Research Article

Comparative study between the use of preoperative Misoprostol and intraoperative bilateral uterine artery ligation versus bilateral uterine artery ligation alone versus Misoprostol alone in reducing blood loss during abdominal myomectomy

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Abstract

Background: Fibroids are benign tumors characterized by the proliferation of uterine muscle cells and the production of a collagenous matrix. Myomectomy can be accomplished by laparotomy, laparoscopy or hysteroscopy. Substantial blood loss associated with the dissection of huge fibroids renders myomectomy a more technically challenging procedure. It was reported in abdominal myomectomy that up to ٢٠٪ of patients need blood transfusion and up to ٢٪ might need hysterectomy. **Methods:** Sixty patient were recruited to this study from the outpatient clinic in Minia university hospital requiring abdominal myomectomy for symptomatic leiomyomas. The patients classified randomly in to ٣ groups: Group (I): including ٢٠ patients received preoperative misoprostol in dose of ٨٠٠ µg vaginal.(Mistoac ٢٠٠ mcg per tablet) and do bilateral uterine artery ligation (combined group), Group (II) including patients ٢٠ do bilateral uterine artery ligation alone (ligation group). Group (III): including patients ٢٠ that received misoprostol alone in dose of ٨٠٠ µg vaginal.(Misotac ٢٠٠ mcg per tablet) (misoprostol group). **Results:** the study resulted in: there is nostatistically significant difference betwn th ٣ groups regarding age, parity and body wight. Blood Loss (ml) was ٣٣٦.٠+٨١, .٥٤٧٢.٥ + ١٨٨.١, ٥٢٧.٥+٨٥.٠ in group ١, ٢, ٣ respectively. Post-operative Hb (gm/dl) was ٩.٩٧ +٠.٩٥, ٩.٠٣+١.٠٥, ٩.٠٢+١.٠٣ in group ١, ٢, ٣ respectively. The Number of patients needed blood transfusion was ١(٥٪), ٤(٢٠٪) and ٥(٢٥٪) in group ١, ٢, ٣ respectively. **Conclusion:** It could be concluded that preoperative use of vaginal misoprostol prior to abdominal myomectomy in combination with intraoperative bilateral uterine artery ligation could be a effective, efficient and reliable methods in reducing blood loss with subsequent reduction in need for blood transfusion associated with minimal drug related adverse effects than the use of bilateral uterine artery ligation alone or the use of misoprostol alone without increasing the operative time

Key words: misoprostol, myomectomy, uterine artery ligation.

Introduction

Uterine fibroids (also termed leiomyomas or myomas) are the most common tumors of the female repro uterine fibroids may be diagnosed by pelvic clinical examination and ultrasound. Sometimes it is not possible clinically to accurately determine whether a pelvic mass involves the uterus or not, but ultrasound is a simple way to confirm this. In doubtful cases, magnetic resonance (MR) imaging or computed tomography may help (Shwayder et al., ٢٠١٤).

The traditional management of symptomatic fibroids has been surgery (hysterectomy or myomectomy).

However, some women do not want invasive surgery and wish to retain their uterus and fertility. Fortunately in this respect, during the last few years new medical and surgical uterine-conserving alternatives have become available as technological advances have been made.

Pharmacological management of symptomatic uterine fibroids has benefited from the introduction of new compounds, although the indications and treatment duration are limited by their side-effects (Borah et al., ٢٠١٣).

Myomectomy can be accomplished by laparotomy, laparoscopy or hysteroscopy. Substantial blood loss associated with the dissection of huge fibroids renders myomectomy a more technically challenging procedure. It was reported in abdominal myomectomy that up to ٢٠٪ of patients need blood transfusion and up to ٢٪ might need hysterectomy (Lethaby et al., ٢٠٠٤). Number of interventions have been introduced to reduce bleeding during myomectomy. Despite these actions, prevention of excessive hemorrhage during myomectomy remains a major task for surgeons (Morita et al., ٢٠٠٤).

It is well known that prostaglandins such as misoprostol or prostaglandin E٢ analog, not only increases myometrial contractions but also reduces uterine artery blood flow and may decrease intraoperative hemorrhage in myomectomies (Rossetti et al., ١٩٩٩). While they may be asymptomatic they can cause abnormal bleeding, pelvic pressure symptoms and infertility. Fibroid growth and regression vary throughout life. Thus, they tend to grow during the patient's reproductive years and regress after the menopause. They affect millions of women and are the leading cause of hysterectomy (Bulun, ٢٠١٣)

Aim of the work

The present study was designed to evaluate the use of pre-operative Misoprostol and intraoperative bilateral uterine artery ligation versus bilateral uterine artery ligation alone versus Misoprostol alone in reducing blood loss during abdominal myomectomy in Minia University hospital.

