Accepted Manuscript

Title: Dextrose intravenous fluid therapy in labor reduces the length of the first stage of labor

Authors: Melissa Riegel, Johanna Quist-Nelson, Gabriele Saccone, Mariavittoria Locci, Vineet K. Shrivastava, Raed Salim, Allan Fisher, Lennart Nordstrom, Allen R. Kunselman, John Repke, Alex Fong, John Smulian, Serena Xodo, Neggin Mokhtari, Fulvio Zullo, Vincenzo Berghella

PII: S0301-2115(18)30346-4
DOI: https://doi.org/10.1016/j.ejogrb.2018.07.019
Reference: EURO 10455

To appear in: *EURO*

Received date: 26-6-2018
Revised date: 13-7-2018
Accepted date: 16-7-2018

Please cite this article as: Riegel M, Quist-Nelson J, Saccone G, Locci M, Shrivastava VK, Salim R, Fisher A, Nordstrom L, Kunselman AR, Repke J, Fong A, Smulian J, Xodo S, Mokhtari N, Zullo F, Berghella V, Dextrose intravenous fluid therapy in labor reduces the length of the first stage of labor, *European Journal of Obstetrics and Gynecology* (2018), https://doi.org/10.1016/j.ejogrb.2018.07.019

Dextrose intravenous fluid therapy in labor reduces the length of the first stage of labor

Melissa Riegel BA[1], Johanna Quist-Nelson MD[1], Gabriele Saccone MD[2], Mariavittoria Locci MD[2], Vineet K. Shrivastava MD[3], Raed Salim MD[4], Allan Fisher MD[5], Lennart Nordstrom MD[6], Allen R. Kunselman MA[7], John Repke MD[8], Alex Fong MD[9], John Smulian MD, MPH[7], Serena Xodo MD[10], Neggin Mokhtari MD[11], Fulvio Zullo MD[2], Vincenzo Berghella MD[1]

[1]Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Sidney Kimmel Medical College of Thomas Jefferson University, Philadelphia, PA

[2]Department of Neuroscience, Reproductive Sciences and Dentistry, School of Medicine, University of Naples Federico II, Naples, Italy

[3]Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, University of California, Irvine, School of Medicine, Orange, CA

[4]Department of Obstetrics and Gynecology, Emek Medical Center, Afula, and Rappaport Faculty of Medicine, Technion, Haifa, Israel

[5]Department of Gynecology and Obstetrics, Saint Louis University School of Medicine

[6]Department of Obstetrics and Gynecology, Karolinska University Hospital and Department of Women's and Children's Health, Karolinska Institutet, 17176 Stockholm, Sweden

[7]Department of Public Health Sciences, Penn State College of Medicine, Hershey, PA

[8]Penn State University College of Medicine-Milton S. Hershey Medical Center

[9]Kaiser Permanente Southern California Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, Irvine, CA

[10]Department of Gynaecology and Obstetrics, School of Medicine, University of Udine, Udine, Italy

[11]Department of Obstetrics, Gynecology, and Reproductive Sciences, Magee-Womens Hospital of University of Pittsburgh Medical Center, Pittsburgh, PA

Financial Disclosure: *The authors did not report any potential conflicts of interest.*

Correspondence: Vincenzo Berghella, MD, Division of Maternal-Fetal Medicine, Department of Obstetrics and Gynecology, Thomas Jefferson University, 833 Chestnut Street, First Floor, Philadelphia, PA 19107, USA.

E-mail: vincenzo.berghella@jefferson.edu

Disclosure: The authors report no conflict of interest

Financial Support: No financial support was received for this study

Running title: Dextrose intravenous fluids therapy for labor

Condensation: Dextrose intravenous fluid therapy in labor reduces the length of the first stage of labor

ABSTRACT

The aim of this systematic review with meta-analysis was evaluate the effect on length of labor when patients receive IVF with or without dextrose. Searches were performed in electronic databases from inception of each database to May 2018. Trials comparing intrapartum IVF containing dextrose (i.e. intervention group) with no dextrose or placebo (i.e. control group) were included. Only trials examining low-risk pregnancies in labor at ≥36 weeks were included. Studies were included regardless of oral intake restriction. The primary outcome was the length of total labor from randomization to delivery. The meta-analysis was performed using the random effects model. Sixteen trials (n=2,503 participants) were included in the meta-analysis.

Women randomized in the IVF dextrose group did not have a statistically significant different length of total labor from randomization to delivery compared to IVF without dextrose (MD -38.33 minutes, 95% CI -88.23 to 11.57). IVF with dextrose decreased the length of the first stage (MD -75.81 minutes, 95% CI -120.67 to -30.95), but there was no change in the second stage. In summary, use of IVF with dextrose during labor in low-risk women at term does not affect total length of labor, but it does shorten the first stage of labor.

Keywords: cesarean delivery; intravenous fluid; labor; operative delivery; vaginal delivery

Abbreviations: CD, cesarean delivery; SVD, spontaneous vaginal delivery; DM, diabetes mellitus; GDM, gestational diabetes mellitus; h, hour; OVD, operative vaginal delivery; IOL, induction of labor; IUGR, intrauterine growth restriction; IVF, intravenous fluid; GA, gestational age; NR, not reported; HR, heart rate; IFD, intrauterine fetal death

Keywords: cesarean delivery, intravenous fluid, labor, operative delivery, vaginal delivery

INTRODUCTION

Length of labor may be a determinant of the health of both mother and neonate. Longer lengths of labor have been shown to be associated with increased rate of cesarean delivery, chorioamnionitis, and admission to the neonatal intensive care unit (NICU).[1] Diminished uterine contractile strength serves a role in prolonging labor, given the oxytocin augmentation.[2] Therefore, identifying interventions that safely decreases the length of labor is beneficial.[3,4] In many countries, patients receive intravenous fluids during induction or labor management. One meta-analysis of randomized controlled trials (RCTs) showed that a policy of intrapartum intravenous fluid (IVF) rate of 250 mL/hr is associated with a reduction in length of labor compared to a policy of 125 mL/hr.[3] Because carbohydrate replacement helps muscle performance during prolonged exercise,[3] it has been hypothesized that carbohydrate replacement may enhance the function of the contracting uterus, and speed up the laboring process. Recent studies have found no significant changes in fetal acid-base status when utilizing IVF with dextrose[4–6]. However, administration of IVF with dextrose during labor is unclear as the size of cohorts in original studies prevents generalizability and the findings are mixed.

Thus, the aim of this systematic review and meta-analysis of RCTs was to evaluate the effect on length of labor of IVF with or without dextrose as well as to examine the effects of IVF with dextrose on other maternal and neonatal outcomes.

