

The use of CA-125 in the assessment of conservative medical treatment of ectopic pregnancies with single dose of methotrexate.

Thesis

*Submitted For Partial Fulfillment Of Master degree
In Obstetrics & Gynecology.*

BY

*Manal Mohamed Mahmoud
Assistant specialist of Obstetrics & Gynecology
At EL Police Authority Hospital.*

Under Supervision Of

*Prof. Dr. Ali Elian Khalaf Allah.
Professor of Obstetrics & Gynecology
Faculty of Medicine Ain Shams University.*

*Dr. Ahmed Mohamed Ibrahim
Lecturer in Obstetrics & Gynecology
Faculty of Medicine
Ain Shams University.*

*Faculty of Medicine
Ain Shams University.*

2008

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

(يرفع الله الذين آمنوا منكم
والذين أوتوا العلم درجات)

(المجادلة : من الآية ١١)

PROTOCOL

INTRODUCTION

- Ectopic pregnancy is still the major cause of maternal mortality in the first trimester of pregnancy and accounts for approximately 10% of maternal deaths (Malatyalioglu E 2006)

- Modern diagnostic methods now permit early recognition of most ectopic pregnancies. Contemporary treatments are more conservative than in the past. The focus of attention has shifted from emergency surgery for the control of life threatening hemorrhage to medical treatment aimed to avoiding surgery and preserving reproductive anatomy and fertility (Speroff L and Marc A.2005)

- The CA-125 tumor marker is a cell-surface antigen derived from the surface coelomic epithelium, including the mucosa of the entire female genital tract and the germinal epithelium of the ovaries the fetal chorion, amniotic fluid and maternal deciduas also have been shown to contain significant amounts of CA-125 protein. Serum CA-125 levels are increased early in pregnancy and immediately after birth.
(Bredanic M 2000)

- Ectopic pregnancy is a unique situation in which maternal extra uterine compartments are exposed to fetal tissues. In normal intrauterine pregnancy, ruptured and unruptured tubal ectopic pregnancies, there are contradictory reports investigating the dynamics and comparison of maternal serum CA-125 levels. (Schmidt T, et al. 2001)

- Reports of Witt et al. and Kobayashi et al. showed very low CA 125 values in the serum of patients with ectopic pregnancy compared to those with normal intrauterine pregnancy or miscarriage.
(Schmidt Tet. al. 2001)

- Sadovsky et al 1991. reported that women with ectopic pregnancies have elevated serum CA-125 levels compared to those with intrauterine pregnancies.

- In intact tubal ectopic pregnancies , expectant or managed with medical treatment , the increase of C A 125 levels in the serial measurements could be a supplementary test for an early diagnosis of tubal rupture
(Malatyalioglu E 2006)



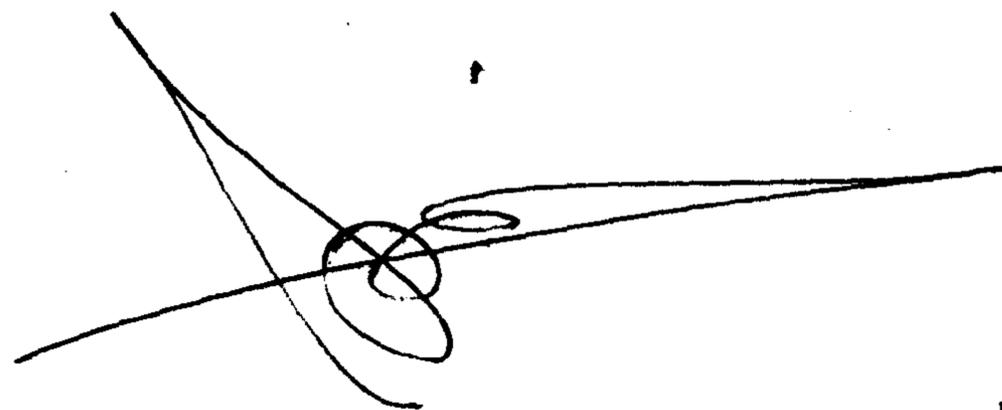
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- Predantic M 2000 reported that the use of CA-125 levels as an adjunct to serial beta-hCG levels shows promise as a means for differentiating tubal abortion from viable ectopic pregnancy.

- Methotrexate was first introduced for the management of ectopic pregnancies in the 1980s. It is a cytotoxic drug that binds to the enzyme dihydrofolate reductase, which is involved in the synthesis of purine nucleotides. As a consequence it interferes with DNA synthesis and disrupts cell multiplication. It can be used both systemically and locally for the treatment of both tubal and non-tubal ectopic pregnancies.

