Methylergonovine Infusion May Decrease Blood Loss During Abdominal Myomectomy: A 3-Year Observational Study

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Submission: June 06, 2018; Published: July 26, 2018

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Abstract

Objective: to ascertain whether the peri-operative administration of methylergonovine infusion can reduce blood loss during abdominal myomectomy or not.

Methods: This prospective observational study was conducted on 82 patients with symptomatic multiple intramural myomas intended for abdominal myomectomy, who were allocated into two groups; study group (n=40) received intravenous infusion of methylergonovine during surgery and control group (n=42) received normal saline infusion. Estimated intraoperative blood loss, postoperative hemoglobin and hematocrit values, the need for blood transfusion, postoperative hospital stay and adverse effects of methylergonovine were the outcome measures.

Results: Patients in the study group experienced lesser estimated intra-operative blood loss, higher post-operative hemoglobin, higher post-operative hematocrit, lower number of received packed RBCs units and shorter postoperative hospital stay (p<0.001) with no difference in the frequency of adverse effects related to methylergonovine infusion (p>0.05) compared to the control group.

Conclusion: methylergonovine infusion during abdominal myomectomy significantly reduced blood loss and the need for blood transfusion. Larger multicenter randomized trials are warranted to prove or refute these findings.

Keywords: Methylergonovine; Blood loss; Abdominal myomectomy

Introduction

Uterine myomas are the most common benign tumour affecting about 20-30% of women above the age of 35 years [1]. Myomas are symptomatic in one third of patients causing heavy uterine bleeding, anaemia in addition to pressure symptoms [2]. Symptoms may be severe enough to warrant surgical removal of myomas (myomectomy) via various routes [1]. Myomectomy is associated with severe bleeding that may require emergency blood transfusion [3].

Several medical therapies were examined to reduce blood loss during myomectomy with variable effectiveness including uterotonics such as prostaglandins misoprostol [4] and dinoprostone [5], oxytocine [6,7] and carboprost [8], and more recently ascorbic acid was tried [9]. This observational study was designed to ascertain whether the peri-operative administration of methylergonovine infusion can reduce blood loss during abdominal myomectomy or not.

Materials and Methods

This prospective observational study was conducted at the department of Obstetrics and Gynecology, Menoufia University hospital, Shihin El-Kom city, Menoufia governorate, Egypt during the period between the beginnings of March 2015 and March 2018. The study protocol was formally reviewed and approved by the ethical committee at the Menoufia Faculty of Medicine with all patients signed the informed consent form before commencement of the study.

Calculation of the sample size was based on the results of previous study conducted by Wang et al. [6] with the need for 40 patients in every single group to get an inter-group mean (SD) difference of 200ml in blood loss during myomectomy at a power of 0.9 and level of significance of 0.05. Eighty two patients with symptomatic multiple intramural uterine myomas (≥4) with different sizes, were enrolled after thorough history taking and ultrasound scanning (Figure 1: the flow diagram).
Figure 1: Flow diagram of recruitment and retention of patients in the study.

Patients with medical disorders as hypertension, heart disease, bronchial asthma, diabetes mellitus, bleeding tendency, preoperative Hemoglobin concentration less than 10gm/dL, Body mass index >35, submucosal myomas, known sensitivity to ergot alkaloids or with any contraindication to surgery or methylergonovine administration were excluded from the study.

None of the patients had received preoperative GnRH analogues or any other hormonal and non-hormonal therapies to decrease the myoma size or bleeding during myomectomy. All patients were operated under spinal anaesthesia to rule out drug interactions between methylergonovine and inhalational agents.

Enrolled Patients were divided into Two Groups

Group 1 (Study group)
Comprised 40 patients who administered 2 ampoules of methylergonovine maleate (Methergine 1m 0.2mg, Novartis Pharmaceuticals Corporation, East Hanover, New Jersey 07936, USA) diluted in 1000ml of normal saline over 2 hours starting after opening the anterior abdominal wall layers.

Group 2 (Control group)
Comprised 42 patients who administered only normal saline infusion.

Outcome Measures

Primary outcome
Estimated intraoperative blood loss (ml), preoperative and postoperative hemoglobin and hematocrit values (measures at 8 hours before and 24 hours after surgery) and the need for blood transfusion both intra-operative and post-operative (based on clinical signs and hemoglobin concentration).

Secondary outcome
Operative time, operative details (number of intramural myomas retrieved), postoperative hospital stay and adverse effects of methylergonovine.

Statistical analysis
Data was analyzed by computer using SPSS version 20, Chi square and Fisher’s exact tests were used to compare the two groups. P≤0.05 was considered to indicate significance and P≤0.001 was considered to indicate high significance.

Results
There was no significant difference between the two groups regarding patients’ characteristics included age, body mass index, size of the uterus and measures of the largest myoma (p>0.05) as depicted in Table 1. Patients in the study group experienced better outcome regarding shorter operative time, lesser estimated intra-operative blood loss, higher postoperative hemoglobin, higher post-operative hematocrit value, lower number of received packed RBC units and shorter post-operative hospital stay (p<0.001) as revealed in Table 2 Patients in both groups suffered comparable changes in the blood pressure as well as nausea and vomiting during surgery (p>0.05) with no patients experienced chest pain or difficult breathing as shown in Table 3.
How to cite this article: Ragab D, El-Sayed El-Shamy, Ayman S. Methylergonovine Infusion May Decrease Blood Loss During Abdominal Myomectomy: A 3-Year Observational Study. J Gynecol Women’s Health. 2018: 10(5): 555796. DOI: 10.19080/JGWH.2018.10.555796

