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The effect of placental removal method at cesarean delivery on perioperative hemorrhage: a randomized clinical trial ISRCTN 49779257

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Abstract

Objectives: To evaluate whether the method of placental removal during cesarean section has an impact on perioperative hemorrhage and maternal infectious morbidity. *Study design*: Three hundred and two patients admitted for abdominal delivery were recruited in a prospective randomized clinical intention-to-treat trial. Participants were assigned to have their placenta removed either manually or spontaneously. The drop in hematocrit was the primary outcome; postpartum maternal infectious morbidity was also assessed. *Results*: Two patients were excluded for incomplete data. One-hundred-fifty-one were randomized to the manual removal group and 149 to the spontaneous group. The demographic characteristics of the two populations were similar. The mean drop (%) in the manual removal group was greater than in the spontaneous group (5.57 ± 3.86 and 2.65 ± 2.67, respectively; $P < 0.01$). the incidence of postpartum infectious morbidity was also significantly greater in the manual group (RR 15.8, 95% CI 2.19–117.5). *Conclusion*: Routine manual removal of placenta at cesarean section significantly increases perioperative blood loss and postpartum maternal infectious morbidity.

Keywords: Placenta; Blood loss; Cesarean section; Uterine hemorrhage

1. Introduction

During the past decades cesarean section safety has improved but it remains a potentially morbid procedure [1]. Obstetric hemorrhage account for one of a major possible complication of abdominal delivery [1] with a reported postpartum hemorrhage rate varying between 4.3 and 8% [2–4] while prospective observational study showed a tendency to under-estimate blood loss [5].

Good knowledge of surgical principles minimize morbidity [1] and some randomized prospective studies evaluated benefits of different procedures to reduce operative blood loss [6–10]. Manual versus spontaneous removal of placenta have been studied in controlled trials [11–14] but according to Wilkinson and Enkin at the Cochrane Collaborative [15] the evidences are not sufficiently strong to make recommendation for current practice.

In view of the above conclusion, we designed a prospective randomized clinical trial to compare manual with spontaneous removal of placenta during cesarean section. The primary outcome was the perioperative hemorrhage estimated by the decrease in hematocrit.

2. Study design

We conducted a randomized, controlled clinical trial between October 2002 and May 2003 at the Gynecologic and Obstetric Department of F. Hached University Teaching Hospital, Sousse, Tunisia. this single-institution protocol was approved by the Institution ethics committee and all patients provided informed consent. As it is now recommended [16,17] the trial was also registered with a International Standard Randomised Controlled Trial Number (ISRCTN49779257 http://www.controlled-trials.com).

For practical reasons the protocol was applied 4 days a week. The study population consisted of women who had an indication for elective or emergency cesarean section after 35 weeks of gestation. Patients diagnosed with gestational diabetes, severe pre-eclampsia, placenta previa,

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chorioamnionitis, multiple gestations, maternal coagulopathy, or <20 years were excluded from the trial.

Following study enrollment, the patient was randomly assigned to one of the two study groups as follows: group A (spontaneous delivery of placenta) or group B (manual removal of placenta). Assignment was made through the use of a computer-generated random numbers table. The assigned treatment was written on a card and sealed in opaque envelopes consecutively numbered that were opened just immediately before the procedure.

Cesarean sections were performed by second, third or fourth-year obstetric residents and under the supervision of a faculty obstetrician. In preoperative preparation patient was shaved and scrubbed with povidone–iodine solution. A Perioperative prophylactic antibiotic was systematic either with a single dose of first-generation cephalosporin or gentamicin. The choice of technical procedure was left at obstetrician discretion.

