

Intratubal Methotrexate versus Laparoscopic Salpingotomy

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ABSTRACT

Introduction: Though laparoscopic salpingotomy is the preferred conservative surgery of choice in patients desirous of future fertility, the management of ectopic pregnancy has changed extensively. Other modalities like medical management with Methotrexate are being reviewed for conservative management of tubal pregnancy.

Objective(s): To compare intratubal Methotrexate instillation with laparoscopic salpingotomy for conservative management of tubal pregnancy.

Method(s): A literature review was conducted using search engines Google, Highwire press. Success rate after treatment and future reproductive outcome were analyzed.

Conclusion(s): Laparoscopic salpingotomy was more superior to with Methotrexate as conservative treatment of ectopic pregnancy.

Keywords: Laparoscopic salpingotomy, pregnancy, tubal, ectopic.

INTRODUCTION

Each year, women all around the world present with ectopic pregnancy, accounting for upto 2% of pregnant women.¹ This pathology occurs due to the implantation of fertilized ovum outside the uterus, the most common site being the fallopian tube. If left untreated, it eventually causes life-threatening hemorrhage following the rupture of the fallopian tube. It is therefore a significant cause of maternal mortality and morbidity.²⁻⁴ It is known to account for 10-12% of maternal mortality.⁵⁻⁶

Ectopic Pregnancy usually occurs 98% of cases in the uterine tube. Trophoblast can be implanted at various sites. These are as follows:

- The ampulla (64%)
- The Isthmus (25%)
- The infundibulum (9%)
- The intramural junction (2%)
- Ovarian (0.5%)
- Cervical (0.4%)
- Abdominal (0.1%)
- Broad ligament (0.05%)

RISK FACTORS ASSOCIATED WITH ECTOPIC PREGNANCY

- Previous tubal surgery
- Previous ectopic pregnancy
- In utero* diethylstilbestrol exposure
- Previous genital infections
- Infertility
- Current smoking
- Previous intrauterine device use^{7,8}

A diagnosis of ectopic pregnancy is made by history and examination, ultrasonography, bHCG serial assays.

HISTORY AND PHYSICAL FINDINGS

Ectopic pregnancy is usually diagnosed around seven weeks of gestation in reproductive women who present with abdominal pain and vaginal bleeding.⁹ The overall risk of developing ectopic pregnancy is 39 percent in a patient with abdominal pain and vaginal bleeding but no other risk factors and increases to 54 percent if the patient has other risk factors.¹⁰ Exclusion of ectopic pregnancy based solely on history and physical examination is not reliable.¹¹⁻¹⁴

BETA HUMAN CHORIONIC GONADOTROPIN (bhCG) MEASUREMENT

Beta-hCG levels increase by at least 53 percent every two days, and reach a level greater than 100,000 mIU per mL (100,000 IU per L) in a normal intrauterine pregnancy.^{1,15} In ectopic pregnancy serial beta-hCG levels do not increase appropriately. Serial assays are only 36 percent sensitive and approximately 65 percent specific for detection of ectopic pregnancy.^{16,17}

SERUM PROGESTERONE MEASUREMENT

Eighty-five percent of patients with ectopic pregnancy will have normal serum progesterone.

Levels.¹⁰ It is, therefore, not diagnostic of ectopic pregnancy, though patients at risk for developing ectopic pregnancy can be identified.

ULTRASOUND IMAGING

Ultrasonography is the test of choice. If transabdominal ultrasonography does not show an intrauterine gestational sac and the patient's beta-hCG level is greater than 6,500 mIU per mL (6,500 IU per L) or Transvaginal ultrasonography does not show an intrauterine gestational sac with beta-hCG level of 1,500 mIU per mL (1,500 IU per L) or greater, ectopic pregnancy can be suspected. Transvaginal ultrasonography and serial beta-hCG measurements have sensitivity of 96 percent and specificity of 97 percent in diagnosing ectopic pregnancy.^{2,18}

The mortality and morbidity has declined in the recent in the recent years due to improvements in diagnosis by transvaginal ultrasonography and serial assays of bHCG.^{19,20} Improved diagnosis, desire for future fertility have changed the treatment modality of tubal pregnancy more in favor of conservative approach with successful results.²¹

The criteria for selecting appropriate candidates for conservative management of an ectopic pregnancy is:

1. A highly compliant and reliable patient, since close follow-up is required and resolution may take up to 7 weeks.
2. Healthy woman, unruptured tubal ectopic pregnancy and hemodynamically stable.
3. Ultrasound without evidence of intrauterine pregnancy and ideally a dilatation and curettage failing to find villi.
4. Ectopic size less than 4 cm in greatest diameter CG titer of less than 5,000 mIU/mL.
5. Absence of fetal heart tones.

Every patient must satisfy Criteria 1 and 2, Criteria 3 to 6 being relative contraindications to medical therapy.²² Conservative approach can be medical or surgical.

