Vaginal Misoprostol versus Bilateral Uterine Artery Ligation in Decreasing Blood Loss in Trans-Abdominal Myomectomy: A Randomized Controlled Trial

Thesis

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By

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List of Abbreviations

Abbr.	Full-term
ABL	: Allowable Blood Loss.
ACOG	: American College of Obstetricians and Gynecologists.
ALT	: Alanine Transferase.
AUB	: Abnormal Uterine Bleeding.
BMD	: Bone Mineral Density.
BMI	: Body Mass Index.
cAMP	: Cyclic Adenosine Monophosphate.
CI	: Confidence Interval.
COCs	: Combined Oral Contraceptives.
E2	: Estradiol.
EBV	: Estimated Blood Volume.
EPO	: Erythropoitin.
ESHRE	: European Society for Human Reproduction and Embryology.
FDA	: Food and Drug Administration.
FIGO	: Fédération Internationale de Gynécologie et d'Obstétrique.
FMDG	: FIGO Menstrual Disorders Group.
FSH	: Follicle-Stimulating Hormone.
GnRH	: Gonadotrophin Releasing Hormone.
Hb	: Hemoglobin.
HBV	: Hepatitis B Virus.
HCV	: Hepatitis C Virus.
H_i	: Initial Hematocrit.
H_f	: Final Lowest Acceptable Hematocrit.
IM	: Intramuscular.

INHB : Inhibin B.

INR : International Normalized Ratio.

IUS : Intrauterine System.

IV : Intravenous.

LH : Leuteinizing Hormone.

LM : Laparoscopic Myomectomy.

LUAO : Laparoscopic Uterine Artery Occlusion.

M.W : Molecular Weight.

Mcg : Micrograms.

MPA : Misoprostol Acid.

MRgFUS : Magnetic Resonance-guided Focused-Ultrasound Surgery.

MRI : Magnetic Resonance Imaging.

NG : Nulligravida.

NSAIDs : Nonsteroidal Anti-inflammatory Drugs.

OCs : Oral Contraceptives.

PALM-COEIN : Polyp, Adenomyosis, Leiomyoma, and Malignancy – Coagulopathy, Ovulatory dysfunction, Endometrial, Iatrogenic, Not yet classified.

PG : Prostaglandin.

PKA : Protein Kinase A.

PRM : Progesterone Receptor Modulators.

PT : Prothrombin Time.

PTHrP : Parathyroid hormone related protein.

PTT : Partial Thromboplastin Time.

PV examination : Pervaginal Examination.

RBCs : Red blood Cells.

rHuEPO : Recombinant Human Erythropoietin.

SOGC : Society of Obstetricians and Gynaecologists.

UAE : Uterine Artery Embolization.

UFE : Uterine Fibroid Embolization.

USA : United States of America.

Vs : Versus.

2D US : Two Dimensional Ultrasound.

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Abstract

Background: Uterine leimyomas are tumors of the smooth muscles and the connective tissues of the uterus. They are considered to be the most common benign pelvic tumor affecting about 20% of women above the age of 35. The diverse symptomatology of fibroids can be attributed to size, number and location of the tumors. The common symptoms include menorrhagia, infertility, abdominal mass and pressure effects. **Aim of the Work:** The aim of this study is to compare between the effect of medical (preoperative vaginal misoprostol) and non-medical (bilateral uterine artery ligation) regarding their efficacy to decrease blood loss in trans- abdominal myomectomy. **Patients and Methods:** Prospective randomized controlled interventional clinical trial. The study was conducted in Ain Shams University Maternity Hospital, Cairo, Egypt in the period between August 2015 till December 2016. It was approved by the Ethical Research Committee, Obstetrics and Gynecology Department, Ain Shams University, Cairo, Egypt. It included 60 women recruited from those attending the outpatient gynecology clinic, seeking treatment for symptomatic uterine myomas. **Results:** The current study revealed that there was no statistically significant difference between both groups regarding operative time, blood loss and postoperative hospital stay. **Conclusion:** A single pre-operative dose of 400 micrograms of vaginal misoprostol is as effective as uterine artery ligation in decreasing blood loss in transabdominal myomectomy. Misoprostol is a simple, cheap, fast, available and applicable tool that can be administered even an hour preoperatively. **Recommendations:** Preoperative vaginal misoprostol is an effective practical tool in decreasing blood loss in transabdominal myomectomy. Investigation of misoprostol use in larger population groups and with different dosages and administration routes, together with comparison of other methods used to reduce bleeding during myomectomy, is recommended.

