BOSTON IVF

CONSENT FOR METHOTREXATE TREATMENT

INTRODUCTION

When a normal pregnancy is established the fertilized egg or the embryo implants in the uterine cavity. However, sometimes the embryo implants outside of the uterine cavity. This situation is referred to as an ectopic pregnancy and cannot lead to a normal pregnancy. The vast majority of ectopic pregnancies (>95%) occur in the fallopian tube but an ectopic pregnancy can also implant in the cervix, ovary, or abdominal cavity. The major concern with an ectopic pregnancy is that it can rupture through the fallopian tube and result in internal bleeding.

In the past, the diagnosis of tubal pregnancy was made when the pregnancy was more advanced and surgical removal of the tube was usually necessary. With the development of vaginal ultrasound and a sensitive pregnancy test, the diagnosis of an ectopic pregnancy can be made earlier. When the diagnosis is made at an earlier stage, there is a greater likelihood that the ectopic pregnancy can be removed surgically and the fallopian tube can be conserved.

Methotrexate administration is available as an alternative to surgery. This medication stops rapidly dividing cells from multiplying (pregnancy tissue grows in this fashion). Methotrexate is a chemotherapy drug, which has been used to treat women with molar pregnancies. Molar pregnancies are non-viable intrauterine pregnancies that are made up of very aggressive placental tissue that can grow into the wall of the uterus. Several studies have demonstrated that properly selected patients with ectopic pregnancies can be successfully treated with methotrexate.

INDICATIONS FOR METHOTREXATE

Methotrexate treatment has several applications in the treatment of ectopic pregnancy, which are discussed below.

1. **Persistent ectopic pregnancy following conservative surgery-** If the diagnosis is made early, an ectopic pregnancy can be removed from the fallopian tube by a surgical procedure called laparoscopy. This procedure is performed under general anesthesia and involves the placement of a telescope-like instrument and other instruments through small incisions in the abdomen. A small incision is made in the tube over the ectopic pregnancy and the pregnancy tissue is removed. However, not all of the tissue can be removed and some remains in the tube. In the majority of cases, the remaining pregnancy tissue goes away on its own but in other cases the tissue can remain in the tube and continue to grow. Following conservative surgery periodic blood samples are taken to follow the level of the pregnancy hormone, human chorionic gonadotropin (hCG). As long as the hCG level decreases no intervention is necessary. However, if the hCG levels plateau or increase, additional treatment is indicated. Treatment options include repeat laparoscopy with possible removal of the fallopian tube or medical treatment with methotrexate.
2. **An ectopic pregnancy in a location that is not amendable to conservative surgery**- If the ectopic pregnancy is located in the cervix, the ovary or in the portion of the tube that is located in the uterine wall, surgical removal may be difficult and potentially complicated. Treatment with methotrexate is another alternative.
3. **A woman who is a poor operative risk**- Medical treatment can be considered for the woman who is at greater risk for surgical or anesthetic complications.
4. **A presumed ectopic pregnancy**- Some women who achieve pregnancy have slowly rising levels of pregnancy hormone. In this situation, there is no chance for a viable pregnancy. This occurrence can be the result of a failed intrauterine pregnancy or an ectopic pregnancy. Another presentation of an ectopic pregnancy is when an ultrasound exam fails to document an intrauterine pregnancy at six weeks of pregnancy and/or when the hCG titer has reached 2000 mIU/mL. In these situations there are several alternatives:
   A) ***Performance of a D&C***- This procedure involves placing an instrument into the uterine cavity to remove the pregnancy tissue. This surgery is performed under anesthesia. A pathologist can examine the tissue and if pregnancy tissue is identified, the presence of a failed intrauterine pregnancy is confirmed and no further treatment is indicated. Alternatively, if the pathologist fails to identify pregnancy tissue, then this raises further suspicion of an ectopic pregnancy. If this occurs, there are two options- medical treatment with methotrexate or surgical treatment by laparoscopy.
   B) ***Methotrexate treatment***- The other option is to <u>not</u> undergo a D&C and be treated with methotrexate initially. A single intramuscular injection will be administered and you will be asked to return for weekly blood work to have the pregnancy hormone level assessed. If the level decreases, then simple observation is indicated. Alternatively, if the level increases or plateaus a second injection of methotrexate or surgery may be indicated.
5) **Confirmed Ectopic Pregnancy**- If an ultrasound exam confirms the presence of a gestational sac (evidence of an early pregnancy) outside of the uterine cavity then the diagnosis of an ectopic pregnancy is established. In this situation there are two options:
   A) ***Laparoscopy***- This is outpatient surgical procedure that is performed under general anesthesia. The procedure involves

