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CLINICAL ARTICLE

Use of second-line therapies for management of massive primary postpartum hemorrhage

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ABSTRACT

Objective: To determine rates of use and success of second-line therapies for massive primary postpartum hemorrhage (PPH). *Methods:* A retrospective cohort study was conducted among 91 women who gave birth at Kwong Wah Hospital, Hong Kong, between January 1, 2006, and December 31, 2011. Inclusion criteria were gestational age of at least 24 weeks and massive PPH (defined as blood loss ≥1500 mL within 24 hours after birth). Second-line therapies assessed were uterine compression sutures, uterine artery embolization, and balloon tamponade after failure of uterine massage and uterotonic agents to stop bleeding. *Results:* The rate of massive PPH was 2.65 per 1000 births. Second-line therapies were used among 42 women with PPH, equivalent to a rate of 1.23 per 1000 births. Only 21.4% of the women who received second-line therapies required rescue hysterectomy. A rising trend was observed for the use of second-line therapies, whereas the incidence of rescue hysterectomy and estimated blood loss were found to concomitantly decrease. *Conclusion:* Increasing use of second-line therapies among women with massive PPH was associated with a decreasing trend for rescue hysterectomy. Obstetricians should, therefore, consider all available interventions to stop PPH, including early use of second-line options.

1. Introduction

Primary postpartum hemorrhage (PPH) is an appreciable cause of maternal morbidity and mortality worldwide. According to the WHO, PPH accounts for approximately one-quarter of all maternal deaths globally and for approximately half of all postpartum deaths in low-income countries [1].

The MOMS-B survey [2], which was conducted in 11 European countries in the 1990s, found a total incidence of severe PPH of 4.6 per 1000 births. The MOMS-B researchers defined severe PPH as measured blood loss of at least 1500 mL, blood loss requiring plasma expanders and/or blood products 2500 mL in 24 hours, or blood loss leading to maternal death. However, the incidence of PPH varies greatly around the world [3]. In Hong Kong, the incidence of severe PPH (defined as an estimated blood loss ≥2000 mL) increased from 2.49 to 3.88 per 1000 births from 2006 to 2010 [4]. Peripartum hysterectomy may be performed within 24 hours after birth in cases requiring definitive management of intractable primary PPH. The UK Obstetric Surveillance System reported a peripartum hysterectomy rate of 0.41 per 1000 births [5], whereas the rates in Hong Kong during the period 2006–2010 ranged from 0.55 to 0.68 per 1000 births [4].

In 2012, the WHO revised its recommendations for the prevention and treatment of PPH, stating that second-line therapies, including surgery, uterine artery embolization (UAE), and intrauterine balloon tamponade, could be adopted when uterotonic agents fail [6]. However, no evidence is available to suggest that any second-line treatment is superior to the others for the management of massive PPH and no consensus exists about the optimal use and timing of these treatments.

The aim of the present study was to evaluate the use of second-line therapies and their effects on maternal outcomes following massive PPH.

2. Materials and methods

A retrospective cohort study was conducted among women who gave birth at Kwong Wah Hospital, Hong Kong, between January 1, 2006, and December 31, 2011. Inclusion criteria were gestational age of at least 24 weeks and massive primary PPH, which was defined as an estimated blood loss of at least 1500 mL within 24 hours after

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birth. The protocol of the present study was approved by the Kowloon West Cluster Research Ethics Committee, Hospital Authority, Hong Kong. Patient data were collected anonymously and coded for statistical analysis. Therefore, no consent was required in advance.

Kwong Wah Hospital has a consultant-led maternity center staffed by experienced midwives, residents, and clinical fellows. Approximately 6000 deliveries are performed each year. Uncomplicated vaginal deliveries are conducted by midwives. Instrumental deliveries and cesarean deliveries are performed by residents under the direct or indirect supervision of clinical fellows or consultants. Overall, the rates of cesarean delivery and instrumental delivery at Kwong Wah Hospital every year are 21% and 3%–4%, respectively.

Blood lost by the mother during vaginal delivery was collected in a bucket placed beneath the woman's perineum. Blood volume was estimated with a measuring jar. Blood on bed sheets or pads was estimated subjectively by midwives or doctors. Blood lost in the operating theater was usually sucked into the measuring bottle and objectively measured, whereas blood on used gauzes was estimated by the theater staff according to a pictorial graph.

Active management of the third stage of labor was adopted for all women. Routine intramuscular oxytocin/ergometrine or intravenous oxytocin was given to every woman after delivery of the anterior shoulder. Other uterotonic agents available at Kwong Wah Hospital were carboprost, rectal misoprostol, and sulprostone (before the suspension of its use in 2008). These drugs were considered to be first-line therapy for massive PPH; second-line therapies were used if first-line therapies failed to stop bleeding.

