Introduction

Haemorrhage remains in the top five causes of maternal death in the UK and other countries, both developed and developing ***(UK/Department of Health, 1998).*** In the developing world at least one woman dies in childbirth every minute, of whom 15-25% die from PPH ***(Baskett, 2000).*** In developing countries, where nearly half the women deliver without the aid of a skilled birth attendant ***(WHO, 1997),*** there is simply not enough time to seek treatment for PPH. The only way to help women is through preventive measures ***(Langenbach, 2006).***

Most of the deaths and disabilities attributed to childbirth are avoidable. It is agiven that each mother and newborn require care that is close to where they live, respectful of their culture, and provided by persons with enough skill to act immediately should a complication occur. The challenge that remains internationally is not technological, but strategic and organizational ***(AbouZahr 1998)***.

Postpartum haemorrhage (PPH) is a leading cause of maternal death, in both developing ***(Li et al., 1996)*** and industrialized countries ***(Berg et al, 1996)***.

In the developing countries, the most common cause of maternal mortality is haemorrhage. In Egypt a maternal mortality rate in (2005) was 65 maternal deaths per 100.000 live births and this equal to 349 maternal deaths due to direct obstetric causes ***(Central Agency for Public Mobilization and Statistics, 2005)***.

Every year, nearly 600000 women between the ages of 15 and 49 die worldwide as a result of complications arising from pregnancy and childbirth ***(WHO/UNICEF, 1999)***. The single most common direct obstetric disorder accounting for 25% of all maternal deathsglobally is severe haemorrhage, generally occurring postpartum ***(WHO, 1986)***.

Nearly all these maternal deaths (99%) occur in the developing world where factors like poverty, ignorance, traditional practices, unbooked emergencies, poor health status of mothers and lack of delivery facilities contribute to increasing the mortality statistics in the presence of severe postpartum haemorrhage ***(Harrison, 1997)***.

The third stage of labor has been described as the most important stage of labor. The normal case can, within a minute, become abnormal and successful delivery can turn swiftly to a disaster ***(Donald, 1979).***

Systematic reviews have concluded that active management of third stage of labor, particularly the prophylactic use of uterotonic agents can significantly decrease the incidence of postpartum haemorrhage compared with that of expectant management ***(Prendiville et al, 1988 & Prendiville et al, 2003 & Elbourne et al, 2003& McDonald et al, 2004).***

The routine use of uterotonic drugs for the management of the third stage of labor has been shown to reduce maternal mortality ***(Jago et al, 2007)***.

An ideal uterotonic agent should promote prompt, strong and sustained uterine contractions without any significant adverse effects ***(Leung et al, 2006).***

McDonals et al., 2004 reported that administration of oxytocin alone is as effective as the use of oxytocin plus ergometrine in the prevention of postpartum haemorrhage, but associated with a significantly lower rate of unpleasant maternal side effects.

Because ergometrine can stimulate smooth muscle contraction and vasoconstriction, it may raise blood pressure, intracerebral haemorrhage ***(Dumoulin, 1981)*** and rarely lead to coronary artery spasm ***(Carey, 1993)*** whereas oxytocin is free of these adverse effects therefore, syntometrine is contraindicated in

women with asthma, hypertension or cardiac disease thus the choice of uterotonic drugs remain controversial ***(Prendiville et al., 1988; McDonald et al., 2004).***

Therefore we will conduct a randomized controlled trial to compare the efficiency and safety of intramuscular oxytocin versus intramuscular ergometrine in the management of the third stage of labor.

Aim Of The Work

To compare the efficiency and safety of intramuscular oxytocin with intramuscular ergometrine in the management of third stage of labor.

Physiological Overview

Definition of labor

Labor is a physiological process during which the products of conception (i.e., the fetus, membranes, umbilical cord, and placenta) are expelled outside of the uterus. Labor is achieved withgradual effacement and dilatation of the uterine cervix as a result of rhythmic uterine contractions of sufficient frequency, intensity, and duration ***(Cunningham 2001).***

Stages of Labor

Although labor is a continuous process, for reasons of study and to assist in clinical management it has traditionally been divided into three stages, the first stage further subdivided into three phases.

