ORIGINAL ARTICLE

Effect of oxytocin infusion on reducing blood loss during abdominal myomectomy: A randomized controlled trial

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Abstract

Objective: To assess oxytocin infusion efficacy in terms of mean blood loss in patients undergoing abdominal myomectomy.

Methods: The single-blind randomised control trial was conducted at the Obstetrics and Gynaecology Department of Military Hospital, Rawalpindi, Pakistan, July 15, 2017, to January 15, 2018, and comprised women with intramural fibroids of American Society of Anaesthesia class I and II who were candidates for elective abdominal myomectomy. The women were randomised into study and control groups. In the study group, an infusion of 30 units of oxytocin in 1000ml normal saline was given at the rate of 15 units/hour during surgery. In the control group, pure normal saline was given. The main outcome measure was intra-operative blood loss. Data was analysed using SPSS 21.

Results: Of the 60 women, there were 30(50%) in the study group with a mean age of 37.10±4.35 years, and 30(50%) in the control group with a mean age of 36.67±3.70 ($p>0.05$). Mean intra-operative blood loss in the study group was 409.67±181.29ml which was significantly lower than the control group 875.33±284.71 ($p<0.05$). The mean surgery time also showed statistically significant difference between the two groups ($p<0.05$). In the study group, 3(10%) patients required blood transfusion, while blood was transfused to 11(36.6%) patients in the control group ($p=0.046$).

Conclusion: Oxytocin, when given as an infusion, was found to be effective in reducing blood loss during abdominal myomectomy.

Keywords: Abdominal myomectomy, Fibroids, Intra-operative blood loss, Oxytocin. (JPMA 70: 969; 2020)
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Introduction

Uterine leiomyomas, commonly known as fibroids, are the most common benign tumours that affect women of reproductive age,[1] with 20% of women aged >35 years having fibroids. Fibroids can be asymptomatic, but they may cause significant problems, such as heavy menstrual bleeding, anaemia, pelvic pain and pressure symptoms in 20-50% patients. Myomectomy, the surgical removal of myomas, is an important treatment option for symptomatic leiomyomas, especially in women who wish to preserve their uteri. This can be accomplished via laparotomy, laproscopy or hysteroscopy.[2]

Myomas have very rich blood supply because of which bleeding is one of the major complications of myomectomy. This can result in significant morbidity and mortality and it remains a major challenge for gynaecologists despite using various techniques to prevent excessive haemorrhage during the procedure.[3]

Following abdominal myomectomy, transfusion is required in up to 20% cases. A number of trials have been conducted to assess the effect of different pharmacological agents to reduce bleeding during myomectomy, such as misoprostol, intra-myometrial infiltration of bupivacaine plus epinephrine, injection of vasopressin into the uterus, pre-operative administration of gonadotropin-releasing hormone (GnRH) agonist, but most of these are ineffective or expensive.[4,5]

Oxytocin, a widely used uterotonic to control bleeding in the postpartum period, is now being considered as a means to reduce bleeding from a non-pregnant uterus. Oxytocin-associated contraction of the uterine musculature leads to contraction of uterine vessels and, thus, causes decrease in the blood supply to myomas and, consequently, reduced blood loss during myomectomy.[6]

A study[2] showed that infusion of 30IU oxytocin during

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abdominal myomectomy caused reduction in intra-operative blood loss, and reduced the need for blood transfusion compared to placebo. Average intra-operative blood loss in the patients who received oxytocin infusion was significantly lower than the placebo group (p<0.0001).

Due to lower concentration of oxytocin receptors in non-gravid uterus, the clinical use of oxytocin outside of pregnancy is limited. As such, not much data is available on the subject. The current study was planned to assess the effect of oxytocin in reducing blood loss during myomectomy.

