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Ping Cheng, Xin-Hua Yang

Department of Gynecology, Women and children's health hospital in Xinjiang, China

Preservation of the fallopian tube in ectopic tubal pregnancy: An analysis of the outcome of two laparoscopic surgical approaches

INTRODUCTION: *The application of laparoscopic partial tubal resection with end-to-end anastomosis can reduce the incidence of persistent ectopic pregnancy. Aim: We aim to compare the therapeutic effects of laparoscopic fenestration and laparoscopic partial tubal resection with end-to-end anastomosis in the treatment of tubal ectopic pregnancy. Material and methods: The patients were randomly divided into the observation group (the group treated with laparoscopic partial tubal resection with end-to-end anastomosis, n=238) and the control group (the group treated with laparoscopic fenestration, n=213). The average operation time, intraoperative blood loss, postoperative exhaust time and hospital stay were observed to evaluate the clinical effect. In addition, the time required for the β-HCG to drop to normal level, the patency of the fallopian tubes and the ovarian function were observed in the two groups after the operation.*
RESULTS: *There was no significant difference between observation group operation time, intraoperative hemorrhagic amount, blood β-HCG recovery time and hospital time and control group ($P > 0.05$). The postoperative fallopian tube patency rate in the observation group was 67.58%, significantly higher than the control group ($P < 0.05$). In addition, there was no significant difference in ovarian function between the two groups.*
CONCLUSIONS: *The method of laparoscopic partial tubal resection with end-to-end anastomosis is more effective in the treatment of tubal ectopic pregnancy, and has less impact on ovarian function, which can effectively improve the probability of normal pregnancy after the operation.*

KEY WORD: Fallopian tube, Ectopic pregnancy, Laparoscopic fenestration, Laparoscopic partial tubal resection with end-to-end anastomosis

Introduction

Ectopic pregnancy is one of the most common complications of pregnancy [1], whose main clinical manifestations are amenorrhea, vaginal bleeding, syncope and even shock. In the worldwide, ectopic pregnancy can cause three-quarters of maternal deaths in the first three months of pregnancy [2]. At the same time, women with ectopic pregnancy have a higher risk of infertility or recurrent ectopic pregnancy [3]. Of all ectopic pregnancy types, tubal pregnancy is the most common type, and its incidence can be as high as 90% [4]. Although with the development of medical technology, With the development of medicine, although the mortality of ectopic pregnancy has decreased in recent years, it still seriously affect women's quality of life [5]. Therefore, it is urgent to find an effective treatment for ectopic pregnancy.

In recent years, laparoscopic therapy in ectopic pregnancy has been widely recognized. Compared with traditional open surgery, laparoscopic surgery has the advantages of less trauma, less interference to organs and faster postoperative recovery. It can save patients' lives and improve the prognosis [6]. For tubal pregnancy, laparoscopic fenestration is often used in clinical practice, and

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Correspondence to: Ping Cheng, Department of Gynecology, Women and children's health hospital in Xinjiang autonomous region, Urumqi, 830001; China (e-mail: chengpingcf@126.com)

its indications are mainly suitable for patients with fertility needs and less involvement of the fallopian tubes [7]. However, some studies have shown that this operation may have the problems of incomplete removal of pregnancy tissue, continued growth of residual trophoblast or implantation in other places, resulting in the increase of blood β - HCG instead of decrease, resulting in persistent ectopic pregnancy [8,9].

At present, many patients with ectopic pregnancy require to maintain the function of fallopian tube and normal reproductive function. Therefore, the application of laparoscopic partial tubal resection with end-to-end anastomosis was born. The operation method can reduce the incidence of persistent ectopic pregnancy and improve the rate of intrauterine pregnancy in the future [10,11], so as to reduce the harm caused by assisted reproduction and reduce the economic burden of female patients, which has good health and economic benefits [12].

Our study aims to compare the efficacy of laparoscopic fenestration and laparoscopic partial salpingectomy with end-to-end salpingostomy in the treatment of ectopic pregnancy of fallopian tube, in order to find a new method to preserve the fallopian tube and improve the incidence of ectopic pregnancy caused by the decrease of fallopian tube patency.

Materials and methods

A random clinical trial conducted from January 2014 to July 2019 in our hospital included selected 451 patients with a diagnosis of tubal ectopic pregnancy who met the inclusion criteria. They were randomly divided into the control group (n=213) and the observation group (n=238). Randomization was performed by using random numbers. The observation group was treated with laparoscopic partial tubal resection with end-to-end anastomosis, while the control group was treated with laparoscopic fenestration. Our study was approved by the ethics committee, and all patients signed an informed consent voluntarily.

