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# **Active Management in the Prevention of Postpartum Hemorrhage**

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## **Abstract**

Postpartum hemorrhage (PPH), an extensive threat to maternal fatalities. Defined as blood loss of more than 500 ml following vaginal delivery, or more than 1000 ml following caesarean delivery in the first 24 hours of birth. To test the hypothesis that the use of active management of third stage of labor (AMTSL) - a combination of, administration of uterotonics, early cord clamping, and controlled cord traction used to speed up delivery of the placenta with the aim of reducing blood loss for lowering the rates of primary PPH - compared to expectant management. This hypothesis was proven through different experiments using descriptive cross-sectional study, descriptive statistical analysis, and lastly cohort analysis to be able to achieve an unbiased settlement, by using population studies. Active management of the third stage reduced the risk of hemorrhage greater than 1000ml at the time of birth, in a population of women at mixed risk of excessive bleeding, but adverse effects were identified. Women should be informed on the benefits and harms of both methods to support informed choice. It is crucial to review the individual components of third-stage management, given the concerns about early cord clamping and the potential adverse effects of some uterotonics. A Recommendation is made for clinical guidelines in hospital settings to advocate active management (with oxytocin alone). However, decisions about individual care should take into account the weights placed by pregnant women and their caregivers on blood loss, compared with an intervention-free third stage.

## Introduction

Postpartum hemorrhage (PPH) is a risk factor for all pregnant women who have progressed beyond 20 weeks' gestation. Although maternal mortality rates have decreased drastically in developed countries, postpartum hemorrhage remains the leading cause of maternal death elsewhere. It is defined as blood loss of more than 500 ml following vaginal delivery, or more than 1000 ml following cesarean delivery.<sup>(1)</sup> A loss of these amounts within 24 hours of delivery is termed early or primary PPH; whereas such losses are termed late or secondary PPH if they occur 24 hours after delivery. It should be noted that estimating blood loss at time of delivery is generally inaccurate. Studies have suggested that caregivers consistently underestimate the amount of actual blood loss. Some might suggest that PPH should be diagnosed with any amount of blood loss that threatens the hemodynamic stability of the woman, keeping in mind that not all patients have the same coping capacity. A healthy woman has a 30-50% increase in her blood volume in a normal singleton (giving birth to one child) pregnancy, and is therefore much more tolerant of blood loss than a woman with a preexisting condition such as anemia, an underlying cardiac condition, or a volume-contracted condition.<sup>(2)</sup> Lastly, as aforementioned the diagnoses of PPH is applied on pregnancies that have made it beyond the 20 weeks' gestation point (end of the second trimester). Deliveries at less than 20 weeks' gestation age are termed as spontaneous or induced abortions. Any bleeding related to a spontaneous abortion may have symptoms, causes, and management in common with those of PPH, but is not diagnosed as PPH.<sup>(3)</sup>

A Practice Bulletin from the American College of Obstetricians and Gynecologists places the estimate at 140,000 maternal deaths per year or 1 woman every 4 minutes.<sup>(4)</sup> Failure of the uterus to contract and retract following delivery of the baby, known as *uterine atony*, is the most common cause of PPH by a wide margin, although PPH has many potential causes uterine atony is the most frequent of them. Another major risk factor of PPH is previous pregnancy, every effort should be made to determine its severity and cause. A famous mnemonic in the obstetrician-gynecologist community known as the "4 T's": Tone, Tissue, Trauma, & Thrombosis; is used as a way of remembering the causes of PPH.

Physiological management of the third stage, also known as expectant management of the third stage refers to spontaneous placental delivery by maternal efforts, no uterotonic drugs are administered to assist in the process. Retention of the placenta for longer than 60 minutes of physiological management, or signs and symptoms of hemorrhage are awaited before active management is used. Active management of the third stage of labor involves the use of interventions including: the use of uterotonics (preferably oxytocin) immediately upon delivery of the baby; early clamping of the umbilical cord; and controlled cord traction with uterine counter-traction when the uterus is well contracted known as the “Brandt-Andrews maneuver” to expedite delivery of the placenta with the aim of reducing blood loss.<sup>(4)</sup> The frequency of PPH is highly related to the management of the third stage of labor. This is the period from the completed delivery of the baby until the completed delivery of the placenta. Data from several sources, including several large randomized trials performed in developed countries, indicate that the occurrence rate of PPH of more than 500 ml following vaginal delivery is approximately 5% when active management is used versus 13% when expectant management is used; and the prevalence rate of PPH of more than 1000 ml in cesarean is approximately 1% when active management is used versus 3% when expectant management is used.<sup>(3)</sup>