the placement of a telescopic instrument through a small incision into the abdominal cavity, allowing visualization of the pelvic organs. When the ectopic pregnancy is localized in the tube then a small incision in the tube to remove the pregnancy tissue. During the postoperative period pregnancy hormone levels will be followed until they are negative. If at the time of the laparoscopy there is significant damage to the tube then partial or complete removal of the tube may be indicated. At the time of surgery the other tube will be examined to determine its condition.

B) ***Methotrexate treatment***-This treatment is reviewed below.

METHOTREXATE TREATMENT

If you elect to proceed with methotrexate treatment, the first step is to obtain routine blood work. If it is determined that you are a candidate for this treatment, the methotrexate will be administered by an intramuscular injection. Side effects may occur but usually don't appear until 2-7 days after administration. Side effects include nausea, vomiting, abdominal pain and loss of appetite. Sores or ulcers of the mouth, tongue, vagina and bowel occur rarely, are usually mild and resolve over a short period of time. Rarely, methotrexate can lower the white blood and platelet counts. Other very uncommon side effects include hair loss, skin rash, dizziness and liver dysfunction. Because of the potential liver toxicity it is important that you do not consume any alcohol while taking this medication.

A pregnancy blood level (hCG) will be determined at weekly intervals. If the level is dropping then the pregnancy hormone level will be followed periodically until it reaches zero. It can take up to 4-5 weeks or sometimes longer after the injection of methotrexate before the pregnancy hormone level reaches zero. If the pregnancy hormone level plateaus or increases, then either another injection can be administered or surgery can be performed.

It is important to remember that even though you have received methotrexate, tubal rupture can still occur and emergency surgery may be required. Therefore, you should contact your doctor immediately if you develop abdominal pain. If you should have any difficulty in contacting your physician you should proceed to the emergency department of the nearest hospital.

Even though your tubal pregnancy totally resolves on methotrexate treatment, scarring may occur in your tube as a result of the tubal pregnancy as it can follow surgical treatment. This could predispose you to a tubal pregnancy in the future and/or subsequent infertility. Your chances of conceiving after medical therapy with methotrexate are the same as after surgery. There is no increased risk of congenital anomalies in babies born to women who have taken methotrexate in the past.

It is important that during and up to two weeks after receiving methotrexate you should not drink any alcohol or take aspirin or aspirin-like compounds (Advil®, Motrin®, etc), folic acid or vitamins containing folic acid. You should also avoid excess exposure to sun or use of sunlamps for 4 weeks following methotrexate therapy because your skin may be more sensitive to sunlight than usual and you can burn excessively. You should also avoid intercourse until resolution.

ACKNOWLEDGEMENT OF INFORMED CONSENT

I acknowledge that I have read and understand this written material. I understand the purpose, risks and benefits of this treatment. I am aware that there may be other risks and complications not discussed that may occur. I also understand that during the course of the treatment, unforeseen conditions may be revealed requiring the performance of additional procedures. I acknowledge that no guarantees or promises have been made to me concerning the results of this treatment or any subsequent treatment that may be required. This treatment has been explained to me in language that I understand. **I have been given the opportunity to ask questions which have been answered to my satisfaction.** I have also considered other options and alternatives**. I consent to the treatment with methotrexate.**

_____ _____

Signature of Patient Signature of Physician

_____

Printed Name

_____

Date of Birth

_____

Date