Patients and Methods

Setting

This study was conducted prospectively in the department of Obstetrics & Gynecology, El-Minia University Hospital during period from January. to September ٢٠١٤. El-Minia University Hospital is a tertiary hospital in Upper Egypt attended by most complicated cases.

Ethics

The study protocol was approved by the clinical research ethics committee of faculty of medicine, El-Minia University.

Recruitment & Consent:

Sixty patients were recruited to this study from the outpatient clinic in Minia university hospital requiring abdominal myomectomy for symptomatic leiomyomas, written informed consent were taken from patients after full explanation of the procedure.

Inclusion criteria

Patients undergoing abdominal myomectomy with the following conditions:

- Anterior wall myoma
- Intra mural myoma
- Single myoma
- Multiple myomas provided that removal will be through one incision line
- Comparable size of myoma in all patients

Exclusion criteria

- Known allergy to prostaglandin.
- Known history of pelvic/ovarian endometriosis.
- Known history of medical disease (hypertension, cardiac, pulmonary disease, chronic endocrine or metabolic diseases such as diabetes).
- Blood diseases affecting coagulation profile.
- Anemic patients (less than ١٠ gm/dl)

History Taking

All women, were included into the study, were subjected to medical history taking including; name, age, education level, residence, history of medications.

Past history of chronic medical disorders as (anemia, hemorrhagic diseases, cardiac diseases, sever chronic allergic conditions, hepatic or renal) was also taken.

Menestrual history including: age of menarche, menstrual cycle, duration,

dysmenorrhea, intermenestrual spotting or discharge & last menstruation.
Obstetric history including, parity, past obstetric history, including the mode of delivery in the previous pregnancies, either spontaneous or instrument-assisted or by cesarean section, also history of previous laparotomy were taken.

Examination
General examination; vital signs were carefully measured intra-operative and every ٣٠ min post-operative for ٢ hours;they include four main items., pulse (P) measured from radial artery, blood pressure (BP), body temperature (T) was measured axillary & respiratory rate.
Also pallor, signs of haemostatic disorders, chest and heart were clinically evaluated during operation.

Abdominal Examination; to determine uterine size (in weeks), number of myoma & size of largest one if multiple myoma.
Local examination; for vaginal bleeding or any local gynecological lesions.
*Bimanual examination; to detect any other lesions than myoma

Investigations
All women included in the study had a real time ultrasound by using (TOSHIBA SSA-٣٤٠A diagnostic ultrasound equipment) to determine size, site (anterior or posterior wall), number of myomas & size of largest one if multiple myoma.
In addition to the ultrasonagraphic examination done with admission, some laboratory investigations were performed including.

Haemoglobin (Hb) concentration, pre-operative Hb was detected as a routine investigation of admission and post-operative Hb was also detected by drawning another sample ١٢ hours after surgery, difference between two samples was calculated. Coagulation profile: which include prothrombin time (PT) prothrombin concentration (PC), and platelets count.

Study design:
This study included sixty patients which were randomly allocated into three groups, nearly equal in number of participants, each group included twenty patients, one as a control groups and the others as intervention groups.after discharge of five patients from the study due to:
Group (I): including patients received preoperative misoprostol in dose of ٨٠٠ µg vaginal. (Mistoac ٢٠٠ mcg per tablet) and do bilateral uterine artery ligation (combined group), Group (II) including patients do bilateral uterine artery ligation alone (ligation group), Group (III): including patients that received misoprostol alone in dose of ٨٠٠ µg vaginal. (Mistoac ٢٠٠ mcg per tablet) (misoprostol group)

Procedure
The drug was given ٦٠ min before the operation. Women in all groups were asked to remain in the supine position for ١٠ min following insertion. Vaginal medications were inserted by one of the investigating team members to ensure proper placement high up into the vagina.

Patients were admitted before the operation by three days. Blood pressure, pulse rate and temperature were recorded at the time of admission and investigations were done in the following days including ultrasound examination and complete blood picture.
Abdominal myomectomy was performed by the usual standard surgical technique through a transverse suprapubic incision and intraoperative bilateral uterine artery ligation was done to all patients of group I and group II before uterine incision started.

