

Vasopressin Effect on Operation Time and Frequency of Electrocauterization during Laparoscopic Stripping of Ovarian Endometriomas: A Randomized Controlled Clinical Trial

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Abstract

Background: The purpose of this study was to assess the vasopressin effect on operation time and the need for electrocauterization frequency and ovarian reserve during laparoscopic stripping of ovarian endometriomas.

Methods: This was a randomized prospective clinical trial, in which twenty patients between 18-35 years with unilateral endometriomas were randomly divided in two groups of cases and controls. Laparoscopic cystectomy was performed by hydrodissection and stripping method in both groups with diluted vasopressin injected in cases, in comparison to only saline injection in controls. Ovarian hemostasis was achieved by bipolar electrocoagulation. The operation time and frequency of electrocoagulation were compared between two groups. The ovarian reserve was determined by ultrasound examination and laboratory assessment one month before and two months after surgery in two groups. Non parametric data was analyzed by Mann-Whitney test. The p-value less than 0.05 was considered statistically significant.

Results: The operation time was less in cases than control group, but the difference was not statistically significant ($p=0.065$). The frequency of electrocoagulation for hemostasis was less in cases than controls but this difference was not statistically significant ($p=0.132$). The antral follicle count decreased in both groups two months later, while no significant difference was found between two groups.

Conclusion: This study shows that diluted vasopressin decreases operation time and electrocauterization frequency during laparoscopic stripping of ovarian endometriomas; however, the difference between case and control group is not statistically significant.

Keywords: Electrocoagulation, Endometriosis, Laparoscopy, Vasopressin.

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Introduction

One of the important issues of recent years is concerned with the methods for preserving ovarian reserve in order to decrease the manipulation and direct harm to ovary. In some studies electrocoagulation was compared to suturing (1, 2).

Endometriomas are defined as cystic formations

of ovarian endometriosis and 35% of benign ovarian cysts require surgery in women of reproductive age (3). Laparoscopic stripping is the choice treatment in conservative treatment of ovarian endometrioma and is considered to be better than fenestration and coagulation because of less pain, low recurrence rate and better spontaneous preg-

nancy rates (4). However, in recent studies, laparoscopic stripping has been shown to be associated with reduction of ovarian reserve due to excessive removal of ovarian tissue and hemostasis through bipolar coagulation of ovarian tissue (thermal injury) or by suturing (local tissue pressure and local hypoxia) (5). Histopathology studies have shown the removal of unintended fragments of nearby healthy ovarian tissue due to cystectomy of endometrium, particularly in areas close to the ovarian hilum (6).

Ebert et al. in 2009 showed that galantine thrombin matrix sealant (FloSeal©) is effective in hemostasis (7). However, this agent has been related to small bowel obstruction in some patients who underwent gynecologic surgery (8, 9).

Saeki et al. suggested that the injection of vasopressin during laparoscopic excision of endometriomas reduces the use of coagulation and thus may protect ovarian reserve (10).

This randomized clinical trial was carried out to determine the effect of diluted vasopressin on operation time and the need for electrocoagulation and ovarian reserve.

Methods

This randomized prospective clinical trial (IRCT 2013012512262N1) was carried out in Women Hospital of Tehran University of Medical Sciences from April 2012 to March 2013. Twenty women between ages 18-35 years participated in this study with confirmed diagnosis of unilateral endometrioma.

Inclusion criteria were as following: unilateral ovarian endometrioma diagnosed by ultrasound examination, diameter of endometrioma between 30-70 mm, no clinical and sonographic suspicion of ovarian cancer and regular menstrual bleeding. Exclusion criteria were pregnancy, body mass index (BMI) of more than 30 kg/m², genital or extra-genital malignancy, postoperative pathologic diagnosis of non-endometriotic ovarian cyst, use of oral contraceptive pills before surgery, previous surgery for endometriosis, combined PCO syndrome and endometrioma, intraoperative diagnosis of another cyst type, any complication during operation or conversion to laparotomy and irregular attendance during follow-up examinations. Due to these criteria, eight patients were excluded (five because of non-endometriotic histopathology and three because of converting to laparotomy) and finally twelve patients enrolled in the study. Randomly, 6 patients underwent laparo-

scopic cystectomy with hydrodissection using only normal saline (control group), and 6 patients underwent laparoscopic hydrodissection cystectomy using normal saline and diluted vasopressin (case group).