Patients and Methods

The single-blind randomised control trial (RCT), was conducted at the Obstetrics and Gynaecology Department, Military Hospital, Rawalpindi, Pakistan, from July 15, 2017, to January 15, 2018, and comprised women with fibroids. After approval from the institutional ethics committee, the sample size was calculated using World Health Organisation (WHO) calculator[7] in the light of literature.[2] The Level of significance was 5%, confidence interval (CI) 95% and Power of test was 80%. The trial was registered at Clinicaltrials.gov with NCT 03702946.[8] Those included in the study were women of American Society of Anaesthesia (ASA) physical status class I and II with intramural fibroids who were due to undergo elective abdominal myomectomy. Women with haemoglobin (Hb) <10g/dl and any respiratory or cardiovascular disease were excluded. None of the included patients had received danocrine or GnRH analogues before the surgery.

After written informed consent was taken from all the patients, they were randomised into study and control groups of equal strength using the lottery method. Data related to demographics, parity and weight was recorded. Uterine size was assessed by bimanual pelvic examination. Only consultant gynaecologists and consultant anaesthetists performed the procedure in order to reduce the operator bias. Also, surgical procedural elements and prophylactic antibiotics were standardised to eliminate any potential confounding effect. In study group, after the induction of general anaesthesia (GA), an infusion of 30IU oxytocin in 1000ml normal saline was started at the rate of 15units/hour by a trained anaesthetist. In the control group, the patients only received 1000ml saline at the rate of 500ml/hour.

The primary outcome measure was intra-operative blood loss which was measured at the end of surgery by calculating the sum of blood in the suction bottle and the blood absorbed in the sponges. Dry sponges were weighed before the surgery and the blood-soaked sponges were weighed at the end of the surgery. There was a single trained person who calculated the intra-operative blood loss and he was blinded to the randomization of the patients and the use of medication.

Secondary outcome measures were frequency of blood transfusion, post-operative Hb, total surgery time and total anaesthesia time.

Data was analysed using SPSS 21. Mean and standard deviation (SD) were calculated for quantitative variables, i.e. age, weight, uterine size, size of the largest fibroid, and intra-operative blood loss. Frequency and percentage were calculated for categorical variables, i.e. need for blood transfusion. Independent sample t-test was used to compare quantitative variables, like intra-operative blood loss in both groups. Chi square test was used for comparison of qualitative data like frequency of blood transfusion. P<0.05 was considered statistically significant.

Results

Of the 60 women, there were 30(50%) in the study group with a mean age of 37.10±4.35 years, and 30(50%) in the control group with a mean age of 36.67+3±0.70 (p>0.05) (Table-1). In the study group, the average blood loss was 409.67±181.29ml while in the control group it was 875.33±284.71ml (p <0.0001). The average amount of intra-operative fluid used also showed similar results with 720±263 ml in the study group and 1016±278 ml in the control group (p<0.0001).

Table-1: Patients' pre-operative characteristics in the two groups.

	Study group (n=30)	Control group (n=30)	p
Age (years)	37.10±4.35	36.67±3.70	0.617
Weight (Kg)	69.97±9.69	66.90±6.46	0.466
Uterine size (weeks)	18.33±4.52	16.67±3.53	0.360
Largest fibroid (cm)			
Length (average)	10.67±3.21	10.45±3.06	0.732
Width (average)	8.48±2.22	8.64±2.62	0.505

In the study group, 3(10%) patients required blood transfusion, while in the control group, blood was transfused to 11(36.6%) patients (p=0.046) (Table-2).

Table-2: Peri-operative variables in the study of the two groups.

	Study group (group 1) n=30	Control group (group 2) n=30	P
Total intra-operative iv fluid (ml)	720±263.14	1016±278.03	(p <0.0001)
Intra-operative calculated blood loss (ml)	406.33±171.67	875.33±284.711	(p <0.0001)
Patients who needed blood transfusion (%)	10	36.6	0.046
Number of removed fibroids	2.17±0.69	2.47±0.63	0.062
Pre-operative Hb (g/dl)	11.53±0.61	11.44±0.51	0.061
Post-operative Hb (g/dl)	11.19±0.77	10.53±0.88	0.522
Duration of surgery (min)	50.50±14.40	71±11.99	(p <0.0001)
Duration of anaesthesia (min)	75.67±16.54	97.83±14.60	(p <0.0001)
Total intra-operative iv fluid (ml)	720±263.14	1016±278.03	(p <0.0001)
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Post-operative Hb (g/dl)	11.19±0.77	10.53±0.88	0.522
Duration of surgery (min)	50.50±14.40	71±11.99	(p <0.0001)
Duration of anaesthesia (min)	75.67±16.54	97.83±14.60	(p <0.0001)

Hb: Haemogloboin.

