Effect of Oxytocin versus Misoprostol on Blood loss during Abdominal Myomectomy: a Randomised Controlled Trial

Thesis

Submitted for partial fulfillment of master degree in
Obstetrics and Gynecology

By

Ahmed Neamatallah Abdelghafar Mohamed

M.B.B.Ch (2003)
Faculty of Medicine, Mansoura University-2009

Supervised by

Prof. Dr. Osama Saleh El Kady
Professor of Obstetrics and Gynecology
Faculty of Medicine-Ain Shams University

Prof. Dr. Amgad Al-Said Abou-Gamra
Professor of Obstetrics and Gynecology
Faculty of Medicine-Ain Shams University

Dr. Ihab Adel Gomaa
Assistant Professor of Obstetrics and Gynecology
Faculty of Medicine- Ain Shams University

Faculty of Medicine
Ain Shams University
2019

Acknowledgments

My deepest gratitude to my supervisor, **Prof. Dr. Osama Saleh El Kady,** *Professor of Obstetrics and Gynecology, Faculty of Medicine-Ain Shams University, for his valuable guidance and expert supervision, in addition to his great deal of support and encouragement. I really have the honor to complete this work under his supervision. God blesses him and keeps him a sun lightening the way for the scientific students.*

I would like to express my great and deep appreciation and thanks to **Prof. Dr. Amgad Al-Said Abou-Gamra,** *Professor of Obstetrics and Gynecology, Faculty of Medicine-Ain Shams University, for his meticulous supervision, and his patience in reviewing and correcting this work.*

I must express my deepest thanks to **Dr. Ihab Adel Gomaa,** *Assistant Professor of Obstetrics and Gynecology, Faculty of Medicine-Ain Shams University, for guiding me throughout this work and for granting me much of his time. I greatly appreciate his efforts.*

Special thanks to my **Parents,** *my* **Wife,** *and all my* **Family** *members for their continuous encouragement, enduring me and standing by me.*

Last but not least, I would also like to thank my colleagues, my patients and everyone helped me in this study.

✍ *Ahmed Neamatallah Abdelghafar Mohamed*

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List of Abbreviations

Abbr.	Full-term
ADH	**:** Anti-diuretic hormone
AI	**:** Aromatase inhibitors
COC	**:** Combined oral contraceptive
CT	**:** Computed tomography
ECM	**:** Extracellular matrix
FIGO	**:** International Federation of Gynecology and Obstetrics
FSH	**:** Follicle-stimulating hormone
GnRHa	**:** Gonadotropin-releasing hormone analogs
HMB	**:** Heavy menstrual bleeding
IU	**:** International unit
IUS	**:** Intrauterine sonography
LH	**:** Luteinizing hormone
LNG-IUS	**:** Levonorgestrel intra-uterine system
MLCK	**:** Myosin Light Chain Kinase
MRgFUS	**:** Magnetic resonance-guided focused ultrasound surgery
MRI	**:** Magnetic resonance imaging
NSAID	**:** Non-steroidal anti-inflammatory drugs

PR **:** Progesterone receptor

PRL **:** Prolactin hormone

RF **:** Radiofrequency

SD **:** Standard deviation

SERMs **:** Selective estrogen receptor modulators

SPRMs **:** Selective progesterone receptor modulators

UAE **:** Uterine artery embolization

3D **:** Three-dimensional

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Effect of Oxytocin versus Misoprostol on Blood loss during Abdominal Myomectomy: A Randomised Controlled Trial

Abstract

Background: Myomectomy is the best option for women who have not completed child bearing or otherwise wish to retain their uterus. Many techniques used to reduce blood loss during myomectomy including preoperative correction of anemia, preoperative GnRH agonists, intraoperative tourniquets and clamps, intra-myometrial vasopressin and other vasoconstrictors and uterotonics (Misoprostol, Oxytocin, etc).

Objective: The purpose of this study was to compare the efficacy of vaginal misoprostol versus IV oxytocin infusion in reducing blood loss during abdominal myomectomy.

Methodology: This is a randomized, controlled study that was conducted in Ain Shams University Maternity Hospital. This study involved sixty women undergoing abdominal myomectomy for symptomatic uterine myoma divided randomly into two groups: Group A (Oxytocin group) which include 30 patients received an infusion of 30 IU oxytocin in 500 ml normal saline at a rate of 120 ml/h immediately before the start of the surgery and Group B (Misoprostol group) which include 30 patients received (200 mcg) misoprostol vaginally one hour before the operation.

