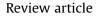


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Uterine massage for preventing postpartum hemorrhage at cesarean delivery: Which evidence?



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ARTICLE INFO	A B S T R A C T	
<i>Article history:</i> Received 13 November 2017 Accepted 22 February 2018 Available online xxx	Background: Cesarean delivery could be complicated by postpartum hemorrhage (PPH), the first cause of maternal death. Objectives: To evaluate the efficacy of uterine massage in preventing postpartum hemorrhage at cesarean delivery.	
<i>Keywords:</i> Postpartum hemorrhage Maternal death Bleeding Cesarean section Maternal mortality	 Data sources: Electronic databases from their inception until October 2017. Study eligibility criteria, participants, and interventions: We included all RCTs comparing uterine massage alone or as part of the active management of labor before or after delivery of the placenta, or both, with non-massage in the setting of cesarean delivery. Data collection and analysis: The primary outcome was PPH, defined as blood loss > 1000 mL. Meta-analysis was performed using the random effects model of DerSimonian and Laird, to produce summary treatment effects in terms of mean difference (MD) or relative risk (RR) with 95% confidence interval (CI). Results: Only 3 RCTs comparing uterine massage vs no uterine massage were found. The quality of these 3 trials in general was very low with high or unclear risk of bias. All of them included only women in the setting of spontaneous vaginal delivery and none of them included cesarean delivery, and therefore the meta-analysis was not feasible. Conclusions: There is not enough evidence to determine if uterine massage prevents postpartum benefore. 	
	hemorrhage at cesarean delivery.	

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Introduction

The first cause of maternal death worldwide is postpartum hemorrhage (PPH), responsible for an estimated 127,000 deaths annually. Failure of the uterus to contract adequately after childbirth is the most common cause of PPH. In the absence of timely and appropriate action, a woman could die within a few hours [1].

One of the most common complications of cesarean delivery (CD) is PPH, which can be life threatening [2–6]. In high-income countries, hemorrhage is reduced by routing active management of the third stage of labor, including removal of the placenta by controlled cord traction, and by using uterotonics after delivery, such oxytocin, to stimulate contraction of the uterus [2], or by using antifibrinolytics agents before CD, mainly tranexamic acid (TXA) [3,4].

As simple and inexpensive intervention, uterine massage, by repetitive massaging or squeezing movements, after delivery of the placenta in the setting of CD can also promote contraction of the uterus. However it is not known whether it is effective [6].

The aim of this systematic review and meta-analysis of randomized controlled trials (RCTs) was to evaluate the efficacy of uterine massage in preventing PPH at CD.

Materials and methods

Search strategy

This review was performed according to a protocol designed a priori and recommended for systematic review [7]. Electronic databases (i.e. MEDLINE, Scopus, ClinicalTrials.gov, EMBASE, Sciencedirect, the Cochrane Library at the CENTRAL Register of Controlled Trials, Scielo) were searched from their inception until October 2017. Search terms used were the following text words: "PPH," "cesarean", "caesarean", "delivery", "labor", "labour", "postpartum hemorrhage," "bleeding," "general anesthesia," "morbidity," "mortality," "meta-analysis," "metaanalysis," "review," "randomized," "oxytocin," "clinical trial," "randomised," "effectiveness," "guidelines," "bleeding," "balloon" and "clinical trial." No restrictions for language or geographic location were applied. In addition, the reference lists of all identified articles were examined to identify studies not captured by electronic searches. The electronic search and the eligibility of the studies were independently assessed by two authors (GS, CC). Differences were discussed with a third reviewer (VB).

Study selection

We included all published, unpublished and ongoing RCTs comparing uterine massage alone or as part of the active management of labor (including uterotonics) before or after delivery of the placenta, or both, with non-massage in the setting of CD. Quasi RCTs (i.e. trials in which allocation was done on the basis of a pseudo-random sequence, e.g. odd/even hospital number or date of birth, alternation) were not included. Studies on uterine massage in the setting of spontaneous or operative vaginal delivery were also excluded.

Risk of bias

The risk of bias in each included study 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].

