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Investigating and Comparing the Effects of Vasopressin Injection around Uterine Myoma and Rectal Misoprostol Injection in open Myomectomy Surgery to Reduce Bleeding: A Randomized Interventional Study

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Abstract--*The objective of this study was to compare the effects of vasopressin injection around the uterine myoma in open myomectomy with misoprostol rectal surgery to reduce bleeding during the surgery and the level of changes in hemoglobin. In a clinical trial study, 66 patients who were candidates for open myomectomy, were randomly divided into two groups (each group included 33 patients). The first group received 400 µg misoprostol 30 minutes before rectal surgery and the second group received a 20-unit vasopressin ampoule in 19 ml of dissolved normal saline 30 minutes before the surgery. The bleeding volume and hemoglobin level before and after the surgery were measured in two groups and compared with independent and paired t-tests. The mean bleeding volume in the two misoprostol and vasopressin groups was 199.4 ±370.9 and 261.5 ±120.3 ml, respectively. The mean lost blood was lower in the vasopressin group (p=0.009). The mean changes in hemoglobin level in the misoprostol and vasopressin groups were 1.68 ± 0.63 and 1.3 ± 0.55 g / dl, respectively, and the difference between two groups was significant (p = 0.01). Based on the results of our study, vasopressin seems to be more effective than misoprostol in controlling bleeding during myomectomy, but due to inconsistencies in the results of different studies, further studies on these two drugs are recommended to determine the most effective drug in controlling bleeding during the myomectomy surgery.*

Keywords--*Vasopressin, Misoprostol, Myomectomy.*

I. INTRODUCTION

Uterine fibroids are benign tumors of smooth muscle cells around the myometrium, where large aggregates of extracellular matrix consisting of collagen, elastin, fibronectin, and proteoglycans can be found (1 & 2). In an epidemiologic study in the United States in 2003, about 80 percent of black women and 70 percent of white women were found to have leiomyoma in sonography examinations (3). Surgical treatment is often required when these fibroids develop symptoms such as menorrhagia, severe dysmenorrhea, urinary recurrence or obstructive symptoms, infertility, and recurrent miscarriages, dyspareunia, and sexual disorders (4). Procedures

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such as uterine artery embolization (5 & 6), myolysis (7), laparoscopic and abdominal myomectomy (8) and preoperative GnRH agonist injection are used to treat uterine fibroids .There is also controversy on the effectiveness and safety of the interventions to reduce bleeding during myomectomy (9). The interventions include intra-myometrium injection of vasopressin (10 & 11), intravascular injection of oxytocin (12), and use of tourniquet (13 & 14), chemical dissection with sodium-2-mercaptoethanesulfonate (mesna) (15), intra-myometrium injection of bupivacaine and epinephrine (16), and complete removal of myoma using morcellation by clamping the uterine and ovarian arteries. In the case of very severe bleeding, both uterine arteries can be closed or ligated (17, 18). Vasopressin is a type of antidiuretic hormone that causes smooth muscles` contraction in the wall of capillaries. Its complications include bradycardia and cardiovascular collapse (18). Misoprostol is an analogue of E1prostaglandin and is currently used around the world for uterine drainage in cases of missed or incomplete abortions and intrauterine death and induction of labor (19). Several studies have indicated that misoprostol causes very strong contractions in the uterine muscles that can reduce myometrium-induced and postpartum bleedings (20-22). Since misoprostol and vasopressin are currently used to reduce the volume of myomectomy-induced bleeding, the efficacy of each of these methods has been controversial, and no ideal methods has been proposed so far for the appropriate control of myomectomy-induced bleeding during the surgery and no study has been conducted in Iran to compare these two drugs. The objective of this study was to compare the effects of vasopressin injection around the uterine myoma in open myomectomy surgery and rectal misoprostol in reducing the volume bleeding during the surgery as well as the level of changes in the hemoglobin.

