بسم الله الرحمن الرحيم

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تم رفع هذه الرسالة بواسطة / حسام الدين محمد مغربي

بقسم التوثيق الإلكتروني بمركز الشبكات وتكنولوجيا المعلومات دون أدنى مسئولية عن محتوى هذه الرسالة.

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Oxytocin Infusion versus Vaginal Misoprostol in Reducing Blood Loss during Abdominal Myomectomy: A Randomized Controlled Trial

Thesis

Submitted for Partial Fulfillment of the M.D in Obstetrics and Gynecology

By

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Marwan Hassan Alsaid Elfar

List of Contents

List of Tables

List of Figures

List of Figures (Cont...)

List of Abbreviations

Abb.	Full term

AUB ..... *Abnormal uterine bleeding (AUB)*

BMI ..... *Body mass index*

CIN ..... *Cervical intraepithelial neoplasia*

ESHRE ..... *European society of human reproduction and embryology*

FDA ..... *Food and Drugs Administration*

FIGO ..... *International Federation of Gynecology and Obstetrics*

GnRH ..... *Gonadotrophine releasing hormone*

HPF ..... *High power field*

IUD ..... *Intrauterine device*

LMSP ..... *leiomyoma-derived side population*

MMPs ..... *Matrix metalloproteinases*

RFA ..... *Radiofrequency Ablation*

SD ..... *Standard deviation*

SPSS ..... *Statistical package for social science*

UAE ..... *Uterine artery Embolization*

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Introduction

Uterine fibroids (also referred to as myomas and leiomyomas) are benign, monoclonal tumors of the uterus that are composed largely of smooth muscle cells. They are the most common tumor of the female genital tract, with some studies estimating over a 70% incidence **(Baird *et al.*, 2003).** About 20–40% of women will be diagnosed with uterine fibroids at some point in their life but only a fraction of those will have problems or require treatment **(Wallach & Vlahos, 2004).**

The exact etiology is not clearly understood, but the current working hypothesis is that it may have a genetic predisposition, prenatal hormone exposure. Known risk factors are African descent, nulliparity, obesity, polycystic ovary syndrome, diabetes, and hypertension **(Okolo, 2008).**

Myomas can cause significant morbidity including menstrual abnormalities (e.g. heavy, irregular, and prolonged uterine bleeding), iron deficiency anemia, bulk symptoms (e.g. pelvic pressure/pain, obstructive symptoms), and fertility issues. Symptomatic fibroids have a considerable impact on women's quality of life as well as their productivity: in one survey of more than 21,000 women from 8 different countries, these symptoms had a negative impact on sexual life (43%), performance at work (28%), and relationship, and family (27%) **(Zimmermann *et al.*, 2012).**

Treatment of women with uterine leiomyomas must be individualized, based on symptomatology, the size and location of fibroids, age, the needs and desires of the patient for preservation of fertility or the uterus, the availability of therapy, and the experience of the therapist. Patients have multiple options in the management of uterine myomas including

observation, medical therapy, uterine artery embolization, high intensity focused ultrasound ablation and as well as surgical methods like myomectomy and hysterectomy (**Kongnyuy & Wiysonge, 2011).**

Surgical intervention is necessary when the myoma is symptomatic and resistant to medical management or interferes with reproduction. The standard treatment of symptomatic leiomyomas is hysterectomy for women who have completed childbearing. Hysterectomy is associated with significant morbidity, mortality, and economic burden on the health care system **(Clark-Pearson & Geller, 2013).**

Myomectomy is an alternative to hysterectomy for women who wish to retain their uterus, regardless of their fertility desire. Although myomectomy allows preservation of the uterus, there is a higher risk of blood loss and greater operative time with myomectomy than with hysterectomy **(Garcia, 1993).**

Myomectomy is associated with intraoperative and postoperative complications including excessive hemorrhage, pyrexia, visceral damage, thrombo-embolism, conversion to hysterectomy, blood transfusions, scar dehiscence in future pregnancy and many others **(Paul *et al.*, 2010).**

Myomectomy can be accomplished by laparotomy, laparoscopy, or hysteroscopy. Open myomectomy is the most adopted surgical strategy in the conservative treatment of uterine fibroids. Massive blood loss associated with the dissection of huge fibroids renders myomectomy a more technically challenging procedure than hysterectomy. The average volume of blood loss during abdominal myomectomy (performed via laparotomy, also referred to as open myomectomy) is 200 to 800 ml **(Sawin *et al.*, 2000; West *et al.*,**

2006 and Iverson *et al.*, 2008) and for laparoscopic myomectomy is 80 to 250 ml **(Sinha *et al.*, 2008 and Paul *et al.*, 2010).**

