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Efficacy of Intravenous Dextrose-containing Fluid in Reducing Labor Duration of Pregnant Women: A randomized controlled trial

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ABSTRACT

Objectives: To evaluate the efficacy of dextrose-containing intravenous fluid and normal saline intravenous fluid in reducing labor duration in pregnant women.

Materials and Methods: In this randomized controlled trial, 164 low-risk term singleton pregnant women with gestational age of 37-42 weeks presenting with labor pain at Sanpasitthiprasong Hospital were equally randomized to receive either 1) dextrose-containing intravenous fluid 5% dextrose-containing in half-strength normal saline (5%D/N/2) or 2) normal saline (NSS) at a rate of 120 ml/hr. Primary outcome was total labor time, defined as duration during active phase plus second stage. Duration of latent phase, active phase, first stage and second stage of labor and maternal and neonatal outcomes were also assessed.

Results: Demographics, gestational age, cervical dilatation at the time of randomization and augmentation were comparable between the two groups. Total labor time was significantly shorter in dextrose group than NSS group (median 177.0, interquartile range 110.0, 258.0) and 206.5 (138.5, 298.3), p = 0.033). Active phase duration was significantly shorter in dextrose group (median 160.0 (100.0, 240.0) and 187.5 (127.3, 281.3), p = 0.029). There was no difference in latent phase, second stage, and third stage duration. Rates of cesarean delivery and maternal complications were comparable between the two groups. Transient tachypnea of the newborn was significantly higher in NSS group than dextrose group (29.3% and 9.8%, p = 0.002). There was no between-group difference in neonatal outcomes including birthweight, Apgar scores, and neonatal hypoglycemia.

Conclusion: Dextrose-containing intravenous fluid administered during intrapartum may shorten total labor time especially active phase duration, without increasing maternal and neonatal complications.

Keywords: Dextrose-containing intravenous fluid, intrapartum, total labor time, active phase duration.

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ประสิทธิภาพของการให้สารน้ำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรสทางหลอดเลือดดำในการลดระยะเวลาคลอดของสตรีตั้งครรภ์: การศึกษาแบบสุ่มมีกลุ่มเปรียบเทียบ

วนัชพร พุทธกูล, ปิยวดี วุฒิกรสัมมากิจ, ปริญญา ชำนาญ

บทคัดย่อ

วัตถุประสงค์: *เพื่อศึกษาประสิทธิภาพของการให้สารน้ำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรสทางหลอดเลือดดำ เปรียบเทียบกับน้ำเกลือ ในการลดระยะเวลาคลอดของสตรีตั้งครรภ์*

วัสดุและวิธีการ: *การทดลองแบบสุ่มมีกลุ่มเปรียบเทียบในอาสาสมัครสตรีตั้งครรภ์เดี่ยวครบกำหนดที่มีความเสี่ยงต่ำ ขณะอายุครรภ์ 37 ถึง 42 สัปดาห์ จำนวน 164 ราย ซึ่งมาเข้ารับการรักษาที่ห้องคลอด โรงพยาบาลสรรพสิทธิประสงค์ ด้วยอาการเจ็บครรภ์คลอด โดยอาสาสมัครจะถูกแบ่งเป็น 2 กลุ่มเท่าๆ กัน โดยวิธีสุ่ม ได้แก่ กลุ่มที่ 1 ได้รับสารน้ำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรส 5% dextrose-containing in half-strength normal saline (5%D/N/2) และกลุ่มที่ 2 ได้รับสารน้ำเกลือ (normal saline; NSS) ในอัตรา 120 มิลลิลิตรต่อชั่วโมง โดยผลลัพธ์หลักคือระยะเวลาคลอด (total labor time) ซึ่งหมายถึงช่วง active phase รวมกับช่วงระยะที่สองของการคลอด (second stage of labor) รวมทั้งเก็บข้อมูลระยะเวลาช่วงปากมดลูกเปิดช้า (latent phase), active phase, ระยะที่หนึ่งและสองของการคลอด (first and second stage of labor) รวมทั้งภาวะแทรกซ้อนต่อมารดาและทารก เพื่อการวิเคราะห์*