METHODS

Eligibility criteria, information sources, search strategy

This review was performed according to a protocol designed a priori by the investigators and recommended for systematic review and meta-analysis.[7] Searches were performed independently by two authors (MR, JQN) in Medline, OVID, Scopus, ClinicalTrials.gov,

Embase, and the Cochrane Library. Appendix S1 shows the search strategy for this review that can be replicated to verify or update the results. Keywords were searched from inception of each database to October 2017. No restrictions for language or geographic location were applied.

Study selection

RCTs comparing intrapartum IVF with dextrose (i.e. intervention group) versus IVF with no dextrose or placebo (i.e. control group) were included in the meta-analysis. Only trials on low-risk women (as defined by individual studies) in labor at ≥36 weeks were included. Studies were included regardless of whether or not oral intake was restricted and irrespective of the type of IVF used. Augmentation of labor with oxytocin was not considered a criterion for exclusion. Trials including high-risk pregnant women (e.g. women with diabetes, preeclampsia, neonates with intrauterine growth restriction) were excluded. We planned to include only trials in which IVF were administered during labor, as this intervention has been proven to be effective. Titles and abstracts for all identified studies were independently reviewed by two reviewers (MR, JQN). Any disagreements were resolved with discussion with a third reviewer (VB).

Data extraction

The primary outcome was the total length of labor from randomization to delivery. Pre-specified secondary outcomes were length of labor from randomization to complete dilation (first stage), length of labor from complete dilatation to delivery (second stage), mode of delivery, augmentation of labor, chorioamnionitis, postpartum haemorrhage, and neonatal outcomes. Neonatal outcomes included Apgar <7 at 5 minutes, neonatal hypoglycemia (serum glucose <40 mg/dL), admission to NICU, and neonatal blood gas parameters at delivery (umbilical artery pH, CO_2, O_2, and base deficit).

We planned to assess the primary outcome (i.e. length of labor from randomization to delivery) in the following subgroup analyses:

1) According to the amount of dextrose
2) According to the rate of fluids used
3) According to restriction of oral fluid intake

We also planned to perform a sensitivity test including only trials, which blinded participants to type of IVF. Only the primary outcome was assessed in subgroup and sensitivity analyses.

Assessment of risk of bias

The risk of bias for each trial was assessed by using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions. Seven domains related to risk of bias were assessed in each included trial since there is evidence that these issues are associated with biased estimates of treatment effect: 1) random sequence generation; 2) allocation concealment; 3) blinding of participants and personnel; 4) blinding of outcome assessment; 5) incomplete outcome data; 6) selective reporting; and 7) other bias. Review authors' judgments were categorized as "low risk", "high risk" or "unclear risk" of bias.[7]

Data synthesis

The data analysis was completed independently by two authors (MR, GS) using Review Manager 5.3 (Copenhagen: The Nordic Cochrane Centre, Cochrane Collaboration, 2014). The completed analyses were then compared and any difference was resolved by discussion with a third reviewer (VB). Meta-analysis was performed using the random effects model of DerSimonian and Laird, to produce summary treatment effects in term of mean difference (MD) or relative risk (RR) with 95% confidence interval (CI). Heterogeneity across studies was

assessed using the Higgins I^2 test. Potential publication biases were assessed statistically by using Begg's and Egger's tests.[7] The meta-analysis was reported following the Preferred Reporting Item for Systematic Reviews and Meta-analyses (PRISMA) statement. The review was registered with the PROSPERO International Prospective Register of Systematic Reviews (Registration Number: CRD42017079583).

RESULTS

Study selection and study characteristics

Sixteen trials were included in the meta-analysis (Figure 1).[8–13,4,14–17,6,5,18–20] A total of 2,503 nulliparous and multiparous women in spontaneous or induced labor at term were included (Table 1). Of the 2,503 women included, 1,271 (50.8%) were in the dextrose group (i.e. intervention group), and 1,232 (49.2%) in the no dextrose group (i.e. control group). All studies that reported this baseline characteristic included only singleton gestations. Of the 14 studies that reported this variable, seven (50%) included women in spontaneous labor, five (36%) included women in spontaneous or induced labor, and two (14%) included only women with induction of labor. When reported, cervical dilatation at enrollment was ranged from 3-5cm (Table 1). In the dextrose group, twelve studies used 5% dextrose, two studies[8,9] used 5% and 10% dextrose, one study 10% dextrose,[10] and one study used 2.5% and 5% dextrose.[11] Regarding the no dextrose (control) group, the majority of the studies (fourteen in total) used 0.9% normal saline solution or lactated Ringer's solution. Two studies used more than one control group, one with lactated Ringer's solution and no IVF, and the other with lactated Ringer's solution and 0.9% normal saline.[8,13] IVF infusions were administered at varying rates, from 20-300 mL/h (Table 2). IVF were generally initiated during 'active labor'. In one study that included induction of labor only, IVF were initiated with oxytocin.[4] Oxytocin use was significant less for the IVF with dextrose

compared to the IVF without dextrose. There were no significant differences in the incidences of induction, nulliparity, or epidural use, between dextrose vs no dextrose groups (Table 3). Individual patient data meta-analysis, while ideal, was not undertaken secondary to the limited response of the individual authors in providing data.

The majority of included trials were judged as low risk of bias (Figure 2). Three articles did not follow the principle of intention to treat, increasing the risk of attrition bias.[14,16,17] These articles received a high risk of bias as they excluded previously randomized patients from the final analysis if they underwent induction of labor or operative vaginal delivery. Figure 3 shows the funnel plot for assessing publication bias. Publication bias, assessed using Begg's and Egger's tests, showed no significant bias (P=0.34 and P=0.33, respectively). Statistically heterogeneity was high, I^2=82% for the primary outcome.

Synthesis of results

There was no significant difference in total length of labor (MD -38.33 minutes, 95% CI -88.23 to 11.57; 8 studies; 1,501 participants; I^2=82%; Figure 3) or second stage of labor (MD -7.63 minutes, 95% CI -19.80 to 4.54; 6 studies; 1,298 participants; I^2=91%; Table 4) between women who received dextrose and those who did not. However, women who received dextrose had a significantly shorter first stage of labor (MD -75.81 minutes, 95% CI -120.67 to -30.95; 4 studies; 873 participants; I^2=84%). Chorioamnionitis, prolonged labor >12 hours, and postpartum haemorrhage occurred at similar rates in the two groups. Most (over three quarters) women had vaginal deliveries, with similar incidence in the two groups, and there was no significant difference in operative vaginal delivery (Table 5).