Two authors (GS, CC) independently assessed inclusion criteria, risk of bias and data extraction. Disagreements were resolved by discussion with a third reviewer (VB).

Outcomes

All analyses were done using an intention-to-treat approach, evaluating women according to the treatment group to which they were randomly allocated in the original trials. Primary and secondary outcomes were defined before data extraction.

The primary outcome was PPH, defined as blood loss >1000 mL after trial entry. The secondary outcomes were blood loss >300, >500, >1500, >2000, and >2500 mL after trial entry; mean blood loss after trial entry; mean time to placenta delivery; use of additional uterotonics; use of other procedure for management of PPH; blood transfusion; and maternal death or severe morbidity.

We planned to assess the primary and secondary outcomes in the following subgroup analyses:

-Uterine massage before or after delivery of the placenta

-With or without uterotonics (e.g. oxytocin)

-With or without controlled cord traction

We also planned to assess the primary and secondary outcomes in the following sensitivity analyses:

-Type of uterine massage

-Trial quality

Statistical analysis

The data analysis was completed independently by two authors (GS, AC) using Review Manager v. 5.3 (The Nordic Cochrane Centre, Cochrane Collaboration, 2014, Copenhagen, Denmark). The completed analyses were then compared, and any difference was resolved by discussion with a third reviewer (VB).

Data from each eligible study were extracted without modification of original data onto custom-made data collection forms. For continuous outcomes means \pm standard deviation were extracted and imported into Review Manager v. 5.3.

Meta-analysis was performed using the random effects model of DerSimonian and Laird, to produce summary treatment effects in terms of mean difference (MD) or relative risk(RR) with 95% confidence interval (CI). Heterogeneity was measured using I-squared (Higgins I²).

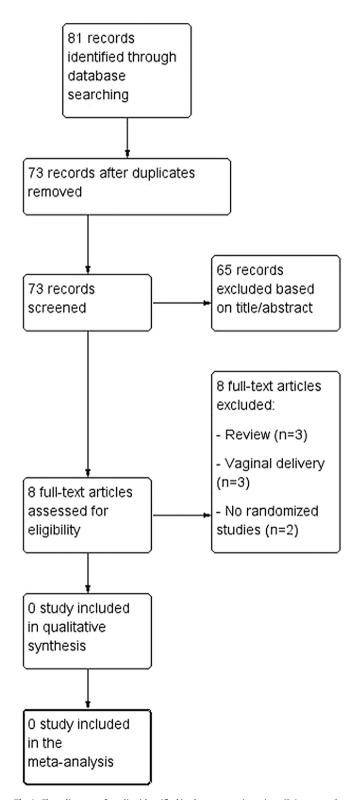
Potential publication biases were assessed statistically by using Begg's and Egger's tests.

The *meta*-analysis was reported following the Preferred Reporting Item for Systematic Reviews and Meta-analyses (PRISMA) statement [8].

Results

Study selection and study characteristics

The flow of study identification is shown in Fig. 1. Only 3 RCTs comparing uterine massage vs no uterine massage were found [9–11]. The quality of these 3 trials in general was very low and



both of them had high or unclear risk of bias in most of the seven Cochrane domains related to the risk of bias (Fig. 2A and B). Table 1 shows the characteristics of the clinical trials. All of them included only women in the setting of spontaneous vaginal delivery and none of them included CD.

Synthesis of results

None of the three RCTs met the inclusion criteria and therefore a *meta*-analysis was not feasible.

Discussion

The results of this review are inconclusive. Only three low quality RCTs comparing uterine massage versus no massage to reduce the risk of PPH were found through a systematic review of the literature. None of them analyzed the efficacy of uterine massage in the setting of cesarean delivery. All of them were low quality trials.