Delivery of the placenta was done similarly as described by others [7,14]: Immediately after delivery of the fetus 20 units of oxytocin placed in 500 cc ringer lactate were rapidly infused while a gentle traction was applied to the umbilical cord until the placenta was delivered in the patients of group A; for patients assigned to manual extraction group, the operator introduced his dominant hand into the uterine cavity and created a cleavage plane then the placenta was grasped and removed. After that, and in both group, the uterine cavity was wiped for exploration and removal of uterine blood clots or placental fragments. The uterus was not exteriorized for repair. Hematocrit and hemoglobin were done immediately before and between 24 to 48 h after operative procedure.

Maternal demographics, medical, biological and delivery characteristics, were examined; the primary outcome measure was the drop in hematocrit level (%); the secondary outcome was infectious morbidity defined as postpartum endometritis (parametrial tenderness, white blood cell count >15.000 ml^{-1}, and at least two temperature >38.5 °C 6 h apart after the first 24 h postpartum), pelviperitonitis, isolated fever (>38 °C 6 h apart) and surgical wound Infection.

On the basis of previous studies [11–14], the sample size for our study was calculated to demonstrate a difference of 3% between groups (assuming alpha = 0.05 and beta = 0.20; power, 80%) a total sample size of 250, with 125 in each arm, was required.

The data were analyzed for statistical significance by using the Student's *t*-test, the Mantel–Haenszel χ^2 analysis, Fisher's exact test or Mann–Whitney *U*-test as appropriate; Significance was assumed at the 5% level. Relative risk (RR) and 95% confidence interval (CI) were reported. All analyses were on an intent-to-treat basis. Data were analyzed with SPSS 10.0 (SPSS Inc.).

3. Results

From October 2002 to May 2003, 4664 patients delivered at our institution. Of these 897 gave birth by cesarean section (19.2%) and 302 entered the trial, the remainder (428) being ineligible or not randomized because of non disposability of investigators. A total of 153 patients were enrolled in the manual removal of placenta group of whom 151 completed trial while 149 were assigned in the spontaneous placenta delivery group but in two cases manual delivery was performed because of failure of spontaneous delivery (Fig. 1).

Base-line demographic and clinical characteristics were similar in the two groups (Table 1); there were no statistically significant differences in the distribution of indications for cesarean deliveries between the two groups (Table 2);

The primary outcome of this study is the perioperative hemorrhage estimated by the drop in hematocrit; the mean drop (%) in the manual removal group was greater that in the spontaneous group (5.57 ± 3.86 and 2.65 ± 2.67, respectively; $P < 0.01$). The change in the hemoglobin (g/100 ml) was also greater in the manual group compared with the spontaneous group (1.88 ± 1.2 and 0.77 ± 0.89,

Table 1
Base-line demographic and clinical characteristics

	Manual ($n = 151$)	Spontaneous ($n = 149$)	*P* value
Age (years)	32.1 ± 5.29	31.6 ± 5.3	0.43
Weight (kg)	77.4 ± 3.4	76.8 ± 4.2	0.17
Height (cm)	157.9 ± 6.1	158.6 ± 5.8	0.27
Nulliparous	37 (24.5)	36 (24.1)	0.94
Prior cesarean delivery	80 (52.9)	79 (53)	0 > 0.99
Gestational age (day)	273 ± 12	274 ± 11	0.64
Duration of ruptured membranes (h)	8 ± 31.8	3.5 ± 9.5	0.09
Antibiotics intrapartum (No.)	8 (5.2)	8 (5.3)	>0.999
Epidural anesthesia	56 (37)	51 (34.2)	0.63
Preoperative hemoglobin (g/100 ml)	12.06 ± 1.5	11.7 ± 1.4	0.06
Preoperative hematocrit (%)	35.8 ± 4.1	34.8 ± 4.2	0.06
New born characteristics			
Birthweight (g)	3528 ± 682	3462 ± 606	0.17
Female	72 (47%)	74 (49.6)	0.81

Continuous data presented as mean ± S.D. Dichotomous data presented as number (percent).

