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Original Article

Obstetrics and Gynaecology Section

Human Chorionic Gonadotropine in Cul-de-sac Fluid in Tubal Ectopic Pregnacy; A New Diagnostic Approach

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ABSTRACT

Introduction: Although new diagnostic abilities are being utilised increasingly yet early detection of tubal pregnancy remains a challenge. The use of highly sensitive hCG kits has facilitated the early diagnosis of a pregnancy. But it takes time to determine the localisation of the pregnancy. Early diagnosis of ectopic pregnancy may reduce the morbidity of ectopic pregnancy.

Aim: This study was conducted to analyse the cul-de-sac and serum βhCG ratio in tubal ectopic pregnancy cases which may be a new diagnostic approach for ectopic pregnancy.

Materials and Methods: Between January 2004 and July 2011, 263 patients with ectopic pregnancy were included in the study. Risk factors of patients and treatment modalities were evaluated. hCG was measured in peripheral serum and peritoneal fluid, obtained by puncture of Douglas pouch in 52 patients with tubal ectopic pregnancy.

hCG level was determined in the cul-de-sac fluid and in the maternal serum for comparison.

Results: Tubectomy (5.3%), history of abortion (9.5%), history of previous surgery (14.8%), previous cesarean section (8%) and pelvic infamatorry disease (15.9 %) were the important risk factors for ectopic pregnancy in our cases. In 51 of 52 patients with tubal pregnancy, the cul-de-sac hCG vaule and the serum hCG value ratio was >1.

Conclusion: It is concluded that the ratio of hCG in cul-de –sac and serum can be used for the verification of tubal ectopic pregnancy in addition to other diagnostic methods. This may help rapid confirmation of the diagnosis of ectopic pregnancy.

Keywords: Douglas hCG, Diagnostic, Puncture

INTRODUCTION

Ectopic pregnancy occurs in 1-2% of pregnant women and may threaten the women's health seriously [1]. Tubal ectopic pregnancy accounts for 95-99% of ectopic pregnancies [2]. Ovarian, abdominal, cornual ectopic pregnancies are rarely seen [3].

History and physical examination alone, does not reliably diagnose or exclude ectopic pregnancy. Quantitave human Chorionic Gonadotropin (hCG) measurement and transvaginal ultrasound are the mainstays for the diagnosis. To make the diagnosis with hCG measurement, ıt is usually necessary to make at least two measurements with a minimum time interval [4,5]. In some cases, endometrial curettage may be necessary for the diagnosis of ectopic pregnancy. Despite all these diagnostic models, the diagnosis of ectopic pregnancy in the early phase still have some difficulties. It has been reported that the cul-de-sac and serum βhCG ratio is greater than unity in ectopic pregnancies and less than unity in intrauterine pregnancies [6]. In our study we have evaluted the cul-de-sac and serum ratio of human chorionic gonodotropin in proven tubal ectopic cases. Simultaneous single measurement of hCG levels in the serum and the cul-de-sac fluid can be a new diagnostic approach for tubal pregnancy in selected cases.

MATERIALS AND METHODS

A total of 263 patients with ectopic pregnancy were treated between January 2004 and July 2011, at the Department of Obstetrics and Gynecology, Süleymaniye Education and Research Hospital. The patients who needs surgical therapy were included in the study. Medical therapy was an exclusion criteria. The study is a cohort study comparing cul-de sac hCG and serum hCG in tubal ectopic pregnancies. Quantitative serum hCG and periteonal fluid hCG were measured simultaneously before the surgery. After the pathologic investigation, the patiens with histologically proven tubal ectopic pregnancy were included in the study.

Peritoneal fluid was obtained by blind puncture of the Douglas pouch. Ethical approval was undertaken and all patients gave written consent prior to puncture. General or local anesthesia was not required in any of the cases. Serum and peritoneal hCG levels were analysed in the patients with tubal ectopic pregnancy.

STATISTICAL ANALYSIS

Statistical analysis was undertaken using NCSS version 2007. Differences were considered significant at the $p< 0.05$ level.

RESULTS

The peak age of incidence was 29.2 years (16-47). Identifiable risk factors were observed in 66.9% of the patients. Tubectomy (5.3%), history of abortion (9.5%), history of previous surgery (14.8%), previous cesarean section (8%) and pelvic inflammatory disease (15.9%) were the important risk factors [Table/Fig-1]. A 183 patients

Tubectomy	15 (5.3%)
Previous cesarean section	21 (8%)
Pelvic infection	42 (15.9%)
Previous abdominal surgery	39 (14.8%)
D&C- R&C- F&C	25 (9.5%)

[Table/Fig-1]: Previous risk factors.

Observation	36 (13.7%)
Observation+ Medical Therapy	17 (6.53%)
Observation+ Surgery	12 (4.61%)
Observation+Medical Therapy+ Surgery	1 (0.38%)
Medical Therapy	22(8.4%)
Medical Therapy + Surgery	10 (3.84%)
Surgery	183 (69.5%)

[Table/Fig-2]: Treatment modalities.