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: 1) accordance with the standard of tubal-sparing surgery for ectopic pregnancy in the 9th edition of the People's Medical Publishing House of Obstetrics and Gynecology; 2) Young women with fertility requirements, especially those with removed contralateral fallopian tube; 3) Non-ruptured tubal pregnancy; 4) Progression of ectopic pregnancy (i.e. blood HCG>3000mIU/ml, or continuous increase, fetal heart beat, adnexal mass); 5) Drug treatment contraindications or ineffective; 6) Persistent ectopic pregnancy.

The exclusion criteria were as follows: 1) Unstable vital signs or intra-abdominal hemorrhage; 2) Severe cardiovascular disease and cardiac dysfunction; 3) Low lung function; 4) Diffuse peritonitis; 5) Blood coagulation disorder or blood disease; 6) Multiple bowel surgery or severe adhesion surgery history; 7) Obesity or hepatitis; 8) Other serious medical diseases.

Operation Methods

Anesthesia methods: All patients were treated with tracheal intubation general anesthesia.

Laparoscopic fenestration:

A 1 cm longitudinal or transverse incision was made in the middle of the umbilicus wheel to establish pneumoperitoneum. A 0.5 cm long puncture was made at the corresponding position of the left lower abdomen and Maxwell's point. Surgical instruments were inserted to explore the pelvic cavity and tubal pregnancy.

Surgical instruments were placed to explore the pregnancy type and select the appropriate surgical method. If the pregnancy site is located at the ampulla near fimbria, the pregnancy tissue from fimbria was directly suck with an aspirator. If the pregnancy is located near the isthmus or isthmus of the ampulla, the proximal end of the fallopian tube should be clamped with non-destructive forceps. And then, the electric hook was used to cut the fallopian tube longitudinally before separating the pregnant substance under the water pressure.

At the implantation position of the pregnancy, bipolar electrocoagulation was performed to fully stop the bleeding, while flushing with the electrocoagulation to observe the absence of bleeding and active bleeding.

Laparoscopic partial tubal resection with end-to-end anastomosis.

After successful anesthesia, the patient took supine position and indwelling catheter. Puncture above the umbilical foramen and inject carbon dioxide into the abdominal cavity. The internal pressure is 12-14 mmHg (1 mmHg = 0.133 kPa). A 10 mm diameter cannula was placed through the umbilical puncture point, and the laparoscope was inserted.

The pelvic cavity was carefully examined to make sure that the operation could be performed under laparoscope. Puncture holes with a diameter of 5 mm were made at the junction of the left anterior iliac spine to the middle and lower 1 / 3 of the umbilicus, 2 cm from the junction of middle and upper 1 / 3 of the umbilicus, and the right lower abdominal Maxwell's point, respectively.

1:1 dilution of pituitrin (pituitrin 5iu + normal saline 5ml) was injected into the uterine corner of the affected side of the fallopian tube and the mesentery of the tubal pregnancy site. The serous layer was cut transversely

at the pregnancy site, and then the tubal pregnancy segment was separated and cut off.
Then the plastic pipe from the umbrella end should be inserted. At the same time, the two broken ends would be fully trimmed and aligned. After resecting the lesion, the fallopian tube was intermittently anastomosed with 3-1 absorbable line at both ends of the fallopian tube. The length of the affected fallopian tube should be kept as much as possible after the operation.
After cleaning the pelvic cavity with normal saline to ensure no active bleeding, the post-treatment nursing should be completed. The detailed surgical procedure can be seen in the display in Video1

Observation Indicators and Evaluation Criteria
The intraoperative bleeding, operation time, hospital stay, the recovery time of β-HCG, number of antral follicles, type 2 hormone level and patency of affected fallopian tube were compared between the two groups.
The β-HCG value was tested on the first and third days after the operation, and the test was stopped until it dropped to the normal level.
At the early stage of menstruation three months after the operation, the B-ultrasound probe was guided to scan the ovaries, and then the sinus follicles were counted directly. Venous blood was collected on the second day of menstrual cycle in the third month after operation to observe the changes of serum estradiol, luteinizing hormone and follicular stimulating hormone. If the number of sinus follicles was less than 5, follicle-stimulating hormone was greater than 12.5, follicle-stimulating hormone/luteinizing hormone was more than 2 and estradiol was greater than 50, it indicated that the ovarian reserve function was not good. If the number of sinus follicles was more than 12, and luteinizing hormone/follicle-stimulating hormone was more than 3, it meant that there might be polycystic ovary syndrome. If the number of sinus follicles was between 5-12, then the ovarian function is normal.
The fallopian tube was examined by lipiodol angiography in the 3-7 days after menstruation. The results were divided into three types: unobstructed (soft tubal development), complete obstruction (incomplete tubal development and/or abnormal expansion), and incomplete obstruction (between the type of unobstructed and complete obstruction) [13].