The second-line therapies evaluated in the present study were uterine compression sutures, UAE, and balloon tamponade. Uterine compression sutures in use at Kwong Wah Hospital were the B-Lynch (first used in 2006) [7], Hwu (first used in 2010) [8], Cho square [9], and Hayman [10]. Interventional radiologists performed UAE during office hours or by special arrangement before scheduled surgeries in selected cases. The procedure was performed in the operating theater or the radiology department. Only Sengstaken–Blakemore tubes were available for balloon tamponade. The first case of massive PPH to be treated with balloon tamponade was in 2008. Neither uterine artery nor iliac artery ligation were performed during the present study period.

Demographic data, details of delivery, and estimated blood loss were entered into an electronic database. Index cases were identified from this database. The chief investigator (L.L.C.) reviewed the medical records of these cases and gathered data for each patient on a standardized form. The data were coded and then analyzed using SPSS version 20.0 (IBM, Armonk, NY, USA). Data were analyzed in groups with or without second-line therapy. Data were also analyzed according to the type of second-line therapy used (uterine compression sutures, UAE, or balloon tamponade). Treatment success was defined as no requirement for rescue hysterectomy. The success rate was calculated as a percentage with a 95% confidence interval. The P values were calculated using the χ^2 test for nominal data or the Mann–Whitney U test for non-parametric continuous data. A P value of 0.05 or below was considered statistically significant.

3. Results

A total of 34 296 women delivered at Kwong Wah Hospital during the present study period, 91 of whom experienced massive PPH (2.65 per 1000 births). Characteristics of the women with massive PPH are shown in Table 1, while their clinical management is outlined in Fig. 1.

In all, 489 twin pregnancies were recorded; 8 of these women experienced massive PPH (16.4 per 1000 twin births). Of the 91 women with massive PPH, 13 (14.3%) required hysterectomy (0.38 per 1000 births). The time to decision for hysterectomy was 18–420 minutes after birth.

Table 1
Characteristics of the women with massive primary postpartum hemorrhage (n = 91).[a]

Characteristic	Distribution
Age, y	33.3 ± 4.6
BMI	21.6 ± 3.2
Parity	0 (0–3)
Gestational age at delivery, wk	38.3 (26.6–41.4)
Multiple pregnancy	8 (8.8)
Cases that occurred during non-office hours	30 (33.0)
Length of hospital stay, d	6 (3–54)
Mode of delivery	
Spontaneous vaginal	21 (23.1)
Instrumental (vacuum or low forceps)	4 (4.4)
Elective cesarean	38 (41.7)
Emergency cesarean	28 (30.8)
Cause of massive PPH	
Uterine atony	38 (41.8)
Placenta previa	14 (15.3)
Placenta accreta	7 (7.7)
Lower genital tract bleeding	9 (9.9)
Uterine wound bleeding	15 (16.5)
Others (uterine rupture, coagulopathy, retained placenta)	8 (8.8)
Outcomes	
Estimated blood loss, L	2 (1.5–20)
Received packed-cell transfusion	79 (86.8)
Volume transfused, pints of packed cells	4 (0–77)
Disseminated intravascular coagulopathy	16 (17.6)
Hysterectomy	13 (14.3)

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by the square of height in meters); PPH, primary postpartum hemorrhage.
[a] Values are given as mean ± standard deviation, median (range), or number (percentage).

A single maternal death occurred in the present study cohort. The affected woman had eclampsia; she underwent normal vaginal delivery, which was complicated by excessive blood loss (6.2 L). Treatment was initiated with uterotonic agents, balloon tamponade, and recombinant activated clotting factor VII (rFVIIa). The episode of massive PPH was controlled but the woman died 11 days after delivery; the primary causes of death were eclampsia and intracerebral hemorrhage.

Hysterectomy was performed directly after failure of uterotonic agents among 4 women. Two of these women were multiparous and underwent cesarean delivery for placenta accreta. Both women consented to a hysterectomy if morbidly adherent placenta or massive hemorrhage were encountered. The third woman had 1 previous cesarean delivery with uterine tear and underwent emergency surgery owing to early onset of labor. This woman developed uterine atony with massive PPH and multiple uterotonic agents and rFVIIa were given intraoperatively. The decision to perform a hysterectomy was taken in light of uncontrolled bleeding; total blood loss was 10.5 L. The fourth woman underwent an uneventful emergency cesarean delivery for cord prolapse at night. However, heavy vaginal bleeding and uterine atony were noted by clinical staff on the postnatal ward. Hysterectomy was subsequently performed owing to persistent hypotension.

All women with massive PPH were initially treated by intravenous infusion of oxytocin. Additional uterotonic agents were administered in 92.9% of cases with second-line therapies. Second-line therapies were used to treat massive PPH among 42 women (1.23 per 1000 women). The characteristics of the women treated with different second-line therapies were not significantly different. In all, 9 (21.4%) of the women who received second-line therapy required hysterectomy owing to treatment failure. The outcomes and success rates of the second-line therapies are shown in Fig. 2. Uterine compression suture was the most frequently used second-line therapy. When used alone, the overall success rate of this approach was 71.4% (Fig. 3), regardless of the cause of massive PPH or the type of compression suture.

Table 2 shows the causes of massive PPH and modes of delivery among the present study group. The causes of massive PPH were