The study was approved by the faculty ethics committee. All patients signed written consent form.

Demographic characteristics of patients were taken using the questionnaire. All subjects underwent transvaginal or abdominal ultrasound examination (5-7.5 MHz transvaginal transducer, Sonoline G50, Siemens, Germany) to determine the antral follicle count (AFC) of both ovaries, preoperatively [in the early follicular phase of the menstrual cycle (Days 3-6)] and postoperatively, on the similar day of second menstrual cycle. Ovarian follicles measuring 3-10 mm on both ovaries were counted using the largest cross-sectional sagittal view of the ovary. Vaginal ultrasound examination was performed by two independent examiners. Both sonologists had a good agreement on the follicular count.

Serum FSH¹ was checked for all patients on same days of ultrasound examinations.

All laparoscopies were performed during late proliferative phase of the cycle by an experienced surgeon under general anesthesia. Operative laparoscopy was performed through a three-port approach with one 11 mm subumbilical port for the scope and two 5.5 mm ancillary ports. Usual operation for laparoscopic ovarian cystectomy was done using stripping the cyst wall by normal saline hydrodissection. The following procedures included careful inspection of pelvic and peritoneal cavity, peritoneal washings, staging of endometriosis and adhesiolysis for release and mobilization of the ovaries from the surrounding structures, the injections of normal saline between the cyst wall and the ovarian cortex, aspiration of chocolate material of the cyst by suction needle. Applying careful traction-counter traction technique over the edges of the cyst wall with two atraumatic graspers, the cyst wall stripped from the healthy surrounding normal ovarian tissue and cortex. Hemostasis was achieved by a 35-W current bipolar electrocoagulation on the cyst bed for the shortest possible time. Finally, the pelvic cavity was irrigated with a large amount of saline.

In the case group, before hydrodissection, vasopressin was prepared by dilution of one ampoule

1- Follicle Stimulating Hormone

(20 units) of Hypress® (Exir Pharmaceutical Co., Boroujerd, Iran) with 200 ml of physiologic saline to dilute it 200-fold (0.1 U/ml). The injection of 3 ml diluted vasopressin was made at one to three points, at the nearby large vessels, but not to the hilum, followed by 30-40 ml saline solution injection in different points to achieve hydrodissection. This was done to avoid the side effects of vasopressin like arrhythmia. In fact, a total of only 0.3 U of vasopressin was used for each patient. In the control group, 3 ml placebo (Normal saline) followed by 30-40 ml saline solution injection was injected while the surgeon and her assistant both were blinded to the injection material.

Operation time was considered from the start of detaching the cyst wall until hemostasis of the normal ovarian tissue. The total number of electrocoagulation used to achieve hemostasis was counted. To confirm the diagnosis and exclusion of malignancy, cyst wall was sent for histological assessment. None of the operated ovaries were sutured. All patients were discharged the following day, then followed by ultrasound examination and serum FSH after 2 regular menstrual cycles as described above.

Statistical evaluation was performed using SPSS version 18.0. Nonparametric data was analyzed by Mann-Whitney test. The p-value less than 0.05 was considered statistically significant.

Results

Ten patients were included in each group (case and control). Eight patients were excluded from the study, three because of conversion of the procedure to laparotomy and five because of non-endometrial pathology. Finally, in each group, six patients remained. There were no statistical differences in demographic characteristics of the two groups except for basal AFC which are shown in table 1.

Table 1. Demographic characteristics in two groups for laparoscopic stripping of ovarian endometriomas

| | Cases Median (percentile 25-75) | Controls Median (percentile 25-75) |
|---------------|------------------------------------|---------------------------------------|
| Age | 27 (20-30.7) | 27.5 (22.5-31) |
| BMI * | 23 (20.7-24) | 21.5 (19.7-24) |
| Cyst size | 51.2 (44.5-64.2) | 51.7 (48.3-61.6) |
| Basal FSH ** | 5.5 (4.6-6.5) | 5 (5-5.6) |
| Basal AFC *** | 5 (4-6) ^a | 2 (2-3.2) ^a |

* BMI: body mass index; ** FSH: follicle stimulating hormone; *** AFC: antral follicle count
a: p<0.01

None of the patients developed complications after surgery. No suture was done to achieve hemostasis.

