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Management and Outcome of Heterotopic Pregnancy

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Abstract

Objective: The aim of this study was to investigate the clinical efficacy of laparoscopic surgery for women with heterotopic pregnancy.

Method: The clinical outcomes of 12 patients with intrauterine and ectopic pregnancy undergoing laparoscopic operation were analyzed retrospectively.

Results: The products of ectopic pregnancy were removed by laparoscopically. The median operation time was 12 minutes, and the average blood loss was 21.4 ml. There were no postoperative complications. The wounds recovered well in all cases. Among these women, ten delivered at term whereas two failed to continue their pregnancies, one had an abortion after 8 days of the surgery and another one had an abortion due to preterm premature rupture of the membrane at 15 gestational weeks.

Conclusion: Laparoscopic surgery is an effective technique in successful management of heterotopic pregnancy.

Keywords: Heterotopic pregnancy; Laparoscopic surgery; Intrauterine pregnancy; Ectopic pregnancy

preserving the intrauterine pregnancy, continuing the intrauterine pregnancy and removing the ectopic embryo completely are vital, and it is a challenge for clinicians.

Ectopic pregnancy of HP can be treated by potassium chloride injection and (or) methotrexate in the gestational sac, laparoscopic surgery and laparotomy. However, conservative management may cause infection, internal hemorrhage, adnexal mass persistence, fetal toxicity and drug allergy. About 55% of HP patients after conservative treatment need surgery. Laparotomy is the treatment method for hemodynamically unstable and pelvic severe adhesion patients, but laparotomy has more complications such as high-volume pelvic haemorrhage, pelvic adhesion, intrauterine embryo abortion, PID etc. [6]. Recently, laparoscopy has been used to treat HP and replaced laparotomy gradually with the advantage of good operative field exposure, less postoperative pain, shorter length of hospital stay and less complication. The objective of this work was to describe our experience, investigate the laparoscopic surgical techniques and value in the treatment of HP.

Methods

A retrospective review was undertaken of 12 cases of HP which were diagnosed via serum β -HCG (human chorionic gonadotropin) level and ultrasound and treated by laparoscopic surgery at the First Affiliated Hospital of Zhengzhou University from January 2013 to January 2016. Data about patients' age, gravidity, the current pregnancy, gestational age, symptoms, serum β -HCG level and general appearance on ultrasound were available from a retrospective review of the hospital and outpatient medical records. Gestational age was calculated either according to the last menstrual period or 2 weeks before the date of embryo transfer. All ectopic embryos were located in the fallopian tubes.

Operative Procedure

11 patients underwent partial salpingectomy on the affected side to reduce the occurrence of persistent postoperative EP or recurrence rate and protect ovarian function. One patient with ruptured EP underwent salpingectomy because of massive bleeding. To minimize the

Introduction

Heterotopic pregnancy (HP) is defined as the coexistence presence of intrauterine and ectopic pregnancy. It was considered a rare event. The incidence is approximately 1 per 30,000 pregnancies in spontaneous pregnancy, in recent years the incidence is up to 1% [1,2]. The incidence of heterotopic pregnancy is arising because of the increasing tubal factor infertility and infertility treatments such as ovulation induction and assisted reproductive techniques [3,4]. Once ectopic pregnancy ruptured, massive hemorrhage can lead to more than three quarters of the first trimester death [5]. Ruptured ectopic pregnancy is one of the outcomes of delayed diagnosis or misdiagnosis, early and accurate diagnosis is crucial for an opportune intervention of a potentially life-threatening condition. For the patients with the intensely need for