(Kirk et al. 2006)

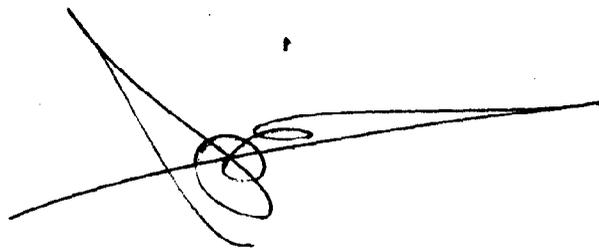
- Among methotrexate regimens, a single dose (50 mg/m^2) of intramuscular methotrexate, which was first described by Stovall et al 1991. is the most commonly used one because of its simplicity and convenience for both clinician and patient. (Dilbaz S et al 2006.)

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AIM OF THE WOKK

The aim of this study is To evaluate the use of C A 125 in the assessment of conservative medical treatment of ectopic pregnancies with single dose of methotrexate

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MATERIALS AND METHODS

1- Patients

This descriptive study will be carried out at the causality and outpatient clinic of Obstetric and Gynecology in Ain Shams University Maternal Hospital .

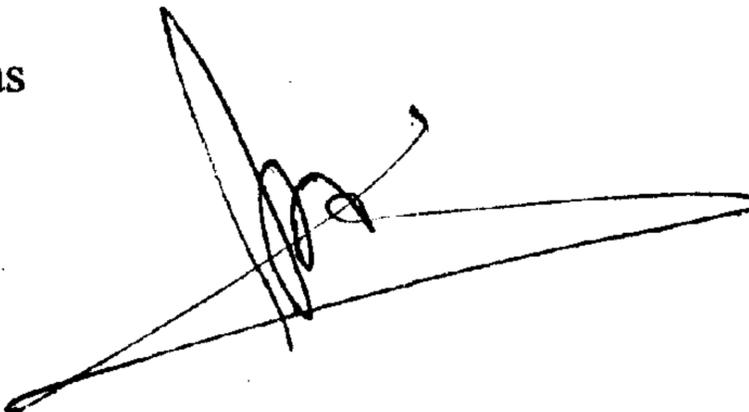
(study group):

Includes 15 patients with undisturbed ectopic pregnancy.who will be managed by conservative medical treatment with single dose of methotrexate All patients will subjected to (1) history taking, (2) general, abdominal and local examinations , (3) investigations as : transvaginal U\S and quantitative β HCG.

Exclusion criteria :

(1) patients with any lesion known to increase serum C A 125 will be excluded from this study . This includes

- 1-Acute or chronic pelvic infection
- 2- Endometriosis
- 3- Benign ovarian cysts
- 4- Uterine leiomyomas
- 5- Endometrioma
- 6- Renal diseases
- 7- Smokers



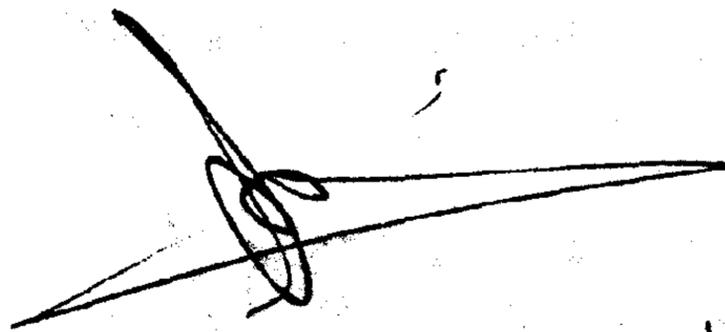
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(2) Contraindications to methotrexate treatment :

- 1- Breast feeding .
- 2- Overt or laparotomy evidence of immunodeficiency
- 3- Alcoholism, alcoholic liver disease, or other chronic liver disease
- 4- Preexisting blood dyscrasias , such as bone marrow hypoplasia , leucopenia , thrombocytopenia , or significant anemia .
- 5- Known sensitivity to methotrexate
- 6- Active pulmonary disease.
- 7- Peptic ulcer disease .
- 8- Hepatic , renal , or hematological dysfunction

(3) patient who don't fit the inclusion criteria for conservative medical treatment of ectopic pregnancy described below:

- 1- The patient is hemodynamically stable, reliable, and compliant
- 2- Ultrasonography should fail to find an intrauterine pregnancy
- 3- The ectopic pregnancy measures 4 cm or less in its greatest diameter .
- 4- There is no evidence of rupture of the ectopic pregnancy
- 5- Pre treatment serum hCG concentration less than 5000 miu/ml

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Prior to methotrexate treatment

1. Rhogam (will administered) if patient is Rh – negative and greater than 8 weeks gestation .
2. Baseline liver and renal function tests , complete blood and platelet counts will be obtained .

