Women Undergoing Goal-Directed Fluid Therapy During Pregnancy: A Systematic Review and Meta-Analysis of Published Randomized Controlled Trials

Original Article

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ABSTRACT

Introduction: Goal-directed fluid therapy "GDFT" is a method of oxygen delivery and hemodynamics optimization using vasoactive and fluid infusions. According to several studies, GDFT has shown better results than traditional fluid therapy to maintain hemodynamic stabilization

Material and Methods: Our systematic review and meta-analysis was carried out according to the PRISMA guidelines for randomized studies. A computer literature search of PubMed, Scopus, Web of Science, and Cochrane Central Register of Controlled Trials was conducted from inception until February 2022. All relevant outcomes were pooled in the meta-analysis using Review Manager Software

Results: Our systematic review included three RCTs. All of them were included in our meta-analysis. There was no significant difference between GDFT group and the control group in the maternal adverse events except in the incidence of hypotension which was less in the intervention group. Also, there is no significant difference between the two groups in terms of PH, PO2, PCO2, lactic acid, and base deficit. GDFT group was better in SO2 than the control group in both artery and vein. Regarding the umbilical vein, the number of neonates who had PCO2 >46 mmHg and PO2 ≤21 mmHg was less in the intervention group than the control group. On the other hand, there were no significant difference between the two groups in the number of neonates whose PH <7.28. Finally, regarding the umbilical artery, the number of neonates who had PCO2 >46 mmHg and PO2 ≤21 mmHg was less in the intervention group.

Conclusion: GDFT shows promising results in controlling the hypotension and blood gases in pregnant women compared with the control group. Also, GDFT may provide benefits to healthy parturient women and their newborns.

Key Words: A systematic review, goal-directed fluid therapy, pregnancy.

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INTRODUCTION

Rapid volume expansion by administration of intravenous fluid is essential for patients undergoing major surgeries or patients with poor volume expansion as they need to maintain tissue perfusion[1]. One of the most efficient methods of intravenous therapy is goal-directed fluid therapy (GDFT)[2]. GDFT is a method of oxygen delivery and hemodynamics optimization using vasoactive and fluid infusions. According to several studies, GDFT has shown better results than traditional fluid therapy to maintain hemodynamic stabilization. In addition, GDFT was found to be able to increase tissue perfusion and decrease postoperative complications. Also, it was reported that GDFT could lead to several clinical benefits during the perioperative period as it can help to reduce the hospitalization and ICU stay time[3,4].

GDFT is guided by dynamic indicators such as pulse pressure variation and stroke volume variation (SVV) to predict fluid responsiveness[5]. Also, techniques like arterial waveform-based analysis, pulmonary artery catheterization, echocardiography, and thoracic bioimpedance-based technologies are needed for the assessment of volume status[6].

Recently, studies have discussed GDFT as suitable management for pregnant women to control maternal hypotension, uteroplacental hypoperfusion, and decreased cardiac preload and output induced by anesthesia used for cesarean section[7,8]. However, there is some conflict about using GDFT. It needs esophageal doppler monitoring, a continuous cardiac output monitoring system, and arterial pressure pulse contour analysis. Some of these measures are considered too invasive for pregnant women undergoing cesarean delivery[9]. In our systematic review

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and meta-analysis, we aim to synthesize evidence from published studies on the efficacy and the impact of GDFT on pregnant women.

MATERIAL AND METHODS

Inclusion criteria

Our meta-analysis was carried out according to the PRISMA guidelines for randomized studies[10]. It was determined that RCTs fulfilled the following requirements: "Pregnant ladies," "Goal-directed Fluid Therapy," and "full-text" English. When a study failed to meet our criteria, it was eliminated from consideration for future research.

Search strategy

We searched PubMed, Cochrane Library, Web of Science, and SCOPUS using the following keywords: Goal-directed Fluid Therapy and pregnancy.

We focused our research on publications written in the English language. Other than that, he double-checked every reference in every article.

Risk of bias assessment

To assess the quality of each study, we used the Cochrane Handbook for Systematic Reviews of Interventions, Second Edition. We examined how biases in selection and performance and detection and attrition biases affected the methodological quality as part of our methodology review. Study quality was evaluated by assigning letters to each criterion: "+" implies the study satisfied all criteria and was low in bias; "?" signifies equivocal quality criteria; and "-" denotes poor quality criteria and a high bias risk. (1)

Data collection

Each research yielded the following:

1. The name of the first author and the publishing year of the article,
2. Study design,
3. Inclusion criteria,
4. Primary outcome,
5. Results for each study,
6. Sample;
7. Age at baseline
8. Weight;
9. Gestational weeks (weeks);
10. Fasting duration (h);
11. Height,
12. Preoperative hemoglobin (g/L).

