8 (0.5–1.3)	**0.5 (0.3–0.7)**	0.7 (0.4–1.2)
Drug use	4.2 (0.9–19.7)	2.8 (0.4–13.6)	0.7 (0.3–1.5)	0.6 (0.3–1.6)	1.1 (0.5–2.6)	1.3 (0.5–3.4)
Alcohol drinking	1.1 (0.2–4.8)	1.0 (0.2–3.7)	1.1 (0.7–1.8)	1.1 (0.7–1.7)	1.2 (0.7–1.9)	1.1 (0.7–2.0)
Hypertension during pregnancy	0.5 (<0.1–3.7)	0.2 (<0.1–2.6)	0.5 (0.3–1.0)	0.6 (0.3–1.3)	0.7 (0.4–1.3)	0.5 (0.2–1.1)
Gestational diabetes	1.3 (0.2–10.1)	1.6 (0.2–7.3)	1.2 (0.6–2.2)	1.4 (0.7–2.8)	0.7 (0.4–1.5)	1.2 (0.5–3.0)
Pre-eclampsia	1.4 (0.2–10.7)	3.8 (0.3–22.8)	**0.4 (0.2–0.8)**	0.6 (0.2–1.4)	1.1 (0.5–2.0)	1.5 (0.7–3.5)
Epidural before caesarean section	1.3 (0.5–3.6)	0.9 (0.2–3.6)	1.3 (0.9–1.6)	1.5 (1.0–2.4)	0.9 (0.6–1.2)	0.9 (0.5–1.4)
Elective caesarean section	0.6 (0.2–1.8)	0.6 (0.2–2.6)	1.2 (0.9–1.6)	**1.7 (1.1–2.6)**	1.3 (1.0–1.9)	**1.8 (1.1–2.9)**
Apgar score	1.4 (0.6–3.2)	1.2 (0.8–3.4)	1.2 (1.0–1.3)	1.2 (1.0–1.4)	1.1 (1.0–1.2)	1.1 (0.9–1.2)
Fever during hospitalization	1.6 (<0.1–13.2)	1.5 (<0.1–13.6)	2.6 (0.9–7.8)	3.3 (1.1–10.4)	0.8 (0.3–2.3)	1.0 (0.3–3.1)
Breastfeeding during hospitalization	0.7 (0.2–2.0)	0.9 (0.3–2.7)	1.3 (1.0–1.8)	1.1 (0.8–1.5)	**1.6 (1.1–2.1)**	1.5 (1.0–2.2)

Phototherapy on day 1	4.0 (0.5–32.9)	7.7 (0.7–46.1)	1.1 (0.4–3.1)	1.4 (0.4–4.8)	0.3 (0.1–1.1)	0.3 (0.1–1.2)
Phototherapy on day 2	N/A	N/A	1.1 (0.5–2.3)	1.6 (0.7–3.9)	0.9 (0.4–2.0)	1.7 (0.7–4.4)
Phototherapy on day 3	N/A	N/A	N/A	N/A	0.7 (0.4–1.3)	0.8 (0.4–1.6)
Urine during day 1	1.0 (0.8–1.4)	0.8 (0.6–1.2)	1.0 (0.9–1.1)	1.0 (0.9–1.2)	1.0 (0.9–1.1)	1.1 (1.0–1.2)
Urine during day 2	N/A	N/A	0.8 (0.8–0.9)	0.9 (0.8–1.0)	**0.8 (0.7–0.9)**	0.9 (0.8–1.0)
Urine during day 3	N/A	N/A	N/A	N/A	**0.8 (0.7–0.9)**	0.9 (0.8–1.0)
Stools during day 1	**1.5 (1.1–2.1)**	**1.6 (1.1–2.3)**	1.1 (1.0–1.2)	1.1 (1.0–1.2)	1.0 (0.9–1.1)	1.0 (0.8–1.1)
Stools during day 2	N/A	N/A	**0.8 (0.7–0.9)**	**0.8 (0.7–0.9)**	**0.8 (0.7–0.9)**	0.9 (0.8–1.0)
Stools during day 3	N/A	N/A	N/A	N/A	**0.7 (0.6–0.8)**	**0.7 (0.6–0.8)**

Model 2 adjusted results were similar to the adjusted results of Model 3 (only results from Model 3 are presented in the table; results of Model 2 are available upon request)

Model 2 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, and election to have a caesarean section.

N/A: not applicable

*Firth penalized maximum likelihood estimation method was used for quasi-complete separation

Table IV. Crude and Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI) for Excess Weight Loss (>7%) According to Doses of Intrapartum IV Fluid Received by Mothers for Caesarean Section

	24 hours postpartum			48 hours postpartum			72 hours postpartum		
	No. cases (%)	*Model 1 (crude)OR (95% CI)**	*Model 3 Adjusted OR (95% CI)**	*No. cases (%)*	*Model 1 (crude)OR (95% CI)*	*Model 3 Adjusted OR (95% CI)*	*No. cases (%)*	*Model 1 (crude)OR (95% CI)*	*Model 3 Adjusted OR (95% CI)**
Regression models for type-specific doses of IV fluid									
Colloids doses (in ml)									
0	12 (2.0)	Reference	Reference	252 (41.9)	Reference	Reference	260 (53.8)	Reference	Reference
>0-500	2 (4.4)	3.3 (0.6–11.8)	2.7 (0.4–11.5)	17 (37.0)	0.9 (0.5–1.7)	1.0 (0.5–2.1)	20 (55.6)	1.1 (0.6–2.3)	1.3 (0.6–2.9)
>500	1 (0.8)	0.7 (0.1–2.8)	0.7 (0.1–3.1)	48 (39.7)	0.9 (0.6–1.4)	1.0 (0.6–1.5)	70 (62.5)	1.4 (0.9–2.1)	1.3 (0.8–2.1)
Crystalloids doses (in ml)									
0	0 (0.0)	Reference	Reference	6 (37.5)	Reference	Reference	9 (75.0)	Reference	Reference
>0-1000	3 (1.4)	N/A	N/A	92 (43.0)	1.1 (0.4–3.4)	0.8 (0.2–2.6)	93 (54.1)	0.5 (0.1–1.9)	0.2 (<0.1–1.1)
>1000-2000	10 (2.6)	N/A	N/A	156 (40.1)	1.0 (0.3–3.0)	0.6 (0.2–2.0)	179 (56.7)	0.5 (0.1–2.1)	**0.2 (<0.1–0.9)**
>2000	1 (0.8)	N/A	N/A	56 (44.8)	1.2 (0.4–3.8)	0.9 (0.2–3.0)	61 (55.0)	0.5 (0.1–2.1)	0.3 (<0.1–1.2)
Regression models for total doses of IV fluid									
Total IV fluid doses (in ml)									
>0-1000	3 (1.7)	Reference	Reference	82 (44.8)	Reference	Reference	81 (55.5)	Reference	Reference
>1000-2000	8 (2.0)	1.1 (0.3–4.4)	1.1 (0.3–4.5)	161 (39.3)	0.8 (0.6–1.1)	0.7 (0.5–1.0)	183 (56.0)	1.0 (0.7–1.5)	0.8 (0.5–1.2)
>2000-3000	3 (2.2)	1.3 (0.3–6.3)	1.2 (0.2–6.1)	64 (45.7)	1.0 (0.7–1.6)	1.0 (0.6–1.6)	71 (55.9)	1.0 (0.6–1.6)	0.9 (0.5–1.6)
>3000	0 (0.0)	N/A	N/A	3 (27.3)	0.5 (0.1–1.8)	0.5 (0.1–2.0)	7 (63.6)	1.4 (0.4–5.0)	1.1 (0.3–4.6)

Model 2 adjusted results were similar to the adjusted results of Model 3 (only results from Model 3 are presented in the table; results of Model 2 are available upon request)
Model 2 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, and election to have a caesarean section.
Model 3 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, election to have a caesarean section, Apgar score, breastfeeding, number of stools, number of urine, presence of fever and phototherapy.
N/A: not applicable
*Firth penalized maximum likelihood estimation method was used for quasi-complete separation

Figures legend

Figure 1. Cohort selection flow diagram

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Intrapartum intravenous fluids for caesarean delivery and newborn weight loss: a retrospective cohort study

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ABSTRACT

Objective: To examine weight loss (WL) and excess weight loss (EWL) among newborns of caesarean delivery, comparing colloids plus crystalloids versus crystalloids only. Also, to examine different doses of intrapartum intravenous (IV) fluids on WL and EWL.

Design: Comparative safety retrospective cohort study.

Setting: University teaching hospital, Moncton, Canada.

Patients: Mothers exposed to IV fluids with caesarean delivery between 2008 and 2016.

Interventions: Exposure to colloids plus crystalloids was compared to crystalloids only, and dose-response analyses were performed for colloids, crystalloids and total IV fluids doses. Linear and logistic regression models were used, adjusting for potential confounders.