Medically, Methotrexate is the drug of choice and can be administered via various routes. One of which is locally, under ultrasound guidance into the gestational sac directly. The main potential advantages of this method are:

1. A greater antitrophoblastic effect;
2. A shorter treatment period;
3. Reduced dosage, and
4. Absence of side effects.²³

Laparoscopic approach is the preferred approach now and laparoscopic salpingotomy is the conservative surgery of choice. The mesosalpinx is infiltrated with vasopressin (5 IU in 20 mL of normal saline). A 1 to 2 cm incision on the antimesenteric side of the tube is made. Copious irrigation is used to dislodge trophoblast. The bed is irrigated well. The products of conception are then removed through the 10 mm sleeve. The opening of fallopian tube was left to heal by secondary intention. This review was carried out to compare treatment for tubal

pregnancy using intratubal Methotrexate or by laparoscopic salpingotomy. Short-term outcome measures (primary treatment success, reinterventions for clinical symptoms or persistent trophoblast, tubal preservation) and long-term outcome measures (tubal patency and future fertility) were focused upon.

MATERIAL AND METHODS

A literature search was performed using the search engine Google and Highwire Press. The following search terms "Laparoscopic salpingotomy, pregnancy, tubal, ectopic" were used. Selected papers were taken for the further references.

INCLUSION CRITERION

Published RCT (randomized controlled trial) were included in the review if it dealt with the comparison of Methotrexate and laparoscopic salpingotomy for the treatment of tubal pregnancy

OUTCOME MEASURES

1. Short-term
 - Evaluation of success of the treatment which was based on uneventful decline of serum bhCG to undetectable levels.
 - Need for reintervention in view of persisting clinical symptoms or inadequately declining serum bhCG levels.
2. Long-term
 - Patency of the fallopian tube on further follow-up which was established by passage of dye on hysterosalpingography
 - Future fertility.
3. Others
 - Hospital stay and
 - Cost effectiveness.

DISCUSSIONS

Success Rate

In a study of one hundred patients, conducted by Shalev E et al, in 1995, to test the effectiveness of laparoscopic intratubal Methotrexate (MTX) injection or salpingotomy in the treatment of ectopic pregnancy, Salpingotomy was successful in 51 of 55 patients (92.7%), whereas intratubal MTX injection was successful in only 27 of 44 women (61.4%). Methotrexate injection particularly was unsuccessful if the initial bhCG was > 2,000 mIU/mL (conversion factor to SI unit, 1.00) or the size of the tubal mass was > 2.0 cm as measured during laparoscopy.²⁴ Fernandez (1998), in a study of Methotrexate (group 1), or laparoscopic salpingotomy (group 2), reported successful treatment in 45 of 51 patients in group 1 (88.2%) and 47 of 49 group 2 (95.9%). success rate.²⁵

That Methotrexate had a lesser success rate as compared

to laparoscopic salpingotomy was also concluded in similar comparative studies, even though criterion for conservative management had been strictly followed.^{26,27}

Reintervention

An advantage of linear salpingotomy was the predictable and consistent decline of circulating bhCG, and consequently a reduced need for reintervention. This was concluded by Porpora et al in a study performed to compare local injection of Methotrexate (MTX) and linear salpingotomy in the conservative treatment of ectopic pregnancy.²⁷

Tubal Patency

No significant difference in tubal patency on follow-up hysterosalpingography was observed between the two groups. This was concluded in a number of studies.

In an original randomized study done by Fernandez in 1995 comparing intratubal Methotrexate with laparoscopic salpingotomy, tubal patency was assessed in 35 women with hysterosalpingography on follow-up after 3 months. No difference was found.²⁸

Two similar randomized controlled trials reported on tubal patency in 36 women and no significant differences were found.^{26,27}

Fertility Outcome

Fertility restoration and pregnancy outcome following conservative approach by minimal access surgery proved no significant difference when compared with Intratubal Methotrexate. The number of intrauterine pregnancies was comparable, 83.5% in the group treated with laparoscopic pregnancy and 81% in the other group treated with Methotrexate.²⁹

Hospital Stay

A randomized control trial conducted by Porpora et al, comparing laparoscopic surgery versus Methotrexate in treatment of ectopic pregnancy, showed longer hospital stay of 2.7 days (range 1-5 days) to 1.7 days (range 1-3 days in the Methotrexate group).²⁷

Cost Effectiveness

It was concluded in various studies that single dose of Methotrexate was more cost effective in comparison to laparoscopic salpingotomy.³⁰⁻³²

CONCLUSION

Methotrexate is not suitable for treatment of every ruptured ectopic even after choosing patients according to the inclusion criterion and is found to be more effective for small tubal pregnancies with low values of bhCG. Thus laparoscopic salpingotomy has an edge over Methotrexate and should be the gold standard for conservative approach in an unruptured tubal pregnancy.

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