The operation time, from beginning of hydrodissection until completing hemostasis between the two groups was different, although it was lesser in the case group 485(325.7-915) minutes [Median (percentile 25-75)] in comparison to controls 583(548-860) minutes [Median (percentile 25-75)] but the difference was not statistically significant (p=0.065).

The frequency of electrocoagulation for hemostasis was less in the cases 2.5(0-4.5) [Median (percentile 25-75)] compared to controls 10(4-11) [Median (percentile 25-75)] but this difference was not also statistically significant (p=0.132).

The level of preoperative basal FSH was similar in the 2 study groups (5.36 mIU/ml in cases, and 5.52 mIU/ml in controls). The FSH level increased in both groups after 2 months post operation, but there was no statistically significant difference between the groups (p=0.286).

The antral follicle count decreased in two groups after two months of follow-up, while this decrease was not statistically significant between two groups (p=0.485). The main results are demonstrated in table 2.

Table 2. Main results of two groups for laparoscopic stripping of ovarian endometriomas

| | Cases Median (percentile 25-75) | Controls Median (percentile 25-75) |
|--------------------------------|------------------------------------|---------------------------------------|
| Operation time | 485 (325.7-915) | 583 (548-860) |
| Electrocauterization frequency | 2.5 (0-4.5) | 10 (4-11) |
| AFC change * | 2.5 (2-3.2) | 2 (1-3) |
| FSH change ** | 1.7 (2.6-0.9) | 2.8 (1.3-4.1) |
| HB change *** | 0.7 (0.5-1) | 0.7 (0.5-1) |

The effect of vasopressin on operation time, electrocauterization frequency and ovarian reserve in cases versus controls

*AFC change: antral follicle count change before and after surgery; **FSH change: follicle stimulating hormone change before and after surgery; ***HB change: hemoglobin change before and after surgery

Discussion

This randomized trial showed that vasopressin decreased operation time and the need for electrocoagulation in hemostasis. Ovarian reserve decreased after laparoscopic cystectomy in both groups but it was not statistically significant.

Laparoscopic cystectomy is the method of choice for the conservative treatment of endometriotic cysts (11). But it is not exactly clarified what would be the appropriate technique. Available surgical laparoscopic techniques are ovarian cystectomy, ablative surgery, three-step procedure (laparoscopic drainage, GnRH analogues for 3 months, laparoscopic laser vaporization) and combined technique of excisional and ablative surgery (partial cystectomy of 80% to 90% of the endometrioma and then vaporization by the CO₂ laser to the remaining 10-20% of the endometrioma near by the hilum) (12).

Different studies have indicated that treatment of endometriomas by fenestration, drainage and coagulation or laser vaporization is related to a higher chance of cyst recurrence (11, 13, 14).

On the other hand, some evidence indicated that cyst drainage and vaporization or thermal coagulation may have less harmful impact on ovarian reserve (15, 16). Some studies suggested decreasing the size of ovarian endometrioma prior to cystectomy like a three-step surgical management of large cysts (17).

Literature review shows that the stripping procedure is associated with a reduced recurrence rate of dysmenorrhoea, dyspareunia, non menstrual pelvic pain and higher spontaneous pregnancy rate (11, 18, 19).

The inadvertent removal of ovarian parenchyma during cystectomy has already been reported by several researchers (20, 21, 22).

Indeed, it cannot be concluded that the cyst may damage the surrounding ovarian tissue per se. Surgery may also damage the ovarian reserve by accidental removal of a consistent amount of ovarian tissue (6). On the other hand, local inflammation due to surgery or vascular injury secondary to electrosurgical coagulation may harm the healthy ovarian tissue (5). Muzii et al. suggested that if the surgeon chooses the proper cyst edge to detach, the stripping of the greatest part of the pseudo-capsule is not associated with removal of healthy tissue, and so the stripping procedure can be considered a tissue-preserving procedure (4, 23). In our technique, after using the hydrodissection, the best surface was used for cleavage.