Regarding neonatal outcomes, there were no statistically significant differences in Apgar scores, hypoglycemia, or admission to NICU (Table 6). Umbilical arterial and venous gases were recorded in 6 of the 16 trials and there were no significant changes between groups (Table 7).[21]

Subgroup and sensitivity analyses

The following subgroup analyses concurred with the overall analysis with no significant differences for the primary outcome:

1) Only RCTs using 5% dextrose: MD -14.72 minutes, 95% CI -63.15 to 33.73
2) Only RCTs with unrestricted policy for oral intake: MD -43.50 minutes, 95% CI -95.46 to 8.45
3) When including only RCTs that blinded participants to type of IVF: MD -78.30 minutes, 95% CI -86.82 to -69.78

Subgroup analysis for only trials using IVF rate at > 125 mL/h (MD -97.82 minutes, 95% CI -184.08 to -11.55), and sensitivity analysis including only double-blind trials (MD -67.97 minutes, 95% CI -112.93 to -11.01) showed significant benefit in the dextrose group with a significant reduction in the length of labor.

DISCUSSION

Main Findings

This meta-analysis of RCTs, evaluating the effectiveness of IVF with dextrose compared to no dextrose, demonstrated no difference in total length or second stage of labor. There was a reduction in first stage of labor. Since this is the longest stage of labor, this finding may indicate there is some benefit to utilizing IVF with dextrose in laboring women. This is to be interpreted with caution as the length of first stage of labor is defined differently between studies, as some did not specify the period that the patient was in active labor. Moreover, in the best quality (e.g.

blinded RCTs), the duration of the total length of labor was statistically different. The addition of dextrose to IVF was also associated with a trend (but no significance) for lower incidence of labor lasting >12hours.

Although the increased rate of hypoglycemia had a confidence interval that crossed 1.0, the RR (95% CI) of 2.25 (0.94, 5.35) there is a trend towards significance. Therefore, it would be prudent to observe neonates exposed to maternal dextrose containing fluids for signs and symptoms of hypoglycemia after delivery until an appropriately powered study confirms whether the risk is clinically important. There are no significant changes in neonatal umbilical artery gas results, suggesting that exposure to dextrose in labor does not lead to a compromised infant.

Strengths and Limitations

Our study has several strengths. To our knowledge, this is the first meta-analysis comparing IVF with dextrose vs no dextrose. The included trials were all RCTs and all examined dextrose administration while in labor, and our primary outcome includes 8 studies with 1,501 participants. Limitations of our study are inherent to the limitations of a meta-analysis and the included studies. There were discrepancies between studies, as some excluded women who had operative deliveries or induction of labour.[11,14–17,6] As this is not an individual patient data meta-analysis, we are unable to differentiate laboring vs induction, cervical dilation at time of presentation, and indication for operative vaginal delivery. One study allowed women to freely eat and drink throughout labor, which may have affected our outcome variables.[4] In general, there were several secondary outcomes not addressed in various studies. Fluid management is only one aspect of labor management and there may be other confounders driving these findings. In original trials is difficult to define the duration of the first stage of labor. There was lack of data regarding lactate concentrations in cord blood.

Interpretation

Different meta-analyses have been published to assess the efficacy of different technique during labor aimed to reduce the length of labor.[22-30] Our meta-analysis appears to be the first to study RCTs strictly comparing IVF with dextrose versus no dextrose. Previous studies have demonstrated the ability of an IVF rate of 250 mL/hr to shorten length of labor compared to IVF rate of 125mL/hr, but did not address dextrose administration.[22,23] In one meta-analysis, an included RCT utilized normal saline in dextrose water, but the authors did not compare dextrose versus no dextrose in the study population.[24] Another meta-analysis could not reach a conclusion regarding the efficacy of dextrose or its impact on length of labour.[25] The studies included in our meta-analysis were heterogeneous as they included both laboring and induced patients, making it more generalizable to a labor and delivery floor. However, without the ability to perform an individual patient level meta-analysis, we were unable to see if particular groups would benefit from IVF with dextrose.

CONCLUSION

The addition of dextrose to IVF appears to shorten the duration of first stage of labor, and the total length of labor in the best quality studies, but not in the overall analysis, for low-risk laboring nulliparous and multiparous women. There were no effects, beneficial or detrimental, of the addition of dextrose in IVF for other maternal or neonatal outcomes. The shortening of the first stage of labor should be probably weighted against the trend for a higher incidence of neonatal hypoglycemia, which increased from 3.2% to 5.7%. Larger RCTs are probably needed to better evaluate effects on maternal and neonatal outcomes.

DISCLOSURE STATEMENT

The authors report no conflict of interest.

AUTHOR CONTRIBUTIONS

VB and MR conceived the study; MR, JQN, and GS collected the data and analyzed the results. VS, RS, AF, LN, AK, JR, AF, and JS provided data from their respective studies. NM translated study data. ML, FZ, and SX helped interpret findings. The manuscript was prepared by MR and JQN with assistance from GS and VB.

DETAILS OF ETHICS APPROVAL

The study was exempt from ethics approval because the research was not conducted with humans or animals.

There was no funding supplied for this research.

REFERENCES

1. Cheng YW, Shaffer BL, Bryant AS, C. A. Length of the first stage of labour and associated perinatal outcomes in nulliparous women. *Obs. Gynecol* **116,** 1127–35 (2010).

2. Dencker A, Berg M, Bergqvist L, Ladfors L, Thorsén LS, L. H. Early versus delayed oxytocin augmentation in nulliparous women with prolonged labour--a randomised controlled trial. *BJOG* **116,** 530–6 (2009).

3. Harger-Domitrovich SG, McClaughry AE, Gaskill SE, R. B. Exogenous carbohydrate spares muscle glycogen in men and women during 10 h of exercise. *Med Sci Sport. Exerc* **39,** 2171–9 (2007).

4. Pare J, Pasquier JC, Lewin A, Fraser W, B. Y. Reduction of total labour length through the addition of parenteral dextrose solution in induction of labour in nulliparous: results of DEXTRONS prospective randomized controlled trial. *Am J Obs. Gynecol* **216,** 508 (2017).

5. Garmi G, Zuarez-Easton S, Zafran N, Ohel I, Berkovich I, S. R. The effect of type and volume of

fluid hydration on labour duration of nulliparous women: a randomized controlled trial. *Arch Gynecol Obs.* **295,** 1407–1412 (2017).

6. Dapuzzo-Argiriou LM, Smulian JC, Rochon ML, Galdi L, Kissling JM, Schnatz PF, Rios AG, Airoldi J, Carrillo MA, Maines J, Kunselman AR, Repke J, L. R. A multi-center randomized trial of two different intravenous fluids during labour. *J Matern Fetal Neonatal Med* **29,** 191–6 (2016).

