Introduction

Postpartum hemorrhage is defined as blood loss greater than 500 mls after giving birth vaginally or as blood loss greater than 1000 mls after cesarean section; however the quantity of blood loss does not always accurately define the pathology since for certain individuals a loss of as much as 500 mls after vaginal birth is considered within normal limits[1].

Based on an estimated blood loss greater than 500 mls, postpartum hemorrhage has been found in about 5% of deliveries [2].

The World Health Organization (WHO) estimated that 529,000 women died from obstetric causes in year 2000 [3].The immediate postpartum period is the most critical time during which almost 90% of deaths occur within the first 4 hours of delivery [4]. Postpartum hemorrhage which afflicts approximately 14 million women annually caused a quarter of the deaths. Most of these deaths occur in the resource poor countries of Africa and Asia, particularly in rural areas [4].

In developing countries, the maternal mortality ratios commonly range from 100 to 1000/100,000 live births, whereas in industrialized countries they range mostly from 3-15/100,000. This enormous difference represents one of the greatest inequalities in all of public health statistics[4].

The prevalence rate of PPH of more than 500 mls is approximately 5% when active management is used versus 13% when expectant management is used. The prevalence rate of PPH of more than 1000 mls is approximately 1% when active management is used versus 3% when expectant management is used [5].

Active management of 3rd stage of labor which includes use of oxytocic drugs, early cord clamping, and placental delivery by controlled cord traction has been demonstrated to be an effective prophylactic measure against postpartum hemorrhage [6].

The uterotonic drugs used in active management of the third stage of labor trials include oxytocics: oxytocin, ergometrine maleate, and combinations of the two (syntometrine). All of which must be administered by injection, which not only requires a sterile needle, syringe and accurate dosing, but someone to administer it. In addition, oxytocics have to be protocted from light as they are light sensitive and require refrigeration to remain pharmacologically active as both ergometrine and syntometrine have been stored at a temperature between 2 ^{o}C and 8 ^{o}C, which limits their use to areas with refrigeration and reliable sources of energy and increases their cost [7].

In rural communities, the lack of refrigeration for storing parenteral uterotonic agents and skilled birth attendants able to administer them, combined with the high incidence of anemia among pregnant women and the unavailability of safe blood transfusion services, worsen the outcome of PPH, underscoring the need for novel approaches and low-cost methods for reducing its occurrence [8].

In developing countries, where nearly half the women deliver without the aid of a skilled birth attendant [9], there is simply not enough time to seek treatment for PPH, and in most cases none is to be done. The only way to help women without access to trained attendants is through preventative measures [7].

The most successful method for reducing PPH, active management of the third stage of labor, requires prophylactic uterotonic drugs which are unsuitable for use in the remote locations where prevention is most

needed. Nonetheless, this nearly universal method has set the precedent for a standard of care unavailable in developing countries [10].

Misoprostol is a prostaglandin E_1 analogue registered for the prevention and treatment of gastric ulcers, is well known for its off-label use as an uterotonic agent. It is affordable, inexpensive, comes in tablets which can be administered orally, rectally, sublingually, or vaginally. It has wide clinical applications in obstetrics as it stimulates uterine contractions and has been used for induction of labor [11], early pregnancy failure [12], induction of abortion [13], and for cervical priming [14].

It does not require refrigeration, dark storage or administration by an attendant as it is stable at room temperature and easy to administer. It has a shelf life of several years [10]. The use of misoprostol has therefore a practical role in uncomplicated low risk spontaneous vaginal delivery, especially in developing countries when resort to parenteral drug administration is difficult [7]. It does not cause hypertension [15] and therefore it can be administered to hypertensive patients and also those with cardiac disease.

Since the first report of the use of misoprostol in the management of the third stage of labor in 1996, there are a number of randomized trials comparing its use with placebo or other uterotonic agents [16]. However, many studies have found it to be slightly less effective than oxytocics in controlled clinical settings. This circumstance has had the result of branding misoprostol as an inferior drug [4], despite repeated praise for the feasibility of its use in resource-poor settings [17].

Joy et al. also concluded that misoprostol was inferior to oxytocin and other uterotonics with regard to any of the third stage of labor outcomes assessed. However, when compared to placebo, misoprostol

had a decreased risk of needing additional uterotonics. Thus, in less-developed countries where administration of parenteral uterotonic drugs may be problematic, misoprostol represents a reasonable agent for the management of third stage of labor [18].

The sublingual mucosal area is rich in blood supply to allow direct absorption of medication. A pharmacokinetic study has shown that sublingual administration of misoprostol has maximum systemic bioavailability and achieves highest serum peak concentrations in comparison to either the oral or vaginal route of administration. Sublingual administration also avoids the first pass effect seen with the oral route and the inconvenience of vaginal and rectal administration [19].