	N	Minimum	Maximum	SS	Z	p-value
Venous BhCG mU/ml	52	106	16400	2093,94	3346,25	<0.00001
Cul-de-sac BhCG mU/ ml	52	1220	76899	11663,58	13741,61	

[Table/Fig-3]: Serum and cul-de-sac hCG levels.

(69.58%) were treated surgically. Totally, 128 salgingectomy and 41 salpingostomy were performed [Table/Fig-2]. A 95% (n:174) of the surgically treated patients were tubal ectopic pregnancy. 88 of surgically treated patients were admitted with severe abdominal pain. Because of the pain, diagnostic puncture of the Douglas pouch was not able to be performed prior to surgery in these patients. Therefore these patients were excluded from the study. Furthermore, the amount of cul-de-sac fluid were not sufficent in 34 (19.6%) patients, so the remaining 52 patients were included.

The results of 52 cul-de-sac punctures of histopathologically proven tubal pregnancy cases were analysed. The hCG values in the serum and cul-de-sac fluid are given in [Table/Fig-3]. The cul-de-sac hCG value was significantly higher than venous blood hcG value in tubal ectopic pregnancy cases.

In 51 of 52 patients , the cul-de-sac hCG value and the serum hCG value ratio was >1. The case with an hCG ratio of <1 was together with ovarian cyst rupture and the low ratio could be attributed to haemodilution.

DISCUSSION

Pregnancy begins with a fertilized egg. Normally, the fertilized egg attaches ıtself to the lining of the uterus. In the case of ectopic pregnancy, the fertilized egg implants somewhere else. If it is undiagnosed, it may lead to high mortality and morbidity rates. If the ectopic pregnancy is detected early, an injection of Methotrexate may be used to stop cell growth and dissolve existing cells successfully [7].

Despite the progress in our diagnostic abilities, the early detection of tubal pregnancy is still controversial. The use of highly sensitive hCG kits has facilitated the early diagnosis of a pregnancy, leaving the problem of the location.

Therefore, it is desirable to make the correct diagnosis as early as possible with a highly accurate simple test. Different testing models has been studied for this purpose [8-10]

The simultaneous determination of hCG concentration in the serum and the cul-de-sac fluid appears to fulfil the prerequisites for such a test [11,12]. In the present study, measurements of cul-de-sac and serum hCG levels were made in histopathologically proven tubal pregnancy cases to prove the accuracy of this ratio. 51(98%) of 52 patients had a ratio of >1. The diffussion of hCG from the fallopian tube into its surrounding tissue was responsible for the elevated hCG levels in the cul-de-sac in patiens with tubal ectopic pregnancy.

But there is still some debate about the cul-de-sac and serum hCG ratio. In 85 cases reported by Hinney and collegues 82 patients had an hCG ratio of >1. In this study, the diagnostic sensitivity of the test was 95.4% and the specificity was 95.2%. The positive predictive value 97.6% and the negative predictive value 91.3% [6]. Conversely, in the study reported by Thorneycroft and colleagues, in the 3 (12%) of 25 cases had an hCG ratio <1. The authors drew the conclusion from this observation that, only in cases of ectopic pregnancy with a serum hCG level lower than 5000mU/ml could show significiant alterations in the hCG ratio than expected [8]. But Hinney et al., reported that, three patients with a ratio of <1 were associated with serum levels between 100 and 1000 mU/ml [6]. Our study do not confirm this assumption too. In our sample 51 of 52 cases had a ratio greater than unity. Only one case with a tubal pregnancy had a ratio of <1. Concominant ovarian cyst rupture may lead to this result by haemodilution. The serum hCG level was lower than 1000m/U/ ml in that case. The sensivity of the test was 98% for tubal ectopic pregnancy. The specifity, positive predictive value, negative predictive value of the test could not be calculated because we have performed this test only in tubal pregnancy cases. Douglas hCG values of intrauterine pregnacy cases are needed as a control group to find the detailed accuracy of this test. This is the limitation of our study. Further studies with control groups are needed to calculate these ratios. These tudies can be conducted with large sample size to determine efficacy and cut off values of this test.

There are however other basic limitations to the procedure. In our study the cul-de-dac fuid was obtained blindly and in 19.6% of the patients the amount of the fluid were not sufficient. Advanced technical properties, puncture systems and simultaneously transvaginal ultrasound usage may solve this problem.

The procedure described in this study may facilitate the correct diagnosis of tubal pregnancy. There is no doubt that the first methods of choice to diagnose a tubal pregnancy are non invasive procedures like transvaginal sonography. If after this, the diagnosis still remains unclear, before the treatment, the determination of hCG ratio could be an alternative approach for the diagnosis. It is an invasive procedure but more invasive procedures as uterine currettage may be necessary in some cases for the diagnosis. It has been reported that uterine currettage is a very sensitive diagnostic method for ectopic pregnancy [13].

CONCLUSION

In our cases with tubal ectopic pregnancy, the cul-de-sac hCG value was significiantly higher than venous blood hCG value. The cul-de-sac examples were taken by easy and simple douglas puncture technique. It is concluded that the ratio of hCG in cul-de –sac and serum can be used for the verification of tubal ectopic pregnancy in addition to other diagnostic methods. But further studies are needed to standardize the test for diagnostic algoritm of ectopic pregnancy.

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