The pregnancy-related mortality ratio in the United States was 17.3 deaths per 100,000 live births in 2013. National statistics suggest that approximately 11.4% of these deaths are caused by PPH. In industrialized countries, PPH usually ranks in the top 3 causes of maternal mortality, along with embolism and hypertension. In the developing world, several countries have maternal mortality rates in excess of 1000 women per 100,000 live births, and World Health Organization statistics suggest that 60% of maternal deaths in developing countries are due to PPH, accounting for more than 100,000 maternal deaths per year.<sup>(4)</sup>

In a recent randomized trial in the United States, birth weight, labor induction and augmentation, chorioamnionitis, magnesium sulfate use, and previous PPH were all positively associated with increased risk of PPH. Additionally, PPH is also associated with obesity, in a study by Blomberg, the risk of atonic uterine hemorrhage rapidly increased with increasing BMI; in women with a BMI over 40, the risk was 5.2% with normal delivery and 13.6% with instrumental delivery.<sup>(5)</sup>

In developing countries, a number of factors contribute to the increased frequency of the negative outcomes of PPH. The first is mostly reflected by the rates for expectant and active management (as mentioned before), due to the lack of availability of medication used in active management of the third stage. The second factor is the lack of experienced caregivers who have the ability to successfully manage postpartum hemorrhage if it happened. Additionally, the same drugs used in the active management of the third stage are also the primary drugs used in the treatment of PPH. Lack of blood transfusion services, anesthetic services, and operating capabilities also play a role.<sup>(2)</sup>

The aim of this report is to highlight the use of active management instead of expectant management in the third stage of labor for all women who are giving birth.

## **Materials and Methods**

This report was gathered from different articles and reviews found on google scholar, PubMed, the British Medical Journal, and the Cochrane Library. Considering case study I, titled “Active vs. expectant management in the third stage of labor.” was collected from PubMed by searching the Cochrane Pregnancy and Childbirth Group trials register.<sup>(1)</sup> Next, case study II was collected from Cochrane Database System Revision titled “Active versus expectant management in the third stage of labor.” Lastly, the third case study titled “The Bristol third stage trial: Active versus physiological management of third stage of labor.” Was collected from the British Medical Journal.<sup>(2)</sup> The formerly stated articles all tested the same methodology, that is the use of active management during the third stage of labor. Descriptive statistical analysis was used to present data, many of the articles reviewed used cohort analysis.

### **Case study I**

Randomised trials comparing active and expectant management of the third stage of labor in women who were expecting a vaginal delivery in the setting of a maternity hospital.

### **Case study II**

Randomised and quasi-randomised controlled trials comparing active versus expectant management of the third stage of labor included seven studies involving 8247 women, all undertaken in hospitals, six in high-income countries and one in a low-income country. Random effects were used in the analyses because of clinical heterogeneity.

### **Case study III**

Randomised trial of active versus physiological management took place at a maternity hospital. Women entered trial on admission to labor ward. Sample size of 3900 was prearranged, a planned interim analysis after the first 1500 deliveries showed continuing high postpartum hemorrhage rate in physiological group and study was stopped. 1695 were admitted to trial and assigned randomly to physiological (849) or active (846) management.