II. MATERIALS AND METHODS

This study was a clinical trial conducted in 2015 and 2016 in Alzahra and Shahid Beheshti hospitals in Isfahan. The statistical population of the study included the patients undergoing myomectomy in these centers . Inclusion criteria included patients at the reproductive age of 15-45 years, having intramural myoma of 4-10 cm (confirmed by ultrasound and physical examination), clinical symptoms, no history of blood and coagulation diseases, and cardiovascular disease, normal platelet count, history of up to 3 laparotomies or previous cesarean section, no pregnancy, and BMI between 20 and 30. The exclusion criteria also included severe bleedings during the surgery causing hysterectomy, any drug complications, and hemodynamic disorders during the surgery, and severe adhesion causing severe bleeding during the dissection.

Sample size was estimated at 33 people for each group using the sample size estimation formula to compare the means with considering 95% confidence level, 80% test power, hemoglobin standard deviation of 1.17, and the minimum significant difference between the groups of 0.8. After obtaining the permission from the Medical Ethics Committee of the University and obtaining written consent from patients to participate in the study and after providing necessary examinations and confirmation of inclusion criteria, the patients were randomly assigned to two groups of misoprostol and vasopressin. The patients' characteristics including age, number of pregnancies, number of previous platelets, BMI, size and number of myomas and hemoglobin before the surgery had been recorded in each patient's data collection form . The first group received 400 µg misoprostol

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as a single dose 30 minutes before the rectal surgery and the second group received a 20-unit vasopressin ampoule in 19 ml of dissolved normal saline 30 minutes before the surgery around the myoma and inside the myometrium. During myomectomy, the number of incisions on the uterus was limited as far as possible and the defect created on the uterus was restored in three layers. Then, all of the removed fibers were weighed and their numbers and the diameter of the largest of them were measured and recorded. In each group, the number of myomas and the size of myomas were classified as one or two myomas and more and classified as 4-7 cm myomas and 7-10 cm myomas and examined separately. In order to estimate the volume of blood lost from sucked blood during the surgery, a number of blood-stained gases and long-gases (each gas included about 20 cc and each blood-saturated long-gas included 100 cc of blood) were used, with checking the hemoglobin before and 6 hours after the completion of surgery, level of blood loss was determined. The data were analyzed using SPSS, version 24, software. Statistical tests used for data analysis included Chi-square test, T-test, paired t-test, and Pearson correlation test.

III. RESULTS

During the study, none of the exclusion criteria was observed in any patient. There were no significant differences between the two groups in terms of age. The mean number of previous pregnancies in both misoprostol and vasopressin groups was 1.5 ± 1.2 (p = 0.84). The mean number of myomas in misoprostol and vasopressin groups was 2.6±2 and 2.3 ± 1.7, respectively (p = 0.46). The mean size of myomas in the misoprostol and vasopressin groups were 7.58 ± 1.49 and 7.43 ± 1.42 mm, respectively (P = 0.68). The mean weight of myomas in the misoprostol and vasopressin groups was 239.8 ± 94.8 and 222.4 ± 99.7 g, respectively (P = 0.68) (Table 1). The mean numbers of incisions on the uterus in the misoprostol and vasopressin groups were 1.8 ± 1 and 1.5 ± 0.8 times, respectively (p = 0.29). The number of incisions was 18 people in the misoprostol group and 20 people in the vasopressin group (54.5% vs. 60.6%). Two incisions were seen in 7 and 9 cases (21.2% vs. 27.3%), 3 incisions were seen in 5 and 3 cases (15.2% vs. 9.1%), and 4 incisions were seen in 3 and 1 case (9.1% vs. 3%). The frequencies of incisions were not different between the two groups (0.6).