Main outcome measures: Infants' WL was measured at days 1, 2 and 3 postpartum, and EWL defined as loss of > 7% of birth weight.

Results: From 801 mother-infant pairs, 176 were exposed to colloids plus crystalloids and 625 were exposed to crystalloids only (overall mean birth weight = 3416 g, EWL = 2%, 41.4% and 55.5% on days 1, 2 and 3 respectively). No significant difference in newborns' WL was observed on any of the days assessed. Adjusted odds ratio (95% CI) of EWL was 1.0 (0.3–3.3) at 24 hours, 1.0 (0.7–1.5) at 48 hours and 1.4 (0.9–2.2) at 72 hours. No dose-response relationship was detected with type-specific and total IV fluids exposures.

Conclusions: The risk of EWL was similar with colloids plus crystalloids and crystalloids only, suggesting that both therapeutic options can be considered during caesarean delivery. The absence of dose-response relationships adds confirmatory evidence to the IV fluids safety profiles.

Keywords: Birth weight, Weight loss, Colloids, Crystalloids, Caesarean section.

INTRODUCTION

Hypotension is the most significant adverse effect in women undergoing spinal anesthesia for caesarean delivery, affecting on average 70% of pregnant women.[1,2] The administration of intravenous (IV) fluids (i.e. crystalloids and colloids) prior to and/or during anesthesia represents one of the most common strategies to prevent maternal hypotension.[1] Among the IV fluids, crystalloid solutions are the most frequently used, with normal saline (NS) and Ringer's lactate (RL) as the most common choices.[3] Colloids are frequently used nowadays for several reasons. Preloading with crystalloids alone have shown poor effectiveness in decreasing hypotension.[3] While crystalloids co-loading is considered superior, variable effectiveness were reported.[1,3] Systematic reviews and meta-analyses indicate that pre- or co-loading with colloids – specifically hydroxyethyl starches (HES) – is superior to crystalloids alone, with volumes larger than 500 ml offering no significant additional benefits.[1–5] Current practice advocate combining colloids and crystalloids solutions rather than colloids alone.[2]

While colloids are becoming an increasingly used choice as IV fluid in pregnant women undergoing caesarean section, no study has examined the impact of colloids – or colloids plus crystalloids combination – on excess weight loss (EWL) among newborns. Although normal physiological weight loss occurs after delivery,[6,7] EWL (i.e. loss of more than 7-10% of birth weight) is considered a complication which increases the risk of hyperbilirubinemia, hypernatremic dehydration, hospitalizations and long-term morbidities.[8–10] Recent literature reports growing evidence of positive association between IV fluids – specifically crystalloids – and EWL (between 7% to 10%),[11–14] and it remains unclear whether different IV fluid combinations present similar safety profiles. The primary objective of the current study was to examine amount of weight loss and EWL among newborns of caesarean delivery, comparing colloids plus crystalloids intrapartum IV fluids versus crystalloids only. The secondary objective was to examine the association between different doses of intrapartum IV fluids and newborn weight loss, as well as EWL.

METHODS

Study Design

A population-based retrospective cohort design was used. The cohort was selected from mothers hospitalized at the Dr. George-L.-Dumont University Hospital Centre (New Brunswick, Canada) between April 2008 and June 2016. The average hospital stay for mothers after caesarean deliveries in New Brunswick is 72 hours. Trained medical staff extracted the information from the hospital medical records of mothers undergoing caesarean deliveries and their linked newborns' files. Data collection was performed on

two periods for logistical and sample size reasons; (1) records from all (n = 320) caesarean deliveries between April 2008 and January 2010 and (2) a random sample of 500 caesarean deliveries between February 2010 and June 2016 were retained. Performing separate primary analysis for the two periods did not show major differences in results.

Cohort Selection

The cohort inclusion criteria were: (1) a pregnancy with a recorded caesarean delivery between April 1, 2008 and June 31, 2016; (2) recorded singleton live birth; (3) maternal age at the beginning of pregnancy of 15-45 years; (4) gestational duration of 30-42 weeks; and (5) exposure to colloids or crystalloids IV fluids before caesarean delivery. The exclusion criteria were: (1) missing data on IV fluids administration in addition to several other important variables and (2) infants with feeding difficulties leading to unsuccessful oral feeding (neither breastfeeding nor formula) during the hospitalization period (i.e nil per os [NPO]).

Weight Loss and EWL

From the infants' medical records, we extracted information on birth weight and infants' weight at 24, 48 and 72 hours. EWL was defined as loss of > 7% of birth weight, calculated at 24, 48 and 72 hours postpartum.[6,7,15]

IV Fluids Exposure

Colloids (Voluven®, Pentaspan® and others/non-specified) plus crystalloids (RL, NS and others/non specified) use was defined as the maternal intrapartum exposure to both colloids and crystalloids IV fluids for caesarean delivery. Crystalloids use (RL, NS and others/non-specified) was defined as the maternal intrapartum exposure to crystalloids

only. Being "non-specified" refers to cases where an indicator was present that a colloid or a crystalloid was administered, but no detail on the specific type was recorded. The doses of colloids were categorized as: 0, > 0-500, > 500 ml and doses of crystalloids were categorized as: 0, > 0-1000, > 1000-2000, > 2000 ml. We calculated the total doses of IV fluids; categorized into: 0-1000, > 1000-2000, > 2000-3000, > 3000ml.

Confounding Variables

Two classes of potential risk factors were included in the analysis. First, gestational and maternal variables, including: maternal age in years at delivery, number of pregnancies, number of viable births, number of lost pregnancies, gestational diabetes (yes/no), hypertension during pregnancy (yes/no), pre-eclampsia (yes/no), cigarette smoking during pregnancy (yes/no), alcohol drinking during pregnancy (yes/no), drug use during pregnancy (yes/no), epidural before caesarean section (yes/no), and elective caesarean section (yes/no). Second, infant related variables, including: gestational age in weeks, Apgar score, fever during hospitalization (yes/no), exclusive breastfeeding during hospitalization (i.e. we excluded only formula and breastfeeding-formula combined) (yes/no), phototherapy on days 1 (yes/no), 2 (yes/no) and 3 (yes/no), number of urine on each of day 1, 2 and 3, and number of stools on each of day 1, 2 and 3.

Statistical Analysis

The descriptive statistics for the characteristics of the mothers-infants pairs were calculated and compared between groups. Four regression forms were employed, two for the difference in weight according to types and doses of IV fluids, and two for EWL according to types and doses of IV fluids. We compared the amount of weight lost by infants in both groups (as absolute measure in grams) at 24, 48 and 72 hours postpartum

using crude and adjusted linear regressions, with crystalloids only users as reference group. Three regression models were constructed: *Model 1* (crude, i.e. single univariate regression model), *Model 2* (adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, and elective caesarean section) and *Model 3* (adjusted for the variables in Model 2, in addition to Apgar score, exclusive breastfeeding, number of stools, number of urine, presence of fever and phototherapy). The purpose of this methodology is that the additional variables in Model 3 were measured during the postpartum period and not at baseline, and through them, the effect of IV fluids on weight loss could be mediated. Additional regression models for colloids and crystalloids doses were used to examine trends and dose-response relationships with newborn weight loss, similarly with the total IV fluid doses. Logistic regression models were used to estimate crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for EWL, with adjustment for potential confounders as listed above. Firth penalized maximum likelihood estimation method was used whenever quasi-complete separation in data was detected in logistic regression models.[16]

Sensitivity Analysis

First, the maximum physiological limits of weight loss for newborns are controversial,[17,18] thus, we reanalyzed our data using EWL defined as (1) loss of > 5% and (2) loss of > 10% of birth weight. Second, suboptimal breastfeeding and delayed onset of lactogenesis can lead to EWL.[11,15] Therefore, we tested its potential effect using 2 different techniques; (1) performed all analyses among the subgroup of breastfed

newborns only and (2) excluded exclusive breastfeeding as potential confounder from Model 3. Using a type I error of 0.05 and 80% power, a sample size of 818 mother-infants pairs was estimated to be sufficient to detect a weight loss difference of 10% between the group exposed to colloids plus crystalloids versus the group exposed to crystalloids only. All statistical analyses were conducted using SAS software, version 9.3 (SAS Institute Inc., Cary, NC). This study was approved by the Research Ethics Committee of the Vitalité Health Network.