ผลการศึกษา: *ข้อมูลทั่วไปของอาสาสมัคร, อายุครรภ์, การขยายตัวของปากมดลูก ณ เวลาที่เข้างานวิจัย และการได้รับยาเร่งคลอดไม่แตกต่างกันระหว่างกลุ่ม โดยพบว่าระยะเวลาคลอดสั้นลงอย่างมีนัยสำคัญในกลุ่มที่ได้รับสารน้ำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรส เปรียบเทียบกับกลุ่มที่ได้รับสารน้ำเกลือ (ค่ามัธยฐาน 177.0 นาที ในกลุ่มที่ได้รับสารน้ำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรสและค่ามัธยฐาน 206.5 นาทีในกลุ่มที่ได้รับสารน้ำเกลือ, p = 0.033) ระยะ active phase สั้นลงอย่างมีนัยสำคัญ ในกลุ่มที่ได้รับสารน้ำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรส (ค่ามัธยฐาน 160.0 นาที ในกลุ่มที่ได้รับสารน้ำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรสและค่ามัธยฐาน 187.5 นาที ในกลุ่มที่ได้รับสารน้ำเกลือ, p = 0.029) แต่ไม่พบความแตกต่างกันอย่างมีนัยสำคัญระหว่างกลุ่มของระยะปากมดลูกเปิดช้า (latent phase) และการคลอดระยะที่สองและสาม เช่นเดียวกันกับอัตราการผ่าตัดคลอด และภาวะแทรกซ้อนของมารดา ที่ไม่มีความแตกต่างกันระหว่างกลุ่ม อย่างไรก็ตามพบภาวะหายใจเร็วชั่วคราวของทารกแรกเกิด (transient tachypnea of newborn) ในทารกที่มารดาได้รับสารน้ำเกลือมากกว่ากลุ่มที่มารดาได้รับสารน้ำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรสอย่างมีนัยสำคัญ (ร้อยละ 29.3 ในกลุ่ม

NSS และร้อยละ 9.8 ในกลุ่มน้ำตาลเด็กซ์โตรส, p = 0.002) ส่วนผลลัพธ์ของทารกในด้านอื่นๆ ได้แก่ น้ำหนักแรกคลอด, คะแนน Apgar, และภาวะน้ำตาลในเลือดต่ำของทารก ไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ

***สรุป**: การให้สารน้ำทางหลอดเลือดดำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรสในช่วงเจ็บครรภ์คลอด ช่วยลดระยะเวลาคลอด โดยเฉพาะอย่างยิ่งระยะเวลาปากมดลูกเปิดเร็วได้ โดยไม่มีผลแทรกซ้อนต่อมารดาและทารกในครรภ์*

***คำสำคัญ**: การให้สารน้ำที่มีส่วนประกอบของน้ำตาลเด็กซ์โตรสทางหลอดเลือดดำ, ระยะคลอด, ระยะเวลาคลอด, ระยะปากมดลูกเปิดอย่างรวดเร็ว*

Introduction

According to stages of labor, the first and second stage of labor potentially affected successful vaginal delivery, decision of managements and neonatal outcomes[1]. From previous studies, many pregnant women who encountered the prolonged duration of labor, would have several adverse effects on pregnancy outcomes, such as increased risk of cesarean section from cephalopelvic disproportion[2], chorioamnionitis, neonatal intensive care unit (NICU) admission[3], neonatal asphyxia, postpartum hemorrhage[4]. In addition, prolonged labor might increase stress for pregnant women and her families.

Intrapartum fluid hydration either oral or intravenous fluid has been reported to reduce labor duration due to glucose playing an important role in the muscle power, especially uterine muscle contraction[5]. Evidence from systematic review[6] indicated that intravenous fluid hydration with the rate of 250 ml/hour could reduce duration of labor in nulliparous women if a policy of no oral intake is applied. However, the effect of intravenous fluid administration still could not conclude in cesarean section rate and operative vaginal delivery rate[7].

Even intravenous fluid hydration was very essential for pregnant women during labor periods; however, there was no conclusion in deciding which type of intravenous fluid is suitable and safely given during labor[8]. The results from previous studies[9-20] were not concordant to determine types and rate of intravenous fluid given in beneficial effect of reducing labor duration. Most of previous studies[5, 9-11, 13, 14, 18, 19] could demonstrate the shorter labor time in dextrose-containing intravenous fluid administration but some studies[12,15, 17] demonstrated the contradicted results. Most previous studies[9, 10, 12-15, 19, 20] suggested that dextrose-containing fluid did not affect cesarean delivery rate, while more recent studies[16, 18] demonstrated the benefit in reducing cesarean section rate. However, the majority of these previous studies were conducted in western population and focused on nulliparous women which may not be generalized in clinical practice with both nulliparous and multiparous women. Therefore, the present study was aimed to investigate the effect of glucose-containing intravenous fluid compared with the normal saline intravenous fluid on labor duration and other maternal and neonatal outcomes in nulliparous and multiparous women giving birth at a tertiary hospital in northeastern Thailand.