Hofmeyr et al. in a prior Cochrane review analyzed the efficacy of uterine massage to prevent PPH [6]. They included only two trials evaluating the efficacy of uterine massage in the third stage of labor after vaginal delivery. They concluded that there is not

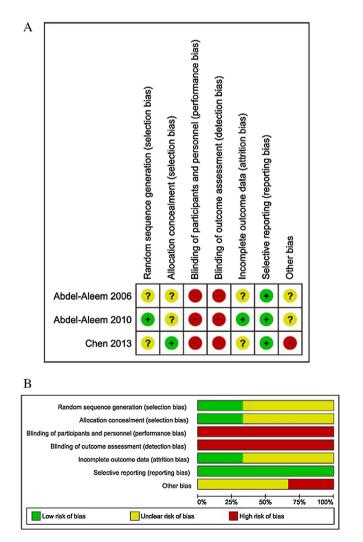


Fig. 2. Assessment of risk of bias. (A) Summary of risk of bias for each trial; Plus sign: low risk of bias; minus sign: high risk of bias; question mark: unclear risk of bias. (B) Risk of bias graph about each risk of bias item presented as percentages across all included studies.

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

Table 1

Characteristics of the trials on uterine massage.

	Abdel-Aleem, 2006 [9]	Abdel-Aleem, 2010 [10]	Chen, 2013 [11]
Study location	Egypt	Egypt	China
Sample size ^a	200 (98/102)	1964 (643/652/659)	2340 (1170/1170)
Inclusion criteria	Singleton undergoing spontaneous vaginal delivery	Singleton undergoing spontaneous vaginal delivery	Singleton undergoing spontaneous vaginal delivery
Exclusion criteria	Cesarean delivery, malpresentation	Cesarean delivery, malpresentation	Cesarean delivery, malpresentation
Intervention group	Uterine massage every 10 min for 60 min promptly after placental delivery	Uterine massage for 30 min promptly after placental delivery	Uterine massage for 30 min promptly after placental delivery
Use of oxytocin ^b	Oxytocin 10 UIM immediately after cord clamping	Oxytocin 10 U IM immediately after delivery of the shoulder	Oxytocin 10 U IM immediately after delivery of the shoulder
Additional manovre ^b	Controlled cord traction	Controlled cord traction	Not stated
N vaginal delivery	100%	100%	100%
N cesarean delivery	0%	0%	0%
Primary outcome	Mean blood loss	Blood loss >300 mL	Blood loss >400 mL

^a Data are presented as number in the uterine massage group vs number in the control group.

^b In both group.

enough evidence to support the use of uterine massage after cesarean or vaginal delivery.

Different strategies have been published to prevent PPH in women at cesarean [2–6]. Prophylactic oxytocin at any dose have been shown to decrease PPH and the need for therapeutic uterotonics compared to placebo alone [2]. Prophylactic TXA given before cesarean skin incision in women undergoing CD, under spinal or epidural anesthesia, significantly decreases blood loss, including postpartum PPH and severe PPH, in addition to the standard prophylactic oxytocin given after delivery of the neonate [3,4]. Different cesarean techniques have also been studies in order to reduce blood loss during the operation. For example expansion of the uterine incision with fingers in a cephalad-caudad direction is associated with better maternal outcomes and should be preferred to transverse expansion during a CD [5].

As simple and inexpensive intervention, uterine massage, by repetitive massaging or squeezing movements, after delivery of the placenta in the setting of CD can also help to reduce the risk of PPH. The International Confederation of Midwives and the International Federation of Gynecologists and Obstetricians (ICM/FIGO) both recommended routine massage of the uterus after delivery of the placenta [12]. However, there is very little empirical research to evaluate the effectiveness of this method. So far, despite this technique can be easy to do, inexpensive and lifesaving, no RCTs have been published so far and none are ongoing.

In summary, there is not enough evidence to determine if uterine massage prevents postpartum hemorrhage at cesarean delivery. Given that this inexpensive and simple intervention may be life saving for women worldwide, especially in low-income countries, where uterotonics can be not available, a large, multicenter, well-designed randomized controlled trial should be a research priority. If shown to be effective, uterine massage would represent an easy intervention with the potential to have a major effect on postpartum hemorrhage and maternal mortality worldwide.

Funding

This study had no funding source

Details of ethics approval

None required

Compliance with ethical standards

* Disclosure of potential conflicts of interest: We declare that we have no conflict of interest.

- * Research involving human participants and/or animals: no
- * Informed consent: no necessary

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