An audit at King Edward Memorial Hospital for Women, Western Australia, identified a 15% transfusion rate of women undergoing open abdominal myomectomy. Although serious reactions are rare, transfusion is not without risks e.g. labeling errors, Transfusion Related Acute Lung Injury and Transfusion Associated Circulatory Overload. Perioperative transfusions and anemia have both been associated with increased complications and length of hospital stay **(Browning *et al.*, 2012).**

Hemorrhage is a major concern in myomectomy operation. Bleeding can be prevented if dissection done through the avascular cleft or decreased with mechanical or pharmacologic methods. Several interventions have been developed to control bleeding during this operation such as dissection and embolization of uterine artery, use of mechanical and hormonal tourniquets, use of uterotonic medications such as oxytocin, ergometrine, misoprostol. Careful planning and considered use of some of those interventions, it should be possible in most cases to avoid the need for transfusion and minimise the impact of postoperative anemia **(Ngeh *et al.*, 2004; Chang*et al.*, 2006 and Kongnyuy & Wiysonge, 2011)**

Misoprostol and Oxytocin are the agents of choice in the management of postpartum uterine atony and bleeding. Misoprostol, a prostaglandin E1 analogue, reduces uterine blood flow by causing uterine contractions and subsequently reduces bleeding during myomectomy **(Wang *et al.*, 2007).**

Placebo-controlled randomized studies have shown that a single dose of misoprostol 400 μg given vaginally 1 hour prior or rectally 30 minutes prior to abdominal myomectomy resulted

in a statistically significant reduction in operative time, operative blood loss, postoperative hemoglobin drop, and need for postoperative blood transfusion. No differences were observed in length of hospital stay **(Celik & Sapmaz, 2003).**

Oxytocin receptors exist in the non-pregnant uterus, although the concentration of the receptors is much lower than in its pregnancy. It is for this reason that the clinical use of oxytocin outside of pregnancy is limited **(Wang *et al.*, 2007).**

In light of the effectiveness of oxytocin on the postpartum uterus, there is interest in the use of oxytocin to reduce uterine perfusion and therefore bleeding during myomectomy. Shokier *et al.* reported that oxytocin infusion reduces the observed reduction in hematocrit after hysteroscopic myomectomy **(Shokeir *et al.*, 2011).** Wang *et al.* discovered the ability of oxytocin to reduce the haemorrhage and subsequent blood transfusion requirement during laparoscopic myomectomy and laparoscopic vaginal hysterectomy **(Wang *et al.*, 2007).**

There is always controversial for choosing the best method with minimal adverse effects and effective results among gynecologists. In view of the lack of sufficient data and comparable studies, this trial will be designed to evaluate the efficacy of uterotonic drugs (intra-operative oxytocin drip versus preoperative vaginal misoprostol) of proven efficacy in management of postpartum haemorrhage and the difference in non pregnant uterus especially in reducing blood loss in abdominal myomectomy.

Aim of the Work

The primary aim of the currnt study is to compare between the efficacy of intraoperative oxytocin infusion and preoperative vaginal misoprostol in reducing blood loss during trans- abdominal myomectomy.

Research question:

In women undergoing trans-abdominal myomectomy; does oxytocin infusion reduce blood loss equally or in similar efficacy as vaginal misoprostol ?

Research hypothesis:

Null hypothesis:

In women undergoing trans-abdominal myomectomy, the use of intraoperative IV oxytocin infusion may reduce blood loss in similar efficacy as vaginal misoprostol.

Patients and Methods

I. Study Design:

Randomized controlled trial (RCT).

II. Study Site:

Inpatient ward and Operative Theatre in Ain Shams University Maternity Hospital.

III. Study Protocol:

The study will be conducted during1 year period starting from July 2017.

IV. Sample Size:

Total sample size in the study is one hundred patients, randomized into two groups

- *Sample Size Justification:*

Using PASS program for sample size calculation version 11, group sample size of 50 patients in each group achieves 100% power to detect a difference of 280 cc in intraoperative blood loss between the null hypothesis that both group means of intraoperative blood loss are 190 cc and the alternative hypothesis that the mean of blood loss of group 2 (Misoprostol) is 470 cc with estimated group standard deviations of 17.0 cc and 77.0 cc and with a significance level (alpha) of 0.05 using a two-sided two-sample t-test. Calculation of the sample size was done according to data obtained from a previous relevant study **(Atashkhoei *et al.*, 2016) (Celik & Sapmaz, 2003).**

V. Study population:

The study will include 100 patients who are consenting to be recruited in the study, and are fulfilling the inclusion criteria. The patients will be randomized into 2 groups; (O, M):