Statistical Analysis

All data was performed using the SPSS21.0. The quantitive variables were presented as means±standard deviations and compared with student's t-test. The enumeration variables were expressed as portions and compared by the χ^2 test. P value<0.05 was considered statistically significant.

Results

Study population

The patients in the control group were 22-37 years old, with an average age of (25.63±4.24) years old; the amenorrhea time was 35-67 days, with an average amenorrhea time of (50.64±12.46) days. In the control group of 213 cases of patients, 101 cases were primiparal, and the rest cases were multipara. At the same time, the patients in the observation group were 23-37 years old, with an average age (26.62±4.28) years old. The amenorrhea time of observation groups was 36-67 days, with an average of (50.66±12.47) days. There were 238 patients in the observation group, including 110 primipara and 128 multipara. There was no significant difference between the two groups in pregnancy times, amenorrhea time and other basic information (P > 0.05).

The results of operation conditions between the control group and observation group.
As shown in Table 1, the operation time of the observation group was 67.7±16.57 min, which was significantly longer than the 35.67±16.21 in the control group. In addition, the laparoscopic partial tubal resection with end-to-end anastomosis could effectively promote the recovery of β-HCG.
The results presented the recovery time of the observation group was about 1.5 times faster than that of the control group (Table I). Although there was no significant difference in the indicator of the length of stay between the control group and the observation group, the observation group still has the trend of reducing the length of hospital stay (Table I). As for the intraoperative blood loss, the results demonstrated that the safety of the two kinds of operation is similar (Table I).

Table I - *The results of operation conditions between control group and observation group* ($\bar{x} \pm s$)

Group	Intraoperative blood loss (ml)	Operation time (min)	Time of blood β-HCG recovery (d)	Length of stay (d)
Observation group (n=238)	20.21±20.23	67.76±16.57[a]	20.13±3.84[a]	4.37±1.58
Control group (n=213)	16.76±20.12	35.67±16.21	31.22±3.86	4.73±1.62

Note: Comparison with control group, [a]P<0.05.

Table II - *The results of fallopian tube conditions between control group and observation group* [n (%)]

Group	The fallopian tubes are partially blocked	The fallopian tubes are unobstructed	The fallopian tube is blocked
Observation group (n=238)	24 (10.08)	161 (67.65)[a]	53 (22.27)[a]
Control group (n=213)	22 (10.31)	78 (36.62)	113 (53.05)

Note: Comparison with control group, [a]P<0.05.

Table III - *The results of ovarian function between control group and observation group* ($\bar{x} \pm s$)

Group	Serum estradiol (U/L)	Luteinizing hormone (pmol/L)	Follicle stimulating hormone (U/L)	Sinus follicle count (a)
Observation group (n=238)	128.83±17.32	7.82±0.27	8.90±2.21	5.37±1.43
Control group (n=213)	122.31±14.12	7.70±0.11	8.60±2.57	5.02±1.03

The results of fallopian tube conditions between the control group and observation group

After one year of follow-up, the lipidodol angiography was used to detect the fallopian tube conditions. The tubal patency rate of the affected side in the observation group was 67.75% and that of the control group was 36.62%. On χ^2 test analysis, this difference was statistically significant (P<0.05). Besides, blocked fallopian tubes on the affected side occurred in 53 cases (22.27 %) of the observation group and in 113 (53.05%) of the control group (P<0.05) as shown in Table II.

The results of ovarian function between the control group and observation group

Our results found that there was no significant difference between the observation group and the control group (Table III). It illustrated that the treatment of laparoscopic fenestration and laparoscopic partial tubal resection with end-to-end anastomosis has the same effect on the process of ovarian function recovery.

Discussion

In recent years, the incidence of tubal ectopic pregnancy has been on the rise. The main symptoms of patients are amenorrhea, irregular vaginal bleeding, abdominal pain, which seriously threaten the health and quality of life of patients. At present, there are many kinds of clinical treatment for ectopic pregnancy, mainly including open surgery, conservative treatment and laparoscopic surgery. Given the low success rate of drug treatment and the narrow scope of application, surgical treatment is mainly used in clinical treatment [14].