7. Higgins JPT, Green S, eds. Cochrane handbook for systematic reviews of interventions, version 5.1.0 (update March 2011). *The Cochrane Collabouration, 2011* (2011).

8. Morton KE, Jackson MC, G. M. A comparison of the effects of four intravenous solutions for the treatment of ketonuria during labour. *Br J Obs. Gynaecol* **92,** 473–9 (1985).

9. Shrivastava VK, Garite TJ, Jenkins SM, Saul L, Rumney P, Preslicka C, C. K. A randomized, double-blinded, controlled trial comparing parenteral normal saline with and without dextrose on the course of labour in nulliparas. *Am J Obs. Gynecol* **200,** 379 (2009).

10. Piquard F, Hsiung R, Schaefer A, Haberey P, D. P. Does fetal acidosis develop with maternal glucose infusion during normal labour? *Obs. Gynecol* **74,** 909–14 (1989).

11. Fong A, Serra AE, Caballero D, Garite TJ, S. V. A randomized, double-blinded, controlled trial of the effects of fluid rate and/or presence of dextrose in intravenous fluids on the labour course of nulliparas. *Am J Obs. Gynecol* **217,** 208 (2017).

12. Rad RH, Najjar S, H. Effects of intravenous normal saline with and without dextrose on labour duration and delivery outcomes in nulliparous women. *Koomesh* **13,** 434–9 (2012).

13. Loong EPL, Lao TTH, C. R. Effects of intrapartum intravenous infusion of 5% dextrose or Hartmann's solution on maternal and cord blood glucose. *Acta Obs. Gynecol Scand* **66,** 241–3

(1987).

14. Nordstrom L, Arulkumaran S, Chua S, Ratnam S, Ingemarsson I, Kublickas M, Persson B, Shimojo N, W. M. Continuous maternal glucose infusion during labour: effects on maternal and fetal glucose and lactate levels. *Am J Perinatol* **12,** 357–62 (1995).

15. Fisher AJ, H. J. Intrapartum maternal glucose infusion reduces umbilical cord academia. *Am J Obs. Gynecol* **177,** 765–9 (1997).

16. Jamal A, Choobak N, T. F. Intrapartum maternal glucose infusion and fetal acid-base status. *Int J Gynaecol Obs.* **97,** 187–9 (2007).

17. Sharma C, Kalra J, Bagga R, K. P. A randomized controlled trial comparing parenteral normal saline with and without 5% dextrose on the course of labour in nulliparous women. *Arch Gynecol Obs.* **286,** 1425–30 (2012).

18. Omigbodun AO, Akindele JA, Osotimehin BO, Fatinikun T, Fajimi JL, A. J. Effect of saline and glucose infusions of oxytocin on neonatal bilirubin levels. *Int J Gynecol Obs.* **40,** 235–9 (1993).

19. Shafaie FS, Mohaddesi H, Mirghafourvand M, Y. F. A randomized, double-blinded, controlled trial comparing parenteral dextrose 5%, Ringer's solution and oral intake on the delivery outcomes in nulliparas. *Int J Womens Heal.* **5,** 283–9 (2017).

20. Omigbodun AO, Fajimi JL, A. J. Effects of using either saline or glucose as a vehicle for infusion of labour. *East Afr. Med. J.* **68,** 88–92 (1991).

21. Riley RJ, J. J. Collecting and analyzing cord blood gases. *Clin Obs. Gynecol* **36,** (1993).

22. Garite TJ, Weeks J, Peters-Phair K, Pattillo C, B. W. A randomized controlled trial of the effect of increased intravenous hydration on the course of labour in nulliparous women. *Am J Obs.*

Gynecol **183,** 1544–8 (2000).

23. Eslamian L, Marsoosi V, P. Y. Increased intravenous fluid intake and the course of labour in nulliparous women. *Int J Gynaecol Obs.* **93,** 102–5 (2006).

24. Ehsanipoor RM, Saccone G, Seligman NS, Pierce-Williams RAM, Ciardulli A, B. V. Intravenous fluid rate for reduction of cesarean delivery rate in nulliparous women: a systematic review and meta-analysis. *Acta Obs. Gynecol Scand* **96,** 804–11 (2017).

25. Dawood F, Dowswell T, Q. S. Intravenous fluids for reducing the duration of labour in low risk nulliparous women. *Cochrane Database Syst Rev* **CD007715,** (2013).

26. Saccone G, Ciardulli A, Baxter JK, Quiñones JN, Diven LC, Pinar B, Maruotti GM, Martinelli P, Berghella V. Discontinuing Oxytocin Infusion in the Active Phase of Labor: A Systematic Review and Meta-analysis. Obstet Gynecol. 2017 Nov;130(5):1090-1096. doi: 10.1097/AOG.0000000000002325

27. Ciardulli A, Saccone G, Anastasio H, Berghella V. Less-Restrictive Food Intake During Labor in Low-Risk Singleton Pregnancies: A Systematic Review and Meta-analysis. Obstet Gynecol. 2017 Mar;129(3):473-480. doi: 10.1097/AOG.0000000000001898

28. Saccone G, Berghella V. Induction of labor at full term in uncomplicated singleton gestations: a systematic review and metaanalysis of randomized controlled trials. Am J Obstet Gynecol. 2015 Nov;213(5):629-36. doi: 10.1016/j.ajog.2015.04.004

29. Budden A, Chen LJ, Henry A. High-dose versus low-dose oxytocin infusion regimens for induction of labour at term. Cochrane Database Syst Rev. 2014 Oct 9;(10):CD009701

30. Jozwiak M, Bloemenkamp KW, Kelly AJ, Mol BW, Irion O, Boulvain M. Mechanical methods for induction of labour. Cochrane Database Syst Rev. 2012 Mar 14;(3):CD001233

FIGURES

Figure 1. Flow diagram of studies identified in the systematic review. *(Prisma template [Preferred Reporting Item for Systematic Reviews and Meta-analyses]).*

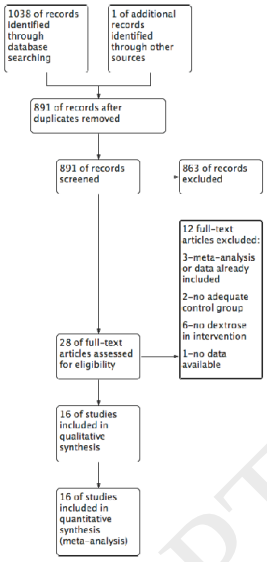

Figure 2. Assessment of risk of bias. (A) Summary of risk of bias for each trial; Plus sign: low risk of bias; minus sign: high risk of bias; question mark: unclear risk of bias. (B) Risk of bias graph about each risk of bias item presented as percentages across all included studies.