Statistical analysis

This meta-analysis was performed using Review Manager 5.4.0 (Cochrane Collaboration, Oxford, UK). When describing the results of this study, researchers employed a risk ratio and a 95% confidence interval (CI) (DerSimonian and Laird 1986). (2,3) The degree of heterogeneity was established using Cochrane's Q tests and I2 stats. There is considerable heterogeneity if the I2 is more than 50% and the *P-value* is less than 0.1. To decrease the heterogeneity, the study used a random-effect model. When the *p-value* was more than 0.1, it was deemed significant statistically. Due to the insufficient number of papers included, we could not conduct a subgroup analysis.

RESULTS

Study selection process and characteristics of studies

Our search strategy found 103 articles in these databases. After reviewing their abstracts and titles, we ruled out 94 articles. Among the remaining nine articles, six articles were excluded. Finally, three studies were involved. (1–3) All of them were included in our analysis (Figure 1). The summary and baseline characteristics of RCTs were listed in (Table 1 and Table 2).

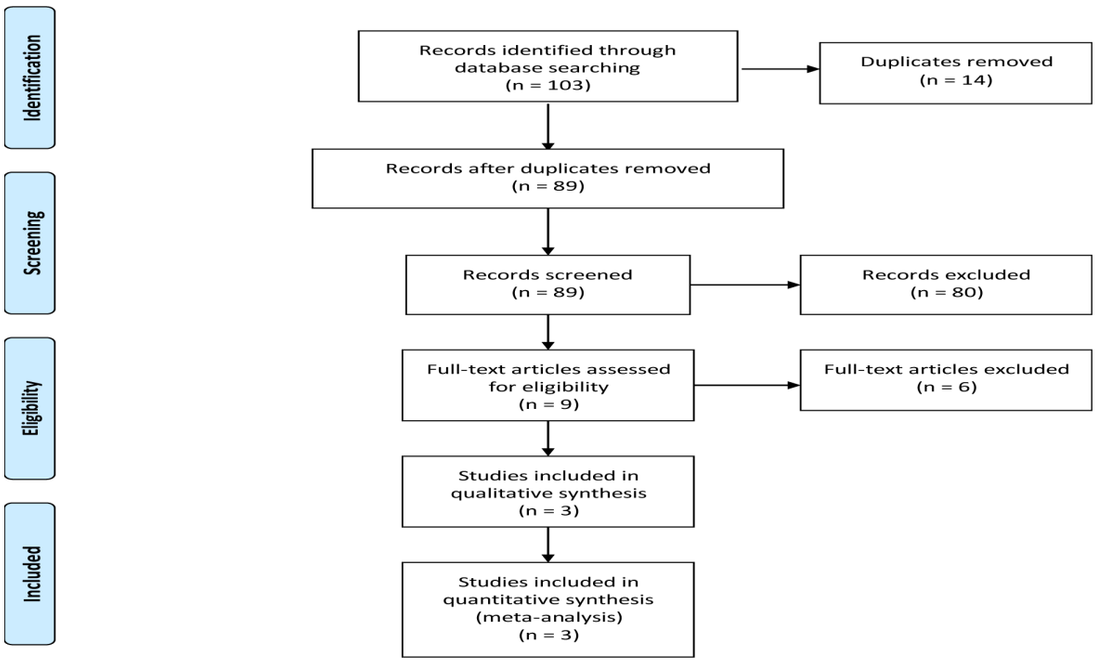

Fig. 1: Prisma flow diagram

Table 1: Summary of included studies. Abbreviations; RCT: Randomized control trial, HDP: Hypertensive disorders of pregnancy, ASA; American Society of Anesthesiologists, and GDFT: Goal-directed fluid therapy.