The average pre-operative haemoglobin in group 1 and group 2 were similar, 11.53±0.61 g/dl and 11.47±0.47 g/dl respectively (Table-2). The average post-operative haemoglobin was found to be lower in control group but the difference was not statistically significant. It was 11.19±0.77 and 10.56±0.85 in group 1 and group 2 respectively (p= 0.09) (Table-2).

The average surgery and anaesthesia time also showed statistically significant difference. The average surgery time was 50.50±14.40 min in group 1 and 71±11.99 min in group 2 (p <0.0001) The average anaesthesia time was 75.67±16.54 min in group 1 and 97.83±14.60 in group 2 (p <0.0001).

Discussion

Surgical myomectomy is currently considered to be the standard surgical treatment in patients who have a desire of future fertility.[9,10] One of the major morbidities associated with myomectomy is a high risk of intra-operative and post-operative bleeding. Haemostasis at the time of surgery is paramount to the success of patient recovery. Excessive bleeding may make complete dissection difficult.[11] It may increase the time of surgery, post-operative pain and prolonged hospital stay. It can also cause need of blood transfusion in up to 20% cases and need of hysterectomy in 2% of myomectomies.[12,13] A number of safe and effective interventions have been proposed for this purpose, including intra-myometrial vasopressin, misoprostol, removal of myoma with prior ligation of bilateral uterine and ovarian arteries.[14,15] But these methods have various side effects and limitations.

Oxytocin is widely used for the prevention and treatment of postpartum haemorrhage (PPH). Most obstetric units use intravenous (IV) oxytocin as the first-line agent to prevent uterine atony after vaginal delivery and also to decrease blood loss during caesarean section (CS).[16]

In our study, the average blood loss in the control group was significantly lower than the control group. Also, 11 patients in the control group required blood transfusion within 24 hours of the surgery which was significantly higher compared to the study group. Patients who received oxytocin infusion also showed a significant reduction in use of intra-operative fluid and operation time.

The findings corresponded to those of an earlier study.[2] Another study[17] with similar findings concluded that the reduction in blood loss was because of reduction in blood supply to the uterus under the effect of oxytocin.

Main side effects caused by oxytocin are tachycardia, hypernatremia and hypotension.[18] We did not find any of these side effects probably due to low dose of oxytocin given as infusion. Intra-myometrial injection of vasopressin is used to reduce blood loss during myomectomy.[19] Vasopressin has vasoconstrictive properties on all the blood vessels, including uterine vessels, but it has many side effects. It is associated with hypertension (HTN) because of its vasoconstrictive action. It causes nausea, vomiting and pain due to uterine contraction.[20] A study conducted to see the effect of intramuscular (IM) injection of carboprost in reducing haemorrhage during myomectomy found that the reduction in blood loss was similar to vasopressin. The reduction was significantly lower if carboprost was combined with IV injection of 20IU of oxytocin. But carboprost has many side effects. It causes nausea, vomiting, diarrhoea, HTN, headaches and it aggravates asthma. When combined with oxytocin, it causes significant uterine pain.[21]

Vascular occlusion techniques known as tourniquet or uterine artery embolisation are also being used to reduce haemorrhage during myomectomy. These methods require additional interventions before the surgery or a separate procedure during the operation. Large and laterally placed myomas make access to uterine artery difficult and require special expertise.[22] oxytocin infusion does not require any special expertise or additional intra-operative procedures.

The current study had some limitations. Firstly, it was a single centre trial with limited number of patients. We were unable to conduct a double-blind RCT. We could not specify one gynaecologist and one anaesthetist for the study because of administrative issues.

Further studies, especially multi-centre double-blind RCTs with larger sample size are needed to confirm the findings of the current study.

Conclusion

Oxytocin, when given as an infusion at the rate of 15 units/hour, was found to be effective in reducing blood loss during abdominal myomectomy.

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