RESULTS

A total of 801 mother-infant pairs fulfilled our inclusion and exclusion criteria (see Figure 1 for the selection process). From these, 176 mother-infant pairs were exposed to colloids plus crystalloids intrapartum and 625 were exposed to crystalloids only. Among the colloids plus crystalloids group, 103 (58.5%) were exposed to Voluven®, 22 (12.5%) to Pentaspan®, and 51 (29%) to other colloids or non-specified. For crystalloids, 546 (87.3%) were exposed to RL only, 44 (7.1%) to RL and NS, and 35 (5.6%) to other crystalloids or non-specified. The most frequently used doses of colloids and crystalloids were > 500 ml and >1000-2000 ml, respectively. Overall, the mean birth weight for the newborns was 3416 g. During the hospitalization period, EWL of > 7% was detected in 15 infants (2%) at 24 hours, 318 infants (41.4%) at 48 hours, 351 infants (55.5%) at 72 hours, and EWL of > 10% was detected in 3 infants (0.4%) at 24 hours, 17 infants (2.2%) at 48 hours and 100 infants (15.8%) at 72 hours.

In both groups, most women were ≤ 35 years of age, with approximately 1 to 4 gravidity, 0 to 1 parity and 0 to1 abortus (Table I). However, based on crude observations, women exposed to crystalloids only were more likely to have suffered from gestational diabetes, to have been exposed to epidural before caesarean section, to report cigarette smoking and alcohol drinking. The incidence of preterm deliveries and phototherapy on day 3 were higher among infants in the colloids plus crystalloids group, while exclusive breastfeeding during hospitalization was more successful in the crystalloids only group.

Differences in Weight

We observed no significant difference in newborns' weight loss between women exposed to colloids plus crystalloids compared to crystalloids only intrapartum on any of the three days assessed (Table II). Moreover, none of the doses of colloids, crystalloids or total IV fluids was found to be associated with a significant difference in weight loss, nor with a trend of increased or decreased risk over time. We obtained similar estimates for Models 2 and 3 (only results from Model 3 are presented, others are available upon request).

Differences in EWL by Group

We observed no significant difference in the risk of EWL (>7%) at 24 hours (adjusted OR: 1.0; 95% CI: 0.3–3.3), 48 hours (adjusted OR: 1.0; 95% CI: 0.7–1.5) or 72 hours (adjusted OR: 1.4; 95% CI: 0.9–2.2) (Table III). Elective caesarean section was associated with a significant increased risk of EWL at 48 hours (adjusted OR: 1.7; 95% CI: 1.1–2.6) and at 72 hours (adjusted OR: 1.8; 95% CI: 1.1–2.9). Number of stools measured on each day was significantly associated with EWL (adjusted OR, 95% CI: 1.6,

1.1–2.3; 0.8, 0.7–0.9; and 0.7, 0.6–0.8 at 24, 48 and 72 hours, respectively). We obtained similar estimates for Models 2 and 3.

Differences in EWL by Dose

At 24 hours postpartum, the number of cases of EWL was too small to examine specific crystalloids doses. However, neither colloids doses nor total IV fluids doses were associated significantly with EWL (Table IV). At 48 and 72 hours postpartum, we observed no significant association between colloids, crystalloids or total IV fluids and EWL, with the exception of a marginal protective effect from EWL at 72 hours postpartum for crystalloids at doses >1000-2000 (adjusted OR: 0.2; 95% CI: <0.1–0.9). No trend or dose-response relationship was observed with the increase in doses of intrapartum IV fluids (Table IV). Results from the 3 sensitivity analyses supported the primary analyses estimates (available in supplementary data Tables E1 to E5)).

DISCUSSION

This comparative safety study revealed two main findings. First, the newborn weight loss and the risk of EWL did not differ when colloids plus crystalloids or crystalloids only IV fluids where administered intrapartum for caesarean delivery. Second, there was no dose-response relationship between colloids, crystalloids or total IV fluids and an increased risk of EWL. The results were consistent in different models and sensitivity analyses on exclusively breastfed newborns and EWL of >5% and >10% showed similar results.

To the best of our knowledge, this study is the first to compare the risk of EWL for different types of intrapartum IV fluids for caesarean delivery. Previous studies have demonstrated comparable neonatal safety profiles of colloids versus crystalloids, specifically for neonatal acidosis (risk ratio [RR] 0.2; 95% CI 0.01-4.1) and Apgar score (meta-analysis of 3 studies with 209 women: RR: 0.2; 95% CI 0.03-2.1).[1] Similarly, no significant difference in Apgar score was found among neonates exposed to colloids plus crystalloids versus crystalloids only (meta-analysis of 2 studies with 107 women: RR: 0.1; 95% CI 0.01-1.2).[1] Still, it is noteworthy that the number of events in those studies was low and medications used in these older trials (e.g dextrans and gelatins) no longer reflect the current practice of using HES as the preferred choice.[2,4,5] Recently, the CAESAR trial compared two treatment regimens similar to the current study and reported no difference in Apgar score or umbilical pH.[2]

Of nine published studies, five reported significant positive associations between doses of intrapartum fluids and weight loss[11–14,19] whereas the other four reported no significant relationships.[20–23] However, studies with significant findings are different from the current study since they were based on vaginal births and breastfed newborns[11,12,19] or very small sample sizes.[13,14] Our results corroborate the results of one case-control[23], two prospective cohort studies[20,22], as well as the only RCT on intrapartum IV fluids and EWL to date.[21]

Previous studies hypothesized that since fluids move freely from the mother to her fetus, newborns may become overhydrated and a consequent correction for the newborns' fluid

balance is an increase in diuresis and weight loss.[20,24] This hypothesis was partially supported by recent reports[11,12], but caution must be exercised as the observed weight loss could be attributed to insufficient feeding, especially among exclusively breastfed infants. Previous studies had suggested that the intrapartum administration of crystalloids could significantly affect the onset of lactogenesis[12,15,25] through the development of breast engorgement, which in turn could negatively affect milk production[25] and increase breast edema.[26] However, our results suggest that if this is the case, it will not lead to an increased risk of EWL. Future studies are warranted to fully examine the effect of IV fluids – and their specific types – on lactogenesis and EWL. In the current study, the rates of discharges (urine and stool) were comparable to similar studies published in the literature.[20,23,27] A noteworthy finding is the significant association between elective caesarean delivery and EWL. It is possible that pregnant women opting for an elective caesarean delivery could have suffered from other obstetric conditions that leave their newborns more prone to EWL.

The present study has some important strengths. Our objective was to compare newborn weight loss and EWL after two widely used prevention and treatment options for hypotension during caesarean delivery. Through comparing similar IV fluid regimens, and accounting for numerous potentially confounding variables, we minimized the potential bias of confounding by indication, in this case hypotension itself. Indeed, maternal hypotension itself – and the associated reduction in utero-placental blood supply – can lead to fetal acidosis, which cause weak rooting and sucking reflexes. The later factors can severely compromise lactogenesis, leading to significant newborn weight loss

that can be erroneously attributed to IV fluids exposure.[1,28–30] In addition, we used a large set of statistical models and sensitivity analyses to confirm the validity of our observed estimates. However, the results should be interpreted with consideration of the following limitations. The retrospective design has its limitations compared to a prospective study with efficient follow-up. We were unable to distinguish between pre- and co-loading of IV fluids administered. We did not have data on intrapartum oral fluids nor the exact onset of successful exclusive breastfeeding (day 1, 2, or 3) and other related factors (e.g. latching, dysfunctional sucking, etc.). We did not have data on the degree of hypertension, the fluid regimens before the caesarean delivery decision, nor the specific indications for caesarean delivery. The study was underpowered for some of the secondary analyses and future larger studies are warranted. Moreover, different tests were performed and no correction was applied for multiple testing. The study was conducted in one hospital center in Canada, and results may not be directly generalizable to other hospital settings. Given that this is a comparative safety study with an active treatment regimen as a reference group, we cannot exclude the possibility that both IV fluid regimens have a deleterious effect on newborn weight loss. We used penalized maximum likelihood estimation, which produces the best estimates given the available information.[31] However, given the very limited number of cases in some of the full models, effect estimates differed from crude models among some variables, with exceedingly inflated variance. The effect estimates of the primary and secondary exposures on the dependent variable (i.e. EWL) are nonetheless valid since the full models were bias adjusted using penalization.

In summary, in the current comparative safety study, the difference in weight loss and the risk of EWL were similar with colloids plus crystalloids and crystalloids intrapartum IV fluids among women undergoing caesarean delivery. The absence of dose-response relationships between both IV fluids types and EWL adds confirmatory evidence to their safety profiles. Future prospective studies are warranted to confirm the current study results. Combined with previous studies, these results suggest that both therapeutic options can be considered as safe during caesarean sections.

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Contribution to Authorship SE, ABa, BS, SD, AM, WH, ABl and MB have contributed to the concept and design of the study. SE and MB performed the analysis and drafted the first draft. SE, ABa, BS, SD, AM, WH, ABl and MB participated in the interpretation of the data. SE, ABa, BS, SD, AM, WH, ABl and MB contributed in drafting and revising of the full manuscript, and have approved the manuscript as submitted. SE, ABa, BS, SD, AM, WH, ABl and MB have met the criteria of authorship, and take public responsibility for the study contents.