Study ID	Site	Study design	Inclusion criteria	Primary outcome	Results
Xiao *et al.* 2014	China	RCT	"Parturients with stable HDP presenting for elective cesarean delivery were recruited to this study."	Intraoperative maternal hemodynamic changes	"Dynamic responsiveness guided fluid therapy with the LiDCO rapid system might provide potential benefits to stable HDP parturient and their babies."
Xiao *et al*. 2015	China	RCT	"Parturient women with ASA physical status one scheduled for elective cesarean section were enrolled in this study."	Maternal adverse events before delivery	"LiDCO rapid-guided GDFT may provide benefit to healthy parturient women and their newborns."
Yang *et al*. 2021	Taiwan	RCT	"Women undergoing elective cesarean delivery were enrolled."	Intraoperative maternal profiles.	"Clear Sight-guided GDFT did not ameliorate post-spinal hypotension but may reduce nausea."

Table 2: Baseline characteristics of included studies. Abbreviations; NR: not reported, AND IQR: Interquartile range

Study ID	Study arms	Sample	Age, m±sd	Weight (kg), m±sd	Height (cm), m±sd	Preoperative hemoglobin (g/L)	Gestational weeks (weeks), median (IQR)	Fasting duration (h), m±sd
Xiao *et al*. 2014	Intervention	26	30.0 ± 4.3	81.8 ± 14.9	162.8 ± 7.8	119.3 ± 9.8	38 (38–40)	10.1 ± 2.8
	Control	26	32.0 ± 4.8	86.4 ± 12.9	64.0 ± 4.5	123.6 ± 13.0	38 (37–39)	10.6 ± 2.4
Xiao *et al*. 2015	Intervention	50	30.74 ± 4.02	75.73 ± 8.66	162.40 ± 4.50	120.90 ± 9.50	NR	12.27 ± 3.12
	Control	50	30.54 ± 3.96	77.22 ± 13.50	162.40 ± 5.50	118.70 ± 9.11	NR	12.43 ± 3.67
Yang *et al*. 2021	Intervention	37	36.6 ± 4.6	69.6 ± 8.2	159.8 ± 4.7	NR	37.5 ± 0.9	NR
	Control	34	35.6 ± 3.7	67.4 ± 7.6	160 ± 5.7	NR	38.1 ± 0.8	NR

Risk of bias assessment

Regarding the quality assessment of included RCTs, all studies were at low risk of randomization allocation, attrition bias, reporting bias, and any other biases. Regarding blinding, Yang *et al*. 2021[11] reported blinding for participants and assessment, while it was not reported in Xiao *et al*. 2014 and Xiao *et al*. 2015[12,13]. The risk of bias summary is shown in (Figures 2,3).

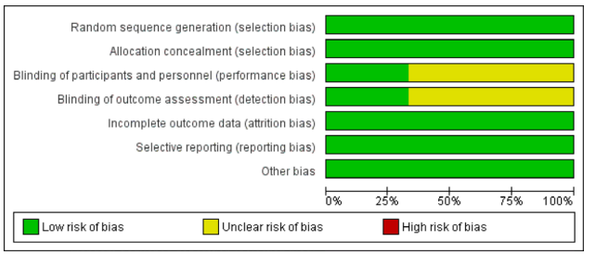

Fig. 2: Risk of bias assessment

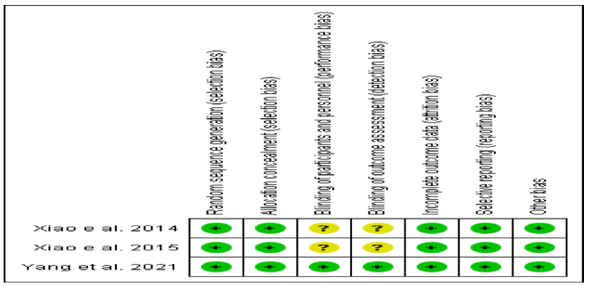

Fig. 3: Risk of bias assessment

Maternal adverse events before fetal delivery

There were no significant differences between Goal-directed Fluid Therapy and control in the Incidence of nausea and vomiting as following; [RR=0.68, CI 95%, (0.43, 1.07), P=0.1], the data was homogenous, Heterogeneity: [(P = 0.34); I² = 8%] (Figure 4).

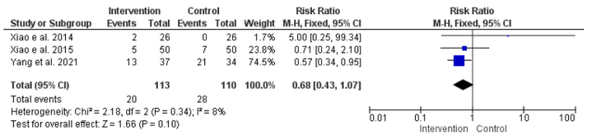

Fig. 4: Nausea & vomiting in both groups

On the other hand, the incidence of hypotension was less in the intervention group as following; [RR=0.32 CI 95%, (0.20, 0.52), *P* < 0.00001)], and the data was homogenous: [(P = 0.95); I² = 0%] (Figure 5).