Materials and Methods

Setting and study population

This was a two-arm parallel-group randomized controlled trial conducted in Sanpasitthiprasong Hospital during April 20th, 2023, to February 1st, 2024. This clinical trial was registered (TCTR20230605004) with http//: www.ClinicalTrials.in.th (Thai Clinical Trials Registry). After approval of institutional ethical committee (081/2566), singleton pregnant women, aged 18-45 years old, who came with labor pain at gestational age of 37 to 42 completed weeks, with

regular uterine contraction and a cervical dilatation of 3-5 cm., were invited to participate in the study. The pregnant women who had pregnancy-induced hypertension, gestational diabetes mellitus, underlying diseases such as renal, heart, or liver disorders, contraindication of vaginal delivery, and abnormal fetal status were excluded.

Randomization and interventions

After given written informed consent, a total of 164 participants were equally randomized to receive one of the two treatments: 1) received 5% dextrose-containing in half-strength normal saline (5%D/N/2) intravenous fluid and 2) received normal saline (0.9% NSS) intravenous fluid starting when participants entered active phase of labor at the same rate of 120 ml/hour. In this study, intravenous fluid was prohibited before randomization in all pregnant women. The randomized sequence generated by Microsoft Excel 2010. The allocated numbers were inserted into identical, opaque, and sealed envelopes placed in the labor room. The attending physicians or nurses opened envelopes to assign the participants to each group. Both types of fluid bottles were prepacked with opaque wrapping. The participants would receive the fluid according to the randomized sequence. The physicians and nurses who took care of the participants were blinded to the intervention. The two treatment groups received identical standard obstetric care included monitoring of fetal heart rate, observing uterine contraction, cervical progression every 2-4 hours, artificial rupture of membranes and augmentation in case of abnormal labor progression from poor uterine contraction and analgesic drugs administration when the participants had pain score of more than 5. To comply with standard practice, all participants were not allowed to eat or drink per oral during active phase. All participants in both groups were evaluated their blood glucose after 1 hour of receiving the intravenous fluid for safety concern of hypo- or hyperglycemic complication.

Data collection and outcome ascertainment

Data on baseline characteristics of participants were collected before allocation. These included age, occupation, education, marital status, income, gravidity, parity, nulliparous, gestational age (weeks), number of antenatal visits, gestational age at first antenatal visit, pre-pregnancy body mass index (BMI) and total weight gain. Data on cervical dilatation, and membrane status at randomization, augmentation with oxytocin and its duration, total volume of intravenous fluid administration were recorded. Primary outcome was total labor time, defined as the duration of active phase of first stage of labor plus the second stage of labor. Secondary outcomes were duration of each stage of labor such as latent, active phase of first stage of labor, second stage, and third stage of labor. Delivery outcomes such as route of delivery, indications for cesarean section and operative vaginal delivery, intrapartum and postpartum complications were recorded. In addition, neonatal outcomes, namely birthweight, Apgar scores at 1,5,10 minutes, and neonatal complications, such as respiratory distress, neonatal jaundice, sepsis, neonatal trauma, neonatal hypoglycemia, and NICU admission, were also recorded. Prolong latent phase was defined as duration from regular uterine contraction until cervical dilatation of 4 cm more than 8 hours and prolong active phase defined as duration from cervical dilatation of more than 4 cm to full dilatation being longer than 12 hours[21].

Statistical analysis

Sample size was calculated based on results from previous study by Swidan et al[13] which showed that the mean (standard deviation; SD) total duration of labor was 395.0 (172.4) minutes in dextrose-containing group and 487.0 (220.5) minutes in normal saline group. With the power of 80%, 2-sided type I error at 5%, and 10% addition for drop out, the sample size of 82 per group was required. An intention-to-treat analysis was done using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov normality test was used to determine the distribution of continuous data. Categorical data were reported

as number (percent) and continuous data were reported as mean ± SD and median (interquartile range; IQR) for normally- and non-normally distributed variables, respectively. Comparisons of outcomes between the two treatment groups were performed using chi-square test, student t-test and Mann-Whitney-U test for categorical variables, normally and non-normally distributed continuous variables, respectively. P value of < 0.05 was considered statistically significant.

Results

Fig. 1 shows enrollment, randomization, and follow-up of the study participants. From 391 pregnant women who met eligible criteria, 227 participants were excluded (139 declined to participate in this study and 88 met exclusion criteria). The final sample of 164 participants were equally randomized to receive either dextrose-containing in half-strength normal saline (5% D/N/2) or normal saline (NSS), at the same rate of 120 ml/hour. No participant was dropped out in this study. Delivery outcomes, maternal and neonatal complications were assessed in all participants.