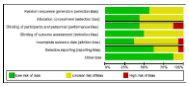

Figure 3. Forest plot for primary outcome, i.e. total length of labour from randomization to delivery. *CI, confidence interval*

Table 1. Characteristics of the included trials

	Study Location	GA at randomization (in weeks)	Spontaneous vs IOL	Cervical dilatation at enrollment (cm)	Exclusion criteria
Morton et al, 1985	United Kingdom	37+0 to 42+0	Both	3-5	Patients likely to give birth within 2h of start of IVF
Loong et al, 1987	China	>37+0	Both	NR	Significant complications during pregnancy, DM, IUGR
Piquard et al, 1989	France	38+0 to 41+0	Both	NR	DM, liver disease, kidney disease, or GDM
Omigbodun et al, 1991	Nigeria	≥37+0	Both	NR	HTN, preeclampsia, DM, jaundice, anemia
Omigbodun et al, 1993	Nigeria	>37+0	IOL	NR	Rhesus positive blood group, HTN, DM, pyrexia, jaundice, anemia
Nordstrom et al, 1995	Singapore	37+0 to 40+4	Spontaneous	4-6	GDM, previous infant >4000 g, glucosuria, polyhydramnios, or excessive fetal growth
Fisher and Huddleston 1997	United States	37+0 to 42+0	Spontaneous	>4	Preeclampsia, IUGR, initial cervical dilatation >9 cm, shoulder dystocia, OVD or CD, IVF exposure of <1h, abnormal 1h glucose screening at 24-28 weeks, abnormal fetal HR tracings, non-vertex presentation
Jamal et al, 2007	Iran	≥37+0 to 40+6	NR	≥4	Pre-eclampsia, IUGR, dilatation >9 cm, OVD or CD, IVF lasting <1h, abnormal 1h glucose screening

	Study Location	GA at randomization (in weeks)	Spontaneous vs IOL	Cervical dilatation at enrollment (cm)	Exclusion criteria
Shrivastava et al, 2009	United States	≥36+0	Spontaneous	3-5	DM, IOL, pre-eclampsia, cardiac disease, renal disease, previous CD, chorioamnionitis, pyelonephritis, febrile illness before random assignment
Sharma et al, 2012	India	≥36+0	Spontaneous	3-5	IOL, DM, pre-eclampsia, cardiac or renal disease, evidence of chorioamnionitis or fetal distress, pyrexia, intrauterine fetal death, planned CD and use of epidural analgesia
Rad et al, 2012	Iran	NR	NR	3-4	Preterm labor, polyhydramnios, pre-eclampsia, IUGR, 3rd trimester bleeding, abnormal 1h glucose screening between 24-28 weeks, maternal height <150 cm, BMI in 1st trimester >26kg/m^2
Dapuzzo-Argiriou et al, 2016	United States	≥36+0	Spontaneous	<6	Contraindication to SVD, IOL, DM or other glucose dysregulation condition, concurrent use of steroids, active labor with cervical dilation of ≥6 cm, or participation in another research study
Garmi et al, 2017	Israel	≥37+0	Both	≥1	HTN disorder, DM, cardiac disease, major

	Study Location	GA at randomization (in weeks)	Spontaneous vs IOL	Cervical dilatation at enrollment (cm)	Exclusion criteria
					fetal malformations, maternal fever upon admission, cervical dilatation >9 cm at randomization, non-vertex presentation, or any other contraindication to a trial of labor; women who had IVF infusion lasting less than 1h from inclusion to delivery were excluded from final analysis
Fong et al, 2017	United States	NR	Spontaneous	3-5	IOL, dilation >5 cm, IUGR, BMI ≥50, DM, preeclampsia, renal disease, any active infection
Paré et al, 2017	Canada	>37+0	IOL	3-5	Diagnosed with GDM and pre-gestational DM, preeclampsia, renal disease, maternal heart disease
Shafaie et al, 2017	Iran	38+0 to 41+0	Spontaneous	≥4	IOL, gestational HTN, nonreassuring fetal status, DM, preeclampsia, gestational DM, IUGR, chorioamnionitis, fetal distress, IFD, epidural, professional athletes

Table 2. Characteristics of IVF in the included trials

	Number of participants dextrose	Number of participants no dextrose	Type of dextrose fluid used	IVF type – control without dextrose	Rate of IVF (mL/h)	IVF initiated in latent vs active labor	PO intake allowed
Morton et al, 1985	20 (10 with 5%; 10 with 10%)	20 (10 with normal saline and 10 with LR solution	5% dextrose 10%dextrose*	NS; LR	1 L over 1 hour, then slow NS infusion	NR	NR
Loong et al, 1987	16	32 (16 with LR and 16 with nothing)	5% dextrose in oxytocin	LR and no IVF administered	Dextrose: 20-240; LR: 80-120	NR	NPO
Piquard et al, 1989	59	66	10% dextrose in water	LR	300	Active	NR
Omigbodun et al, 1991	36	34	5% dextrose in water	NS	NR	NR	Unrestricted
Omigbodun et al, 1993	40	42	5% dextrose in water	NS	NR	Both	Unrestricted
Nordstrom et al, 1995	12	11	5% dextrose*	NS	180	Active	NPO
Fisher and Huddleston 1997	43	48	5% dextrose in LR	LR	125	Active	NR
Jamal et al, 2007	89	89	5% dextrose in NS	LR	120	Active	NR
Shrivastava et al, 2009	192 (94 with 5%; 98 with 10%)	97	5% dextrose in NS; 10% dextrose in NS	NS	125	Active	Ice chips or NPO
Sharma et al, 2012	125	125	5% dextrose in NS	NS	175	Active	Ice chips or NPO

	Number of participants dextrose	Number of participants no dextrose	Type of dextrose fluid used	IVF type – control without dextrose	Rate of IVF (mL/h)	IVF initiated in latent vs active labor	PO intake allowed
Rad et al, 2012	43	54	5% dextrose in NS	NS	120	Active	NPO
Dapuzzo-Argiriou et al, 2016	153	156	5% dextrose in LR	LR	125	Active	NR
Garmi et al, 2017	98	202 (101 at 125 mL/h;101 at 250 mL/h)	5% dextrose in NS	LR	125 or 250	NR	Ice chips, water, tea with sugar
Fong et al, 2017	182 (92 with 5%; 90 with 2.5%)	92	5% dextrose in NS; 2.5% dextrose in NS	NS	125 or 250	Active	Ice chips, sips of water
Paré et al, 2017	96	97	5% dextrose in NS	NS	250	Latent	Unrestricted
Shafaie et al, 2017	67	67	5% dextrose with oral fluids**	LR with oral fluids**	125	Active	Oral fluids**

