

Effects of a single rectal dose of Misoprostol prior to abdominal hysterectomy in women with symptomatic leiomyoma: a randomized double blind clinical trial

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Abstract

Background: Fibroma, the most common benign pelvic tumor in women, affects 25 to 30% of women of reproductive age. Primary treatment for patients with symptomatic or large fibroma is surgery.

Objective: The purpose of this study was to investigate the effect of a single rectal dose of Misoprostol on bleeding during abdominal hysterectomy.

Methods: This double blind randomized clinical trial was conducted with 80 candidates for abdominal hysterectomy, due to uterine myoma, in the Shahid Sadoughi hospital of Yazd in 2012. The aim of this study was to assess the effect of single rectal dose of Misoprostol on peri-operational abdominal hysterectomy bleeding. Following administration of 400 micrograms of Misoprostol in the case group (n=40), predetermined criteria were compared with control group (n=40).

Results: Volume of bleeding during the operation was significantly lower in cases where Misoprostol was used. (268.71 ± 156.85 vs. 350.38 ± 152.61 cc in the case and control groups, respectively). Our findings also showed that Hemoglobin (Hb) levels before, 8, and 30 hours following the operation differed significantly ($p=0.001$), but these changes were similar in both groups. Pre-operative Hb levels were 11.90 ± 1.7 and 11.90 ± 2.0 in the case and control groups, respectively.

Conclusion: A single rectal dose of Misoprostol has positive effect on reducing peri-operational bleeding in women undergoing abdominal hysterectomy due to symptomatic leiomyoma.

Trial registration: The trial is registered at the Thailand Clinical Trial Registry (<http://www.clinicaltrials.in.th>) with the TCTR identification number TCTR20151011001.

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1. Introduction

Fibroids (uterine fibroma) are common benign tumors of uterine smooth muscle cells. During reproductive years, approximately 25-30% of women experience symptoms due to non-cancerous elastic tissue growth in uterine wall (1). These tumors consist of smooth muscle cells and extracellular matrix (collagen, prostaglandin, and fibronectin). Leiomyomas (Fibroma) are often multiple, separated, round or lobulated, and irregular. Different locations these tumors occur are classified as sub mucosal, intramural (interstitial), or sub serousal. The latter two types are more common and only 5% of fibroids are sub mucosal (2). Leiomyomas are not seen before puberty and only grow during reproductive ages due to their hormone dependence. Although fibromas are typically asymptomatic, some women may experience metrorrhagia, menorrhagia, pain, and rarely infertility (3).

Women with large or symptomatic leiomyomas primarily undergo hysterectomies. In the United States, more than 175000 hysterectomies occur annually due to leiomyomas (4). According to most studies, uterine fibromas are the leading cause of hysterectomies (5). A hysterectomy is a permanent solution to fibroids and is recommended only as last option in women who do not wish to become pregnant (4). In many cases, Gonadotropin-releasing hormone (GnRH) agonists are used to minimize uterine and tumor size in order to reduce peri-operational bleeding (6).

2. Material and Methods

This double blind randomized clinical trial was done on patients hospitalized due to uterine myoma in the Gynecology ward of Shahid Sadoughi hospital in Yazd during 2012 and were candidate for abdominal hysterectomy. The patients were randomly divided into two equal groups, according to a coding list by the head nurse of the ward, who was blind to the study. To obtain study power of 80%, a standard deviation of 200 cc bleeding volume, and a significant difference of at least 80 cc, 40 patients were enrolled in each group. Eligible women were defined as candidates for abdominal hysterectomy due to uterine fibroma.

In the case group, 400 micrograms rectal Misoprostol was administered 30 minutes prior to operation. The controls received a placebo. The patients were hospitalized one day prior to operation. Age, previous operations, and BMI were registered. Total bleeding was assessed by blood volume in the suction set and surgical gauzes (15 cc for each gauze and 50 cc for each long gauze). Before, 8, and 30 hours following surgery, Hb levels were registered. The patients, nurses and investigators were all blind to this study. The medications were encoded and given to the patients by the head nurse. Data was reported in each questionnaire separately and the analyzed by independent t and paired t-tests ($p=0.05$). Required information was extracted through check lists. Data was analyzed with SPSS version 16 (SPSS Inc. Chicago Illinois, USA) using t-test and Chi-square test. The desired confidence level (0.95) was necessary for consideration in data analysis.

3. Results

The mean age of patients was 46.4 (32-67 years). As shown in Table 1, there was no significant difference between the two groups in terms of history of C/S or laparotomy. According to Table 2, prior to operation, Hb levels were 11.86 and 11.9 in the case and control groups, respectively. However, after 8 and 30 hours following the operation, Hb levels were 11.19 vs. 11.06 and 11.12 vs. 10.94 in the case and controls groups, respectively. Our findings showed a significant difference ($p=0.001$) between 8 and 30 hours post-op Hb mean levels, but the changes were similar in both groups. In other words, Hb levels dropped at 30 hours post-operation respective to Hb levels at 8 hours after the operation, but misoprostol did not have an effect. Hb levels were 11.90 ± 1.7 and 11.90 ± 2.0 in Misoprostol and placebo groups, respectively. The mean volume of preoperative bleeding in the study group was 268.71 ± 156.85 and was 350.38 ± 152.61 in the control group, indicating that there was a significant difference between these two groups ($p=0.002$).