Data Collection
The total volume of intraoperative blood loss was estimated by measuring the amount of blood accumulated in the aspiration equipment.
Postoperative hemoglobin was measured ١٢ h after the operation. Any intraoperative and postoperative transfusion was recorded. The patient was discharged from hospital according to the clinical situation, and was scheduled to return for a follow-up assessment ٦ weeks after the surgery, or earlier if medically indicated.

Study outcome
Primary outcome
Visually estimated amount of blood loss

Secondary outcome

١. Drop in Hb level
٢. Need for blood transfusion
٣. Operative time
٤. Post- operative stay
٥. Occurrence of side effects

Statistical analysis:

The results were recorded, tabulated and statistically analyzed. The data of all patients were fed into an IBM- compatible personal computer and analyzed using SPSS (version ١٦.٠.٠, California, USA).

Continuous and ordinal data were established as mean ±standard deviation (SE) and other data as nominal scale (present ١; absent ٠). Chi-square (Fischer's exact test) was used for ordinal and continuous data and the Mann-Whitney U test for continuous data in the comparison between groups. P≤.٠٥ was considered statistically significant. In repeated measurements, Freidman variance analysis was employed; on finding P≤.٠٥, a double measurement was made with Wilcoxon Rank test and P≤.٠٥ was considered statistically significant.

Results

Table (١): Patients characteristics in the studied groups

Variables (mean+/-SD)	Group I (Combined Group) (N = ٢٠)	Group II (Ligation Group) (N = ٢٠)	Group III (Misoprostol Group) (N = ٢٠)	P-VALUE
Age (years)	٣٧.٠ ± ٢.٨	٣٦.٣ ± ٣.٢	٣٦.٥ ± ٣.٢	٠.٧٧
Body wt. (Kgs)	٨١.٨ ± ٦.١	٨٣.٥ ± ١٠.٩	٨٢.٤ ± ١٠.٨	٠.٨٥
Parity				٠.٩١
٠	٨ (٤٠٪)	٦ (٣٠٪)	٧ (٣٥٪)	
١	٧ (٣٥٪)	١٠ (٥٠٪)	٩ (٤٥٪)	
٢	٥ (٢٥٪)	٤ (٢٠٪)	٤ (٢٠٪)	
Previous Laparotomy	٧(٣٥٪)	٥ (٢٥٪)	٦ (٣٠٪)	٠.٧٩

** Significant.*

Table (٢): Features of myoma in the studied groups

Variables (mean+/-SD)	Group I (Combind group) (n = ٢٠)	Group II (Ligation group) (n = ٢٠)	Group III (Misoprostol Group) (n = ٢٠)	P-value
Uterine Size (weeks)	١٣.٧ ± ٢.٢	١٤.٤ ± ٢.١١	١٤.٣ ± ١.٩	٠.٥٣
No. of Myomas	٢.٦٥ ± ٠.٩١	٢.٩٥ ± ٠.٩٤	٣.١ ± ٠.٨٣	٠.٢٨
Largest Myoma (cms)	٨.١ ± ١.٦	٧.٨ ± ١.٤	٨.٣ ± ١.٨	٠.٦٢

Table (٣): Mean values of pre-operative Hb among the studied groups

Variables (mean+/-SD)	Group I (Combind group) (n = ٢٠)	Group II (Ligation group) (n = ٢٠)	Group III (Misoprostol Group) (n = ٢٠)	P-value
Pre-operative Hb (gm/dl)	١٠.٨٩ ± ٠.٤	١٠.٧٣ ± ٠.٧٨	١١ ± ٠.٤٦	٠.٣٣

Table (٤): Mean values of Post-operative Hb for the studied groups

Variables (mean+/-SD)	Group I (Combind group) (n = ٢٠)	Group II (Ligation group) (n = ٢٠)	Group III (Misoprostol Group) (n = ٢٠)	P-value		
Post-operative Hb (gm/dl)	٩.٩٧ ±٠.٩٥	٩.٠٣ ± ١.٠٥	٩.٠٢ ± ١.٠٣	٠.٠٠٥*		
				I vs II	I vs III	II vs III
				٠.٠٠٥*	٠.٩٧٥	٠.٠٠٤*

*** Significant.**

Table (٥): Mean values of operative time for the studied groups.