Key words: uterine leimyoma, smooth muscles, connective tissues, vaginal misoprostol, bilateral uterine artery ligation, blood loss, transabdominal myomectomy

Introduction

Uterine leiomyomas are tumors of the myometrium that have a prevalence as high as 70% to 80% at the age of 50 ***(Okolo et al., 2008)***, the etiology and prevalence seem to vary with a number of factors including age, race, and possibly geographic location. Prevalence in the United States is almost 40% in white patients and more than 60% in women of African descent in the same age group ***(Parker, 2007)***.

Leiomyomas are listed as the diagnosis for about 39% of the approximately 600,000 hysterectomies performed each year in the United States ***(Zimmermann et al., 2012)***.

These benign tumors, are usually asymptomatic, and may be only detectable through ultrasound examination, or associated with a number of clinical issues including abnormal uterine bleeding (AUB) especially heavy menstrual bleeding (HMB), infertility, recurrent pregnancy loss, and complaints related to the impact of the enlarged uterus on adjacent structures in the pelvis, which are often referred to as ‘‘bulk’’ symptoms. It is generally perceived that the symptoms of HMB, infertility, and recurrent pregnancy loss largely occur as a result of lesions that distort the endometrial cavity that are therefore adjacent to the endometrium and consequently referred to as submucous leiomyomas ***(Zimmermann et al., 2012)***.

Treatment options for leiomyoma vary; treatment strategies are typically individualized based on the severity of the symptoms, the size and location of the leiomyoma lesions, the patient's age and their chronological proximity to menopause, and the patient's desire for future fertility. The usual goal of therapy is the relief of the symptoms. The treatment options range from the use of acupuncture (ancient Chinese method) to the total removal of the uterus and its myoma contents (hysterectomy) ***(American College of Obstetricians and Gynecologists, 2008)***.

Treatment of fibroids should be individualized, and symptomatology may be a decisive factor in whether or not a fibroid is removed. Myomectomy remains the gold standard for treatment for patients who wish to preserve their uteri and desire future pregnancy. The procedure can be accomplished by either laparotomy (through an incision into the abdomen) or laparoscopically ***(William et al., 2013)***.

The presence of leiomyomas in the uterus distorts normal vascular architecture, thus, the arcuate arteries may run in any axis, rather than transversely, therefore, either vertical or transverse incisions during myomectomy may transect these vessels and increase blood loss during the procedure ***(Discepola et al., 2007)***.

Many interventions have been performed to reduce bleeding during myomectomy. According to ***(Kongnyuy et al., 2011)*** four categories of interventions can be identified:

- *Interventions on uterine arteries:* such as uterine artery embolization ***(Dumousset et al., 2008)***, pericervical mechanical tourniquet ***(Helal et al., 2010)***, vasopressin (natural or synthetic) ***(Tulandi et al., 1996)*** and ***(Lurie and Mamet 2000)*** a vasoconstrictive solution of bupivacaine plus epinephrine ***(Zullo et al., 2004)*** and bilateral uterine artery ligation ***(Sapmaz and Celik 2003).***
- *Utero-tonics:* such as oxytocin ***(Agostini et al., 2005)*** and misoprostol ***(Celik and Sapmaz 2003)***.
- *Myoma dissection techniques:* which include fibroid enucleation by morcellation ***(Sinha et al., 2005)*** and the use of chemical dissectors such as sodium-2-mercaptoethane sulphonate (mesna) ***(Benassi et al., 2000).***
- Pharmacologic *manipulation of the coagulation cascade:* with antifibrinolytic agents such as tranexamic acid ***(Caglar et al., 2008)*** and gelatin-thrombin haemostatic sealant ***(Raga et al., 2009).***