Table 1. Demographic data of both the study and control groups

Variables	Groups		p-value
	Study group (Misoprostol)	Control group (placebo)	
Prevalence	40	40	
Age (mean \pm SD)	46.2 ± 5.67	46.5 ± 5.63	0.08
Previous C/S (mean \pm SD)	0.31 ± 0.62	0.52 ± 0.94	0.27
HX of laparotomy (mean \pm SD)	0.3 ± 0.56	0.3 ± 0.27	1.0

Table 2. Mean Hb level of both the study and control groups

Index	Study group (n=40)	Controls group (n=40)	p-value
Pre-op Hb level	11.86 ± 1.7	11.9 ± 2	0.891
8 hrs post-op Hb level	11.19 ± 1.2	11.06 ± 1.4	0.564
30 hrs post-op Hb level	11.12 ± 1.25	10.94 ± 1.46	0.579
Pre-op and 8 hrs post-op Hb levels difference	0.66 ± 1.2 p=0.001	0.83 ± 1.4 p=0.001	0.57
Pre-op and 30 hrs post-op Hb levels difference	0.74 ± 1.04 p=0.001	0.96 ± 1.5 p=0.001	0.475
8 hrs and 30 hrs post-op Hb levels difference	0.07 ± 0.47 p=0.385	0.12 ± 0.62 p=0.250	0.713

4. Discussion

For the first time, effect of single rectal dose of misoprostol was compared with placebo on peri- and post-operative bleeding during abdominal hysterectomy. Uterine myoma is the most common benign tumor during reproductive ages and up to 25-30 % of cases are symptomatic and require treatment (1). Different medications, including progestin, androgens, GnRHa1, and mifepristone, have been tried, but, can be used for a short period due to side effects (7, 8). Women with symptomatic and large myomas who don't want children can undergo Total abdominal hysterectomy (TAH). Bleeding, blood transfusion, and iron administration following TAH are not uncommon (9). Misoprostol, a prostaglandin E1 analogue, is cheap and can be stored at room temperature. It is used extensively in the obstetric field due to its low level of side effects. Misoprostol induces uterine contractions and vascular constriction. Our findings show that Misoprostol decreases peri-operative bleeding in women who undergo hysterectomies due to uterine myoma. We show that single rectal dose of Misoprostol significantly decreases peri-operative bleeding in comparison to a placebo dose, but this treatment has no significant effect on 8 and 30 hours post-operative bleeding. It should be noted that Hb levels decrease significantly 8 hours following the operation, but this change was similar in both groups. These findings were similar to Chang et al. (10), which showed that a single rectal dose of Misoprostol plus oxytocin prior to operation significantly decreases peri-operational bleeding and Hb changes. In our study, 30 hours post-op mean Hb levels were 11.12 and 10.94 in cases and controls, respectively, which was similar to Celik et al. (11). They reported volume of bleeding in patients who received Misoprostol and placebo as 472 and 621, respectively. Celik reported that post-op Hb levels were 9.7 and 8.9 in the case and control groups, respectively, indicating a significant decrease in peri-operational bleeding in women receiving vaginal Misoprostol. Biswas et.al showed that sublingual Misoprostol 30 minutes prior to operation could significantly decrease peri-operational bleeding. However, post-op Hb levels were higher in cases than controls. These findings show that a pre-operative single rectal dose of Misoprostol can decrease bleeding following abdominal hysterectomy in patients with symptomatic uterine myomas. Misoprostol can be administered through different routes, including sublingually or vaginally, at different doses.

In our current study, according to pharmacokinetic studies, we opted for a 400 microgram rectal dose, which has been shown to act more rapidly and reach its peak level soon after 30 minutes. The effects of Misoprostol on uterine contractions lasted for 3 hours. Bioavailability of Misoprostol is higher in rectal use than when administered vaginally or orally. As the vagina should be cleaned before TAH, vaginal uses of Misoprostol interfere and are less effective. In Chang et al., a combination of Misoprostol and oxytocin was administered, so evaluation of Misoprostol effect alone is difficult. It should be noted that we did not observe any side effects in our study, which confirms the superiority of rectal administration to sublingual administration, which was studied by Biswas et al. (12).

5. Conclusions

We conclude that a single rectal dose of Misoprostol decrease peri-operative bleeding, but has no significant effect on 80 and 30 hours post-op Hb levels. Misoprostol is cost effective in comparison with GnRH analogue or vasopressin, so we recommended further studies to compare the efficacy and side effects of Misoprostol to GnRH and vasopressin in different doses.

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Conflict of Interest:

There is no conflict of interest to be declared.

Authors' contributions:

All authors contributed to this project and article equally. All authors read and approved the final manuscript.

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