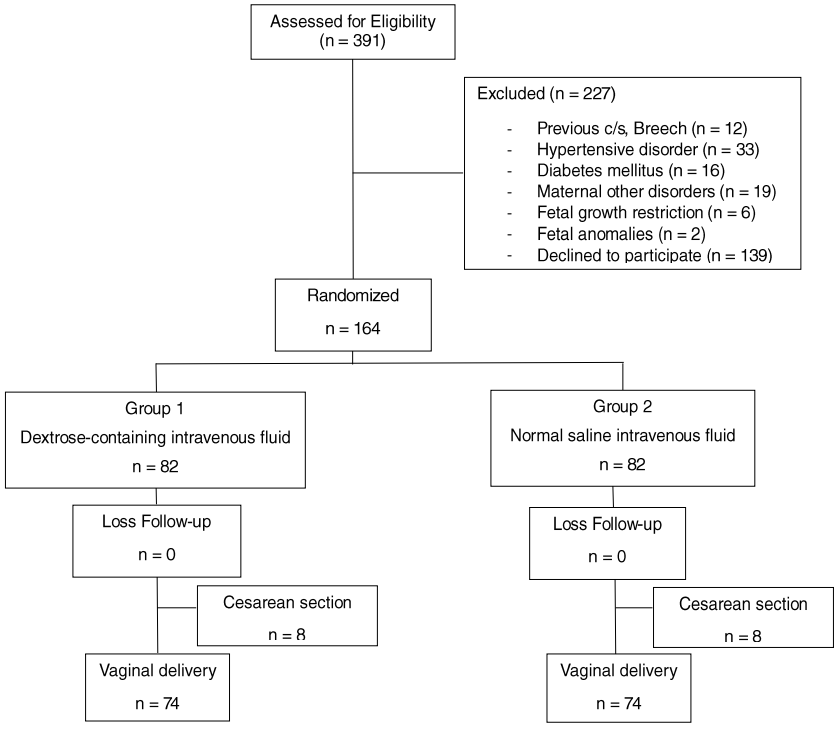

Fig. 1. Flow chart of participants recruitment.

Table 1 shows the baseline characteristics of participants, overall and by treatment groups. Among all participants, 81 (49.4%) were nulliparous with the median (IQR) gestational age of 39.0 (38.0, 39.0) weeks. The median (IQR) of cervical dilatation was 3.0 (3.0, 4.0) cm, and 29 (17.7%) had membranes ruptured at the time of randomization. Participants' age, occupation, education, marital status, and income were comparable between the two groups. Obstetric characteristics including gravidity, parity, nulliparous, gestational age, number of antenatal visits, gestational age at first antenatal visit,

prepregnancy BMI, total weight gain, cervical dilatation, and membrane status at the time of randomization were comparable between the two groups.

Table 1. Baseline characteristics of participants, overall and by treatment groups (n = 164).