The mean number of blood gases in the misoprostol and vasopressin groups were 10 ±7.8 and 6.6 ±1.9, respectively (p = 0.017). Also, the mean number of long-gases in the two groups was 0.76 ±0.8 and 0.4 ± 0.7, respectively, and there was no significant differences between the two groups (p = 0.08). The mean volume of suctioned blood in the two groups was 94.5 ± 48.2 and 87 ±43.1 ml, respectively, and the difference between the two groups was not significant (p = 0.51). The mean bleeding volume in the misoprostol and vasopressin groups was 370.9 ±199.4 and 261.5 ±120.3 ml, respectively. Vasopressin group patients had lower bleeding volume (p = 0.009). The mean preoperative hemoglobin level in the misoprostol and vasopressin groups was 12 ± 1.1 and 11.5 ± 0.81 g / dl, respectively, and the vasopressin group had lower hemoglobin (p = 0.028). Postoperative hemoglobin levels in the misoprostol and vasopressin groups were 10.36 ± 0.85 and 10.21 ± 0.74, respectively (p = 0.44). T-paired test also showed that hemoglobin level was significantly reduced in both groups (p <0.001). The levels of change in the hemoglobin in the misoprostol and vasopressin groups were 1.68 ± 0.63 and 1.3 ± 0.55, respectively (p = 0.01). The percentage of reduction in hemoglobin level was 0.14 ± 0.05 in the

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misoprostol group and 0.11 ± 0.04 in the vasopressin group. The hemoglobin level was significantly lower in the misoprostol group (p = 0.025) (Chart 1). Based on the Pearson correlation tests, there was a significant relationship between changes in hemoglobin level and myoma number, myoma weight, number of surgical incisions, previous laparotomy and volume of suctioned blood, so that with increasing each of these variables (myoma number, myoma weight, number of incisions, previous laparotomy, and volume of suctioned blood, the hemoglobin levels), the hemoglobin level significantly reduced. Also, the number of previous laparotomies was significantly correlated with changes in hemoglobin levels in the vasopressin group, but such a correlation was not observed in the misoprostol group. There was a significant correlation between the number of pregnancies and hemoglobin levels (p = 0.024) (Table 2).

Table 1. Distribution of demographic variables in two groups of patients

Variable		**Group**		
		Misoprostol	**Vasopressin**	
Mean age (year)		4.6 ±4.32	6.3±9.31	49.0
Number (%) of previous pregnancies	0	2).7(21	3).9(27	84.0
	1	3).11(33	2).8(24	9.0
	2	2).7(21	3).9(27	
	3	2).6(18	2).5(15	
	4	1).2(6	1).2(6	
Mean BMI		58.2±83.26	64.1±28.26	3.0
Number (%) of myomas	1	5).15(45	5).18(54	65.0
	2-3	3).9(27	2).6(18	
	4 and more	3).9(27	3).9(27	
Mean weight of myomas		8.94±8.239	7.99±4.222	47.0
Mean size of myomas		49.1±58.7	42.1±43.7	68.0
Number (%) of previous laparotomies		5).16(48	5).18(54	62.0

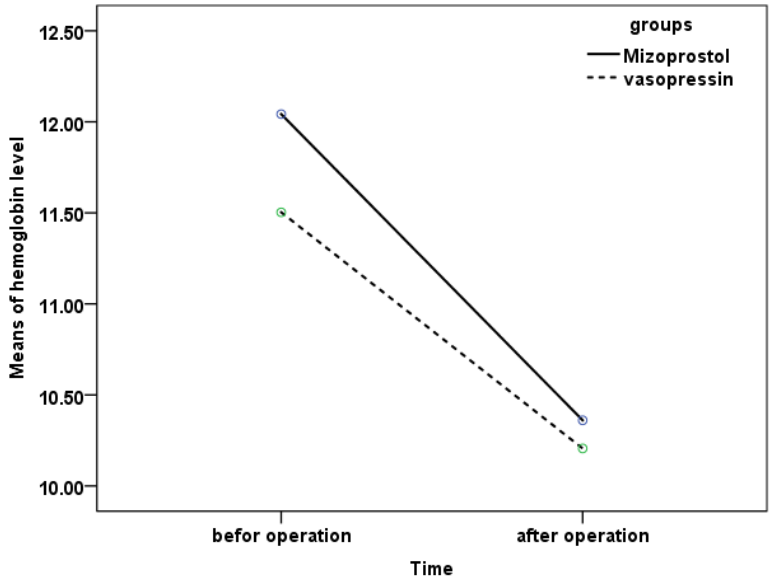

Chart 1. Mean hemoglobin level before and after surgery in both groups

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Table 2. Correlation between hemoglobin level changes and demographic and clinical variables in the two groups