Our study found that laparoscopic partial tubal resection with end-to-end anastomosis has the following advantages: firstly, this operation requires complete removal of the diseased part of the fallopian tube, so there is no risk of residual pregnancy tissue. Secondly, the operation can preserve the fallopian tube and mesosalpinx, which has little effect on the blood supply of the ovary and does not damage the ovarian reserve capacity and ovulation function. Lastly, the disease-free tubal anastomosis, scar area is small, up to 1 mm, so the impact on the fallopian tube is very small, the impact on subsequent pregnancy is very small.

The effect of laparoscopic partial tubal resection with end-to-end anastomosis on the operation time

The clinical use of tubal pregnancy resection and end-to-end anastomosis is gradually increasing, and its field of view is generally 4-10 times larger than that of laparoscopic surgery [15]. Laparoscopic end-to-end anastomosis saves the patient's fallopian tubes, but also has the advantages of less bleeding, small incisions, and less tissue damage [16], which can avoid the occurrence of infection of the fallopian tubes due to prolonged exposure to the air.

Our study found that the operation time of the observation group was two times longer than that of the control group (observation group: 67.76±16.57 min vs control group: 35.67±16.21 min). Our results are similarly with some domestic research results. For example, Jiang et al. [17] took 60 patients with a second fallopian tube ampulla or isthmus pregnancy as the research object. The results of the study showed that the operation time of the group of laparoscopic partial tubal resection with end-to-end anastomosis was also nearly 2 times longer than that of the group of laparoscopic fenestration (74.5±5.3 min vs 53.3±4.7min). Therefore, it can be explained that end-to-end anastomosis has higher requirements for doctors and requires doctors to have a more accurate grasp of endoscopy.

The effect of laparoscopic partial tubal resection with end-to-end anastomosis on the β-HCG recovery

β-HCG is a glycoprotein hormone secreted by trophoblast cells in human placenta after implantation of [18]. In patients

with ectopic pregnancy, due to poor blood supply to the site of pregnancy, the nutritional level of villi tissue is poor. Therefore, the fluctuation of blood HCG is more obvious, and it can be used as a sensitive and objective indicator of the treatment effect of ectopic pregnancy in this life [19,20].

It is worth mentioning that there is currently a large amount of evidence that β-HCG is an important marker of the number and vitality of trophoblasts [21]. The integrity of the muscularis of the fallopian tube is closely related to the degree of infiltration of trophoblast cells on the wall of the fallopian tube [22]. If β-HCG continues to increase and does not return to the normal level, after the simultaneous enhancement of trophoblast proliferation activity, it may strengthen its ability to infiltrate the fallopian tube wall and damage the muscularis of the fallopian tube again.

In our study, the time of β-HCG recovery was 20.13±3.84d after the treatment of the laparoscopic partial tubal resection with end-to-end anastomosis. However, this indicator presented 31.22±3.86d after the treatment of laparoscopic fenestration. Compared with the control group, the β-HCG recovery time of the observation group was shortened by two times, and the difference was statistically significant.

Our results proved that the laparoscopic partial tubal resection with end-to-end anastomosis had a faster β-HCG recovery time, which suggested that it could remove trophoblast cells more cleanly and had less possibility of invasive damage to fallopian tubes.

The effect of laparoscopic partial tubal resection with end-to-end anastomosis on the ovarian function

The number of sinus follicle refers to the total number of follicles of 2 to 10 mm in bilateral ovaries, and is one of the commonly used indicators for clinical evaluation of ovarian reserve [23]. Clinically, the number of follicles with unilateral or bilateral ovaries of 2-9 mm is often used as one of the diagnostic criteria for polycystic ovary syndrome [24].

Follicle-stimulating hormone is a hormone secreted by the pituitary gland to promote follicles. It interacts with luteinizing hormone and follicle-stimulating hormone is regulated by estradiol. Through the level of follicle-stimulating hormone, the female ovarian function status can be assessed. If the level of follicle-stimulating hormone is too high, it indicates that the woman's ovarian function is poor. If the level of follicle-stimulating hormone is too low, it indicates that the woman may have polycystic ovary syndrome [25]. In the presence of follicle-stimulating hormone, luteinizing hormone can act synergistically with the ruptured ovary to form the corpus luteum, which secretes estrogen and progesterone [26].