	Total (n = 164)	Normal saline (n = 82)	Dextrose (n = 82)	p value*
Age (years), median (IQR)	26.0 (22.0, 30.0)	26.0 (22.0, 30.0)	26.0 (23.0, 30.3)	0.562
Occupation				0.505
No job, n (%)	43 (26.2)	26 (31.7)	17 (20.7)	
Student, n (%)	2 (1.2)	0 (0.0)	2 (2.4)	
Employee, n (%)	69 (42.1)	33 (40.2)	36 (43.9)	
Government official, n (%)	10 (6.1)	5 (6.1)	5 (6.1)	
Own-business, n (%)	31 (18.9)	14 (17.1)	17 (20.7)	
Medical personnel, n (%)	3 (1.8)	2 (2.4)	1 (1.2)	
Agriculturist, n (%)	6 (3.7)	2 (2.4)	4 (4.9)	
Education				0.553
Primary and secondary, n (%)	88 (53.7)	42 (51.2)	46 (56.1)	
Vocational, n (%)	33 (20.1)	15 (18.3)	18 (22.0)	
Bachelor, n (%)	39 (23.8)	22 (26.8)	17 (20.7)	
Master's degree or more, n (%)	4 (2.4)	3 (3.7)	1 (1.2)	
Marital status				0.587
Single, n (%)	15 (9.1)	8 (9.8)	7 (8.5)	
Married, n (%)	148 (90.2)	74 (90.2)	74 (90.2)	
Divorced, n (%)	1 (0.6)	0 (0.0)	1 (1.2)	
Income (baht), median (IQR)	10,000 (8,000, 15,000)	12,000 (8,000, 15,250)	10,000 (7,000, 15,000)	0.327
Gravidity, median (IQR)	2 (1, 2)	2 (1, 2)	2 (1, 2)	0.412
Parity, median (IQR)	0 (0, 1)	0 (0, 1)	0.5 (0, 1)	0.745
Nulliparous, n (%)	81 (49.4)	41 (50.0)	40 (48.8)	0.876
Gestational age (weeks), median (IQR)	39.0 (38.0, 39.0)	39.0 (38.0, 39.0)	39.0 (38.0, 40.0)	0.697
Number of antenatal visits, median (IQR)	10.0 (8.3, 12.8)	10.0 (8.0, 13.0)	10.0 (8.8, 12.3)	0.718
Gestational age at first antenatal visit, median (IQR)	10.0 (8.0, 13.0)	10.0 (7.0, 13.0)	10.0 (8.0, 13.0)	0.812
Pre-pregnancy body mass index (kg/m2), median (IQR)	20.7 (18.8, 24.0)	20.7 (18.9, 24.4)	20.7 (18.7, 23.6)	0.593
Total weight gain (kg), median (IQR)	13.0 (10.0, 17.0)	13.0 (10.0, 17.0)	12.5 (10.0, 16.0)	0.165
Cervical dilatation at randomization (cm), median (IQR)	3.0 (3.0, 4.0)	3.0 (3.0, 4.0)	3.0 (3.0, 4.0)	0.701
Effacement at randomization (%), median (IQR)	80 (70, 100)	80 (70, 100)	80 (70, 100)	0.275
Membrane status at randomization				0.072
Intact, n (%)	132 (80.5)	71 (86.6)	61 (74.4)	
Leakage, n (%)	3 (1.8)	2 (2.4)	1 (1.2)	
Ruptured, n (%)	29 (17.7)	9 (11.0)	20 (24.4)	
Pethidine administration, n (%)	7 (4.3)	2 (2.4)	5 (6.1)	0.246
Systemic blood pressure (mmHg), median (IQR)	120.0 (114.0, 127.0)	120.0 (114.0, 126.3)	120.5 (113.8, 127.0)	0.970
Diastolic blood pressure (mmHg), median (IQR)	76.0 (70.0, 80.0)	76.0 (70.0, 80.0)	76.5 (70.0, 80.0)	0.628
Pulse rate (beats/min), median (IQR)	90.0 (82.0, 100.0)	90.0 (81.5, 100.0)	91.0 (81.5, 100.0)	0.421

IQR: interquartile range

* p value for comparison between the two treatment groups, using chi-square test and Mann-Whitney-U test for categorical and non-normally distributed continuous variables, respectively

Table 2 shows duration of stages of labor, overall and by treatment groups. The duration of total labor was significantly shorter in dextrose-containing group than the normal saline group (median (IQR) of 177.0 (110.0, 258.0) minutes vs 206.5 (138.5, 298.3) minutes, respectively, p = 0.033). The duration of active phase of first stage of labor was also significantly shorter in dextrose-containing group than normal saline group. (median (IQR) of 160.0 (100.0, 240.0) minutes vs 187.5 (127.3, 281.3) minutes, respectively, p = 0.029). However, the median durations of latent phase, first stage, second stage, and third stage of labor were not significantly different between the two treatment groups. Prolonged latent phase was equally observed in both treatment groups (28.0% vs 24.4%, p = 0.594). There was no participant having prolonged active phase in both groups. The total intravenous fluid administration, augmentation with oxytocin and its duration were comparable between the two treatment groups.

Table 2. Duration of stages of labor, overall and by treatment groups (n = 164).

	Total (n = 164)	Normal saline (n = 82)	Dextrose (n = 82)	p value*
Total labor time[a] (minutes), median (IQR)	194.0 (124.0, 266.5)	206.5 (138.5, 298.3)	177.0 (110.0, 258.0)	0.033
(Active phase + Second stage)	300.0 (180.0, 480.0)	300.0 (180.0, 487.5)	300.0 (210.0, 480.0)	0.618
Latent phase, (minutes), median (IQR)	170.0 (115.0, 257.5)	187.5 (127.3, 281.3)	160.0 (100.0, 240.0)	0.029
Active phase[a], (minutes), median (IQR)	480.0 (350.5, 775.0)	457.5 (350.0, 815.0)	490.0 (370.0, 710.0)	0.885
First stage of labor[a], (minutes), median (IQR)	11.0 (7.0,16.0)	10.0 (8.0, 16.0)	11.0 (7.0, 16.0)	0.633
Second stage of labor[a], (minutes), median (IQR)	5.0 (4.0,8.0)	5.0 (4.0, 8.0)	5.0 (4.0, 8.0)	0.910
Third stage of labor[a], (minutes), median (IQR)	501.0 (369.0, 790.0)	473.5 (365.0, 839.5)	505.0 (385.0, 730.0)	0.888
First stage + Second stage + Third stage[a], (minutes), medain (IQR)	43.0 (26.2)	23.0 (28.0)	20.0 (24.4)	0.594
Prolong latent phase	73.0 (44.5)	33.0 (40.2)	40.0 (48.8)	0.271
Augmentation with oxytocin, n (%)	181.0 (90.8, 267.8)	120.0 (79.0, 242.0)	200.0 (129.0, 281.0)	0.057
Augmentation duration (min), median (IQR)	524.0 (339.0, 766.5)	539.0 (365.0, 751.5)	498.0 (316.0, 797.5)	0.383
Total fluid volume (ml), median (IQR)	524.0 (339.0, 766.5)	539.0 (365.0, 751.5)	498.0 (316.0, 797.5)	0.383

IQR: interquartile range

* p value for comparison between the two treatment groups, using chi-square test and Mann-Whitney-U test for categorical and non-normally distributed continuous variables, respectively

[a] Percentage of the outcome compared to total vaginal births in each treatment group.

Table 3 shows maternal outcomes overall and by treatment groups. Overall, 15 (9.1%) participants underwent Cesarean delivery, and 23 (14.0%) participants delivered by vacuum extraction with the remaining undergoing normal vaginal delivery. Overall, 9 (5.5%) participants had postpartum

hemorrhage, and there was no chorioamnionitis. When comparing the two treatment groups, there was no significant difference in routes of delivery, intrapartum and postpartum complications.

Table 3. Maternal outcomes, overall and by treatment groups (n = 164).

	Total (n = 164)	Normal saline (n = 82)	Dextrose (n = 82)	p value*
Route of delivery				0.259
Spontaneous Vertex delivery, n (%)	126 (76.8)	59 (72.0)	67 (81.7)	
Vacuum extraction, n (%)	23 (14.0)	15 (18.3)	8 (9.8)	
Cesarean section, n (%)	15 (9.1)	8 (9.8)	7 (8.5)	
Indication of vacuum extractiona				0.782
Fetal distress, n (%)	5 (21.7)	3 (20.0)	2 (25.0)	
Poor maternal effort, n (%)	18 (78.3)	12 (80.0)	6 (75.0)	
Indication for Cesarean sectionb				0.398
Fetal distress, n (%)	6 (40.0)	4 (50.0)	2 (28.6)	
Cephalopelvic disproportion, n (%)	9 (60.0)	4 (50.0)	5 (71.4)	
Intrapartum complications				0.301
Fetal distress, n (%)	10 (83.3)	6 (100.0)	4 (66.7)	
Shoulder dystocia, n (%)	1 (8.3)	0 (0.0)	1 (16.7)	
Failed vacuum extraction, n (%)	1 (8.3)	0 (0.0)	1 (16.7)	
Postpartum complications				
Postpartum hemorrhage, n (%)	9 (5.5)	3 (3.7)	6 (7.3)	0.304
Fourth degree perineum tear, n (%)	2 (1.2)	1 (1.2)	1 (1.2)	1.000
Perineum hematoma, n (%)	2 (1.2)	2 (2.4)	0 (0.0)	0.155
Blood glucose at 1 hour (mg%), median (IQR)	94.0 (86.0, 105.0)	91.0 (84.0, 97.0)	97.0 (89.3, 117.3)	< 0.001

IQR: interquartile range

* p-value for comparison between the two treatment groups, using chi-square test and Mann-Whitney-U test for categorical and non-normally distributed continuous variables, respectively

[a] Percentage of the outcome compare to total participants delivered by vacuum extraction in each treatment group

[b] Percentage of the outcome compare to total participants delivered by caesarean section in each treatment group

Concerning neonatal outcomes, the median infant birthweight was 3,042.5 grams and median Apgar scores at 1 and 5 minutes were 9, and 10, respectively (Table 4). There was no difference in birthweight, Apgar scores at 1, 5, and 10 minutes between the two groups. Respiratory distress was the most common neonatal complication (31.1%) with no significant difference between the two groups. Respiratory distress from transient tachypnea of newborn (TTNB) was significantly increased in normal saline group (29.3% in normal saline group vs 9.8% in dextrose-containing group, p = 0.002). There was no significant difference in other neonatal complications between groups.

Table 4. Neonatal outcomes, overall and by treatment groups (n = 164).

	Total (n = 164)	Normal saline (n = 82)	Dextrose (n = 82)	p value*
Birth body weight (grams), median (IQR)	3042.5 (2797.5, 3372.5)	3055.0 (2806.3, 3390.0)	3027.5 (2765.0, 3338.8)	0.579
Apgar score				
At 1 minute, median (IQR)	9 (9,9)	9 (9,9)	9 (9,9)	0.523
At 5 minutes, median (IQR)	10 (10,10)	10 (10,10)	10 (10,10)	0.322
At 10 minutes, median (IQR)	10 (10,10)	10 (10,10)	10 (10,10)	1.000
Respiratory distress, n (%)	51 (31.1)	30 (36.6)	21 (25.6)	0.129
Cause of respiratory distress, n (%)				
Delay adaptation, n (%)	14 (8.5)	6 (7.3)	8 (9.8)	0.576
TTNB, n (%)	32 (19.5)	24 (29.3)	8 (9.8)	0.002
Sepsis, n (%)	3 (1.8)	0 (0.0)	3 (3.7)	0.080
Pneumonia, n (%)	1 (0.6)	0 (0.0)	1 (1.2)	0.316
MAS, n (%)	1 (0.6)	0 (0.0)	1 (1.2)	0.316
Neonatal jaundice, n (%)	41 (25.0)	22 (26.8)	19 (23.2)	0.589
Sepsis, n (%)	3 (1.8)	0 (0.0)	3 (3.7)	0.080
Neonatal trauma, n (%)	16 (9.8)	11 (13.4)	5 (6.1)	0.114
Cause of neonatal trauma				
Caput succedaneum, n (%)	3 (1.8)	2 (2.4)	1 (1.2)	0.560
Cephalhematoma, n (%)	3 (1.8)	2 (2.4)	1 (1.2)	0.560
Subgaleal hematoma, n (%)	9 (5.5)	6 (7.3)	3 (3.7)	0.304
Scalp abrasion, n (%)	1 (0.6)	1 (1.2)	0 (0.0)	0.316
Fracture clavicle, n (%)	1 (0.6)	0 (0)	1 (1.2)	0.316
Neonatal hypoglycemia, n (%)	4 (2.4)	1 (1.2)	3 (3.7)	0.311
NICU admission, n (%)	9 (5.5)	5 (6.1)	4 (4.9)	0.732

TTNB: transient tachypnea of the newborn, MAS: meconium aspiration syndrome, NICU: neonatal intensive care unit, IQR: interquartile range
*p value for comparison between the two treatment groups, using chi-square test and Mann-Whitney-U test for categorical and non-normally distributed continuous variables, respectively.

Discussion

In this two-arm parallel group randomized controlled trial, dextrose-containing intravenous fluid had beneficial effect in shortening total labor time, especially active phase of labor. However, the duration of other stages of labor such as latent phase, first stage, second stage, and third stage of labor were not significantly different between dextrose-containing intravenous fluid and normal saline groups. There was no difference between groups in maternal and neonatal outcomes except for TTNB, which was observed more frequently in normal saline group.

Consistent with many previous studies[9-11,13, 16,18], our study showed the significant effect of dextrose-containing intravenous fluid to reduce the total labor time. However, some other studies[15, 17, 19] did not find this effect. The differences between these studies and our study may be explained by different types, concentration and administration rates of fluid, whether the mothers were allowed to eat or not. This may also be explained by the differences in participant's parity. That is, previous studies mainly investigated in nulliparous mothers, while our study included both nulliparous and multiparous. The reasons for the

beneficial effect of dextrose-containing intravenous fluid on duration of labor may be that glucose plays an important role in generating adenosine triphosphate (ATP), the major fuel to enhance effective contraction of uterine smooth muscle[6], especially during the period that the women had limited energy from nil-per-oral (NPO). It is possible that timing of dextrose-containing intravenous fluid administration may have impact on labor duration. A few studies[12,17] examining the effect of dextrose-containing intravenous fluid starting at different times when cervical dilatation ranged from 1 to 6 cm. showed negative results. However, to the best of our knowledge, there is no trial investigating head-to-head comparisons between different timing of dextrose-containing intravenous fluid, and this merits further studies.