Results: The study demonstrated that using 200 mcg misoprostol administered vaginally one hour before abdominal myomectomy resulted in a significant reduction of blood loss than using 30 IU oxytocin in 500 ml normal saline at a rate of 120 ml/h immediately before the start of the surgery (359±70 ml misoprostol group vs. 530±62.5 ml in oxytocin group), and also a significant reduction of operative time (56.7± 8.3 min in the misoprostol group vs. 68.1± 9.1 min in oxytocin group) and so the reduction in hemoglobin(1.0 ±0.5 vs. 1.9±0.5 g/dl) and hematocrit (3.2 ±1.3 % vs. 5.9 ± 1.0 %) was significantly lower in the misoprostol group than oxytocin group respectively. Misoprostol lead to statistically insignificant in the need for blood transfusion when compared with oxytocin group (6.7% in the misoprostol group vs. 20% in the oxytocin group). Misoprostol lead to statistically insignificant in the hospital length of stay when compared with oxytocin group (2.2 day in the misoprostol group vs. 2.3 day in the oxytocin group).

Conclusion: In this study, we demonstrated that misoprostol is more effective than oxytocin for reducing intraoperative blood loss during abdominal myomectomy operations.

Keywords: Oxytocin, Misoprostol, Blood loss, Abdominal Myomectomy

PROTOCOL OF THESIS SUBMITTED FOR PARTIAL FULFILMENT OF MASTER DEGREE INOBSTETRICS AND GYNECOLOGY

Title of the Protocol: Effect of Oxytocin Versus Misoprostol on Blood loss during abdominal myomectomy: a randomised controlled trial

Postgraduate Student: Ahmed Neamatallah Abdelghafar Mohamed
Degree: M.B.B.CH-Mansoura University-2009

DIRECTOR: Professor / Osama Saleh El Kady
Academic Position: Professor
Department: Obstetrics and Gynecology

Co-DIRECTOR: Professor / Amgad Al-Said Abou-Gamra
Academic Position: Professor
Department: Obstetrics and Gynecology

Co-DIRECTOR: Dr / Ihab Adel Gomaa
Academic Position: Assistant professor
Department: Obstetrics and Gynecology

Ain Shams University
Faculty of Medicine - 2017

What is already known on this subject? AND
What does this study add?

Several methods have been developed to reduce blood loss during abdominal myomectomy.These Methods include Oxytocin and Misoprostol.

This study is to compare the efficacy of vaginal misoprostol versus IV oxytocin infusion in reducing blood loss during abdominal myomectomy.

1.INTRODUCTION:

Uterine leiomyomas (fibroids) are the most common benign tumours among women. Fibroids are found in approximately 20% of women over 35 years of age **(Kongnyuy et al., 2008).**

Leiomyomas are mostly asymptomatic, but become symptomatic in 20–50 % of affected cases, presenting with menorrhagia, pelvic pain or pressure, or urinary complaints. The occasion and severity of symptoms depend on size, number of tumors, and location of the lesions **(Frederick et al., 2013).**

Surgery is indicated for symptomatic uterine leiomyomas; hysterectomy for women who have completed childbearing (women > 40 years old), and myomectomy for women <40 years old who wish to preserve uterine and fertility **(Biswas et al., 2013)**.

Uterine embolization is a new technique that has recently been evaluated, and its use for this indication in women who want to preserve their fertility needs further study, so surgical treatment is still the only radical treatment for uterine fibroids **(Verma et al., 2008).**

Myomectomy can be accomplished by laparotomy, laparoscopy, or hysteroscopy (transvaginal) approaches. This surgical procedure may be associated with substantial morbidity, in particular major blood loss, especially in abdominal myomectomy **(Schüring et al., 2011).**

Hemorrhage is one of the most common complications in cases undergoing myomectomy. Literature shows that about 20% of the cases

who underwent myomectomy need blood transfusion **(Marret et al., 2012)**.

Several methods have been developed to reduce blood loss. These Methods include use of preoperative GnRH agonist, tourniquet method**,** clamping of the bilateral uterine and /or ovarian artery**,** injection of intraoperative vasopressin or terlipressin into the myometrium**,** intra-myometrial infiltration of bupivacaine plus epinephrine and Preoperative uterine artery embolization**.** However, these strategies may be associated with some complications, and some of these are ineffective or expensive or required extra steps before the actual procedure **(Conforti et al., 2015).**

Oxytocin is a hormone secreted mainly from the pituitary gland. Its main function is uterine contraction during labour and delivery. It is the agent of choice in the prevention of postpartum uterine atony and bleeding. Oxytocin receptors exist in the non-pregnant uterus, although the concentration of the receptors is much lower than in its pregnancy. An infusion of 30 IU oxytocin during abdominal myomectomy affected on oxytocin receptors in the myometrium and fibroid tissue, which stimulates synthesis and release of contractile prostaglandins with the vaso-constrictive effect of oxytocin **(Atashkhoei et al., 2016).**