Ethics Approval This research project was approved by the Research Ethics Committee of the Vitalité Health Network (first approval 23-12-2009, amendment approved on 26-5-2016).

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What is already known on this topic?

- Use of intravenous fluids (i.e. crystalloids and colloids) prior to and/or during anesthesia is a common strategy to prevent maternal hypotension during caesarean sections.
- Published literature provides conflicting evidence of association between intravenous fluids – specifically crystalloids – and excess weight loss.

What this study adds?

- Weight loss difference and the risk of excess weight losswere similar with colloids plus crystalloids and crystalloids among women undergoing caesarean delivery.
- No dose-response relationship observed between colloids, crystalloids or total intravenous fluids and an increased risk of excess weight loss.
- Primary and sensitivity analyses suggest that both therapeutic options can be considered as safe during caesarean sections.

References

1 Cyna AM, Andrew M, Emmett RS, *et al.* Techniques for preventing hypotension during spinal anaesthesia for caesarean section. In: *Cochrane Database of Systematic Reviews*. John Wiley & Sons, Ltd 2006. doi:10.1002/14651858.CD002251.pub2

2 Mercier FJ, Diemunsch P, Ducloy-Bouthors AS, *et al.* 6% Hydroxyethyl starch (130/0.4) vs Ringer's lactate preloading before spinal anaesthesia for Caesarean delivery: The randomized, double-blind, multicentre CAESAR trial. *Br J Anaesth* 2014;**113**:459–67. doi:10.1093/bja/aeu103

3 Teoh WHL, Westphal M, Kampmeier TG. Update on volume therapy in obstetrics. *Best Pract Res Clin Anaesthesiol* 2014;**28**:297–303. doi:10.1016/j.bpa.2014.07.004

4 Mercier FJ. Cesarean delivery fluid management. *Curr Opin Anaesthesiol* 2012;**25**:286–91. doi:10.1097/ACO.0b013e3283530dab

5 Ripolles Melchor J, Espinosa, Martinez Hurtado E, *et al.* Colloids versus crystalloids in the prevention of hypotension induced by spinal anesthesia in elective cesarean section. A systematic review and meta-analysis. Minerva Anestesiol. 2015;**81**:1019–30.

6 Flaherman VJ, Schaefer EW, Kuzniewicz MW, *et al.* Early weight loss nomograms for exclusively breastfed newborns. *Pediatrics* 2015;**135**:16–23. doi:10.1542/peds.2014-1532

7 Miller JR, Flaherman VJ, Schaefer EW, *et al.* Early weight loss nomograms for formula fed newborns. *Hosp Pediatr* 2015;**5**:263–8. doi:10.1542/hpeds.2014-0143

8 Moritz ML, Manole MD, Bogen DL, *et al.* Breastfeeding-associated hypernatremia: are we missing the diagnosis? *Pediatrics* 2005;**116**:e343–7. doi:10.1542/peds.2004-2647

9 Escobar GJ, V.M G, Armstrong MA, *et al.* Rehospitalization for neonatal dehydration: A nested case-control study. *Arch Pediatr Adolesc Med* 2002;**156**:155–61. doi:poa10396 [pii]

10 Van Amerongen RH, Moretta AC, Gaeta TJ. Severe hypernatremic dehydration and death in a breast-fed infant. *Pediatr Emerg Care* 2001;**17**:175–80. doi:10.1097/00006565-200106000-00006

11 Chantry CJ, Nommsen-Rivers LA, Peerson JM, *et al.* Excess Weight Loss in First-Born Breastfed Newborns Relates to Maternal Intrapartum Fluid Balance. *Pediatrics* 2011;**127**:e171–9. doi:10.1542/peds.2009-2663

12 Noel-Weiss J, Woodend a K, Peterson WE, *et al.* An observational study of associations among maternal fluids during parturition, neonatal output, and breastfed newborn weight loss. *Int Breastfeed J* 2011;**6**:9. doi:10.1186/1746-4358-6-9

13 Hirth R, Weitkamp T, Dwivedi A. Maternal Intravenous Fluids and infant weight. *Clin Lact* 2012;:59–63.

14 Sheehan K FB. The Role of Intrapartum Intravenous Therapy and Newborn Weight Loss: Challenging the 7% Rule. *Clin Mother Child Heal* 2015;**12**:8–12. doi:10.4172/2090-7214.1000181

15 Dewey KG, Nommsen-rivers LA, Heinig MJ, *et al.* Risk Factors for Suboptimal Infant Breastfeeding Behavior, Delayed Onset of Lactation, and Excess Neonatal

Weight Loss. *Pediatrics* 2003;**112**.

16 Firth D. Bias Reduction of Maximum-Likelihood-Estimates. *Biometrika* 1993;**80**:27–38. doi:10.1093/biomet/80.1.27

17 Tawia S, Mcguire L. Early weight loss and weight gain in healthy , full-term , exclusively-breastfed infants. *Breastfeed Rev* 2014;**22**:31–42.

18 Mezzacappa MA, Ferreira BG. Excessive weight loss in exclusively breastfed full-term newborns in a Baby-Friendly Hospital. *Rev Paul Pediatr (English Ed* 2016;**34**:281–6. doi:10.1016/j.rppede.2016.03.003

19 Moen V, Brudin L, Rundgren M, *et al.* Hyponatremia complicating labour--rare or unrecognised? A prospective observational study. *BJOG* 2009;**116**:552–61. doi:10.1111/j.1471-0528.2008.02063.x

20 Lamp JM, Macke JK. Relationships among intrapartum maternal fluid intake, birth type, neonatal output, and neonatal weight loss during the first 48 hours after birth. *J Obstet Gynecol Neonatal Nurs* 2010;**39**:169–77. doi:10.1111/j.1552-6909.2010.01106.x

21 Watson J, Hodnett E, Armson BA, *et al.* A randomized controlled trial of the effect of intrapartum intravenous fluid management on breastfed newborn weight loss. *J Obstet Gynecol Neonatal Nurs* 2012;**41**:24–32. doi:10.1111/j.1552-6909.2011.01321.x

22 Grossman X, Chaudhuri JH, Feldman-Winter L, *et al.* Neonatal Weight Loss at a US Baby-Friendly Hospital. *J Acad Nutr Diet* 2012;**112**:410–3. doi:10.1016/j.jada.2011.10.024

23 Thulier DJ. Maternal hydration and infant weight: A case-control study in

breastfeeding infants delivered by cesarean section. *ProQuest Diss Theses* 2013;:126.http://digitalcommons.uri.edu/oa_diss

24 Zetterström R. Excessive fluid intake before and during delivery causing water intoxication in the mother and her offspring. *Acta Paediatr* 2007;**91**:867–8. doi:10.1111/j.1651-2227.2002.tb02846.x

25 Cotterman KJ. Reverse Pressure Softening: A Simple Tool to Prepare Areola for Easier Latching During Engorgement. *J Hum Lact* 2004;**20**:227–37. doi:10.1177/0890334404264224

26 Kujawa-Myles S, Noel-Weiss J, Dunn S, *et al.* Maternal intravenous fluids and postpartum breast changes: a pilot observational study. *Int Breastfeed J* 2015;**10**:18. doi:10.1186/s13006-015-0043-8

27 Mulder PJ, Johnson TS, Baker LC. Excessive weight loss in breastfed infants during the postpartum hospitalization. *JOGNN - J Obstet Gynecol Neonatal Nurs* 2010;**39**:15–26. doi:10.1111/j.1552-6909.2009.01085.x

28 Lyons G. Epidural is an outmoded form of regional anaesthesia for elective caesarean section. Proposer. *Int J Obstet Anesth* 1995;**4**:34–6.

29 Robson SC, Boys RJ, Rodeck C, *et al.* Maternal and fetal haemodynamic effects of spinal and extradural anaesthesia for elective caesarean section. *Br J Anaesth* 1992;**68**:54–9.

30 Roberts SW, Leveno KJ, Sidawi JE, *et al.* Fetal acidemia associated with regional anesthesia for elective cesarean delivery. *Obstet Gynecol* 1995;**85**:79–83.