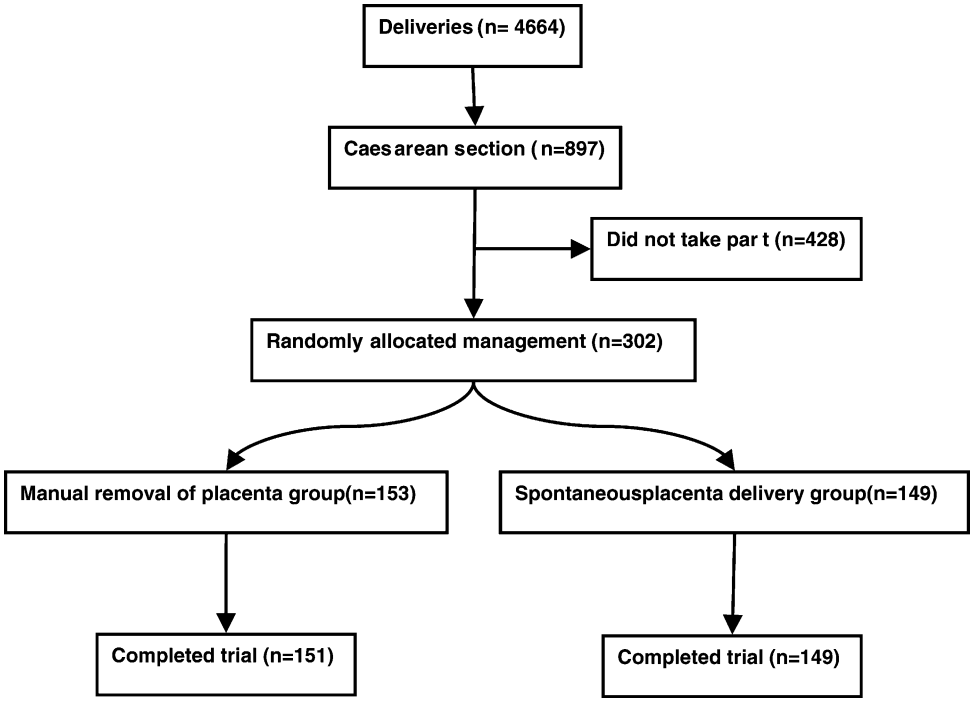

Fig. 1. Trial profile.

respectively; $P < 0.01$). The number of patients with a >10% drop in hematocrit is significantly greater in the manual removal group (RR 22.69, 95% CI 10.34–49.78). The use of more than 40 UI of oxytocin was not significantly more frequent in manual group (20 versus 11; RR 1.06, 95% CI 0.98–1.15) and the mean oxytocin dose (UI) used was more important (35.3 ± 10.59 versus 31.4 ± 7.9, respectively; $P < 0.01$).

In elective repeat cesarean group, the drop in hematocrit after manual removal of placenta was $5.68 \pm 3.89\%$ versus $2.94 \pm 2.82\%$ in the spontaneous group; this difference is significant ($P < 0.01$).

When done during labor the drop in hematocrit after manual removal of placenta was $5.64 \pm 4.3\%$ versus $2.33 \pm 2.42\%$ when placenta was removed manually ($P < 0.01$).

Table 2
Distribution of cesarean delivery indications; membranes and labor status

Indication (No.)	Manual ($n = 151$)	Spontaneous ($n = 149$)	P value
Elective repeat	75	81	0.42
Second stage failure to descend	37	36	0.94
Non reassuring fetal surveillance	20	16	0.59
Suspected IUGR	3	5	0.49
Failed VBACS	2	1	>0.999
Failed induction	2	2	>0.999
Fetal malpresentation	8	7	>0.999
Other	4	1	0.37
Rate of intact membranes	101	100	>0.999
Rate of labor	60	58	0.9

IUGR: Intra uterine growth restriction. VBACS: Vaginal birth after cesarean section.