On the other hand, Misoprostol is as a synthetic PGE1 analogue, is commonly used for medical abortion, management of miscarriage, induction of labor and management of postpartum hemorrhage. A single preoperative dose of misoprostol (200mcg) increased myometrium contractions and lead to a reduction in myometrial hemorrhage. It can be given also orally, buccally or rectally **(Niroomand et al., 2015).**

Based on the hypothesis that uterotonic agents may decrease intraoperative haemorrhage during abdominal myomectomy, we used a randomised controlled trial to investigate the effectiveness of pre-operative misoprostol and intravenous oxytocin on reducing blood loss in abdominal myomectomy.

2.AIM/ OBJECTIVES

The aim of this study is to compare the efficacy of vaginal misoprostol to IV oxytocin infusion in reducing blood loss during abdominal myomectomy.

3.METHODOLOGY:

Study design:

This is a prospective randomized controlled trial.

Study setting:

This study will be conducted in Ain Shams University, Maternity Hospital.

Study population:

This study will be include a sample of (60) women requiring abdominal myomectomy. All patients seeking treatment for symptomatic leiomyomas will be invited to participate in the study.

Sample Size Calculation:

The required sample size has been calculated using the Power Analysis and Sample Size 2008 software version 08.0.15 (PASS© 2008, NCSS, LLC, Keysville, Utah, USA).

The primary outcome measure is the amount of operative blood loss. A previous study reported that the mean ± SD operative blood loss associated with single-dose misoprostol was 458 ± 287 ml. **(Niroomand et al., 2015).**

Another study reported that the mean ± SD operative blood loss associated with oxytocin infusion was approximately 190 ± 17 ml **(Atashkhoei et al., 2017).**

So, it is estimated that a sample size of 30 patients per group would achieve a power of 87% (type 2 error, .13) to detect a statistically significant difference between the 2 groups as regards the operative blood loss using a two-sided unpaired t-test with a confidence level of 95% (type 1 error, .05).

Patients will be divided into two group:

Group A: (Oxytocin group): (n=30) will receive an infusion of 30 IU oxytocin in 500 ml normal saline at a rate of 120 ml/h immediately before the start of the surgery.

Group B: (Misoprostol group):(n=30) will receive 200 mcg misoprostol vaginally 1 hour before the start of the surgery.

Randomization :

Patients will be randomized to either group using a computer-generated random number list (attached appendix).

Computer-Generated Random Number List*

roup	SN	Group	SN	Group	SN	Group	SN	Group	SN	G
roup B	11	Group B	21	Group A	31	Group A	41	Group B	51	G
roup A	12	Group A	22	Group A	32	Group A	42	Group B	52	G
roup B	13	Group A	23	Group A	33	Group A	43	Group A	53	G
roup A	14	Group B	24	Group B	34	Group A	44	Group B	54	G
roup B	15	Group A	25	Group B	35	Group A	45	Group A	55	G
roup A	16	Group B	26	Group A	36	Group B	46	Group A	56	G
roup B	17	Group A	27	Group B	37	Group A	47	Group B	57	G
roup A	18	Group B	28	Group B	38	Group B	48	Group A	58	G
roup A	19	Group B	29	Group A	39	Group B	49	Group A	59	G
roup B	20	Group A	30	Group B	40	Group B	50	Group B	60	G

*Generated using MedCalc© version 15 (MedCalc© Software bvba, Ostend, Belgium).

Allocation Concealment :

The randomization table will be concealed until the time of randomization and will be accessed by a personnel not involved in the study immediately prior to randomization to determine the group to which the patient will be assigned.

Inclusion criteria:

1. Age between 20 and 39 years.
2. Five or less symptomatic Uterine leiomyomas.
3. Maximum diameter of the largest myoma 7 cm.
4. Uterine size <24 weeks' gestation.

Exclusion criteria:

1. History of pelvic infection.
2. History of endometriosis.
3. Cardiac, pulmonary and hepatic diseases.
4. Allergy to oxytocin or prostaglandins.
5. Bleeding disorders ortaking anticoagulant medications.
6. Chronic endocrine diseases such as diabetes.
7. Obesity (body mass index > 30 kg/m^2).
8. Preoperative embolization or preoperative administration of GnRH agonists.

Procedure:

All included women will be subjected to the following:

Preoperative:

History:

Full history taking (personal,present,past and obstetrics and gynecological history).

Physical examination including:

-General examination

- Assesment of vital data.
- Assesment of general condition.

-Abdominal and pelvic examination:

- Assesment of the uterus size.