Abbreviations: CD, cesarean delivery; VD, vaginal delivery; IVF, intravenous fluid; NR, not reported; NS, 0.9% normal saline solution; LR, Lactated Ringer's solution; PO, oral intake; NPO, no oral intake

Number of participants presented as total

*IVF vehicle for dextrose administration not indicated

**Oral fluids included water, apple juice, or orange juice

Table 3. Descriptive labor characteristics and primary outcomes of the included trials

	% Induced n/N (%)	% Nulliparous n/N (%)	Oxytocin use n/N (%)	Epidural use n/N (%)	Primary outcome
Morton et al, 1985	NR by group; 27/40 (67.5%)	11/20 vs 10/20	9/20 (45%) vs 8/20 (40%)	NR by group; 1/40 (2.5%)	Intermediary metabolites
Loong et al, 1987	NR	5/16 (3.1%) vs 14/32 (4.4%)	16/16 (100%) vs 32/32 (100%)	NR	Maternal blood glucose
Piquard et al, 1989	NR	NR	NR	3/59 (5.1%) vs 3/66 (4.5%)	NR
Omigbodun et al, 1991	16/36 (44.4%) vs 14/34 (41.2%)	NR	36/36 (100%) vs 34/34 (100%)	NR	Sodium
Omigbodun et al, 1993	20/40 (50%) vs 20/42 (47.6%)	NR	40/40 (100%) vs 42/42 (100%)	NR	Bilirubin
Nordstrom et al, 1995	0/12 (0%) vs 0/11 (0%)	6/12 (50%) vs 3/11 (27.3%)	7/12 (58%) vs 2/11 (18%)	1/12 (5%) vs 2/11 (18%)	NR
Fisher and Huddleston 1997	0/48 (0%) vs 0/43 (0%)	NR	NR	20/48 (41.7%) vs 18/43 (41.8%)	UA pH
Jamal et al, 2007	NR	NR	NR	NR	UA pH
Shrivastava et al, 2009	0/192 (0%) vs 0/97 (0%)*	192/192 (100%) vs 97/97 (100%)	178/192 (93%) vs 80/97 (82%)	149/192 (77.6%) vs 76/97 (80%)	DOL
Sharma et al, 2012	0/125 (0%) vs 0/125 (0%) *	125/125 (100%) vs 125/125 (100%)	7/125 (5.6%) vs 23/125 (18.4%)	0/125 (0%) vs 0/125 (0%)	DOL

	% Induced n/N (%)	% Nulliparous n/N (%)	Oxytocin use n/N (%)	Epidural use n/N (%)	Primary outcome
Rad et al, 2012	NR	43/43 (100%) vs 54/54 (100%)	3/43 (7%) vs 13/54 (24.5%)	NR	DOL
Dapuzzo-Argiriou et al, 2016	0/153 (0%) vs 0/156 (0%)*	83/151 (55.0%) vs 86/156 (55.1%)	92/153 (60.1%) vs 88/156 (56.4%)	NR	Rate of CD
Garmi et al, 2017	66/98 (67.3%) vs 140/202 (69.3%)	98/98 (100%) vs 202/202 (100%)	38/98 (38.8%) vs 81/202 (40%)	75/98 (76.5%) vs 150/202 (74%)	DOL
Fong et al, 2017	0/182 (0%) vs 0/92 (0%)*	182/182 (100%) vs 92/92 (100%)	NR	NR	DOL
Paré et al, 2017	96/96 (100%) vs 97/97 (100%)	96/96 (100%) vs 97/97 (100%)	96/96 (100%) vs 97/97 (100%)	NR	DOL
Shafaie et al, 2017	0/67 (0%) vs 0/67 (0%)	67/67 (100%) vs 67/67 (100%)	7/67 (10.4%) vs 38/67 (56.7%)	0/67 (0%) vs 0/67 (0%)	Rate of CD
Total	198/1049 (18.9%) vs 271/966 (28.1%)	897/982 (91.3%) vs 837/933 (89.7%)	504/862 (58.5%) vs 498/885 (56.3%)	247/464 (53.2%) vs 247/475 (52%)	N/A
I^2	0%	0%	88%	0%	N/A
RR or MD (95% CI)	0.99 [0.66, 1.48]	0.94 [0.61, 1.43]	0.68 [0.29, 1.58]	1.04 [0.73, 1.48]	N/A

Abbreviations: NR, not reported; CD, cesarean delivery; UA, umbilical artery; DOL, duration of labor; N/A, not applicable; RCT, randomized controlled trial

Data are presented as dextrose n/N (%) vs control IVF n/N (%)

**Represents an exclusion criteria from the RCT*

Table 4. Primary outcomes and secondary labor outcomes

	Total length of labor (min±SD)	Length 1st stage labor (min±SD)	Length 2nd stage labor (min±SD)	% prolonged labor (>12h)	Chorioamnionitis n/N (%)	Postpartum Hemorrhage n/N (%)
Morton et al, 1985	NR	NR	NR	NR	NR	NR
Loong et al, 1987	NR	NR	NR	NR	NR	NR
Piquard et al, 1989	NR	NR	23.5±17.4 vs 17.6±12.3	NR	NR	NR
Omigbodun et al, 1991	556±156.7 vs 574±174.3	NR	NR	NR	NR	NR
Omigbodun et al, 1993	570±152 vs 576±164	NR	NR	NR	NR	NR
Nordstrom et al, 1995	361.7±156.2 vs 344.1±218.21	NR	NR	NR	NR	NR
Fisher and Huddleston 1997	NR	NR	NR	NR	NR	NR

