



Effect of Oxytocin Infusion on Reducing the Blood Loss during Abdominal Myomectomy: a Double- Blind Randomized Controlled Trial

Thesis

*Submitted for Partial Fulfillment of Master Degree
in Obstetric and Gynecology*

By

Othman Mohammed Othman Abu-Elela
M.B.B.Ch 2012

Under Supervision of

Prof. Mohammad AbdElHameed Mohammad Nasr AdDeen

*Professor of Obstetrics and Gynecology
Faculty of Medicine – Ain Shams University*

Prof. Ahmed Hamdy Nageeb

*Professor of Obstetric and Gynecology
Faculty of Medicine - Ain Shams University*

Dr. Mohamed Abdelfattah Elsenity

*Lecturer of Obstetrics and Gynecology
Faculty of Medicine - Ain Shams University*

Faculty of Medicine - Ain Shams University

2019

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قالوا

سبحانك لا علم لنا
إلا ما علمتنا إنك أنت
العليم العظيم

صدق الله العظيم

سورة البقرة الآية: ٣٢

Acknowledgments

First and foremost, I feel always indebted to Allah the Most Beneficent and Merciful.

To *Prof. Mohammad AbdEl Hameed Mohammad Nasr Ad Deen* Professor of Obstetrics and Gynecology Faculty of Medicine, Ain Shams University, for his generous concern, sincere supervision, valuable suggestions and cooperation, continuous advice and support, saving no effort or time in reading each word in this work, To him I will always grateful.

My deepest gratitude, Appreciations and thanks to *Prof. Ahmed Hamdy Nageeb* Professor of Obstetrics and Gynecology, Faculty of Medicine, Ain Shams University, for his sincere supervision, cooperation and continuous support throughout this work, saving no effort or time in reading each word in this work, to him I am always grateful.

I wish also, to express my sincere gratitude and thanks to *Dr. Mohamed Abdelfattah Elsenity*, Lecturer of Obstetrics and Gynecology Faculty of Medicine, Ain Shams University for her kind supervision, sincere encouragement, valuable advices and instructions throughout this work.

I would like also to express my thanks and appreciation to *my Family* for their continuous encouragement and support, I ask god a happy and healthy life for them.

Last but not, least I express my gratitude to everyone who helped me to complete this work.

Othman Mohammed Othman Abu-Elela

List of Contents

Title	Page No.
List of Tables	5
List of Figures	6
List of Abbreviations.....	7
Abstract	9
Protocol.....	
Introduction.....	- 1 -
Aim of the Work	14
Review of Literature	
▪ Oxytocin	15
▪ Uterine Fibroid	29
▪ Abdominal Myomectomy	41
Patients and Methods	85
Results	93
Discussion.....	102
Recommendations	108
Summary and Conclusion.....	109
References	112
Arabic Summary	

List of Tables

Table No.	Title	Page No.
Table (1):	Demographic characteristics among the studied groups	94
Table (2):	Estimated blood loss (mL) among the studied groups.....	95
Table (3):	Hemoglobin (gm/dL) among the studied groups.....	96
Table (4):	Hematocrit (%) among the studied groups.....	98
Table (5):	Operative duration (minutes) among the studied groups.....	100
Table (6):	Blood transfusion among the studied groups.....	100
Table (7):	Ampulation time (hours) among the studied groups.....	101
Table (8):	Hospital stay (day) among the studied groups.....	101

List of Figures

Fig. No.	Title	Page No.
Fig. (1):	Oxytocin (OT) receptor signalling in the myometrium leading to contraction.....	19
Fig. (2):	Fibroid location.....	33
Fig. (3):	Hystroscopic classification of submucous fibroids	34
Fig. (4):	FIGO classification system (PALM-COEIN) for causes of abnormal uterine bleeding,.....	35
Fig. (5):	Classification system including leiomyoma subclassification system.....	36
Fig. (6):	Myomectomy technique.....	53
Fig. (7):	Management of myoma	74
Fig. (8):	CONSORT, Patient flow chart.....	93
Fig. (9):	Estimated blood loss among the studied groups.	95
Fig. (10):	Hemoglobin among the studied groups.	97
Fig. (11):	Hematocrit among the studied groups.....	99

List of Abbreviations

Abb.	Full term
<i>AFS</i>	<i>American Fertility Society</i>
<i>BMD</i>	<i>Bone mineral density</i>
<i>CPI-17</i>	<i>C-kinase-activated protein phosphatase-1 inhibitor 17 kDa</i>
<i>DAG</i>	<i>Diacylglycerol</i>
<i>FDA</i>	<i>Food and Drug Administration</i>
<i>FIGO</i>	<i>Fédération Internationale de Gynécologie et d'Obstétrique</i>
<i>FMDG</i>	<i>FIGO Menstrual Disorders Group</i>
<i>GnRH</i>	<i>Gonado-tropin-releasing hormone</i>
<i>IP3</i>	<i>Inositol-tris-phosphate</i>
<i>IUS</i>	<i>Intrauterine system</i>
<i>MAPK</i>	<i>Mitogen-activated protein kinase</i>
<i>MLCK</i>	<i>Myosin light-chain kinase</i>
<i>MLCP</i>	<i>Myosin light chain phosphatase</i>
<i>MRgFUS</i>	<i>Magnetic resonance guided focused ultrasound surgery</i>
<i>MU</i>	<i>Montevideo-Units</i>
<i>mU/min</i>	<i>Milliunits per minute</i>
<i>NSAIDs</i>	<i>Nonsteroidal anti-inflammatory drugs</i>
<i>OT</i>	<i>Oxytocin</i>
<i>OTR</i>	<i>Oxytocin receptor</i>
<i>PALM</i>	<i>Polyp, Adenomyosis, Leiomyoma, and Malignancy</i>
<i>PGE2</i>	<i>Prostaglandin E2</i>
<i>PIP2</i>	<i>Phosphoinositide-bis-phosphate</i>
<i>PKC</i>	<i>Protein kinases type C</i>

List of Abbreviations cont...

Abb.	Full term
<i>PLA2</i>	<i>Phospholipase A2</i>
<i>PPH</i>	<i>Postpartum hemorrhage</i>
<i>PRM</i>	<i>Progesterone receptor modulators</i>
<i>ROCK</i>	<i>RhoA-associated protein kinase</i>
<i>SR</i>	<i>Sarcoplasmic reticulum</i>
<i>UAE</i>	<i>Uterine artery embolization</i>
<i>UFE</i>	<i>Uterine fibroid embolization</i>

Abstract

Introduction: An increase frequency of symptomatic fibroids is present nowadays. The only curative management of this problem is by surgical intervention either Hysterectomy or myomectomy resulting in a significant blood loss especially abdominal myomectomy. All interventional trial failed to solve the problem of blood loss. Few trials investigate the usage of oxytocin infusion with lacking of data about its safety and effectiveness.

Objective: Assess the efficacy of oxytocin infusion on reducing blood loss during abdominal myomectomy.

Subjects & Methods: Sixty patients divided in two equal groups. The first group received intraoperative oxytocin during myomectomy and the second group receive saline as a placebo.

Results: Oxytocin infusion is significant associated with a lower post-operative Blood loss, hemoglobin and hematocrit reduction with subsequent less blood transfusion. As well as significantly shorter operative duration, amputation time and hospital stay.

Conclusion: Oxytocin infusion could be used to reduce blood loss during myomectomy.

INTRODUCTION

Oxytocin is a hormone secreted mainly from the pituitary gland. Its main function is uterine contraction during labour and delivery. Oxytocin is the agent of choice in the prevention of postpartum uterine atony and bleeding, (*Wang et al., 2007; Yamaguchi et al., 2011*) but should be used cautiously because an intravenous bolus of 10 IU oxytocin could be detrimental to women with heart disease or to women who are hypovolemic (*Langesæter et al., 2006*).

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 (*Shokeir et al., 2011; Agostini et al., 2005*).

Wang et al. (Wang et al., 2007; Wang et al., 2004) discovered the ability of oxytocin to reduce the haemorrhage and subsequent blood transfusion requirement during laparoscopic myomectomy and laparoscopic vaginal hysterectomy. The one published randomized double-blind study did not show any benefit of using oxytocin in preventing bleeding during abdominal and vaginal myomectomy (*Agostini et al., 2005*).

Uterine leiomyomas (fibroids) are the most common benign tumours among women (*Kongnyuy et al., 2008*). Fibroids are found in approximately 20% of women over 35 years of age (*Thomas et al., 2010*).

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 the uterus and fertility (*Kongnyuy et al., 2008*).

Blood transfusion can be required in up to 20% of the women during abdominal myomectomy (*Raga et al., 2009*). A number of interventions have been introduced to reduce bleeding rate during myomectomy, such as use of tourniquets, vaginal misoprostol, intra-myometrial infiltration of bupivacaine plus epinephrine, injection of vasopressin into the uterus, preoperative administration of gonadotropin-releasing hormone (GnRH) agonist, and perioperative injection of ascorbic acid. 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 (*Kongnyuy et al., 2008; Lethaby et al., 2002; Helal et al., 2010; Wang et al., 2007*).

Complications included intraoperative hemorrhage, injury to adjacent organs (such as bowel, ureter and urinary bladder) and anesthetic complications (*Kunde et al., 2009*).

However, data about oxytocin infusion was insufficient and contradictory about the safety and efficacy of oxytocin infusion to minimize blood loss during myomectomy.

AIM OF THE WORK

This study aims at assessment of the efficacy of oxytocin infusion on reducing blood loss during abdominal myomectomy.

Research hypothesis

In women undergoing abdominal myomectomy oxytocin infusion may reduce blood loss during the operation.

Research Question

In women undergoing abdominal myomectomy does oxytocin infusion reduce blood loss during the operation?

OXYTOCIN

Oxytocin is a principal uterine-contracting and milk-ejecting hormone of the posterior pituitary and produced in the hypothalamus (nucleus paraventricularis). It is also used for prevention of PPH as well as for induction of labour (**Dale, 1909**).

Many studies showed that the use of oxytocin (OT) may help to optimize delivery without disastrous side effects. The knowledge about its structure, origin and effects gave rise to research projects from different points of view. In 1992, a nocturnal peak in the concentrations of plasma oxytocin was found correlated with the nocturnal peak in uterine activity in late pregnancy (**Fuchs et al., 1992**).

Recent investigation prove that oxytocin, this small nine amino acid peptide is now believed to be involved in a wide variety of physiological and pathological functions such as sexual activity, penile erection, ejaculation, pregnancy, uterine contraction, milk ejection, maternal behavior, social bonding, stress and probably many more, which makes oxytocin and its receptor potential candidates as targets for drug therapy (**Magon et al., 2011**).

For labor induction or augmentation, oxytocin is used as an intravenous infusion of a dilute solution. While there is no universal standard for dilution, clinicians must be aware of and