effects of the anesthetic drugs on the fetus, general anesthesia was initiated after the preparations for operation were completed. Patients were under endotracheal general anesthesia with propofol, fentanyl, midazolam. Blood pressure, transcutaneous oxygen saturation, electrocardiograms, and carbon dioxide (CO₂) pressure were monitored continuously. Patients were placed in supine position, once CO₂ pneumoperitoneum created the head end was lowered to approximately 15 degrees (15 Trendelenburg position). A 1 cm incision was made just supra the umbilicus. The primary puncture was made by a 10 mm trocar-cannula and laparoscope was inserted. The abdomen was inflated with CO₂ and maintained pressure at 10 mm Hg. Under direct visualization of the videolaparoscope, 5 mm and 10 mm ancillary ports were introduced for instruments in the left lower quadrant. During intraoperative 2 cases were found with severe pelvic adhesions, and then the fourth 5 mm port was added in the right lower quadrant. Cold scissors dissection with bipolar coagulation was used to adhesiolysis. Both sides of the mass (gestational sac) and mesosalpinx were clamped by tissue closure clip (Hem-o-lock clip) and then the mass was cut off using scissors. In one case the EP was ruptured, and then salpingectomy was performed. The proximal portion of the fallopian tube and mesosalpinx were clamped by Hem-o-lock clip and then the fallopian tube was removed by scissors. The abdomen was rinsed till clear at the end of the procedure. During the procedure manipulation about uterus was minimal and special attention should be taken to avoid irritating the ovary in hyperstimulation state. Operations were finished as soon as possible.

Results

Twelve patients underwent laparoscopic surgery for heterotopic pregnancy. Of these women, 6 patients had conceived via *in vitro* fertilization and embryo transfer, 5 patients via ovulation induction with clomiphene, and one patient was spontaneous pregnancy. 3 patients had a history of previous adnexal surgery, 7 had PID history. The median age, gravidity, and gestational age at the time of laparoscopic operation were 28.5 years (range, 26–35 years), 2 (range, 1–3), and 6+5 gestational weeks (range, 5+6–8 gestational weeks), respectively. All patients were diagnosed by transvaginal ultrasound: gestational sacs were visible in 5 cases, while the others were showed with an adnexal mass. 9 cases' ectopic embryos were located in the ampullary of fallopian tube, 2 were found in the isthmus and was in the interstitium. Serum β -HCG measurements ranged from 79324 to 127805 mIU/ml. The median operating time was 12 min (range, 8-20 min) and the average blood loss was 21.4 ml (range, 2-200 ml). In one case with a ruptured right ampullar pregnancy, there was hemoperitoneum approximately 200 ml. No one needed blood transfusion. The median postoperative hospital stay time was 3 days (range, 2–6 days). All the women were discharged from hospital after laparoscopic surgery without any complications. Pathological examination of the excised tissue revealed chorionic villi which confirmed the diagnosis of a tubal pregnancy.

10 women carried their pregnancies to term. Among the women who delivered, eight women underwent cesarean deliveries, two women delivered vaginally. Two women failed to maintain their pregnancies. One had a missed abortion eight days after surgery. The other had a miscarriage due to preterm premature rupture of membrane at 15 weeks. The new borns' Apgar scores ranged from 9 to 10 points, birth weight ranged from 2.8 ~ 3.7 Kg. All newborns in this group were born with no congenital anomalies.

Discussion

Etiology of heterotopic pregnancy

Heterotopic pregnancy is usually a serious emergency and potentially life-threatening condition for the woman and the intrauterine pregnancy. Many predisposing factors causing heterotopic pregnancy are identical to those predisposing to ectopic pregnancy [7]. First, there are ovulation factors such as multiple ovulation or ovulation hyperstimulation syndrome caused by using drugs for ovulation induction application of drugs (controlled ovarian hyperstimulation: COH). The probability of the occurrence of HP is significantly higher in COH associated pregnancy than in non-COH pregnancy. Second, ectopic pregnancy is associated with *in vitro* fertilization and embryo transfer (IVF-ET). And for IVF-ET, the meaningful risk factors for HP included a history of ectopic pregnancy, abortion history, and OHSS [8]. Third, tubal factor is the most prominent risk factor related to ectopic pregnancy. In this group, 8 women had HP after the treatment of tubal factor infertility.