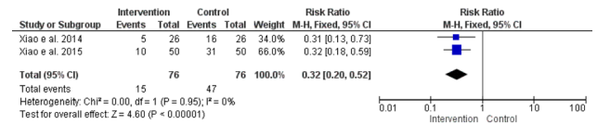

Fig. 5: hypotension in both groups

Umbilical cord vessels

There was no significant difference between the two groups regarding the PH of both umbilical artery and vein as following respectively; [MD=0.01 CI 95%, (-0.01, 0.02), P=0.29] and [MD=0.01 CI 95%, (0, 0.02), P=0.08], but the data was heterogenous, [(P = 0.03); I² = 72%) and [(P = 0.004); I² = 82%]. This heterogeneity was resolved by using the random-effect model and excluding yang *et al*. 2021, and the results showed no significant difference in artery PH, but the PH was more in the control arm in the vein as following respectively; [MD=0.02 CI 95%, (0, 0.03), P=0.08) and [MD=0.02, CI 95%, (0.01, 0.03), P=0.0006). the data was homogeneous as following respectively [(P = 0.25); I² = 25%] and [(P = 0.53); I² = 0%] (Figure 6).

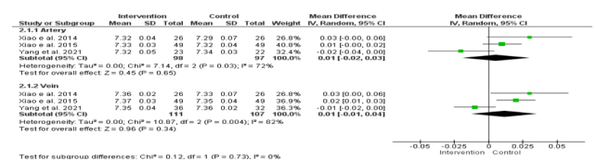

Fig. 6: uterine artery PH in both groups

There was no significant difference between the two groups regarding the PO2 (mmHg) of both umbilical artery and vein as following respectively; [MD=1.06 CI 95%, (-1.05, 3.18), P=0.33] and [MD=1.21 CI 95%, (-0.55, 2.97), P=0.18], but the data was heterogenous, [(P = 0.09); I² = 58%) and [(P = 0.03); I² = 71%]. This heterogeneity was resolved by using the random-effect model and excluding yang *et al*. 2021, and the results showed no significant difference in artery PH, but the PO2 was more in the control arm in the vein as following respectively; [MD=1.88 CI 95%, (-0.37, 4.14), P=0.48) and [MD=2.53, CI 95%, (0.48, 4.59), P=0.02). the data was homogenous as following respectively [(P = 0.48); I² = 0%] and [(P = 0.33); I² = 0%] (Figure 7).

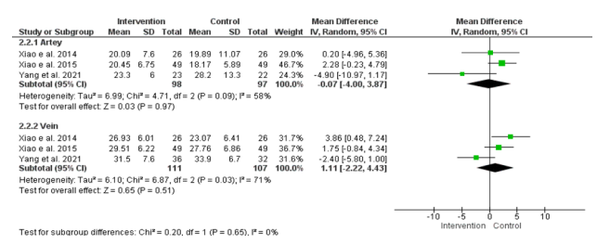

Fig. 7: O2 saturation in both groups

Also, there was no significant difference between the two groups regarding the PCO2 (mmHg) of both umbilical artery and vein as following respectively; [MD=-1.04 CI 95%, (-2.83, 0.75), P=0.26] and [MD=-0.55 CI 95%, (-1.87, 0.77), P=0.41], but the data was heterogenous, [(P = 0.006); I^2 = 81%) and [(P = 0.009); I^2 = 79%]. This heterogeneity was resolved by using the random-effect model and excluding yang *et al*. 2021, and the results showed that PCo2 was artery less in both artery and vein in the intervention arm as following respectively; [MD=-2.8 CI 95%, (-4.9, -0.7), P=0.009) and [MD=-2.3, CI 95%, (-4.02, -0.57), P=0.009). the data was homomgenous as following respectively [(P = 0.51); I^2 = 0%] and [(P = 0.82); I^2 = 0%] (Figure 8).

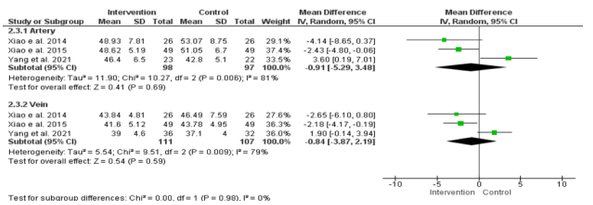

Fig. 8: Co2 level in both groups

There was no significant difference between the two groups regarding the Lactic acid (mmol/L) of both umbilical artery and vein as following respectively; [MD=-0.04 CI 95%, (-0.15, 0.08), P=0.52] and [MD=0.09 CI 95%, (-0.01, 0.18), P=0.07], and the data was homogenous, [(P = 0.36); I^2 = 0%) and [(P = 0.47); I^2 = 0%] (Figure 9).