Variables (mean+/-SD)	Group I (Combind group) (n = ٢٠)	Group II (Ligation group) (n = ٢٠)	Group III (Misoprostol Group) (n = ٢٠)	P-value		
Operative time (min)	٩٠.٥ ± ٩.٨٥	٩١..٢٥ ± ٨.٢٥	٩١.٧٥ ± ١٣.٤	٠.٥١٩		
				I vs II	I vs III	II vs III
				٠.٥٢٤	٠.٦١٨	٠.٦٠٢

Table (٦): Mean values of blood loss among the studied groups.

Variables (mean+/-SD)	Group I (Combind group) (n = ٢٠)	Group II (Ligation group) (n = ٢٠)	Group III (Misoprostol Group) (n = ٢٠)	P-value		
Blood Loss (ml)	٣٣٦.٠ ±٨١.٥	٤٧٢.٥ ± ١٨٨.١	٥٢٧.٥ ± ٨٥.٠	<٠.٠٠١*		
				I vs II	I vs III	II vs III
				٠.٠٠١*	<٠.٠٠١*	٠.١٨٠

*** Significant.**

Table (٧): Need for blood transfusion among the studied groups

Variables	Group I (Combind group) (n = ٢٠)	Group II (Ligation group) (n = ٢٠)	Group III (Misoprostol Group) (n = ٢٠)	P-value		
Number of patients needed blood transfusion	١ (٥٪)	٤ (٢٠%)	٥ (٢٥%)	٠.٠٢٦*		
				I vs II	I vs III	II vs III
				٠.٠١٨*	٠.٠٠٨*	٠.٧٤٤

Table (٨): Post-operative stay for the studied groups.

Variables	Group I (Combind group) (n = ٢٠)	Group II (Ligation group) (n = ٢٠)	Group III (Misoprostol Grou (n = ٢٠)	P-value
Post-operative Stay	١.٨٠ ± ٠.٦١	١.٧٥ ± ٠.٦٣	١.٩ ± ٠.٧٨	٠.٧٨

Table (٩): Frequency of side effects among the studied groups.

Variables	Group I (Combind group) (n = ٢٠)	Group II (Ligation group) (n = ٢٠)	Group III (Misoprostol Group) (n = ٢٠)	P-value	Variables (mean+/-SD)
No side effects	١٣ (٦٥٪)	٧ (٣٥٪)	١٨ (٩٠٪)	١٣.٠٦	٠.٠٠١*
Nausea,Vomiting	١ (٥٪)	٢ (١٠٪)	١ (٥٪)	٠.٥٤	٠.٧٦
Fever	٣ (١٥٪)	٥ (٢٥٪)	١ (٥٪)	٣.١٤	٠.٢٠
Abd pain	٢ (١٠٪)	٤ (٢٠٪)	٠ (٠٪)	٤.٤٤	٠.١٠
Diarrhea	١ (٥٪)	٢ (١٠٪)	٠ (٠٪)	٢.١١	٠.٣٤
X٢	٧٢.١٦				
P-value	< ٠.٠٠١*				

*** Significant.**

Discussion

This current research, including sixty patients, divided into three groups (twenty patients in each group) compares the use of preoperative Misoprostol and intraoperative bilateral uterine artery ligation versus bilateral uterine artery ligation alone versus Misoprostol alone in reducing blood loss during abdominal myomectomy in reducing blood loss during abdominal myomectomy.

- **As regard mean blood loss:**

It was significantly greater in misoprostol group than in combined group and were respectively ٥٢٧.٥±٨٥ml vs. ٣٣٦±٨١.٥ ml (p value <٠.٠٠١). It was also greater in misoprostol group than in ligation group and were respectively ٥٢٧.٥±٨٥ml vs. ٤٧٢.٥ + ١٨٨.١ml (p value ٠.١٨).

Mean blood loss was significantly greater in misoprostol group and ligation group than combind group (p value ٠.٠٠١). Shokeir et al., ٢٠١٢; in a double-blind randomized controlled pilot study that was conducted in the Department of Obstetrics and Gynecology, Mansoura University Hospital, Mansoura, Egypt, included ١٠٨ patients with ٥٤ patient in each group comparing the efficacy of vaginal dinoprostone vs. placebo revealed mean blood loss in dinoprostone group ٣٦٤±٢٧٩ ml with (P value <٠.٠٢). Husnu celik et al., ٢٠٠٣; in a study included ٢٦ patients divided into ٢ groups requiring abdominal myomectomy in university of Firat,Turkey. Misoprostol group (thirteen patient) received ٤٠٠ microgram vaginal tablet ١ hour before abdominal myomectomy while control group (thirteen patients) received placebo.