Early diagnosis

Early diagnosis of HP is defined before 7 weeks of gestation or before the rupture of HP [9]. The early diagnosis of heterotopic pregnancy is quite arduous due to the absence of clinical symptoms. Adnexal torsion, haemorrhagic corpus luteum, ovarian cyst, tubo-ovarian abscess and appendicitis can mimic ectopic pregnancy symptoms [10]. Ultrasonographic evaluation is the gold standard for diagnosis, with findings of a second gestational sac or complex mass in addition to the intrauterine pregnancy [11]. The detection rate of heterotopic pregnancy with transvaginal ultrasound scans can vary from 41% to 84% [12]. The possibility of HP should be suspected in women undergoing assisted reproduction techniques, use of ovulation induction drugs and presenting with acute lower abdominal pain, peritoneal irritation, hypovolemic shock. In high-risk patients, especially that underwent an ART treatment, a transvaginal ultrasound scan should be performed at 5 weeks of gestation (18 days after ET) to diagnosis [9]. And a study suggests 21 days after implantation, if the serum HCG level >1000 mIU/ml then it has been suspected as multiple pregnancy or HP [13]. When blood β -HCG level is significantly higher than those in singleton pregnancy while the ultrasonography detects single intrauterine pregnancy, even though ultrasonography does not show any adnexal mass, or the unconfirmed exact localization of pregnancy, HP should be highly considered, intensive follow-

up including repeated ultrasonography and serial serum β -HCG test should be performed. But, someone considers that the diagnostic role of β -HCG levels in heterotopic pregnancy is debatable [12]. Ultrasound examination combining serial serum β -HCG tests is important ways to diagnose heterotopic pregnancy.

Anesthesia management of laparoscopic surgical treatment for HP

Teratogenic effects of anesthesia drugs often capture our attention. Although there are no known teratogenic effects from the use of commonly administered anesthetic agents at standard concentrations at any gestational age [14], certain precautions should be undertaken to minimize adverse effect. Anesthesia was commenced after disinfection process and the preparation of all the laparoscopic surgical instruments. Anesthetic drugs which make minimal adverse effect on fetus should be used. In this group, propofol, fentanyl and midazolam were used to anesthesia. Fentanyl provides rapid onset, cardiovascular stability and has a short half-life. It has been mentioned that a combination of propofol, fentanyl, and midazolam was used frequently in IVF patients with a relatively low risk for adverse effects on oocyte and embryo quality and pregnancy rates [15-18]. A review of nonobstetric surgery involving pregnant women between 4 and 20 gestational weeks suggested anesthesia between 4 and 20 gestational weeks was safe [19,20].

Safety, feasibility and skills of laparoscopic surgical treatment for HP

The management of heterotopic pregnancy aims to remove the extrauterine pregnancy completely, while as minimally invasive as possible in order to preserve the normal development of the intrauterine pregnancy. Favorable perioperative management and prophylactic treatment should be given on time in case of miscarriage. There is no standard surgical management protocol has yet been established but laparoscopic surgery is accepted as the standard treatment for the surgical management of ectopic pregnancies in many studies [21]. The advantages of laparoscopic surgery were proved, including good operative field exposure, fewer surgical wounds, less intraoperative blood loss, less postoperative pain, shorter hospitalization and quicker return to regular activity. Laparoscopic surgery has the added benefits in the pregnant patient of less uterine manipulation, potentially leading to a decreased rate of miscarriage and preterm labor. In this group, there were no major intraoperative or postoperative complications. We believe these results prove that laparoscopic surgery for ectopic pregnancy of HP is safe, feasible and effective, although additional investigations are needed. Regarding the pressure of pneumoamnios, some reports suggested intra-abdominal insufflation pressures be maintained at less than 12 mmHg to avoid worsening pulmonary physiology in gravid women [22]. In this group, the patients' intraperitoneal pressure was set at 10 mmHg and all newborns were normal. Mechanical stimulation on the uterus

and ovaries should be minimized in order to prevent miscarriage and avoid the endocrine changes.

Conclusion

In conclusion, heterotopic pregnancy is no longer a rare event due to history of PID, widespread and increasing use of ART and induction of ovulation. Laparoscopic surgery performed by an experienced surgeon is feasible and safe for the treatment of heterotopic pregnancy and is worth being advocated.

Conflict of Interest

We declare that we have no conflict of interest.

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