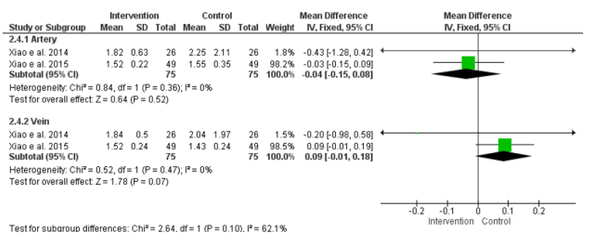

Fig. 9: Lactic acid level in both groups

Also, there was no significant difference between the two groups regarding the Base deficit (mmol/L) of both umbilical artery and vein as following respectively; [MD=0.12 CI 95%, (-0.38, 0.62), P=0.64] and [MD=0.23 CI 95%, (-0.35, 0.82), P=0.43], and the data was homogenous, [(P = 0.18); I^2 = 43%) and [(P = 0.35); I^2 = 0%] (Figure 10).

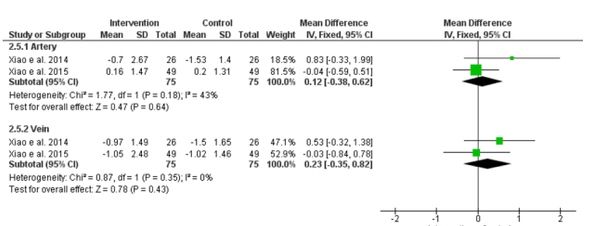

Fig. 10: Base deficit in both groups

Finally, the intervention group was better in SO2(%) in both artery and vein as following respectively; [MD=6.34 CI 95%, (1.07, 11.61), P=0.02] and [MD=6.7 CI 95%, (1.24, 12.16), P=0.02], and the data was homogenous, [(P = 0.98); I^2 = 43%) and [(P = 0.85); I^2 = 0%] (Figure 11).

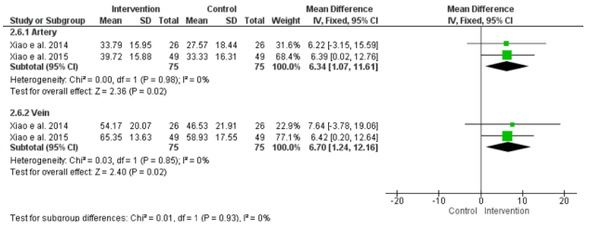

Fig. 11: Neonatal PH in both groups

Neonatal adverse events after delivery

Regarding umbilical vein, the number of neonates who had PCO2 >46 mmHg and PO2 ≤21 mmHg were less in the intervention group as following; [RR=0.46 CI 95%, (0.26, 0.82), P=0.008] and [RR=0.38 CI 95%, (0.16, 0.91), P=0.03], and the data was homogenous, [(P = 0.79); I^2 = 0%) and [(P = 0.31); I^2 = 0%]. On the other hand, there were no significant difference between the two groups in the number of neonates whose pH <7.28 as following; [RR=0.17 CI 95%, (0.02, 1.35), p=0.09] and the data was homogenous [(P = 0.87); I^2 = 0%] (Figure 12).

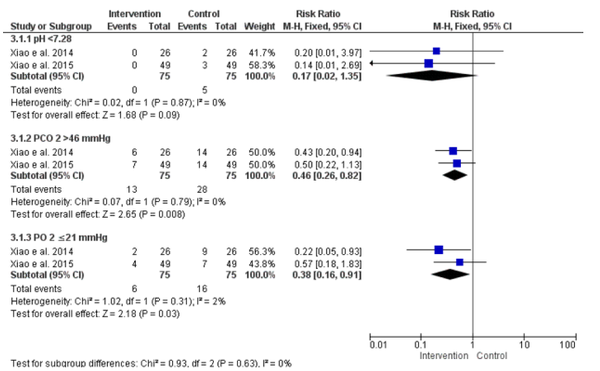

Fig. 12: Neonatal adverse event in both groups

Regarding umbilical artery, the number of neonates who had PCO2 >46 mmHg and PO2 ≤21 mmHg were less in the intervention group as following; [RR=0.42 CI 95%, (0.20, 0.90), P=0.02] and [RR=0.43 CI 95%, (0.24, 0.77), P=0.005], and the data was homogenous, [(P = 0.29); I^2 = 11%) and [(P = 0.30); I^2 = 8%]. On the other hand, there were no significant difference between the two groups in the number of neonates whose PH <7.28 as following; [RR=0.20 CI 95%, (0.02, 1.67), P=0.14] and the data was homogenous [(P = 1.00); I^2 = 0%] (Figure 13).