Mean blood loss in misoprostol group was ٤٧٢±٧٧ml (p value < ٠.٠٥) which is consistent with our study. Kongnyuy et al., ٢٠١٤; in a Conchare review that included ١٨ RCTs studies were performed on ١٢٥٠ women to assess the effectiveness, safety, tolerability and costs of interventions to reduce blood loss during myomectomy.

Another two RCTs with vaginal misoprostol were conducted on ٨٩ patient and revealed significant reduction in blood loss with MD ٩٧.٨.which is consistent with our study. Kongnyuy et al., ٢٠٠٧; in a Conchare review that included ١٧ RCTs studies with ٣٧١ patients, two RCTs assessed the role of vaginal misoprostol in ٥٨ patient and showed significant decrease in blood loss compared to placebo with MD-١٤٩ ml .

- **As regards postoperative haemoglobin**

Post-operative haemoglobin was signifi-cantly greater in combined group than both of ligation group and misoprostol groups and were respectively ٩.٩٧±٠.٩٥ g/dl,

٩.٠٣±١.٠٥g/dl, ٩.٠٢±١.٠١٣g/dl (p value ٠.٠٠٥).

It was also greater in ligation group than in misoprostol group but with no significant

difference (p value ٠.٩٧٥). Shokeir et al., ٢٠١٢; reported that there was no statistically significant difference in post - operative haemoglobin in the ligation group when compared to the misoprostol group that were respectively (٩.٥±١.٢g/dl vs. ٩.٤±١.٤ g/dl) (p value ٠.٧) which is consistent with our study.

Husnu celik et al., ٢٠٠٣; reported statistically significant difference between misoprostol group and ligation group in post-operative haemoglobin which were respectively ٩.٧±٠.٧g/dl vs.٨.٩±٠.٥g/dl (p value <٠.٠٥) which is consistent with our study.

Kongnyuy et al., ٢٠١٤; also reported statistically significant difference between misoprostol group and ligation group in post-operative haemoglobin which were respectively (٩.٨٥±٠.٦ g/dl vs. ٩.٢±.٧ g/dl) (P value<٠.٠٥) which is consistent with our study.

- **As regards operative time:**

There was no statiscally significant difference in operative time among the three groups with reduced time in combind group in comparison with ligation and misoprostol groups which were respectively, ٩٠.٥±٩.٨٥ min, ٩١..٢٥±٨.٢٥ min, ٩١.٧٥±١٣.٤٠min (p value ٠.٠٠١). Shokeir et al., ٢٠١٢; reported no statistically significant difference between misoprostol group and ligation regarding operative time (٨٢.٨±٣٠min vs. ٨٥.٤±٢٠) (p value ٠.٢) which is consistent with our study.

- **As regards need for blood transfusion**

It was found that combind group had less blood transfusion rate than ligation group and misoprostol group which were respectively ١(٥٪) ,٧(٣٥٪) , ٨(٤٠٪) (p value ٠.٠٢٦) while no significant difference was noticed between the dinoprostone and the placebo groups regarding blood transfusion rate (p value ٠.٧٤٤) .

- **As regards post-operative stay:**

It was found that there was no statistically significant difference regarding post-operative stay between combined , ligation and Misoprostol groups that were respectively ١.٧٥±٠.٦٣, ١.٨٠±٠.٦١ and ١.٩±٠.٧٨ days (p value ٠.٧٨).

- **As regards side effects:**

There was no statistically significant differrence between the three groups regarding the occurrence of side effects in the ٣ groups had fewer incidences of side effects in misoprostol group. Husnu celik et al., ٢٠٠٣; reported no statistically significant side effects in misoprostol group and ligation group (p value ٠.٤).

Conclusion

It could be concluded that preoperative use of vaginal misoprostol prior to abdominal myomectomy in combination with intraoperative bilateral uterine artery ligation could be a effective, efficient and reliable methods in reducing blood loss with subsequent reduction in need for blood transfusion associated with minimal drug related adverse effects than the use of bilateral uterine artery ligation alone or the use of misoprostol alone without increasing the operative time

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