Variable	Misoprostol group		Vasopressin group		Total patients	
	Correlation value	P	Correlation value	P	Correlation value	P
Age	14.-0	44.0	15.-0	39.0	18.-0	15.0
Number of pregnancies	32.-0	07.0	26.-0	15.0	28.-0	024.0
BMI	001.0	99.0	21.0	25.0	07.0	58.0
Number of myomas	81.-0	001.<0	81.-0	001.<0	79.-0	001.<0
Weight myoma	83.-0	001.<0	88.-0	001.<0	87.-0	001.<0
Size of the largest myoma	07.0	68.0	05.-0	79.0	04.-0	77.0
Number of surgical incisions	77.-0	001.<0	70.-0	001.<0	73.-0	001.<0
Number of previous laparotomies	29.-0	11.0	49.-0	001.<0	37.-0	002.0
The volume of suctioned blood	64.-0	001.<0	35.-0	047.0	65.-0	001.<0

IV. DISCUSSION AND CONCLUSION

The objective of this study was to evaluate the effect of vasopressin injection around uterine myoma compared with rectal misoprostol administration in open myomectomy in reducing bleeding and hemoglobin levels. In a study conducted on 25 women in Turkey in 2002, intravenous administration of 400 µg of misoprostol alone in a vaginal and single-dose manner caused a significant reduction in intraoperative bleeding (24). Several studies have shown that vasopressin alone reduces blood loss at myomectomy time (10, 12 and 24).

In one of the conducted studies, the efficacy of vasopressin injection around the vessels in the broad ligament was compared with simultaneous consumption of it with misoprostol in reducing myomectomy-inducing bleeding. The results showed that simultaneous consumption of vasopressin with misoprostol was more effective than the use of vasopressin alone (24).As simultaneous consumption of more drugs increases the risk of drug complications and as the use of vasopressin may be risky in some diseases, such as cardiovascular disorders, and the use of a lower-risk drug such as misoprostol may be helpful in these patients in reducing the volume of myomectomy-induced bleeding, this study was conducted with a larger sample size to compare the effects of these two drugs independently in reducing the volume of myomectomy-induced bleeding. The results of our study showed that there was a significant relationship between hemoglobin level and BMI, number of myomas,

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weight of myomas, number of surgical incisions and volume of bleeding, but this correlation was observed in both misoprostol and vasopressin groups. Thus, the level of effect of these factors was almost similar in both groups. The volume of intraoperative bleeding and changes in postoperative hemoglobin level might be related to the type of used drug.

V. CONCLUSION

Based on the results of our study, vasopressin seems to be more effective in controlling bleeding during myomectomy compared to misoprostol. However, due to inconsistencies in the results of different studies, it is recommended to conduct further studies to determine the most effective drug in controlling the bleeding during the myomectomy.