## **Results**

### **Case study I**

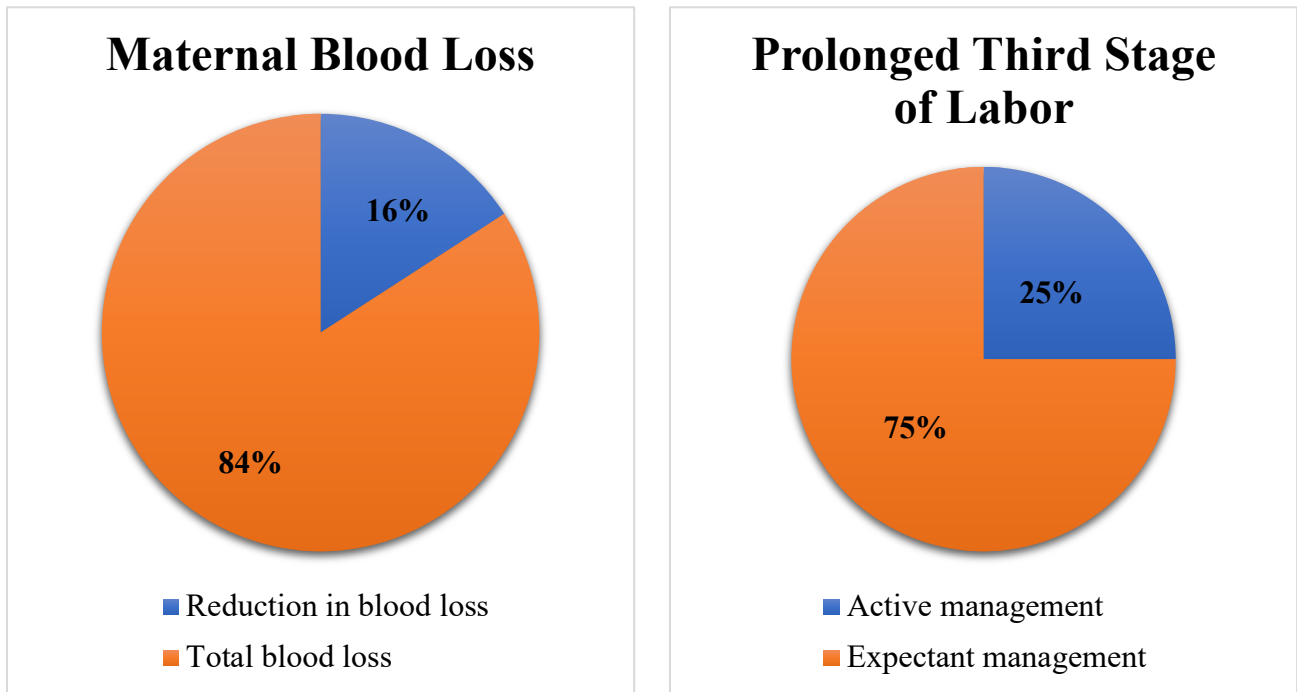
Compared to expectant management, active management was associated with the following reduced risks: maternal blood loss (weighted mean difference -79.33 ml, 95% confidence interval -94.29 to -64.37) (Figure 1); postpartum hemorrhage of more than 500 ml (relative risk 0.38, 95% confidence interval 0.32 to 0.46); prolonged third stage of labor (weighted mean difference -9.77 minutes, 95% confidence interval -10.00 to -9.53). Active management was associated with an increased risk of maternal nausea (relative risk 1.83, 95% confidence interval 1.51 to 2.23), vomiting and raised blood pressure (probably due to the use of ergometrine a uterotonic).

### **Case study II**

The evidence suggested that for women at mixed levels of risk of bleeding, active management showed a reduction in the following: average risk of maternal primary hemorrhage at time of birth more than 1000 ml (average risk ratio (RR) 0.34, 95% confidence interval (CI) 0.14 to 0.87, three studies, 4636 women); maternal haemoglobin (Hb) less than 9 g/dL following birth (average RR 0.50, 95% CI 0.30 to 0.83, two studies, 1572 women). Active management also showed a significant decrease in primary blood loss greater than 500 ml, mean maternal blood loss at birth, maternal blood transfusion, and therapeutic uterotonics during the third stage. An increase in maternal diastolic blood pressure, vomiting after birth, after-pains, use of analgesia from birth up to discharge from the labour ward and more women returning to hospital with bleeding (outcome not pre-specified).

### Case study III

Incidence of PPH was 5.9% in active management group and 17.9% in physiological group (odds ratio 3.13; 95% confidence interval 2.3 to 4.2.) In physiological group third stage was longer (median 15 min vs. 5 min) (Figure 2). More women needed therapeutic uterotonics (29.7% vs. 6.4%). When women allocated to and receiving active management (840) were compared with those who actually received physiological management (403) active management still produced lower rate of postpartum hemorrhage (odds ratio 2.4; 95% CI 1.6 to 3.7).



**Figure 1.** Case study I; weighted mean difference. **Figure 2.** Case study III; median time.

## Discussion

The report's findings demonstrated that active management practiced in this trial reduced the risk of PPH and shortened third stage period. <sup>(1)</sup> In terms of blood loss, PPH and other serious complications of the third stage routine active management proved to be superior to expectant management. Although associated with increased risk of unpleasant side effects, women expecting to deliver a baby by vaginal delivery in a maternity hospital should be recommended to active management. Consequences are less clear for domiciliary practice used more often in developing and industrialized countries. Maternal anaemia (Hb less than 9 g/dL) following birth was reduced by use of active management; however, uncertainty lies in women at low risk of excessive bleeding. It is ambiguous whether there was a difference between active and expectant management in this specific situation. <sup>(2)</sup> Overall prevention of PPH reduced the risk of hemorrhage greater than 1000ml at the time of birth in a population of women at mixed risk of severe bleeding; but harms such as pain, nausea, vomiting, return to hospital due to bleeding and postnatal hypertension where ergometrine is used were identified. Some may argue that although adverse effects were recognized, compared to the major severe fatal outcomes of PPH the risks taken presented less harm to patients. <sup>(5)</sup>