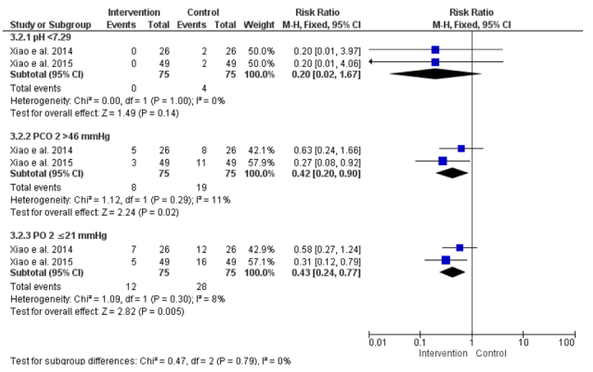

Fig. 13: Ph <7.28 in both groups

DISCUSSION

Summary of the findings

Our systematic review included three RCTs. All of them were included in our meta-analysis. The results of our results showed that there is no significant difference between GDFT group and the control group in the maternal adverse events except in the incidence of hypotension, it was less in the intervention group. Also, there is no significant difference between the two groups in terms of PH, PO2, PCO2, lactic acid, and base deficit, while the intervention group was better in SO2 than the control group in both artery and vein. Regarding the umbilical vein, the number of neonates who had PCO2 >46 mmHg and PO2 ≤21 mmHg was less in the intervention group than the control group. On the other hand, there was no significant difference between the two groups in the number of neonates whose PH <7.28. Finally, regarding the umbilical artery, the number of neonates who had PCO2 >46 mmHg and PO2 ≤21 mmHg was less in the intervention group. On the other hand, there was no significant difference between the two groups in the number of neonates whose PH <7.28.

Agreements and disagreements

Recently, there is wide debate about using GDFT in pregnancy to control maternal hypotension, uteroplacental hypoperfusion, and decreased cardiac preload and output induced by anesthesia used for a cesarean section as it needs esophageal doppler monitoring, continuous cardiac output monitoring system, and arterial pressure pulse contour analysis, and some of these measures are considered too invasive for pregnant women undergoing cesarean delivery. Our meta-analysis is the first meta discussing this topic, and we provided class 1 evidence about the efficacy of GDFT in pregnancy. The results of our meta are in the same direction as Xiao *et al*. 2014, and Xiao *et al*. 2015[12,13], who showed that the incidence of hypotension prior to delivery was significantly higher than that in the GDFT group. However, our results are inconsistent with their results regarding the incidence of maternal adverse events (nausea and vomiting) as their results showed that this incidence was similar in the two groups. Also, our results are consistent with Yang *et al*. 2021[11], who showed that the incidence of post-spinal hypotension was comparably high in the two groups, while regarding the incidence of maternal adverse events, they showed that there were fewer women who experienced nausea in the GDFT group compared with the control group.

Strength points and limitations

Our study has several strength points (1) we conducted all steps in strict accordance with the Cochrane Handbook of Systematic Reviews for interventions, (2) we followed the standard reporting guidelines of PRISMA statement to report this work, (3) we ran a comprehensive search of multiple electronic databases to identify all relevant studies, and finally (4) Our study reported class 1 evidence about the efficacy of GDFT during pregnancy. Nonetheless, our study has a few limitations. We noticed a lack of the RCTs investigating the effect of the GDFT in pregnancy, so we recommend future well-designs RCTs to investigate this impact, address an unmet clinical need, and fill this evidence gap in the literature.

CONCLUSION

In conclusion, our meta-analysis showed no significant difference between the GDFT group and the control group in terms of maternal, neonatal adverse events PH, PO2, PCO2, lactic acid, and base deficit. However, GDFT shows promising results in controlling the hypotension and blood gases compared to the control group. Also, GDFT may provide benefit to healthy parturient women and their newborns

CONFLICT OF INTERESTS

There are no conflicts of interest.

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