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REFERENCES

1. Zaloudek CJ, Hendrickson MR, Soslow RA. Mesenchymal tumors of the uterus. Blaustein's pathology of the female genital tract. 2011:453-527.
2. kongnyuy Ej, Wiysonge CS. intervention to reduce haemorrhage during myomectomy for fibroids. Cochrane Database syst Rv.2014; 15:8CD005355-58
3. Day Baird D, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. Am J Obstet Gynecol 2003; 188: 100–7.
4. Saadatnia G, Saremi A, Salehian B, Salehian P. Uterine Leiomyoma and Reproductive Tract Infections Detected by Polymerase Chain Reaction. Iranian Journal of Pathology. 2019 Jan 1; 14(1):15-17
5. Goodwin SC, Spies JB, Worthington-Kirsch R, Peterson E, Pron G, Li S, et al.Uterine artery Embolization for treatment of leiomyomata: long term out-comes from thefibroid registry. Obstet Gynecol 2008; 111:22–3.
6. Tulandi T, Salamah K. Fertility and uterine artery embolization. Obstet Gyne-col 2010;115:857–60.
7. Kim CH, Kim SR, Lee HA, Kim SH, Chae HD, Kang BM. Trans-vaginal-ultrasound-guided radiofrequency myolysis for uterine myomas. Hum Re-prod 2012; 26:559–63.
8. Dubuisson J, Fauconnier A, Deffarges J, Norgaard C, Kreiker G, Chapron C.Pregnancy outcome and deliveries following laparoscopic myomectomy.Hum Reprod 2000;15:869–73.
9. Neilson JP. Interventions to reduce haemorrhage during myomectomy for fibroids [Comment on Kongnyuy EJ, Wiysonge CS. Cochrane Database SystRev 2007; 1: CD005355.]. Obstet Gynecol 2007; 109: 1197–8.
10. 10.Alyssa W,Chun C,Sik Y.Transcervical intralesional vasopressin injection compared with placebo in hysteroscopic myomectomy.The American college of obstetricians and Gyn 2014;897-903.
11. Protopapas A, Giannoulis G, Chatzipapas I, Athanasiou S, Grigoriadis T, Kathopoulis N, Vlachos DE, Zaharakis D, Loutradis D. Vasopressin during Laparoscopic Myomectomy: Does It Really Extend Its Limits?. Journal of minimally invasive gynecology. 2019 Mar 1; 26(3):441-9.
12. Agostini A, RondaI, Franchi F, Ronda B, Ludovic RC, Bernard B. Oxytocin during myomectomy: a randomized study. Eur J Obstet Gynecol Reprod Biol; 2005; 118:235–8.
13. Samanta S, Samanta S, Jain K, Chatterjee D. Intramyometrial terlipressin in atonic postpartum hemorrhage: A uterine salvage decision. Anaesthesia, Pain & Intensive Care. 2019 May 20.
14. Taylor A, Sharma M, Tsirkas P, Di Spiezio Sardo A, Setchell M, Magos A.Reducing blood loss at open myomectomy using triple tourniquets: a randomized controlled trial. Int J Gynecol Obstet 2005; 112:340–5.
15. Benassi L, Lopopolo G, Pazzoni F, Ricci L, Kaihura C, Piazza F, et al. Chemi-cally assisted dissection of

tissues: an interesting support in abdominal myo-mectomy. J Am Coll Surg 2000; 191: 65–9.
16. Zullo F, PalombaS, Corea D, PellicanoM, RussoT, Falbo A, et al.Bupivacaineplus epinephrine for laparoscopic myomectomy: a randomized placebo-controlled trial. Obstet Gynecol 2004; 104:243–9.
17. Chen C. Laparoscopic myomectomy for large myomas. Int Surg 2006; 91(Suppl):S77–80.
18. Jonathan s b. Berek and novaks Gynecology.15th edition 2012; vol.1:423-40.
19. SinhaR, Sundaram M,Lakhotia S,Mahajan C, RajeS,KadamP,RaoG.Lapa-roscopic myomectomy with uterine artery ligation: review article andcomparative analysis. J Gynecol Endosc Surg 2012; 2:3–10.
20. Elsheikh A, Antsaklis A, Mesogitis S, Papantoniou N, Rodolakis A, Vogas E,et al. Use of misoprostol for the termination of second trimester pregnan-cies. Arch Gynecol Obstet 2001; 265:204–6.
21. Bugalho A, Daniel A, Faundes A, Cunha M. Misoprostol for prevention of postpartum hemorrhage. Int J Gynaecol Obstet 2001; 73:16.
22. Muhammad R, Isah A, Agida T, Akaba G. A prospective study to compare the effectiveness of adjunctive rectal misoprostol or oxytocin titration in the prevention of primary post-partum haemorrhage in at risk patients. African health sciences. 2019; 19(1):1517-24.
23. Celik H, Sapmaz E. Use of a single preoperative dose of misoprostol is efficacious for patients who undergo abdominal myomectomy. Fertil Steril2003; 79:1207–10
24. Sharifa F, Joseph F, Horance F.A trial comparing the use of rectal misoprostol plus perivascular vasopressin alone to decrease myometrial bleeding at the time of abdominal myomectomy. Fertility and Sterility 2013; vol.100:1044-49.

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