Table 1: Patients’ characteristics.

|                          | Study Group (N=40) | Control Group (N=42) | Student T-Test | P-Value |
|--------------------------|--------------------|----------------------|----------------|---------|
| Age (in years)           | 33.9±2.2           | 34.1±2.7             | 0.37           | >0.05   |
| Body mass index (Kg/m²)  | 27.2±6.1           | 26.9±6.9             | 0.21           | >0.05   |
| Size of the uterus (in weeks) | 14.9±0.6      | 15.1±0.4             | 1.78           | >0.05   |
| Measures of the largest fibroid: |          |                      |                |         |
| length (cm)              | 7.2±2.9            | 7.8±2.2              | 1.06           | >0.05   |
| Width (cm)               | 5.8±1.2            | 5.3±1.7              | 1.53           | >0.05   |

Table 2: Perioperative details (*Fisher’s exact test.).

|                          | Study Group (N=40) | Control Group (N=42) | Student T-Test | P-Value |
|--------------------------|--------------------|----------------------|----------------|---------|
| Duration of operation (min) | 80.2±15.4       | 118.6±10.9           | 13.08          | <0.001  |
| Estimated intra-operative blood loss (ml) | 320.6±60.3    | 580.5±76.2           | 17.07          | <0.001  |
| Number of removed myomas | 6.2±2.4           | 5.9±2.7              | 0.53           | <0.05   |
| Pre-operative Hemoglobin (gm%) | 12.9±0.6       | 13.1±0.8             | 1.28           | >0.05   |
| Post-operative Hemoglobin (gm%) | 11.6±0.4      | 10.1±0.7             | 11.83          | <0.001  |
| Pre-operative Hematocrit (%) | 37.3±0.2        | 37.2±0.3             | 1.77           | >0.05   |
| Post-operative Hematocrit (%) | 35.6±0.5        | 31.8±0.7             | 28.2           | <0.001  |
| Number of patients needed blood transfusion | 3 (7.5%)       | 12 (28.6%)           | 4.76*          | <0.05   |
| Number of packed RBCs units transfused | 1.8±0.2        | 2.7±0.6              | 9.02           | <0.001  |
| Postoperative hospital stay (days) | 2.03±0.04      | 3.4±0.06             | 121.03         | <0.001  |
| Venous Thromboembolism   | 0                 | 0                    | -              | -       |
| Admission to Intensive care unit | 0             | 0                    | -              | -       |

Table 3: Adverse effects of methylergonovine administration (*Chi square test).

|                          | Study Group (N=40) | Control Group (N=42) | Fisher’s Exact Test | P-Value |
|--------------------------|--------------------|----------------------|---------------------|---------|
| Changes in blood pressure | 6 (15%)            | 2 (4.8%)             | 1.41                | >0.05   |
| Nausea and vomiting      | 8 (20%)            | 6 (14.3%)            | 0.16*               | >0.05   |
| Chest pain               | 0                  | 0                    | -                   | -       |
| Difficult breathing      | 0                  | 0                    | -                   | -       |

Discussion

This study shows that intravenous infusion of 0.4mg Methylergonovine diluted in 1000ml normal saline significantly lead to reduction of blood loss during abdominal myomectomy with fewer patients required blood transfusion in addition to shorter post-operative hospital stay. Methylergonovine infusion during myomectomy was not associated with considerable adverse effects that warranted interventions as changes in blood pressure, nausea and vomiting, chest pain or difficult breathing.

In the current study, blood transfusion was needed in 12/42 (28.6%) of patients in the control group compared to only 3/40 (7.5%) in the study group. Previous studies demonstrated that about 20-30% of patients undergoing myomectomy required blood transfusion [2,10-12].

A previous Cochrane review concluded that the perioperative use of misoprostol, bupivacaine plus epinephrine, tranexamic acid, gelatin-thrombin matrix, a peri-cervical tourniquet, ascorbic acid, dinoprostone, loop ligation and a fibrin sealant patch may reduce bleeding during myomectomy while there is no evidence that oxytocin, morcellation and temporary clipping of the uterine artery reduce blood loss [3].

Although refuted by previous Cochrane review [3], the use of intravenous infusion of oxytocin to decrease blood loss during laparoscopic myomectomy was extensively studied over the past few years with proved efficacy [6,7].

The effect of methylergonovine on uterine contractility of non-pregnant uterus was previously explored in an observational study to evaluate the pharmacodynamic and pharmacokinetic properties of oral versus intravenous methylergometrine upon uterine motility during menstruation which revealed that after intravenous administration, a fast increase of the frequency and basal tone of uterine contractions occurred with a decrease of its amplitude, lasting for at least 30 minutes [13].

Laparoscopic myomectomy was no adopted in this series secondary to lack of pre-requisites for laparoscopic approach which is limited by the size, number and localization of myomas as well as technique difficulty. To the authors’ knowledge, this is the first trial to explore the effect of intravenous infusion of
Methylergonovine to decrease blood loss during abdominal myomectomy.

Inability to conduct a randomized trial and to include larger sample constitutes unintended limitation of the current study. Future research should focus on the safety and tolerability of Methylergonovine as a potential drug to decrease blood loss during abdominal myomectomy.

Conclusion

Methylergonovine infusion during abdominal myomectomy significantly reduced blood loss and the need for blood transfusion. Larger multicenter randomized trials are warranted to prove or refute these findings.

Acknowledgement

The authors would like to acknowledge the contribution of the residents and nursing staff of the operating room and the blood bank at Menoufia university Hospital.

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