	Total length of labor (min±SD)	Length 1st stage labor (min±SD)	Length 2nd stage labor (min±SD)	% prolonged labor (>12h)	Chorioamnionitis n/N (%)	Postpartum Hemorrhage n/N (%)
Jamal et al, 2007	NR	NR	NR	NR	NR	NR
Shrivastava et al, 2009	NR	NR	NR	12/148 (8%) vs 18/84 (22%)	28/192 (14.6%) vs 7/97 (7%)	12/192 (6.3%) vs 5/97 (5.2%)
Sharma et al, 2012	297.8±154.4 vs 473.8±220.5	NR	NR	4/125 (3.2%) vs 15/125 (12%)	3/125 (2.4%) vs 8/125 (6.4%)	NR
Rad et al, 2012	NR	163.73±39.5 vs 291.5±89.3	33.12±10.48 vs 58.88±33.58	NR	NR	NR
Dapuzzo-Argiriou et al, 2016	820±473 vs 831±484	710±433 vs. 734±453	73±105 vs 82±154	NR	5/150 (3.3%) vs 6/152 (3.9%)	2/149 (1.3%) vs 9/151 (6.0%)
Garmi et al, 2017	629.95±325.11 vs 571.9±309.5	NR	88.4±69.16 vs 96.16±76.55	28/98 (28.6%) vs 50/202 (24.8%)	NR	5/98 (5.1%) vs 14/202 (6.9%)
Fong et al, 2017	593.86± 368.955 vs 607.64± 358.586	486.66±346.207 vs 509.63±345.139	106.90±94.208 vs 98.01±67.286	36/132 (27.3%) vs 23/73 (31.5%)	30/182 (16.5%) vs 15/92 (16.3%)	NR
Paré et al, 2017	423±35.3 vs 499±25.8	320±22.8 vs 390±37.0	80±9.6 vs 95±15.3	NR	NR	NR
Shafaie et al, 2017	NR	NR	NR	2/67 (3%) vs 5/67 (7.5%)	0/67 (0%) vs 0/67 (0%)	NR
Total	N/A	N/A	N/A	82/570 (14.4%) vs 111/551 (20.1%)	66/716 (9.2%) vs 36/533 (6.8%)	19/439 (4.3%) vs 28/450 (6.2%)
I^2	82%	84%	91%	66%	44%	40%

	Total length of labor (min±SD)	Length 1st stage labor (min±SD)	Length 2nd stage labor (min±SD)	% prolonged labor (>12h)	Chorioamnionitis n/N (%)	Postpartum Hemorrhage n/N (%)
RR or MD (95% CI)	-38.33 [-88.23, 11.57]	**-75.81 [-120.67, -30.95]**	-7.63 [-19.80, 4.54]	0.56 [0.30, 1.07]	1.03 [0.54, 1.96]	0.66 [0.27, 1.61]

Abbreviations: NR, not reported; CD, cesarean delivery; N/A, not applicable. Boldface data, statistically significant
Data are presented as dextrose n/N (%) vs control IVF n/N (%) or as dextrose mean±SD vs control IVF mean±SD

Table 5. Mode of delivery

Reference	Spontaneous VD n/N (%)	Operative VD (vacuum or forceps) n/N (%)	CD rate n/N (%)	CD indicated for labor dystocia n/N (%)	CD indicated for fetal well-being n/N (%)
Morton et al, 1985	7/20 (35%) vs 6/20 (30%)	NR	NR	NR	NR
Loong et al, 1987	NR	NR	NR	NR	NR
Piquard et al, 1989	47/59 (79.7%) vs 53/66 (80.3%)	8/59 (13.6%) vs 12/66 (18.2%)	4/59 (6.8%) vs 12/66 (18.2%)	NR	NR
Omigbodun et al, 1991	NR	NR	NR	NR	NR
Omigbodun et al, 1993	34/40 (85%) vs 36/42 (85.7%)	0/40 (0%) vs 0/42 (0%)	6/40 (15%) vs 6/42 (14%)	NR	NR
Nordstrom et al, 1995	9/12 (75%) vs 10/11 (90.9%)	1/11 (9.1%) vs 0/12 (0%)	2/12 (16.7%) vs 1/11 (9.1%)	1/12 (8.3%) vs 2/11 (18.2%)	1/12 (8.3%) vs 0/11 (0%)

Reference	Spontaneous VD n/N (%)	Operative VD (vacuum or forceps) n/N (%)	CD rate n/N (%)	CD indicated for labor dystocia n/N (%)	CD indicated for fetal well-being n/N (%)
Fisher and Huddleston 1997	43/43 (100%) vs 48/48 (100%)	0/43 (0%) vs 0/48 (0%)	0/43 (0%) vs 0/48 (0%)	N/A	N/A
Jamal et al, 2007	NR	*	NR	N/A	N/A
Shrivastava et al, 2009	127/192 (66.1%) vs 69/97 (71.1%)	22/192 (11.5%) vs 13/97 (13.4%)	42/192 (21.9%) vs 14/97 (14%)	28/192 (14.6%) vs 12/97 (12.4%)	10/192 (5.2%) vs 2/97 (2.1%)
Sharma et al, 2012	112/125 (89.6%) vs 104/125 (83.2%)	10/125 (8%) vs 17/125 (13.6%)	3/125 (2.4%) vs 4/125 (3.2%)	2/125 (1.6%) vs 0/125 (0%)	1/125 (0.8%) vs 3/125 (2.4%)
Rad et al, 2012	42/43 (97.7%) vs 51/54 (94.4%)	NR	1/43 (2.3%) vs 3/54 (5.6%)	0/43 (0%) VS 2/54 (3.7%)	1/43 (2.3%) vs 1/54 (1.9%)
Dapuzzo-Argiriou et al, 2016	122/153 (79.7%) vs 131/156 (84.0%)	8/153 (5.2%) vs. 7/156 (4.5%)	23/153 (15%) vs 18/156 (11.5%)	NR	NR
Garmi et al, 2017	81/98 (82.7%) vs 155/202 (76.76%)	6/98 (6.1%) vs 23/202 (11.4%)	11/98 (11.2%) vs 24/202 (11.9%)	NR	NR
Fong et al, 2017	117/182 (64.3%) vs 68/92 (73.9%)	15/182 (8.2%)vs 5/92 (5.4%)	50/182 (27.5%) vs 19/92 (20.7%)	36/182 (19.8%) vs 14/92 (15.2%)	13/182 (7.1%) vs 5/92 (5.4%)
Paré et al, 2017	49/96 (51%) vs 46/97 (47.4%)	20/96 (20.8%) vs 29/97 (29.9%)	27/96 (28.1%) vs 22/97 (22.7%)	NR	NR
Shafaie et al, 2017	65/67 (97%) vs 63/67 (94%)	0/67 (0%) vs 0/67 (0%)	2/67 (3%) vs 4/67 (6%)	NR	NR
Total	775/1032 (75.1%) vs 685/875 (78.3%)	181/1024 (17.7%) vs 106/955 (11.1%)	129/875 (14.7%) vs 113/912 (12.4%)	67/554 (12.1%) vs 30/379 (7.9%)	26/554 (4.7%) vs 11/379 (2.9%)
I^2	0%	92%	0%	0%	0%
RR or MD (95% CI)	0.93 [0.73, 1.18]	1.46 [0.46, 4.59]	1.10 [0.82, 1.48]	1.24 [0.77, 1.98]	1.40 [0.65, 3.00]