Efforts to reduce adverse effects such as the use of a longer-acting oxytocin derivative, *Carbetocin*, in the prevention of PPH. In the context of caesarean delivery *Carbetocin* is licensed specifically for the indication of prevention of PPH in the UK. <sup>(3)</sup> Compared with *oxytocin*, *Carbetocin* resulted in a statistically major reduction in the need for further uterotonics for those undergoing a caesarean delivery. However, there were no statistically significant differences between *Carbetocin* and oxytocin in terms of risk of PPH. <sup>(2)</sup> Active management for delivery of the placenta results in a decrease in incidence of PPH and retained placenta. Additionally, it resulted in less need for uterotonic drugs. <sup>(5)</sup> Oxytocin administration and Controlled cord traction were the most utilized components of AMTSL. This can be explained by the fact that these two components were in the former guidelines of management of third stage of labor. The former guidelines recommended intramuscular *oxytocin* should be administered with the birth of the anterior shoulder, or immediately after the birth of the baby and before the cord is clamped and cut; current guidelines recommend oxytocin administration strictly within a minute of childbirth.



Given the concerns about the potential adverse effects of some uterotonics, and early cord clamping, it is crucial to review constituents of third-stage management for each individual; patient education for expecting mothers on the benefits and harms of both methods, encourages informed choice.

As visual estimation often underestimates blood loss, more accurate methods may be used, such as blood collection drapes for vaginal deliveries and the weighing of swabs. However, a study comparing visual estimation of blood loss with the use of a collector bag after vaginal delivery concluded that the latter did not significantly reduce the risk of severe PPH.<sup>(4)</sup> Participating in clinical reconstructions may encourage early diagnosis and prompt treatment of PPH. Clinical signs and symptoms of hypovolemia should be included in the assessment of PPH. However, clinicians should be aware that the physiological increase in circulating blood volume during pregnancy means that the signs of hypovolemic shock become less sensitive in pregnancy. In pregnancy, pulse and blood pressure are usually maintained in the normal range until blood loss exceeds 1000 ml; tachycardia, tachypnoea and a slight recordable fall in systolic blood pressure occur with blood loss of 1000–1500 ml. <sup>(4)</sup> A systolic blood pressure below 80 mmHg, associated with worsening tachycardia, tachypnoea and altered mental state, usually indicates a PPH in excess of 1500 ml.<sup>(2)</sup>

## **Conclusion**

Active management of the third stage including its three components, has proven to be an extra measure that can save a mother's life. With its uncompromising adverse effects, caregivers are not putting patient's life at risk, but instead are ensuring and enforcing safe, preventative measures for both the mother and her child. Active management of the third stage is on the rise to becoming a mandatory procedure, soon to be implemented by all guidelines.

## **Future Work**

We recommend that clinical guidelines in hospital settings advocate active management. However, decisions about individual care should take into account the weights placed by pregnant women and their caregivers on blood loss compared with an intervention-free third stage.

## Reference

1. Begley C, Gyte G, Devane D, McGuire W, Weeks A, Biesty L. Active versus expectant management for women in the third stage of labour. Cochrane Database of Systematic Reviews. 2019. [cited 9 January 2020].
2. Prendiville W, Harding J, Elbourne D, Stirrat G. The Bristol third stage trial: active versus physiological management of third stage of labour. *BMJ*. 1988;297(6659):1295-1300. [cited 9 January 2020].
3. Rogers J, Wood J, McCandlish R, Ayers S, Truesdale A, Elbourne D. Active versus expectant management of third stage of labour: the Hinchingsbrooke randomised controlled trial. *The Lancet*. 1998;351(9104):693-699. [cited 9 January 2020].
4. ACOG Practice Bulletin: Clinical Management Guidelines for Obstetrician-Gynecologists Number 76, October 2006: postpartum hemorrhage. 2020 [cited 9 January 2020].
5. Government of USA - ClinicalTrials.gov. Clinicaltrials.gov. 2020 [cited 9 January 2020].