Perioperative prophylactic internal iliac artery balloon occlusion for prevention of postpartum haemorrhage in placenta praevia: a randomised controlled trial (abridged secondary publication)

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KEY MESSAGE

Prophylactic internal iliac artery balloon occlusion during caesarean section did not reduce the postpartum haemorrhage and had no effect on the maternal and neonatal morbidity for patients with placenta praevia.

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Introduction

Placenta praevia (PP) is a major cause of massive postpartum haemorrhage (PPH) and maternal mortality. 5.3% of patients with PP required hysterectomy, which is 30 times higher than those without PP.[1] The prevalence of PP and its related complications including placenta accreta spectrum have increased because of the increasing caesarean section (CS) rate, resulting in an increased cost of obstetric care.[2]

Preoperative placement of internal iliac artery (IIA) catheters followed by intraoperative arterial balloon occlusion is a popular prophylactic method to prevent PPH. After caesarean delivery of the baby and clamping of the umbilical cord, the intra-arterial balloons are inflated to occlude the arteries. They do not arrest blood flow to the uterus completely but decrease the pulse pressure distal to the occlusion site. By reducing the rate of blood loss, the haemostatic procedures could be easier and shorter. The intra-arterial catheters also allow therapeutic embolisation to be performed if bleeding persists. There are case series reporting the use of prophylactic balloon catheter insertion in PP and accreta spectrum.[3] In a randomised controlled trial on this approach in placenta accreta spectrum, the beneficial role of balloon occlusion was not supported, and procedure-related adverse effects were noted in 15.4% of cases.[4] Evidence of IIA on PP is not yet available. Hence the current study aims to determine whether prophylactic IIA balloon occlusion during CS for PP can reduce PPH and other maternal morbidity such as blood product transfusion, need of hysterectomy, and intensive care unit admission.

Methods

This was an open-label randomised controlled trial conducted at a university hospital in Hong Kong. This trial was approved by the Joint Chinese University of Hong Kong-New Territories East Cluster Clinical Research Ethics Committee (CRE ref. no.: 2015.260-T). Pregnant women who were diagnosed to have a low-lying placenta in the mid-trimester morphology scan were scheduled for ultrasonography at 34 weeks of gestation to determine the placental location. Pregnant women who were diagnosed to have PP at 34 weeks and required CS were invited to participate. Exclusion criteria were (1) age of <18 years, (2) mentally handicapped or severely ill, (3) fetus diagnosed with in-utero death, (4) contraindication for IIA balloon occlusion, (5) unstable clinical condition in which patients could not be sent to interventional radiology suite for pre-operative internal IIA catheter placement, (6) unable to understand English or Chinese to give consent, and (7) ultrasonic features suggestive of placenta accreta spectrum. PP was defined as lower placenta edge within 2 cm from the internal os, and the grading of PP was defined according to the Royal College of Obstetricians and Gynaecologists guideline.[2] Participants were reassessed within 1 week before the operation, during which transvaginal ultrasonography was repeated to double-check the distance between the placental edge and the internal os. CS was arranged for women between 37 and 38 weeks of gestations if PP persisted at this gestation. Those with placental edge >2 cm away from the internal os were allowed to undergo vaginal delivery. Eligible participants were randomly assigned to either IIA balloon occlusion (occlusion group, n=20)

or standard management (control group, n=20) at 1:1 ratio.

Those randomised to the occlusion group underwent IIA balloon catheter placement in the interventional radiology suite by an interventional radiologist before CS, as described in the literature.[4] They were then sent to the operating theatre for CS. After the baby was delivered, the occlusion balloons were inflated immediately. The placenta was then delivered and CS was continued in the usual manner. After haemostasis was achieved, the balloon was deflated. If bleeding could not be well controlled and uterine artery embolisation was indicated, the balloons were left inflated until embolisation was performed by the interventional radiologist. Otherwise, the vascular sheaths were left in situ for 12-24 hours after surgery in case emergency embolisation was required. All CS of both groups were performed by a qualified obstetrician with experience and expertise in operating with PP.

The primary outcome was the reduction in intrapartum blood loss in the occlusion group. Secondary outcomes included any drop of haemoglobin level on day 1 and day 3 after the operation, the amount of blood products transfused, the incidence of hysterectomy, maternal complications (including renal failure, ischaemic liver, disseminated intravascular coagulation, and adult respiratory distress syndrome), days of stay in the hospital after the operation, admission to an intensive care unit, and maternal death.