Compared with the spontaneous group, the incidence of postpartum infectious morbidity (that we defined as postpartum endometritis, pelviperitonitis, isolated fever and surgical wound Infection) were significantly greater in the manual group (respectively 16 versus 1; relative risk 15.8, 95% CI 2.19–117.5); this incidence remained higher when only patients with intact membranes at time of abdominal delivery were considered (RR 2.09, 95% CI 1.8–2.42).

4. Discussion

To the best of our knowledge, this is the second largest trial to study the effect of placental removal method during cesarean section with blood loss as a primary outcome [13]. Our study, demonstrated that manual removal of placenta is associated with a significant difference in the change in hematocrit (5.57 ± 3.86 versus 2.65 ± 2.67, respectively; $P < 0.01$).

This is in agreement with some earlier studies: Magann et al. [8], in a clinical trial involving 100 women delivered by cesarean reported that manual extraction of the placenta was associated with a significant increase in hematocrit drop (9.6 ± 4.5 versus 3.9 ± 1.3; $P < 0.05$); the study of McCurdy et al. [12], found a significant greater measured blood loss in the manually delivered group than in the spontaneously delivered group (62 patients; 967 ± 248 ml versus 666 ± 271 ml; $P < 0.0001$). In contrast, two recent reports did not find manual removal to cause excessive blood loss: in a prospective randomized study including 375 patients Chandra et al. [13] found a similar drop in

hemoglobin (1.81 g/100 ml versus 1.72 g/100 ml N.S) this is in accordance to the findings by Atkinson et al. [14] who did not find a significant fall in hematocrit (manual group: 4.9 ± 3 versus 4.6 ± 3.4 spontaneous group) but in their study blood loss was a secondary outcome. The American College of Obstetricians and Gynecologists has defined postpartum hemorrhage as a drop of >10% in hematocrit during delivery [18]. In our study the relative risk of this situation was significantly greater in the manual removal group (RR 22.69, 95% CI 10.34–49.78); we acknowledge the limitation of hematocrit in blood loss estimation [19,20] but when done by the obstetrician who is aware of delivery placenta technique blood loss estimation can be influenced and on the other hand clinical estimation is reported to under-estimate effective blood loss when it exceeds 600 ml [5]. To perform the direct measurement method the minimum is to dispose of impermeable plastic drapes [12]. We do not have them in our institution. An alternative method is described by Nelson et al. [21], but this method is very time consuming: approximately 2–4 h per patients this appears to be prohibitive when dealing with a large sample size.

Delivery of the infant causes a sudden diminution in uterine size which is inevitably accompanied by a decrease in the area of the placenta implantation; placenta increases in thickness, but because of its limited elasticity it is forced to buckle so the cleavage takes place [22]; when uterus contracts, area of myometrial vasculature is reduced and bleeding decreases. When placenta is grasped and manually removed this physiological mechanism does not have time to take place and we think this explain in a part why bleeding is more important.

The secondary outcome of the study was postoperative infectious morbidity, we found a significant increased risk in the manual group (RR 15.8, 95% CI 2.19–117.5) even when procedure was done with intact membranes (RR 2.09, 95% CI 1.8–2.42), this is in agreement with previous studies: Atkinson et al. [14] found a relative risk of 1.4 (95% CI 1.1–1.8; $P = 0.01$), McCurdy et al. [12] an increase in endometritis rate (23% versus 3%; $P < 0.05$). Magann et al. [11] also found an increase in incidence of postcesarean Endometritis (45 versus 29; $P < 0.05$). In contrast a recent study by Chandra et al. [13] found no difference in postoperative endometritis (375 patients; 1.7% in spontaneous group versus 2.5% manual group). Here again, in absence of complete uterine contraction, Atkinson et al., [14] postulated that greater areas of the decidua basalis and myometrial vasculature are exposed to contaminated membranes increasing infectious morbidity.

5. Conclusion

Our study suggests that manual delivery of the placenta significantly increases perioperative blood loss as estimated by the mean drop in hematocrit. The postoperative infection rate was also higher in the manual group.

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