Patient instructions

The following are avoided until HCG titers are negative alcohol use, sexual intercourse, and the use of folic acid containing vitamins.

* Before medical treatment β hCG and CA125 will be measured.

Single dose methotrexate protocol

Day 1 : **Baseline studies**
Methotrexate **50mg/m² intramuscular.**

Day 4 : **HCG titer, and CA125 titer**

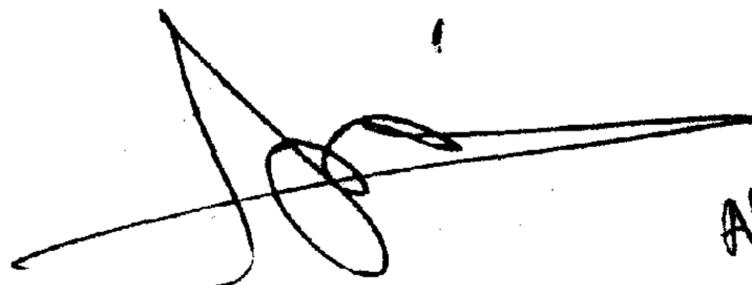
Day 7 : **HCG titer, and CA125 titer**

Complete blood and platelet count

Liver and renal function tests.

Weekly : **HCG titer until negative and CA125.**

Methotrexate is administered a single-dose if the serum β -hCG declines 15% or more between days 4 and 7. thereafter, β -hCG concentration are monitored on a weekly basis until levels become undetectable if the serum β -hCG dose not declines by more than 15% a second dose can be given .



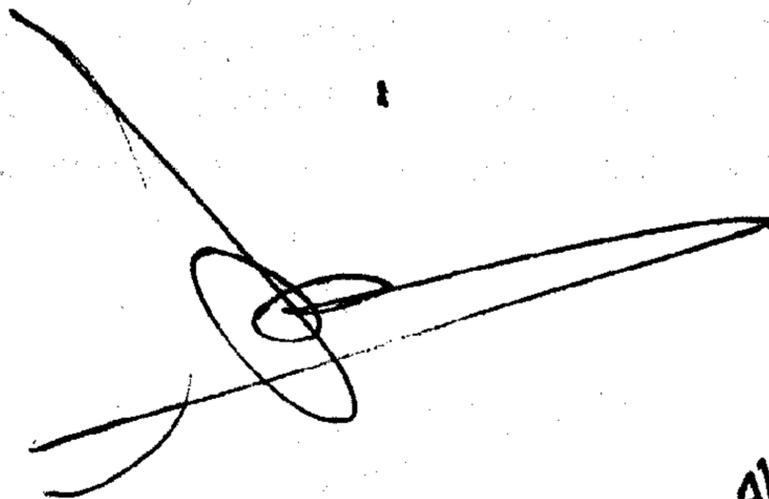
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• **2. Blood samples and biochemical assay:**

- Blood samples will be withdrawn by routine vein puncture at time of admission to the hospital and should be free of haemolysis.
- The collected sample will be assayed quantitatively for maternal serum CA 125 by ELISA. method.
- . The collected sample will be also assayed quantitatively for maternal serum β -hCG by ELISA. method.

3. Statistical analysis:

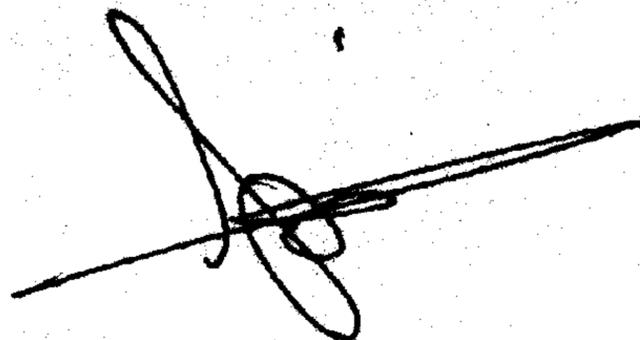
Data will be collected, tabulated and analyzed statistically.