Some recommend that the accurate use of bipolar coagulation during the stripping of bilateral endometriomas does not have a major effect on ovarian reserve (2). Yet, every surgeon using this technique even very carefully would agree on this point that even gentle bipolar coagulation of the cyst bed can harm the surrounding ovarian tissue (24). The risks are known, the most important question is how to reduce the damage.

The point of successful surgery is to prevent bleeding, trauma to the ovary that requires hemostasis. Coric et al. showed that suturing of ovarian tissue and reconstruction of ovary following the stripping of endometrioma had less adverse effect on ovarian reserve than bipolar electrocoagulation in a 6 month post-surgical follow up period (5). However, it makes operative time longer and needs proper laparoscopic suturing training of the surgeon. Electrocoagulation is easier and less time consuming.

On the other hand, another study did not report long-term adverse effects of electrocoagulation versus suture after laparoscopic stripping of ovarian endometriomas over 12-month follow-up (6).

Other authors proposed the use of a gelatine-thrombin-matrix sealant (FloSeal) to control post-cystectomy ovarian wound bleeding (7). This agent has been associated with small bowel obstruction in patients undergoing gynecologic surgical procedures (8, 9).

In our study, hemostasis after stripping was achieved by electrocoagulation and suturing was not needed.

To the best of our knowledge, there is only one study on the effect of vasopressin in decreasing the time of operation and the need for electrocoagulation for laparoscopic stripping of the endometriomas. It seems that our findings are not in agreement with the observations of that study (10). In their randomized prospective study including 15 women with single endometrioma in 3 subgroups of stripping alone, stripping with hydrodissection using only normal saline and stripping with hydrodissection using normal saline plus diluted vasopressin, Saeki et al. suggested that the injection of vasopressin during laparoscopic excision of endometriomas reduces the use of coagulation and operation time and thus may protect ovarian reserve. Although our results could not support those reported by Saeki et al., the operation time and use of electrocoagulation decreased in cases of our study but this difference was not statistically significant ($p=0.065$, $p=$

0.132, respectively). It may be related to different study designs and different procedures such as injection of more diluted vasopressin from outside the cyst before evacuating the cyst fluid in our study instead of injection of vasopressin with higher concentration from inside the cyst after evacuating the cyst fluid in their study.

Local injection of vasopressin due to its tourniquet effect has been used for over 15 years (25). There are some other agents like vasopressin that are used for a tourniquet effect including oxytocin or epinephrine but the longer half-life of vasopressin and not having great effect on systemic circulation makes it a reasonable choice to decrease blood loss during surgery in various clinical fields (26, 27). Shimanukiet et al., have demonstrated that local administration of vasopressin to the uterus can be a safe and practical hemostatic technique due to its tourniquet effect for laparoscopic myomectomy (28). A known side effect of vasopressin during surgery is mild arrhythmia (mainly bradycardia). There are some reports of more severe complications due to administration of vasopressin, but, in these reports, more concentrated vasopressin has been injected (40 times diluted comparing to our study which is 200 times diluted) (25, 29, 30). In our study, none of the patients encountered any complications of vasopressin during or after surgery.

One of the noticeable features in our study is assessment of ovarian reserve by means of both ultrasound and biochemistry. In a recent study, Hansen et al. have demonstrated that AFC is reflective of the true ovarian reserve like histological assessment by the ovarian primordial follicle number (31). As mentioned before, Coric et al. declared that postoperative AFC showed significant functional reduction in operated ovaries, which ever hemostatic technique used (1). In another study, after 6 months following surgery, antral follicle count was higher in patients treated with the 3-step procedure than in those who underwent cystectomy (5). Our findings showed decreased AFC and increased FSH levels over a 2 month follow-up evaluation, but the difference between two groups was not statistically significant. If we had followed for 6 months, the results would be different. Important limitations of our study were the small number of patients and short follow up period. Further studies with larger number of patients are needed to address this point.

Conclusion

This study shows that diluted vasopressin may decrease operation time and electrocauterization frequency during laparoscopic stripping of ovarian endometriomas; however, the difference between case and control groups was not statistically significant.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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