First Stage

The first stage of labor refers to the interval between the onset of labor and full cervical dilatation. It has been subdivided by ***Friedman, (1995)***, in his classic studies on the course of labor in primigravida into three phases according to the rate of cervical dilatation.

Second Stage

The second stage of labor is the interval between full cervical dilatation (10cm) and delivery of the infant ***(ACOG, 1994).***

Third stage of labor

The third stage of labor is the interval between delivery of the infant and complete delivery of the placenta, umbilical cord, and fetal membranes; it lasts less than 10 minutes in most women. A prolonged third stage of labor is defined asgreater than 30 minutes. Separation of the placenta is a result of continued uterine contractions and retraction after delivery of the infant. These contractions reduce the area of the uterine placental bed, with placental separation occurring along a plane in the spongiosa layer of the decidua vera. Blood loss is controlled by compression of spiral arteries by the continued contractions, which transport the placenta from the fundus into the lower uterine segment and through the cervix ***(Robinson and Jasica, 1999).***

Fourth stage of labor

The hour immediately following delivery is critical and it has been designated by some as the "fourth stage of labor." Even though ecobolics are administered, postpartum hemorrhage as the result of uterine atony is more likely at this time. The uterus is frequently evaluated during this time. The perineum is

inspected frequently to detect excessive bleeding. The ***American Academy of Pediatrics and the American College of Obstetricians andgynecologists, (1997)*** recommend that maternal blood pressure and pulse should be recorded immediately after delivery and every 15 minutes for the first hour.

Physiology of third stage

Changes also occur in the coagulation system, with a marked increase in clotting factors and a decrease in fibrinolytic activity. The platelet count may fall slightly during pregnancy because of dilution related to the increased plasma volume however, individual platelet volume is increased and activity is maintained. Although uterine contraction is initially responsible for controlling blood loss at the placental site, clot formation and fibrin deposition occur rapidly and are essential in maintaining hemostasis and promoting involution in the days following delivery ***(Sleep, 1993)*.**

Anatomical and physiological considerations of the myometrium:

During pregnancy, uterine enlargement involves stretching and marked hypertrophy of existing muscle cells, whereas the appearance of new muscle cells is limited. The myometrial smooth muscle cell is surrounded by an irregular array of collagen fibrils. The force of contraction is transmitted

from the contractile proteins of the muscle cell to the surrounding connective tissue through the reticulum of collagen ***(Cunningham et al., 1997)*.**

Arrangement of the muscle cells:

The uterine musculature during pregnancy is arranged in three strata:

1- An outer longitudinal layer, which arches over the fundus and extends into the various ligaments.

2- A middle layer composed of a dense network of muscle fibers perforated in all directions by blood vessels.

3- An internal layer, consisting of sphincter-like fibers around the orifices of the fallopian tubes and the internal os of the cervix.