The sample size calculation was based on a reduction of blood loss by half in the IIA balloon occlusion group as compared with the control group. Based on a previous report[3] and our observation, the average blood loss in patients undergoing caesarean sections for PP was 800-1000 mL (standard deviation, 300 mL). To detect a difference of 400 mL blood loss, with a power of 80% and a significance level of 5%, 10 subjects were required in each arm. 20% more subjects were added to the sample size because of the skewed distribution of blood loss. The sample size was increased to 16 in each arm to allow abandoning of the procedure because of unforeseen emergency. Statistical analysis was performed using the intention-to-treat (ITT) method and was repeated using the on-treatment approach.

Results

The two groups were comparable in terms of baseline characteristics, except that the occlusion group had more previous CS than did the control group (60.0% vs 10.0%, P=0.019, Table 1). Four women in the occlusion group did not have the planned IIA procedure. Three of them required emergency CS because of severe antepartum haemorrhage before the planned IIA balloon catheter insertion. They were included in the ITT analysis but were excluded from the analysis by the on-treatment method. The remaining one was reassessed at 36 weeks and showed that the placental edge was 2 cm from the internal os. She opted for a trial of vaginal delivery and thus was excluded.

In the ITT analysis, the two groups were comparable in terms of intraoperative blood loss and

TABLE 1. Baseline characteristics of the occlusion group and the control group.

Baseline characteristic	Occlusion group (n=20)*	Control group (n=20)*	P value
Maternal age, y	35.3 (31.5-37.6)	36.6 (32.7-39.1)	0.289
Gestational age, wk	36.6 (35.2-37.2)	36.1 (34.8-37.7)	0.968
Nulliparous	10 (50.0)	10 (50.0)	0.999
Previous caesarean section	6 (60.0)	1 (10.0)	0.019
Body mass index at caesarean section, kg/m^2	27.0 (24.9-29.4)	26.9 (24.5-29.7)	0.862
Assisted reproduction pregnancy	1 (5.0)	2 (10.0)	0.999
Active smoker	4 (20.0)	1 (5.0)	0.342
Gestational diabetes	3 (15.0)	4 (20.0)	0.999
Pregnancy-induced hypertension	2 (10.0)	0 (0)	0.487
Placenta praevia grade at recruitment			0.999
I & II	5 (25.0)	6 (30.0)	
III & IV	15 (75.0)	14 (70.0)	
Placental site			
Anterior	7 (35.0)	4 (20.0)	0.479
Non-anterior	13 (65.0)	16 (80.0)	
Antepartum haemorrhage before procedure	11 (55.0)	10 (50.0)	0.752

* Data are presented as median (interquartile range) or No. (%)

all other maternal and neonatal outcomes, except that the use of carboprost was significantly higher in the occlusion group than in the control group (36.8% vs 5.0%, P=0.020, Table 2). After excluding the three cases that required an emergency CS before the planned IIA procedure, the results remained the same, except that the occlusion group had a significantly lower base excess than the control group (-5.10 [-9.13 to -2.98] vs -2.90 [-5.00 to -1.00], P=0.017), but the difference was not clinically significant.

TABLE 2. Intra-operative, post-operative, neonatal, and maternal outcomes analysed using the intention-to-treat method.