31 Greenland S, Mansournia MA, Altman DG. Sparse data bias: a problem hiding in plain sight. *BMJ* 2016;:i1981. doi:10.1136/bmj.i1981

Table I. Characteristics of Mothers-Infants Pairs According to Intrapartum Colloids and Crystalloids Exposure for Caesarean Section

	Missing data	Colloids plus Crystalloids	Crystalloids only
	No. (%)	*No. of deliveries (%)*	
		176 (22.0)	625 (78.0)
Gestational and maternal variables			
Maternal age in years (Mean ± SD)	0 (0)	29.7 (±4.9)	29.2 (±5.2)
≤35		155 (88.1)	547 (87.5)
>35		21 (11.9)	78 (12.5)
Gravida	2 (0.2)		
1		89 (50.9)	285 (45.7)
2-4		79 (45.1)	311 (49.8)
≥5		7 (4.0)	28 (4.5)
Para	2 (0.2)		
0		104 (59.4)	363 (58.2)
1		55 (31.4)	200 (32.0)
≥2		16 (9.2)	61 (9.8)
Abortus	2 (0.2)		
0		135 (77.1)	439 (70.4)
1		33 (18.9)	128 (20.5)
≥2		7 (4.0)	57 (9.1)
Cigarette smoking	2 (0.2)	21 (11.9)	105 (16.9)
Alcohol drinking	4 (0.5)	14 (8.0)	85 (13.7)
Drug use	4 (0.5)	6 (3.4)	24 (3.9)
Gestational diabetes	0 (0)	5 (2.8)	38 (6.1)
Hypertension during pregnancy	0 (0)	9 (5.1)	41 (6.6)
Pre-eclampsia	0 (0)	11 (6.3)	29 (4.6)
Epidural before caesarean section	0 (0)	53 (30.1)	272 (43.5)
Elective caesarean section	4 (0.5)	73 (41.7)	233 (37.5)
Infant related variables			
Birth weight in grams (Mean ± SD)	12 (1.5)	3383 (±572)	3449 (±544)
Gestational age in weeks (Mean ± SD)	12 (1.5)	38.6 (±1.4)	39.0 (±1.6)
Preterm delivery	12 (1.5)	19 (11.1)	43 (7.0)
Low Apgar score (< 7) at 1 min	14 (1.7)	8 (4.7)	34 (5.5)
Fever during hospitalization	14 (1.7)	4 (2.3)	11 (1.8)
Phototherapy on day 1	13 (1.6)	5 (2.9)	9 (1.5)
Phototherapy on day 2	13 (1.6)	9 (5.2)	21 (3.4)
Phototherapy on day 3	14 (1.7)	18 (10.5)	36 (5.9)
Exclusive breastfeeding during hospitalization	15 (1.9)	46 (26.9)	290 (47.2)
Urine during day 1 (Mean ± SD)	15 (1.9)	2.5 (±1.9)	2.8 (±1.8)
Urine during day 2 (Mean ± SD)	17 (2.1)	4.0 (±1.7)	3.8 (±1.7)
Urine during day 3 (Mean ± SD)	73 (9.1)	4.1 (±1.7)	4.0 (±1.8)

Stools during day 1 (Mean ± SD)	15 (1.9)	2.5 (±1.6)	2.6 (±1.6)
Stools during day 2 (Mean ± SD)	17 (2.1)	3.4 (±1.7)	3.0 (±1.5)
Stools during day 3 (Mean ± SD)	73 (9.1)	3.0 (±1.6)	3.0 (±1.6)
Colloids doses in ml*	1 (0.1)		
0		0 (0)	625 (78.1)
>0-500		47 (5.9)	-
>500		128 (16.0)	-
Crystalloids doses in ml	26 (3.2)		
0		16 (2.1)*	0 (0)
>0-1000		54 (7.0)	168 (21.7)
>1000-2000		84 (10.8)	320 (41.3)
>2000		18 (2.3)	115 (14.8)
Total IV fluid doses in ml	26 (3.2)		
>0-1000		22 (2.8)	168 (21.7)
>1000-2000		102 (13.2)	320 (41.3)
>2000-3000		42 (5.4)	108 (13.9)
>3000		6 (0.8)	7 (0.9)

*Deliveries with missing data on crystalloids doses but available data on colloids doses (16 patients' records) were included in the Colloids plus Crystalloids group in the statistical analysis.

Table II. Beta Coefficients and 95% Confidence Intervals of the Linear Regression Models for Difference in Weight at 24, 48, and 72 Hours Postpartum According to Maternal Intrapartum Colloids and Crystalloids Exposure

	Difference in weight in grams (β and 95% CI)					
	24 hours postpartum		48 hours postpartum		72 hours postpartum	
	Model 1 (crude)	*Model 3*	*Model 1 (crude)*	*Model 3*	*Model 1 (crude)*	*Model 3*
Colloids plus Crystalloids	-0.6 (-12.6, 11.4)	-5.2 (-17.5, 7.0)	-0.4 (-15.9, 15.0)	-10.8 (-26.1, 4.5)	-5.4 (-28.2, 17.4)	-9.2 (-32.0, 13.7)
Crystalloids only	Reference	Reference	Reference	Reference	Reference	Reference
Colloids doses in ml (*vs* 0)						
>0-500	-5.8 (-27.9, 16.4)	-9.3 (-31.3, 12.7)	-3.1 (-31.9, 25.7)	-9.5 (-37.3, 18.3)	-11.0 (-55.5, 33.4)	-13.1 (-56.8, 30.6)
>500	-0.4 (-14.6, 13.8)	-5.8 (-20.1, 8.5)	1.6 (-16.8, 20.1)	-9.8 (-27.8, 8.1)	-8.2 (-35.2, 18.8)	-7.9 (-34.5, 18.7)
Crystalloids doses in ml (*vs* 0)						
>0-1000	4.2 (-33.0, 41.4)	-2.6 (-40.9, 35.7)	5.0 (-43.3, 53.3)	13.9 (-34.3, 62.1)	-0.03 (-73.6, 73.5)	39.8 (-35.6, 115.1)
>1000-2000	2.9 (-33.9, 39.6)	-1.5 (-39.4, 36.4)	9.5 (-38.2, 57.2)	21.9 (-25.8, 69.6)	-7.6 (-80.1, 64.9)	39.5 (-35.1, 114.1)
>2000	-0.5 (-38.8, 37.8)	-6.8 (-46.0, 32.4)	2.8 (-46.9, 52.6)	9.8 (-39.4, 59.1)	-21.6 (-97.2, 53.9)	15.2 (-61.5, 91.9)
Total IV fluid doses in ml: (*vs* >0-1000)						
>1000-2000	-4.5 (-16.6, 7.6)	-2.9 (-15.0, 9.2)	4.3 (-11.5, 20.1)	8.1 (-7.1, 23.3)	-7.4 (-31.7, 17.0)	3.5 (-20.2, 27.3)
>2000-3000	-1.6 (-16.9, 13.7)	-2.7 (-17.8, 12.3)	0.8 (-19.1, 20.7)	-0.3 (-19.2, 18.6)	-24.8 (-54.6, 4.9)	-22.1 (-50.9, 6.6)
>3000	-26.7 (-67.7, 14.3)	-27.3 (-66.9, 12.2)	-14.4 (-38.9, 67.7)	-6.4 (-43.4, 56.2)	-3.9 (-81.1, 73.3)	-0.6 (-73.0, 71.8)

The regression coefficient represents the estimated difference in weight since birth

Model 2 adjusted results were similar to the adjusted results of Model 3 (only results from Model 3 are presented in the table; results of Model 2 are available upon request)

Model 2 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, and election to have a caesarean section.

Model 3 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, election to have a caesarean section, Apgar score, exclusive breastfeeding, number of stools, number of urine, presence of fever and phototherapy.

Table III. Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI) for Excess Weight Loss (>7%) According to Type of Intrapartum IV Fluid Received by Mothers for Caesarean Section