Our results demonstrated that there was no significant difference between the control group and the observation group. In the one of domestic study, the results are similar to this study. Li [27] observed 50 cases of tubal pregnancy patients and found that there was no significant difference in the level of luteinizing hormone level, follicle-stimulating hormone and serum estradiol between the laparoscopic fenestration and laparoscopic partial tubal resection with end-to-end anastomosis.

At present, there is not enough clinical evidence to prove that laparoscopic partial tubal resection with end-to-end anastomosis is better than laparoscopic fenestration in terms of ovarian function. The main reasons for this situation may be as follows: firstly, the follow-up time for patients is too short; secondly, the sample size included is relatively single; finally, there is a lack of records of the postoperative fertility status of patients.

The clinical application value of laparoscopic partial tubal resection with end-to-end anastomosis

Although the traditional open surgery can stop bleeding quickly and save patients' lives, if the lesion is too large or the fallopian tube ruptures, the open surgery will cause greater trauma. In addition, there are many postoperative complications, which seriously affect the daily life of patients. With the continuous development of medical technology, laparoscopy has been widely used in the treatment of tubal ectopic pregnancy because of its advantages of small trauma, less complications and fast recovery [28]. The most commonly used laparoscopic surgery in clinic is to preserve the fallopian tube and remove the fallopian tube. However, the pregnancy rate will be reduced by half after salpingectomy, which is easy to affect the blood supply of the ovary, damage the ovarian reserve capacity and destroy the ovulation function. The above two surgical methods will greatly reduce the probability of normal pregnancy, which can not meet the reproductive needs of patients [29].

Now, it has been proved that laparoscopic partial tubal resection with end-to-end anastomosis is the best treatment for isthmus pregnancy [30]. Our study found that laparoscopic partial tubal resection with end-to-end anastomosis has the following advantages: firstly, this operation requires complete removal of the diseased part of the fallopian tube, so there is no risk of residual pregnancy tissue. Secondly, the operation can preserve the fallopian tube and mesosalpinx, which has little effect on the blood supply of the ovary and does not damage the ovarian reserve capacity and ovulation function.

Lastly, the disease-free tubal anastomosis, scar area is small, up to 1 mm, so the impact on the fallopian tube is very small, the impact on subsequent pregnancy is very small.

Conclusion

In conclusion, compared with laparoscopic fenestration, laparoscopic partial tubal resection with end-to-end anastomosis has a significant effect on patients with ectopic tubal pregnancy, which can effectively preserve the function of the affected side of the fallopian tube. The ovarian function of the patients recovered well after the operation, which has practical application value.

Riassunto

L'esecuzione della resezione tubarica parziale laparoscopica con anastomosi end-to-end può ridurre l'incidenza di gravidanze ectopiche ricorrenti. Lo scopo di questo studio è quello di confrontare gli effetti terapeutici della fenestrazione laparoscopica e della resezione tubarica parziale laparoscopica con l'anastomosi end-to-end nel trattamento della gravidanza ectopica tubarica.
Le 451 pazienti studiate sono stati suddivise a caso in un gruppo di osservazione (il gruppo trattato con fenestrazione laparoscopica, n=238 casi) e in un gruppo di controllo (il gruppo trattato con resezione tubarica parziale laparoscopica più anastomosi end-to-end, n=213 casi). Il tempo medio dell'operazione, la perdita di sangue intraoperatoria, il tempo di dimissione postoperatoria e la degenza ospedaliera sono stati osservati per valutare il loro effetto clinico. Inoltre, nei due gruppi dopo l'operazione sono stati osservati il tempo necessario affinché la -HCG scenda a livelli normali, la pervietà delle tube di Falloppio e la funzione ovarica.
Risultati: non c'è stata alcuna differenza significativa tra il gruppo di osservazione ed il gruppo di controllo riguardo la durata dell'intervento, l'entità dell'emorragia intraoperatoria, il tempo di recupero di -HCG nel sangue e la durata del ricovero (P> 0,05). Il normale tasso di gravidanza del gruppo di osservazione era del 67,58%, significativamente più alto rispetto al gruppo di controllo (P <0,05). I valori dell'indice della funzione ovarica erano significativamente migliori di quelli del gruppo di controllo (P <0,05).
Conclusioni: Rispetto al gruppo di controllo, il metodo della resezione parziale laparoscopica delle tube più anastomosi end-to-end è più efficace nel trattamento della gravidanza ectopica tubarica e ha un impatto minore sulla funzione ovarica, che può effettivamente migliorare la probabilità di una gravidanza normale dopo l'operazione.

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