Outcome	Occlusion group (n=19)*	Control group (n=20)*	P value
Intra- and post-operative outcome			
Intra-operation blood loss, mL	1451 (1024-2388)	1454 (888-2300)	0.945
Postpartum haemorrhage ≥1500 mL	9 (47.4)	10 (50.0)	0.869
Postpartum haemorrhage ≥1000 mL	15 (78.9)	15 (75.0)	0.999
Length of surgery, minutes	49 (30-62)	37 (30-51)	0.204
Blood transfusion at operation	11 (57.9)	10 (50.0)	0.621
Transfusion of packed red blood cells	11 (57.9)	10 (50.0)	0.621
Units of packed red blood cells transfused	2 (0-4)	0.5 (0-2.75)	0.550
Transfusion of platelets	4 (21.1)	5 (25.0)	0.999
Units of platelets transfused	0 (0-4)	0 (0-3)	0.945
Transfusion of fresh frozen plasma	2 (10.5)	4 (20.0)	0.661
Units of fresh frozen plasma transfused	0	0	0.411
Transfusion of cryoprecipitate	1 (5.3)	1 (5.0)	0.999
Units of cryoprecipitate transfused	0	0	0.999
Syntocinon infusion during operation	17 (89.5)	20 (100.0)	0.231
Misoprostol during operation	7 (36.8)	5 (25.0)	0.501
Carboprost during operation	7 (36.8)	1 (5.0)	0.020
Intrauterine balloon during operation	0	1 (5.0)	0.999
Compression suture during operation	6 (31.6)	4 (20.0)	0.480
Uterine artery or internal iliac artery ligation during operation	2 (10.5)	0	0.231
Uterine artery embolisation after operation	2 (10.5)	0	0.231
Hysterectomy	0	0	-
Maternal outcome			
Post-operative hospital stay, d	4.0 (3.0-6.0)	3.0 (3.0-4.0)	0.070
Intensive care unit admission	0	1 (5.0)	0.999
Rebleeding after operation	0	0	-
Relaparotomy	0	0	-
Maternal death	0	0	-
Occlusion-related complications	0	0	-
Other maternal complications (adult respiratory distress syndrome, renal failure, ischaemic liver and disseminated intravascular coagulation)	0	0	-
Neonatal outcomes			
Birthweight, g	2690 (2530-2980)	2895 (2673-3190)	0.149
Male	10 (52.6)	11 (55.0)	0.882
Apgar score <7 at 5 minutes	0	1 (5.0)	0.999
Umbilical cord arterial pH	7.29 (7.26-7.30)	7.29 (7.27-7.32)	0.459
Umbilical cord arterial base excess	-4.50 (-8.93 to -2.3)	-2.90 (-5.0 to -1.0)	0.109
Neonatal intensive care unit admission	1 (5.3)	1 (5.0)	0.999

* Data are presented as median (interquartile range) or No. (%)

Discussion

Our study is the first randomised controlled trial on the use of prophylactic IIA balloon occlusion in women with PP undergoing CS. It showed that IIA balloon occlusion did not reduce the obstetrics blood loss during CS or had any significant effect on the maternal or perinatal outcomes.

The study design of randomised controlled trial avoided selection bias and minimised confounding factors. However, the nature of the treatment made double blinding unfeasible. Nonetheless, intra-operative blood loss was measured objectively. Thus, the median blood loss of 1400 to 1500 mL in our study was higher than that in another study.[3] The sample size of 20 per group was nearly double that of a RCT for placenta accrete (12 per group).[4] Our sample size was estimated to detect a difference of 400 mL blood loss, which is considered clinical significant. The median blood loss in both groups was within the range of 1400 to 1500 mL; it is not likely that further study with a larger sample size can demonstrate a clinically significant difference. Nonetheless, a study with a larger cohort may help to identify any predictive factor for the success or failure of IIA prophylaxis. Although there were more women with previous CS in the occlusion group, it is not likely to be a confounding factor in blood loss, as placenta accreta spectrum was excluded in our study. Although four cases in the occlusion group did not have the assigned treatment, the result was the same in terms of the intention-to-treat analysis or the on-treatment analysis.

In a retrospective study comparing 42 women with PP managed with IIA balloon occlusion and 26 women without PP, the incidence of heavy blood loss (≥1000 mL) during CS was significantly lower in the former group (38% vs 69%), although the median amount of blood loss was not significantly different (800 mL vs 1000 mL).[3] However, our results did not support their findings. IIA balloon occlusion did not add any beneficial effect because surgical haemostasis was adequate for most of the PP cases, and collateral circulation such as ovarian arterial supply could not be controlled by IIA occlusion.

Infra-renal intra-aortic balloon has been proposed for control of obstetric haemorrhage. A retrospective study comparing pre-CS aortic balloon occlusion and IIA balloon occlusion suggested that the former may be a better prophylactic choice for patients with PP; the median blood loss was reduced from 3750 mL with IIA occlusion to 1600 mL with aortic occlusion.[5] However, the blood loss was not significantly different in patients with accrete or increta. Yet RCT is required to investigate the value of aortic occlusion in accreta spectrum or PP.

Safety of IIA catheterisation-related complications is a major concern. In our study, no patient had catheterisation-related complication. IIA balloon occlusion appears to be a safe treatment for women with PP.

Conclusion

Prophylactic IIA balloon occlusion for patients with PP undergoing CS did not reduce PPH or had any effect on maternal or neonatal morbidity. Although perioperative placement of internal iliac artery occlusion balloon is a safe and minimally invasive procedure, unnecessary radiological intervention should be avoided.

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Disclosure

The results of this research have been previously published in:

1. Yu SCH, Cheng YKY, Tse WT, et al. Perioperative prophylactic internal iliac artery balloon occlusion in the prevention of postpartum hemorrhage in placenta previa: a randomized controlled trial. Am J Obstet Gynecol 2020;223:117.e1-117.e13.

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