Reference	Spontaneous VD n/N (%)	Operative VD (vacuum or forceps) n/N (%)	CD rate n/N (%)	CD indicated for labor dystocia n/N (%)	CD indicated for fetal well-being n/N (%)

Abbreviations: NR, not reported; VD, vaginal delivery; CD, cesarean delivery. Boldface data, statistically significant

Data are presented as dextrose n/N (%) vs control IVF n/N (%)

**Category represents an exclusion criterion for the trial*

Table 6. Prespecified neonatal outcomes

	5 min Apgar <7 n/N (%)	Hypoglycemia n/N (%)	Admission to NICU n/N (%)	BW (g±SD)
Morton et al, 1985	NR	NR	NR	NR

	5 min Apgar <7 n/N (%)	Hypoglycemia n/N (%)	Admission to NICU n/N (%)	BW (g±SD)
Loong et al, 1987	NR	NR	NR	NR
Piquard et al, 1989	0/59 (0%) vs 0/66 (0%)	0/59 (0%) vs 0/66 (0%)	NR	3470±494 vs 3335±532
Omigbodun et al, 1991	NR	NR	NR	3230±390 vs 3230±360
Omigbodun et al, 1993	NR	NR	NR	3270±420 vs 3210±360
Nordstrom et al, 1995	0/12 (0%) vs 0/11 (0%)	1/12 (8.3%) vs 2/11 (18.2%)	0/12 (0%) vs 0/11 (0%)	2982±345 vs 3257±394
Fisher and Huddleston 1997	0/43 (0%) vs 0/48 (0%)	NR	NR	3300±500 vs 3200±400
Jamal et al, 2007	0/89 (0%) vs 0/89 (0%)	0/89 (0%) vs 0/89 (0%)	NR	NR
Shrivastava et al, 2009	3/192 (1.6%) vs 1/97 (0.3%)	4/192 (2.1%) vs 1/97 (1%)	16/192 (8.3%) vs 8/97 (2.8%)	NR
Rad et al, 2012	NR	NR	NR	NR
Sharma et al, 2012	NR	NR	NR	NR
Dapuzzo-Argiriou et al, 2016	4/153 (2.6%) vs 0/155 (0%)	18/55 (32.7%) vs 7/50 (14.0%)	17/153 (11.1%) vs 19/156 (12.2%)	3408±417 vs 3428±404
Garmi et al, 2017	0/98 (0%) vs 1/202 (0.5%)	NR	NR	NR
Fong et al, 2017	2/182 (1.1%) vs 1/92 (1.1%)	NR	48/182 (26.4%) vs 20/92 (21.7%)	NR
Paré et al, 2017	NR	NR	NR	3405±493 vs 3491±490
Shafaie et al, 2017	NR	NR	NR	NR
Total	9/785 (1.1%) vs 3/712 (0.4%)	23/407 (5.7%) vs 10/313 (3.2%)	81/539 (15%) vs 47/356 (13.2%)	N/A
I^2	0%	2%	0%	30%
RR or MD (95% CI)	1.70 [0.46, 6.33]	2.25 [0.94, 5.35]	1.09 [0.73, 1.63]	1.27 [-71.12, 73.67]

Abbreviations: NR, not reported; UA, umbilical artery; UV, umbilical vein; RR, relative risk; GA, gestational age; IVF, intravenous fluid; BW, birthweight; R/O, rule out; CD, Cesarean delivery

Data are presented as dextrose n/N (%) vs control IVF n/N (%) or as dextrose mean±SD vs control IVF mean±SD

Table 7. Neonatal umbilical blood gas outcomes at delivery

Reference	**UA cord pH (pH±SD)** (mean 7.27; 5th to 95th percentile 7.15-7.38)*	**UA pCO_2 (mmHg±SD)** (mean 50.3; 5th to 95th percentile 32-68)*	**UA pO_2 (mmHg±SD)** (mean 18.4; 5th to 95th percentile 9-32)*	**UA Base deficit (mEq/L±SD)** (mean -2.7; 5th to 95th percentile -8.1-0.9)*
Morton et al, 1985	NR	NR	NR	NR
Loong et al, 1987	NR	NR	NR	NR
Piquard et al, 1989	7.19±0.06 vs 7.24±0.07	52.9±6.8 vs 47.4±7.4	17.0±5.3 vs 16.8±5.4	-5.9±2.1 vs -5.7±2.6
Omigbodun et al, 1991	NR	NR	NR	NR
Omigbodun et al, 1993	NR	NR	NR	NR
Nordstrom et al, 1995	7.25±0.07 vs 7.28±0.08	46.50±4.50 vs 43.50±3.00	18.75±4.5 vs 16.50±5.25	6.0±3.3 vs 5.0±3.9
Fisher and Huddleston 1997	7.30±0.07 vs 7.27±0.09	44.8±9.9 vs 50.6±12.9	NR	-4.5±3.1 vs -5.0±2.5

Reference	UA cord pH (pH±SD) (mean 7.27; 5th to 95th percentile 7.15-7.38)*	UA pCO_2 (mmHg±SD) (mean 50.3; 5th to 95th percentile 32-68)*	UA pO_2 (mmHg±SD) (mean 18.4; 5th to 95th percentile 9-32)*	UA Base deficit (mEq/L±SD) (mean -2.7; 5th to 95th percentile -8.1-0.9)*
Jamal et al, 2007	7.28±0.06 vs 7.25±0.07	41.6±4.1 vs 44.8±5.6	NR	-6.6±1.8 vs -7.3±2.1
Shrivastava et al, 2009	NR	NR	NR	NR
Sharma et al, 2012	NR	NR	NR	NR
Rad et al, 2012	NR	NR	NR	NR
Dapuzzo-Argiriou et al, 2016	7.22±0.08 vs. 7.24±0.07	55±11.4 vs 54.8±11.1	20.3±8.8 vs 21.1±20.0	NR
Garmi et al, 2017	NR	NR	NR	NR
Fong et al, 2017	NR	NR	NR	NR
Paré et al, 2017	7.21±0.7 vs 7.22±0.7	NR	NR	NR
Shafaie et al, 2017	NR	NR	NR	NR
Total	N/A	N/A	N/A	N/A
I^2	71%	92%	0%	12%
RR or MD (95% CI)	0.00 [-0.02, 0.02]	0.07 [-4.22, 4.35]	0.50 [-1.12, 2.12]	0.40 [-0.09, 0.88]

Abbreviations: NR, not reported; UA, umbilical artery; N/A, not applicable

Data are presented as dextrose mean±SD vs control IVF mean±SD

**Reference values are from Riley RJ, Johnson JWC. Collecting and analyzing cord blood gases. Clin Obstet Gynecol 1993; 36:13 (Reference #23)*