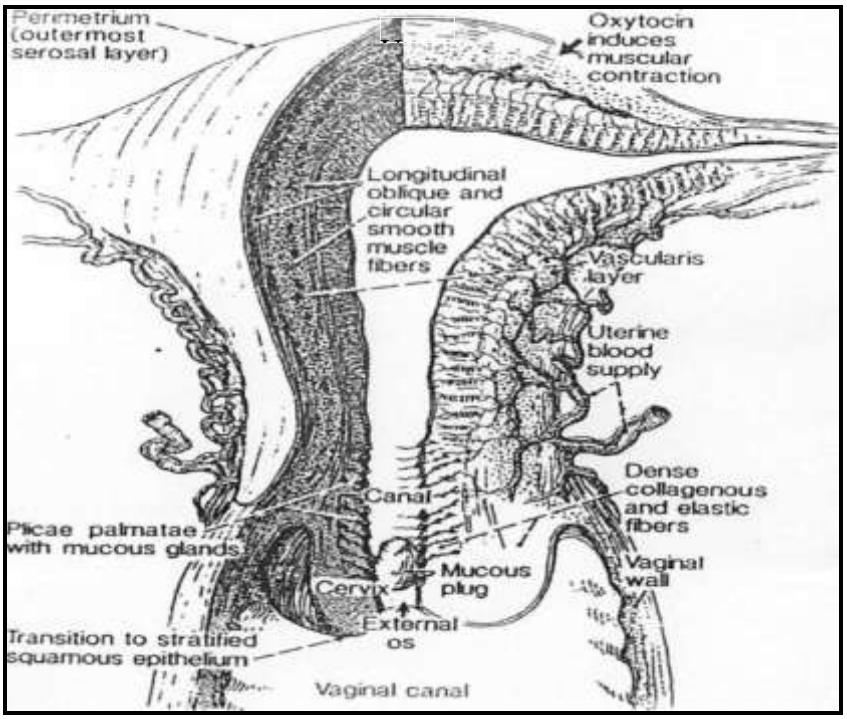

Fig. (1): Anatomy of the uterus. The uterus comprises three muscle layers, derived from the layers of the mullerian ducts. The muscle fibres in the inner layer are arranged in a predominantly circular pattern. The thicker intermediate layer comprises interlocked muscle fibres. The outer layer of muscle fibres runs longitudinally, over the fundus. Quoted from ***(Telford and Bridgman, 1995).***

The main portion of the uterine wall is formed by the middle layer, which consists of an interlacing network of muscle fibers between which extend the blood vessels. Each cell in this layer has a double curve, so that the interlacing of any two muscle fibersgives approximately the form of a figure eight. As a result of this arrangement, when the cells contract after delivery, they constrict the penetrating blood vessels and thus act as ligatures ***(Cunningham et al., 2001).***

Physiology of uterine contraction:

The myometrium is considered one of the unitary smooth muscle. The term "unitary" is confusing because it does not mean single muscle fibers. Instead, it means a whole mass of hundreds to thousands of smooth muscle fibers that contact together as a single unit. The fibers usually are aggregated into sheets or bundles, and their cell membranes are adherent to one another at multiple points so that forcegenerated in one muscle fiber can be transmitted to the next. In addition, the cell membranes are joined by manygap junctions through which ions can flow freely from one cell to the next so that action potentials or simple ion flow can travel from one fiber to the next and cause the muscle fibers to contract together. This type of smooth muscle also is known as syncytial smooth muscle because of its syncytial interconnections among fibers ***(Guyton and Hall, 2001).***

It is shown that the myometrial cells are electrically coupled, such that electrical stimulation of one cell is followed by stimulation of adjacent smooth muscle cells. This results in a wave of contraction as in peristalsis. Moreover, this wave of electrical activity, and hence contraction, may be initiated by a pacemaker cell (i.e., a smooth muscle cell that exhibits a spontaneous depolarization ***(Ganong, 2003; Berne et al., 2004 and Baker, 2006)***.

Major stimulator of myometrial contractions is oxytocin. Although the concentration of oxytocin in maternal plasma does not increase consistently just before labor, the frequency of oxytocin pulses does increase. Furthermore, myometrial oxytocin receptor content rises dramatically at term, as does the local synthesis of oxytocin by the decidua and the fetal membranes. Oxytocin may therefore reinforce labor contractions, and it probably maximizes the contractions immediately after delivery, and thereby minimizes maternal blood loss ***(Berne et al., 2004).***

Immediately after the placenta has separated from the wall of the uterus, the interlocking muscle fibers of the uterus contract. This occludes the blood vessels that were supplying the placenta and reduces blood loss. If the placenta has been attached to the lower uterine segment, the relative lack of muscle in this part of the uterus makes the haemostatic mechanism less efficient, and postpartum haemo-rrhage can occur ***(Baker, 2006).***