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REFERNECES

- 1 - Erdal Malatyalioglu , Sinan Ozer , Arif Kokcu , Mehmat B. Cetinkaya , Tayfun Alber and Migraci Tosun CA 125 levels in ruptured and unruptured tubal ectopic pregnancies J. Obstet. Gynecol. Res. vol. 32, No. 4: 422-427, August 2006
- 2 - Speroff L and Fritz .Ma Ectopic pregnancy Ectopic pregnancy. In Clinical Gynecologic Endocrinology and Infertility Seventh Edition, U.S.A.
LIPPINCOTT WILLIAMS & WILKINS 2005 , 1 2 7 5
- 3 - Schmidt T, Rein DT,Foth D . Prognostic value of repeated serum CA125 Measurements in first trimester pregnancy .Eur J Obstetric Gynecol reprod boil 2001; 97: 168 _ 173 .
- 4 - E.Kirk G.Condous and T.Bourne. The non-surgical management of ectopic pregnancy. Ultrasound Obstet Gynecol 2006,27;91-100.
- 5 - Predanic M. Differentiating tubal abortion from viable ectopic pregnancy with serum CA-125 and beta-human chorionic gonadotropin determinations. Fertile Steril2000,73:522-525
- 6 - Hornstein Md. Check JH. Hill AJ. Serum CA125 levels and spontaneous abortion Am J Obstet Gynecol 1995; 172: 695 – 9
- 7 - Sadovsky Y, Pineda J, Collins JL.Serum CA 125 levels in women with ectopic and intrauterine pregnancies J Reprod Med 1991, 36:875 878
- 8 - Sedar Dilbaz , Eray Caliskan , Berna Dilbaz , Ozlem Degirmenci , and Ali Haberal Predictors of Methotrexate Treatment Failure in Ectopic Pregnancy. The Journal of Reproductive Medicine.2006.
- 9 - Torsten Schmidt , Danien T . Rein , Dolores Foth , Hans- Walter Eibach , Christian M.Kurbacher , Peter Mallmann , Thomas Romer Prognostic value of repeated serum CA-125 measurements in first trimester pregnancy. European Journal of Obstetries & Gynecology and productive Biology 97 (2001)168-173.



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• أسبوعياً: يجرى تحليل كمي لهرمون المشيم

الأدمى التناسلى.

• وإذا لم ينخفض تحليل كمي لهرمون المشيم

الأدمى التناسلى بنسبة 10% تعطى المريضة

جرعة أخرى من الميزوتركسيت.

• عينات الدم والتجربة الكيميائية الحيوية:

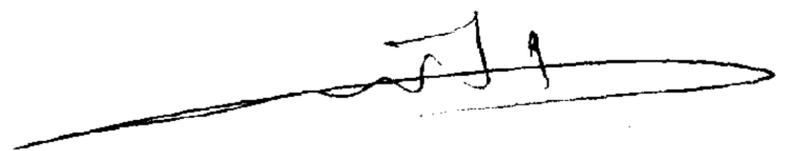
العينات المبيعة ستجرب بشكل كمي للهرمون

المشيم الأدمى التناسلى و (CA-125) بطريقة

إليسا.

• التحليل الإحصائى:

البيانات ستكون مبيعة، جدول و تحليل إحصائى.



٢. وجود أحد موانع استخدام الميزوتر كثيبت

أ- الرضاعة الطبيعية.

ب- انخفاض المناعة.

ج- الكحوليات.

د- أمراض الكبد المزمنة والكلية.

هـ- أمراض الدم مثل: الانيميا، وانخفاض عدد كرات

ج- الدم البيضاء والصفائح الدموية.

ز- الحساسية تجاه الميزوتر كسيبت.

د- قرحة المعدة وأمراض الرئة.

٣. المريضة التي لا تلتزم المعايير المدرجة للمعالجة

الطبية وهذه المعايير هي:

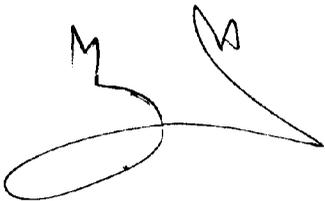
أ. حالة المريضة ثابتة .

ب. التأكد من عدم وجود حمل داخل الرحم.

ج. قياس الحمل خارج الرحم بقياس β سم او اقل فهي

قطره الاعظم.

د. ليس هناك دليل على انفجار الحمل.



المواد و الطرق

- تضم الدراسة 10 مريضة يحمل سليم خارج الرحم واللاتى سوف يتم علاجهن بجرعة واحدة من الميزوتركسيت.
- سوف تخضع المريضة للفحص الشامل , موجات صوتية, تحليل كمي لهرمون الحمل .
- أستثنى من هذه الدراسة الحالات الاتية:
 1. الأمراض التى تؤدى إلى ارتفاع (CA-125) بالدم.

أ- الالتصاق الحاد و المزمن للحوض.

ب- التندد الرحمى .

ت- الأكتياس الحميدة للمبيض.

ث- الأورام الليفية.

ج- أمراض الكلى .

ح- المدخات.