The benefit of dextrose-containing intravenous fluid on active phase duration, oxytocin use, and risk of prolonged labor remains inconclusive. Our study showed consistent results with a few previous studies[11,13] suggesting that dextrose-containing intravenous fluid significantly reduced active phase duration for approximately 27.5 minutes. However, many other studies[9, 14, 15, 20] showed no such benefit. This inconsistency was observed regardless of rates of intravenous fluid administration (varying rates in different studies ranging from 120 to 250 ml/hours). Of note, dextrose-containing intravenous fluid did not impact on the second stage duration in our study. This may be because the second stage of labor was relatively short and therefore the impact of dextrose-containing intravenous fluid may be modest. Our study found no difference in oxytocin use and augmentation time between groups which was consistent with many previous studies[11-13, 15, 17]. However, other studies[10, 20] found less oxytocin use in dextrose group. While some studies[9, 10, 13, 16] showed the effect of dextrose-containing intravenous fluid on reducing prolonged labor, other studies[15, 17, 19] failed to demonstrate such benefit. Of note, no participants in our study had prolonged labor, hence we could not demonstrate the difference between groups in the risk of prolonged labor. The reason for the benefit of dextrose-containing intravenous fluid on this outcome may be likely similar to that of total labor time. However, further research is needed to explore other mechanisms underpinning the impact of dextrose-containing fluid on these outcomes.

Despite its likely benefit on duration of labor, the dextrose-containing intravenous administration has been consistently reported to have no effect on cesarean delivery rate and other maternal outcomes (chorioamnionitis, postpartum hemorrhage, and severe perineal tear). Many previous studies[5, 9, 10, 12-17, 19, 20] showed that cesarean section rate did not differ between mothers receiving dextrose- and non-dextrose-based intravenous fluid. This is confirmed by a recent meta-analysis[18] of 7 trials which suggested a trend toward a reduction in rate of cesarean section in dextrose-group, but the pooled relative risk reduction did not reach statistically significant.

Among all neonatal outcomes, only outcome that was different between normal saline and dextrose-containing group was TTNB. Although there was no previous study mentioning about this outcome, our study revealed higher risk of TTNB in normal saline group than dextrose-containing group. This might be explained by certain cellular level pathophysiology mechanisms. TTNB results from delayed lung fluid clearance. With the onset of labor, maternal epinephrine and glucocorticoid activate the epithelium sodium channel (ENaC) on the apical membrane of type II pneumocytes which creates the osmotic gradient to absorb fluid into the pulmonary circulations[22]. However, human birth is associated with many inflammatory processes, and correlated with many cytokines and chemokines[23]. TNF- α is one of these proinflammatory mediators, which can downregulate ENaC expression in alveolar epithelium cells[24]. It is possible that prolonged labor time, which was observed in normal saline group, would probably result in an increase in TNF- α, hence downregulation of ENaC receptors and compromised reabsorption

process in the neonatal lungs. Consistent with many previous studies[12-15,17-19], our study found no difference in other neonatal outcomes such as Apgar scores, neonatal hypoglycemia, jaundice, pneumonia, sepsis, birth trauma and NICU admission. However, a study by Shafaie et al[16] reported a statistically significant lower Apgar score at 1 min in dextrose-containing group (8.8 in dextrose group vs 9.0 in ringer lactate solution group). However, such a difference in Apgar score was likely to be of no clinical significance.

This study was a well-designed randomized controlled trial, with double blinding (both participants and caregivers). The outcomes were completely investigated without drop out of participants. The participants (both pregnant women and fetuses) were safely monitored to prevent the inadvertent events such as random blood sugar testing, electronic fetal monitoring, and standard obstetric care. This study is among the first to examine in the effect of dextrose-containing intravenous fluid on duration of labor in both nulliparous and multiparous, so the results can be generalizable to all low-risk pregnant women, not limited to only nulliparous mothers. However, our study had a number of limitations. Firstly, our study focused mainly on comparison of dextrose versus non-dextrose containing intravenous fluid supplements, while there were also a number of other approaches to fluid supplementation that have reportedly been effective in reducing labor time; for example, ringer lactate solution[25], oral fluid supplement[26], and anticholinergic agents[27]. Secondly, the onset of labor to determine duration of latent phase of first stage of labor depended largely on mother's recall. Thirdly, our study did not include specific certain groups such as teenage under 18 years old, pregnancy induced hypertension, gestational diabetes mellitus, and other high-risk pregnant women. Therefore, the generalizability of our findings to these high-risk groups may be limited. Lastly, this study only compared normal saline with 5% dextrose-containing fluid at a fixed rate of 120 ml/hour, further studies on different types, concentration and administration rates of intravenous fluid may be needed.

Conclusion

Dextrose-containing intravenous fluid administered during intrapartum may help shorten total labor time especially active phase duration, without increasing in maternal and neonatal complications.

Potential conflicts of interest

The authors declare no conflicts of interest.

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