	24 hours postpartum		48 hours postpartum		72 hours postpartum	
	Model 1 crude OR (95% CI)	*Model 3 Adjusted OR (95% CI)**	*Model 1 crude OR (95% CI)*	*Model 3 Adjusted OR (95% CI)*	*Model 1 crude OR (95% CI)*	*Model 3 Adjusted OR (95% CI)**
Colloids plus Crystalloids	0.9 (0.2–3.2)	1.0 (0.3–3.3)	0.9 (0.6–1.3)	1.0 (0.7–1.5)	1.3 (0.9–2.0)	1.4 (0.9–2.2)
Crystalloids only	Reference	Reference	Reference	Reference	Reference	Reference
Maternal age in years	0.9 (0.8–1.0)	1.0 (0.9–1.1)	1.0 (>0.9–1.1<)	1.0 (>0.9–1.0)	1.0 (>0.9–1.1)	1.0 (>0.9–1.1)
Gravida	0.9 (0.6–1.4)	0.3 (0.1–>99)	0.9 (0.8–1.0)	0.7 (0.2–2.5)	0.8 (0.7–0.9)	8.8 (0.7–>99)
Para	0.9 (0.4–1.8)	3.8 (<0.1–24.6)	0.8 (0.7–1.0)	1.2 (0.3–4.7)	**0.7 (0.5–0.8)**	**0.1 (<0.1–0.8)**
Abortus	0.9 (0.4–1.8)	3.3 (<0.1–19.7)	0.9 (0.7–1.1)	1.3 (0.4–5.0)	0.8 (0.6–1.0)	0.1 (<0.1–1.2)
Gestational age	1.1 (0.8–1.6)	0.9 (0.6–1.4)	1.1 (1.0–1.3)	1.0 (0.9–1.2)	1.1 (1.0–1.2)	0.9 (0.8–1.1)
Cigarette smoking	2.8 (0.9–8.3)	1.9 (0.5–5.9)	0.7 (0.5–1.1)	0.8 (0.5–1.3)	**0.5 (0.3–0.7)**	0.7 (0.4–1.2)
Drug use	4.2 (0.9–19.7)	2.8 (0.4–13.6)	0.7 (0.3–1.5)	0.6 (0.3–1.6)	1.1 (0.5–2.6)	1.3 (0.5–3.4)
Alcohol drinking	1.1 (0.2–4.8)	1.0 (0.2–3.7)	1.1 (0.7–1.8)	1.1 (0.7–1.7)	1.2 (0.7–1.9)	1.1 (0.7–2.0)
Hypertension during pregnancy	0.5 (<0.1–3.7)	0.2 (<0.1–2.6)	0.5 (0.3–1.0)	0.6 (0.3–1.3)	0.7 (0.4–1.3)	0.5 (0.2–1.1)
Gestational diabetes	1.3 (0.2–10.1)	1.6 (0.2–7.3)	1.2 (0.6–2.2)	1.4 (0.7–2.8)	0.7 (0.4–1.5)	1.2 (0.5–3.0)
Pre-eclampsia	1.4 (0.2–10.7)	3.8 (0.3–22.8)	**0.4 (0.2–0.8)**	0.6 (0.2–1.4)	1.1 (0.5–2.0)	1.5 (0.7–3.5)
Epidural before caesarean section	1.3 (0.5–3.6)	0.9 (0.2–3.6)	1.3 (0.9–1.6)	1.5 (1.0–2.4)	0.9 (0.6–1.2)	0.9 (0.5–1.4)
Elective caesarean section	0.6 (0.2–1.8)	0.6 (0.2–2.6)	1.2 (0.9–1.6)	**1.7 (1.1–2.6)**	1.3 (1.0–1.9)	**1.8 (1.1–2.9)**
Apgar score	1.4 (0.6–3.2)	1.2 (0.8–3.4)	1.2 (1.0–1.3)	1.2 (1.0–1.4)	1.1 (1.0–1.2)	1.1 (0.9–1.2)
Fever during hospitalization	1.6 (<0.1–13.2)	1.5 (<0.1–13.6)	2.6 (0.9–7.8)	3.3 (1.1–10.4)	0.8 (0.3–2.3)	1.0 (0.3–3.1)
Exclusive breastfeeding during hospitalization	0.7 (0.2–2.0)	0.9 (0.3–2.7)	1.3 (1.0–1.8)	1.1 (0.8–1.5)	**1.6 (1.1–2.1)**	1.5 (1.0–2.2)

Phototherapy on day 1	4.0 (0.5–32.9)	7.7 (0.7–46.1)	1.1 (0.4–3.1)	1.4 (0.4–4.8)	0.3 (0.1–1.1)	0.3 (0.1–1.2)
Phototherapy on day 2	N/A	N/A	1.1 (0.5–2.3)	1.6 (0.7–3.9)	0.9 (0.4–2.0)	1.7 (0.7–4.4)
Phototherapy on day 3	N/A	N/A	N/A	N/A	0.7 (0.4–1.3)	0.8 (0.4–1.6)
Urine during day 1	1.0 (0.8–1.4)	0.8 (0.6–1.2)	1.0 (0.9–1.1)	1.0 (0.9–1.2)	1.0 (0.9–1.1)	1.1 (1.0–1.2)
Urine during day 2	N/A	N/A	0.8 (0.8–0.9)	0.9 (0.8–1.0)	**0.8 (0.7–0.9)**	0.9 (0.8–1.0)
Urine during day 3	N/A	N/A	N/A	N/A	**0.8 (0.7–0.9)**	0.9 (0.8–1.0)
Stools during day 1	**1.5 (1.1–2.1)**	**1.6 (1.1–2.3)**	1.1 (1.0–1.2)	1.1 (1.0–1.2)	1.0 (0.9–1.1)	1.0 (0.8–1.1)
Stools during day 2	N/A	N/A	**0.8 (0.7–0.9)**	**0.8 (0.7–0.9)**	**0.8 (0.7–0.9)**	0.9 (0.8–1.0)
Stools during day 3	N/A	N/A	N/A	N/A	**0.7 (0.6–0.8)**	**0.7 (0.6–0.8)**

Model 2 adjusted results were similar to the adjusted results of Model 3 (only results from Model 3 are presented in the table; results of Model 2 are available upon request)

Model 2 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, and election to have a caesarean section.

N/A: not applicable

*Firth penalized maximum likelihood estimation method was used for quasi-complete separation

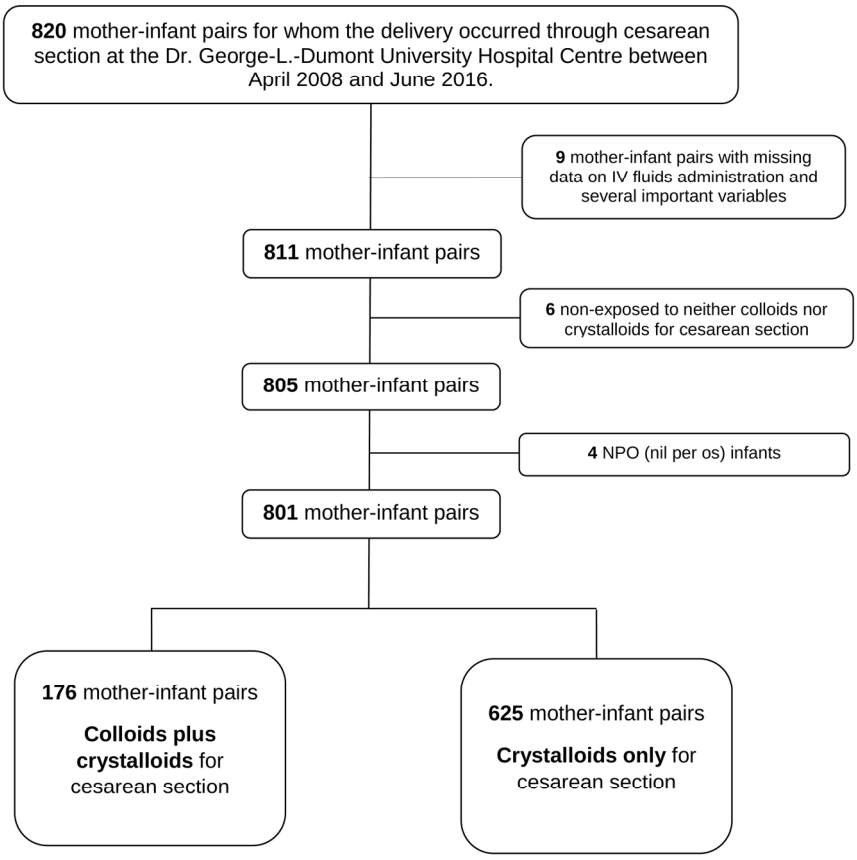
Table IV. Crude and Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI) for Excess Weight Loss (>7%) According to Doses of Intrapartum IV Fluid Received by Mothers for Caesarean Section

	24 hours postpartum			48 hours postpartum			72 hours postpartum		
	No. cases (%)	*Model 1 (crude)OR (95% CI)**	*Model 3 Adjusted OR (95% CI)**	*No. cases (%)*	*Model 1 (crude)OR (95% CI)*	*Model 3 Adjusted OR (95% CI)*	*No. cases (%)*	*Model 1 (crude)OR (95% CI)*	*Model 3 Adjusted OR (95% CI)**
Regression models for type-specific doses of IV fluid									
Colloids doses (in ml)									
0	12 (2.0)	Reference	Reference	252 (41.9)	Reference	Reference	260 (53.8)	Reference	Reference
>0-500	2 (4.4)	3.3 (0.6–11.8)	2.7 (0.4–11.5)	17 (37.0)	0.9 (0.5–1.7)	1.0 (0.5–2.1)	20 (55.6)	1.1 (0.6–2.3)	1.3 (0.6–2.9)
>500	1 (0.8)	0.7 (0.1–2.8)	0.7 (0.1–3.1)	48 (39.7)	0.9 (0.6–1.4)	1.0 (0.6–1.5)	70 (62.5)	1.4 (0.9–2.1)	1.3 (0.8–2.1)
Crystalloids doses (in ml)									
0	0 (0.0)	Reference	Reference	6 (37.5)	Reference	Reference	9 (75.0)	Reference	Reference
>0-1000	3 (1.4)	N/A	N/A	92 (43.0)	1.1 (0.4–3.4)	0.8 (0.2–2.6)	93 (54.1)	0.5 (0.1–1.9)	0.2 (<0.1–1.1)
>1000-2000	10 (2.6)	N/A	N/A	156 (40.1)	1.0 (0.3–3.0)	0.6 (0.2–2.0)	179 (56.7)	0.5 (0.1–2.1)	**0.2 (<0.1–0.9)**
>2000	1 (0.8)	N/A	N/A	56 (44.8)	1.2 (0.4–3.8)	0.9 (0.2–3.0)	61 (55.0)	0.5 (0.1–2.1)	0.3 (<0.1–1.2)
Regression models for total doses of IV fluid									
Total IV fluid doses (in ml)									
>0-1000	3 (1.7)	Reference	Reference	82 (44.8)	Reference	Reference	81 (55.5)	Reference	Reference
>1000-2000	8 (2.0)	1.1 (0.3–4.4)	1.1 (0.3–4.5)	161 (39.3)	0.8 (0.6–1.1)	0.7 (0.5–1.0)	183 (56.0)	1.0 (0.7–1.5)	0.8 (0.5–1.2)
>2000-3000	3 (2.2)	1.3 (0.3–6.3)	1.2 (0.2–6.1)	64 (45.7)	1.0 (0.7–1.6)	1.0 (0.6–1.6)	71 (55.9)	1.0 (0.6–1.6)	0.9 (0.5–1.6)
>3000	0 (0.0)	N/A	N/A	3 (27.3)	0.5 (0.1–1.8)	0.5 (0.1–2.0)	7 (63.6)	1.4 (0.4–5.0)	1.1 (0.3–4.6)

Model 2 adjusted results were similar to the adjusted results of Model 3 (only results from Model 3 are presented in the table; results of Model 2 are available upon request)
Model 2 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, and election to have a caesarean section.
Model 3 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, election to have a caesarean section, Apgar score, exclusive breastfeeding, number of stools, number of urine, presence of fever and phototherapy.
N/A: not applicable
*Firth penalized maximum likelihood estimation method was used for quasi-complete separation

Figures legend

Figure 1. Cohort selection flow diagram



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Supplementary Tables: Intrapartum intravenous fluids for caesarean delivery and newborn weight loss: a retrospective cohort study

Table E1. Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI) for Excess Weight Loss According to Type of Intrapartum IV Fluid Received by Mothers for Caesarean Section in Different Sensitivity Analysis

	24 hours postpartum		**48 hours postpartum**		**72 hours postpartum**	
	Model 1 crude OR (95% CI)	*Model 3 Adjusted OR (95% CI)**	*Model 1 crude OR (95% CI)*	*Model 3 Adjusted OR (95% CI)*	*Model 1 crude OR (95% CI)*	*Model 3 Adjusted OR (95% CI)**
Excess Weight Loss (>5%)						
Colloids plus Crystalloids	0.9 (0.5–1.4)	0.9 (0.5–1.5)	1.2 (0.8–1.8)	1.4 (0.9–2.3)	1.4 (0.8–2.3)	1.5 (0.9–2.8)
Crystalloids only	Reference	Reference	Reference	Reference	Reference	Reference
Excess Weight Loss (>10%)						
Colloids plus Crystalloids	0.5 (<0.1–5.2)	0.4 (<0.1–4.7)	1.1 (0.4–3.4)	1.0 (0.3–3.0)	1.1 (0.7–1.8)	0.9 (0.5–1.5)
Crystalloids only	Reference	Reference	Reference	Reference	Reference	Reference
Among Exclusively Breastfed newborns						
Colloids plus Crystalloids	0.6 (<0.1–5.4)	0.5 (<0.1–3.9)	0.5 (0.3–1.0)	0.6 (0.3–1.2)	1.4 (0.7–3.1)	1.6 (0.7–3.9)
Crystalloids only	Reference	Reference	Reference	Reference	Reference	Reference

Model 2 adjusted results were similar to the adjusted results of Model 3 (only results from Model 3 are presented in the table; results of Model 2 are available upon request)

Model 2 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, and election to have a caesarean section.

N/A: not applicable

*Firth penalized maximum likelihood estimation method was used for quasi-complete separation

Table E2. Crude and Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI) for Excess Weight Loss (>5%) According to Doses of Intrapartum IV Fluid Received by Mothers for Caesarean Section

	24 hours postpartum		48 hours postpartum		72 hours postpartum	
	*Model 1 (crude)OR (95% CI)**	*Model 3 Adjusted OR (95% CI)**	*Model 1 (crude)OR (95% CI)*	*Model 3 Adjusted OR (95% CI)*	*Model 1 (crude)OR (95% CI)*	*Model 3 Adjusted OR (95% CI)**
Regression models for type-specific doses of IV fluid						
Colloids doses (in ml)						
0	Reference	Reference	Reference	Reference	Reference	Reference
>0-500	0.7 (0.3–1.7)	0.9 (0.3–2.1)	1.1 (0.5–2.4)	1.3 (0.5–2.9)	1.5 (0.6–4.1)	1.4 (0.5–2.9)
>500	0.9 (0.5–1.6)	1.0 (0.5–1.7)	1.1 (0.7–1.9)	1.4 (0.8–2.6)	1.6 (0.9–2.8)	1.6 (0.8–2.1)
Crystalloids doses (in ml)						
0	Reference	Reference	Reference	Reference	Reference	Reference
>0-1000	0.6 (0.2–2.1)	0.7 (0.2–3.2)	1.1 (0.3–4.3)	0.9 (0.2–4.5)	1.1 (0.2–5.5)	0.6 (0.1–3.5)
>1000-2000	0.4 (0.1–1.5)	0.5 (0.1–2.4)	0.9 (0.2–3.2)	0.6 (0.1–3.1)	1.3 (0.3–6.3)	0.6 (0.1–3.2)
>2000	0.6 (0.2–2.2)	0.8 (0.2–3.8)	0.9 (0.2–3.5)	0.8 (0.2–4.3)	1.2 (0.2–6.2)	0.7 (0.1–4.1)
Regression models for total doses of IV fluid						
Total IV fluid doses (in ml)						
>0-1000	Reference	Reference	Reference	Reference	Reference	Reference
>1000-2000	0.7 (0.5–1.2)	0.8 (0.5–1.3)	0.8 (0.5–1.3)	0.7 (0.4–1.2)	1.2 (0.7–1.9)	0.9 (0.5–1.6)
>2000-3000	0.9 (0.5–1.6)	1.1 (0.6–1.9)	0.8 (0.5–1.4)	0.9 (0.5–1.6)	1.2 (0.6–2.1)	1.1 (0.5–2.1)
>3000	2.5 (0.7–8.2)	2.8 (0.7–9.8)	1.1 (0.2–5.1)	1.7 (0.3–10.0)	1.2 (0.2–6.9)	0.9 (0.2–5.6)

Model 2 adjusted results were similar to the adjusted results of Model 3 (only results from Model 3 are presented in the table; results of Model 2 are available upon request)

Model 2 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, and election to have a caesarean section.
Model 3 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, election to have a caesarean section, Apgar score, breastfeeding, number of stools, number of urine, presence of fever and phototherapy.
N/A: not applicable
*Firth penalized maximum likelihood estimation method was used for quasi-complete separation

Table E3. Crude and Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI) for Excess Weight Loss (>10%) According to Doses of Intrapartum IV Fluid Received by Mothers for Caesarean Section

	24 hours postpartum		48 hours postpartum		72 hours postpartum	
	*Model 1 (crude)OR (95% CI)**	*Model 3 Adjusted OR (95% CI)**	*Model 1 (crude)OR (95% CI)*	*Model 3 Adjusted OR (95% CI)*	*Model 1 (crude)OR (95% CI)*	*Model 3 Adjusted OR (95% CI)**
Regression models for type-specific doses of IV fluid						
Colloids doses (in ml)						
0	Reference	Reference	Reference	Reference	Reference	Reference
>0-500	1.5 (<0.1–20.6)	0.5 (<0.1–12.4)	0.5 (<0.1–1.7)	0.4 (<0.1–3.3)	0.8 (0.3–2.3)	0.7 (0.2–1.9)
>500	0.6 (<0.1–6.8)	0.7 (<0.1–7.9)	1.7 (0.5–1.4)	1.4 (0.4–4.5)	1.0 (0.6–1.8)	0.8 (0.4–1.5)
Crystalloids doses (in ml)						
0	Reference	Reference	Reference	Reference	Reference	Reference
>0-1000	0.2 (<0.1–44.8)	0.1 (<0.1–27.2)	0.7 (0.1–3.4)	0.7 (<0.1–96.5)	0.3 (0.1–1.3)	**0.2 (<0.1–0.8)**
>1000-2000	0.2 (<0.1–36.4)	0.1 (<0.1–32.1)	1.2 (0.1–3.0)	1.1 (0.1–159.4)	0.4 (0.1–1.4)	**0.2 (<0.1–0.7)**
>2000	0.1 (<0.1–28.5)	0.1 (<0.1–29.6)	0.5 (<0.1–3.8)	0.3 (<0.1–57.9)	0.3 (0.1–1.2)	**0.2 (<0.1–0.8)**
Regression models for total doses of IV fluid						
Total IV fluid doses (in ml)						
>0-1000	Reference	Reference	Reference	Reference	Reference	Reference
>1000-2000	0.7 (0.1–8.1)	0.9 (0.1–15.9)	2.7 (0.8–13.5)	2.6 (0.8–12.8)	0.9 (0.6–1.6)	0.7 (0.4–1.3)
>2000-3000	0.4 (<0.1–8.2)	0.7 (<0.1–22.5)	0.8 (0.1–5.9)	0.6 (0.1–4.9)	0.9 (0.4–1.7)	0.8 (0.4–1.6)
>3000	5.2 (<0.1–103.4)	3.2 (<0.1–151.2)	3.2 (<0.1–41.9)	4.3 (<0.1–60.6)	0.2 (<0.1–1.7)	0.2 (<0.1–1.6)

Model 2 adjusted results were similar to the adjusted results of Model 3 (only results from Model 3 are presented in the table; results of Model 2 are available upon request)

Model 2 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, and election to have a caesarean section.
Model 3 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, election to have a caesarean section, Apgar score, breastfeeding, number of stools, number of urine, presence of fever and phototherapy.
N/A: not applicable
*Firth penalized maximum likelihood estimation method was used for quasi-complete separation

Table E4. Crude and Adjusted Odds Ratios (OR) and 95% Confidence Intervals (CI) for Excess Weight Loss (>7%) According to Doses of Intrapartum IV Fluid Received by Mothers for Caesarean Section among Exclusively Breastfed Newborns

	24 hours postpartum		48 hours postpartum		72 hours postpartum	
	*Model 1 (crude)OR (95% CI)**	*Model 3 Adjusted OR (95% CI)**	*Model 1 (crude)OR (95% CI)*	*Model 3 Adjusted OR (95% CI)*	*Model 1 (crude)OR (95% CI)*	*Model 3 Adjusted OR (95% CI)**
Regression models for type-specific doses of IV fluid						
Colloids doses (in ml)						
0	Reference	Reference	Reference	Reference	Reference	Reference
>0-500	2.3 (<0.1–35.3)	2.0 (<0.1–38.2)	0.8 (0.2–2.8)	1.2 (0.3–4.6)	1.1 (0.3–4.7)	NA[§]
>500	1.0 (<0.1–9.8)	0.6 (<0.1–5.9)	0.5 (0.2–1.1)	0.6 (0.3–1.3)	1.7 (0.8–4.3)	NA[§]
Crystalloids doses (in ml)						
0	Reference	Reference	Reference	Reference	Reference	Reference
>0-1000	0.3 (<0.1–89.5)	0.2 (<0.1–76.9)	1.8 (0.3–21.5)	1.9 (0.2–25.6)	1.8 (0.1–26.2)	NA[§]
>1000-2000	0.4 (<0.1–90.8)	0.3 (<0.1–89.4)	1.8 (0.3–20.4)	1.4 (0.2–18.5)	1.2 (0.1–10.3)	NA[§]
>2000	0.2 (<0.1–56.6)	0.1 (<0.1–48.8)	2.1 (0.3–24.7)	1.9 (0.2–25.7)	1.4 (0.1–12.9)	NA[§]
Regression models for total doses of IV fluid						
Total IV fluid doses (in ml)						
>0-1000	Reference	Reference	Reference	Reference	Reference	Reference
>1000-2000	1.1 (0.2–11.5)	1.2 (0.2–10.8)	0.9 (0.5–1.5)	0.7 (0.4–1.3)	0.7 (0.4–1.4)	0.7 (0.3–1.4)
>2000-3000	0.5 (<0.1–9.7)	0.5 (<0.1–6.4)	1.2 (0.6–2.4)	1.1 (0.5–2.3)	0.9 (0.4–2.1)	0.8 (0.3–1.9)
>3000	4.9 (<0.1–105.0)	1.8 (<0.1–70.0)	0.4 (<0.1–2.1)	0.3 (<0.1–1.8)	1.5 (0.3–15.9)	0.8 (0.1–9.2)

Model 2 adjusted results were similar to the adjusted results of Model 3 (only results from Model 3 are presented in the table; results of Model 2 are available upon request)

Model 2 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, and election to have a caesarean section.
Model 3 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, election to have a caesarean section, Apgar score, number of stools, number of urine, presence of fever and phototherapy.
N/A: not applicable
*Firth penalized maximum likelihood estimation method was used for quasi-complete separation
§ Models did not converge efficiently due to quasi-complete separation (i.e. impossible to estimate even with penalized maximum likelihood)

Table E5. Beta Coefficients and 95% Confidence Intervals of the Linear Regression Models for Difference in Weight at 24, 48, and 72 Hours Postpartum According to Maternal Intrapartum Colloids and Crystalloids Exposure among Exclusively Breastfed Newborns Only

	Difference in weight in grams (β and 95% CI)					
	24 hours postpartum		48 hours postpartum		72 hours postpartum	
	Model 1 (crude)	*Model 3*	*Model 1 (crude)*	*Model 3*	*Model 1 (crude)*	*Model 3*
Colloids plus Crystalloids	18.6 (-2.7, 39.8)	17.3 (-4.1, 38.7)	23.3 (-2.5, 49.0)	18.8 (-7.1, 44.7)	3.6 (-26.8, 34.0)	-2.5 (-33.9, 29.0)
Crystalloids only	Reference	Reference	Reference	Reference	Reference	Reference
Colloids doses in ml (*vs* 0)						
>0-500	29.4 (-15.1, 73.8)	23.3 (-21.3, 70.7)	18.3 (-35.9, 72.7)	20.8 (-33.3, 75.3)	-2.6 (-37.5, 32.4)	-17.1 (-87.8, 53.6)
>500	16.7 (-8.4, 41.7)	16.8 (-8.1, 41.5)	22.3 (-7.8, 52.1)	15.5 (-14.8, 45.1)	-4.6 (-60.2, 69.8)	-0.6 (-35.5, 36.7)
Crystalloids doses in ml (*vs* 0)						
>0-1000	34.3 (-52.3, 80.4)	20.6 (-52.9, 94.7)	-31.7 (-113.3, 53.3)	-18.9 (-107.3, 71.1)	-17.7 (-125.6, 90.5)	-3.8 (-131.6, 125.1)
>1000-2000	33.0 (-51.1, 81.6)	18.5 (-54.4, 91.4)	-20.5 (-101.2, 57.2)	-8.9 (-96.8, 79.6)	-4.6 (-101.1, 111.9)	20.5 (-105.1, 147.1)
>2000	-34.0 (-57.1, 78.8)	15.8 (-58.0, 89.4)	-27.8 (-110.9, 52.6)	-9.9 (-99.4, 80.0)	-13.2 (-122.2, 95.9)	13.2 (-115.5, 141.9)
Total IV fluid doses in ml: (*vs* >0-1000)						
>1000-2000	-1.5 (-18.6, 16.6)	-1.9 (-19.0, 15.2)	10.3 (-10.5, 31.1)	9.1 (-11.1, 30.3)	17.1 (-10.7, 44.0)	15.5 (-12.2, 42.3)
>2000-3000	-8.6 (-14.9, 31.7)	6.7 (-15.8, 29.3)	10.8 (-17.1, 38.7)	13.3 (-14.2, 40.6)	1.8 (-33.6, 36.9)	9.1 (-25.9, 45.6)
>3000	**-64.9 (-125.6, -4.5)**	-48.3 (-107.9, 11.2)	-15.4 (-89.9, 59.7)	-6.9 (-79.4, 65.2)	-22.9 (-104.1, 59.3)	13.6 (-67.0, 95.8)

The regression coefficient represents the estimated difference in weight since birth

Model 2 adjusted results were similar to the adjusted results of Model 3 (only results from Model 3 are presented in the table; results of Model 2 are available upon request)

Model 2 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, and election to have a caesarean section.

Model 3 adjusted for maternal age, gestational diabetes, hypertension during pregnancy, number of pregnancies, viable births, lost pregnancies, gestational age, pre-eclampsia, cigarette smoking, alcohol use, drug use, epidural before caesarean section, election to have a caesarean section, Apgar score, number of stools, number of urine, presence of fever and phototherapy.