Following delivery of the fetus, uterine contractions continue and the placenta is sheared from the underlying endometrium. This separation primarily occurs by a reduction in the surface area of the placental site as the uterus shrinks. This decrease is caused by myometrial retraction, which is a unique characteristic of the uterine muscle to maintain its

shortened length following each successive contraction. In this way, the placenta is undermined, detached, and propelled into the lower uterine segment ***(Baskett, 1999).***

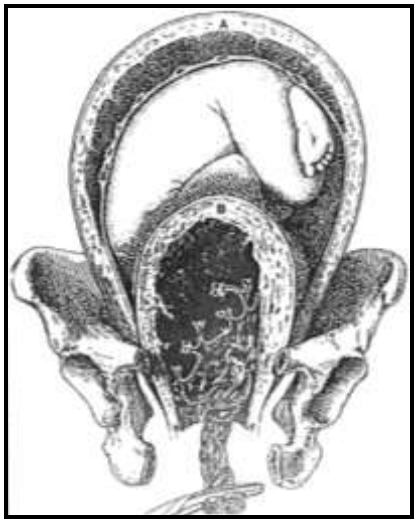

Fig. (2): Diminution in the size of the placental site after birth of the infant Quoted from ***(Cunningham et al., 2005)***.

The second mechanism of separation is through hematoma formation due to venous occlusion and vascular rupture in the placental bed caused by uterine contractions. As the placenta detaches, the spiral arteries are exposed in the placental bed; massive hemorrhage would occur if not for the structure of uterus. The vessels supplying the placental bed traverse a latticework of crisscrossing muscle bundles that occlude and kink-off the vessels as they contract and retract following expulsion of the placenta. This arrangement of muscle bundles has been referred to as the "living ligatures" or "physiologic sutures" of the uterus ***(Baskett, 1999).***

Fig. (3): Diagram showing how the uterine muscle forms a "living ligature" to occlude blood vessels ***(Baker, 1990).***

Separation of amniochorion:

Thegreatest decrease in the surface area of the cavity of the uterus immediately causes the fetal membranes and decidua to be thrown into innumerable folds that increase the thickness of the layer from less than 1mm to 3-4 mm. The membranes usually remain in situ until separation of placenta is nearly completed then they are peeled off the uterine wall partly by contraction of the myometrium and partly by traction by the separated placenta ***(Cunningham et al., 2005).***

Signs of placental separation:

1. The uterus becomesglobular and as a rule, firmer. This sign is the earliest to appear.
2. Suddengush of blood.
3. Elongation of the umbilical cord.
4. The uterus rises in the abdomen because the placenta has separated passing down into the lower uterine segment and vagina where its bulk pushes the uterus upward. These

signs appear within one minute after delivery of the infant and within 5 minutes the placenta is separated so any attempts to pull on the placenta prior to its separation are dangerous so it is important to wait until the appearance of signs of placental separation.

(Cunningham et al., 2005)

Mechanism of placental expulsion:

There are two methods for expulsion of placenta either Schultze mechanism or Duncan mechanism.

Schultze mechanism:

The central part of placenta starts to separate so the retroplacental hematoma is believed to push the placenta towards the uterine cavity first the central portion and then the rest of the placenta is separated. As the surrounding membranes are still attached to the decidua; the placenta can descend only by dragging the membranes then pull off its periphery. So the sac formed by the membranes is inverted with theglistening amnion over the placental surface presenting at the vulva and the retroplacental hematoma either follows the placenta or found within the inverted sac.

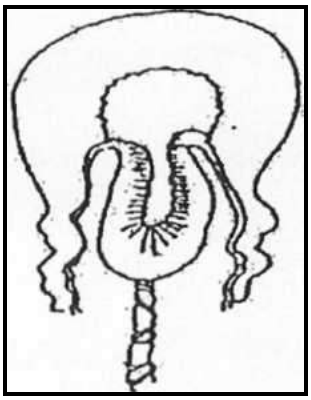

Fig. (4): Schultze mechanism of placental expulsion; Quoted from ***(Cunningham et al., 2005)***

Duncan Mechanism: