

ECTOPIC PREGNANCY MANAGEMENT

BY A NON INVASIVE PROTOCOL

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Summary: The hemodynamic stable patient suspected of extrauterine pregnancy may be a diagnostic challenge. Dilatations and curettage, Douglas puncture and laparoscopy are significant diagnostic aid in the investigation of the suspected ectopic pregnancy patient; but they are among the invasive methods.

The introduction of non invasive methods such as serum beta subunit hCG and sophisticated ultrasound techniques seems to institute a more conservative approach to the "stable patient" prior to exposing her to anaesthetic and operative risks.

A prospective study on "stable patients" suspected of "subacute" extrauterine pregnancy was undertaken in order to assess the diagnostic usefulness of a suggested non invasive protocol to determine whether its use has an advantage over the traditional invasive methods.

108 patients were evaluated in this study. 31 women were managed according to the non invasive protocol; patients presenting positive sonography signs underwent immediate operative procedure, patients in whom sonography revealed suggestive signs of E.U.P., expectant management was undertaken till serum beta subunit hCG confirmed or excluded the diagnosis.

77 patients were managed according to the invasive method protocol.

Results indicate that the non invasive protocol has high diagnostic accuracy. Among the 31 patients no unnecessary intervention was performed. On the other hand, among the 77 patients, 43 laparoscopies were unnecessary.

INTRODUCTION

Ectopic pregnancy is still a major factor in maternal mortality, with an estimated mortality rate of 2-4/1000⁽¹⁾.

The incidence of the disease varies from 0.2% to 1.0% of live births⁽²⁾ and it is apparently increasing. In the United States between 1965-1977 the number of ectopic pregnancies increased from 15000 to 41000 per year⁽³⁾. This increase may be due to the use of intra-uterine contraception, venereal disease, pelvic inflammatory disease, tubal surgery for infertility, sterilization, post conservative surgery for ectopic pregnancy and the recent legalization of artificial abortions^(4, 5, 6). It is uncertain how much is due to the increased incidence of the disease per se, or the rapid change in diagnostic methods that occurred over the last few years⁽⁷⁾.

Diagnostic laparoscopy, rapid assays of beta subunit hCG and ultrasound equip-

ment have all been popular and significant diagnostic aids in the investigation of the stable subacute ectopic pregnancy.

In stable patients presented with irregular bleeding, abdominal pain or tenderness and amenorrhea, a positive diagnosis using anamnesis and clinical examination was established in only about 33%⁽⁸⁾.

Therefore, the use of the above refined mentioned diagnostic techniques has resulted in improved early diagnosis of the unruptured ectopic pregnancy which cut down the mortality rate⁽¹⁾ and improved prognosis for future fertility by development of new surgical approaches^(9, 10).

Among the new diagnostic tools available for the diagnosis of subacute ectopic pregnancy, culdocentesis and laparoscopy are invasive methods that allow a more aggressive approach⁽¹¹⁾.

The use of laparoscopy in these cases confirmed diagnosis in 92%⁽¹²⁾; therefore it is highly recommended⁽¹³⁾. But in the

same series, laparoscopy revealed no intra-abdominal pathologic condition in 40%. Accordingly, the liberal use of laparoscopy exposed the patient to severe complications^(14, 15) from the procedure itself, while it is done only to exclude the disease.

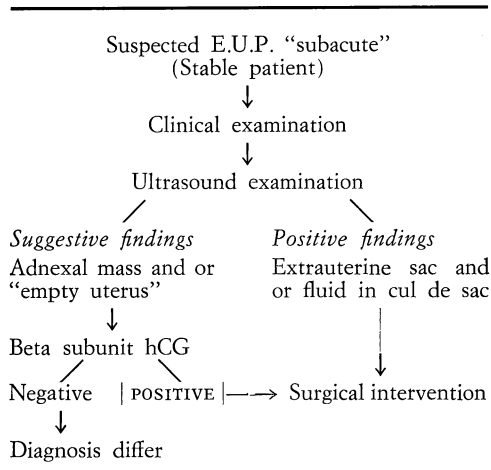
The introduction of the noninvasive methods such as serum beta subunit hCG and sophisticated ultrasound seems to institute a more conservative approach prior to exposing the suspected patient to anaesthetic and operating risks⁽¹⁶⁾.

Based on this premise a clinical follow-up protocol was designed and used over a one year period for the investigation of the stable patient suspected of ectopic pregnancy.

The suggested protocol was introduced as a routine procedure in order to assess its diagnostic accuracy in the evolution of the suspected ectopic pregnancy in stable patient as a prospective study.

This protocol was composed of detailed ultrasound scan coupled with serum beta subunit hCG (scheme 1):

Scheme 1. — *Follow-up protocol in the evaluation of a stable patient suspected of ectopic pregnancy*



The intention of the study was:

a) to examine the diagnostic usefulness of the suggested protocol;

b) to determine whether the use of a noninvasive protocol will reduce the number of unnecessary laparoscopic procedures.

MATERIAL AND METHODS

During the period between 1.6.1982-31.8.1983, the Department of Obstetrics and Gynecology at the Edith Wolfson Hospital, Holon, admitted 108 patients with the presumptive diagnosis of ectopic pregnancy and they were included in this study.

Patients were divided into two groups:

Group A: 31 women suspected ectopic pregnancy stable (subacute) patients; the symptomatology consisted of intermittent mild to moderate abdominal pain and irregular vaginal bleeding, clinically they were stable patients.

Group B: 77 suspected ectopic pregnancy patients who were not evaluated according to the protocol and were examined in the same time period by other staff members.

In the prospective study group, ultrasound scans were performed on admission. The presence of extrauterine sac or fluid in cul de sac were defined as positive evidence of ectopic pregnancy – and therefore immediate surgical procedure was carried out as by scheme 1.

The presence of an empty uterus or adnexal mass were defined as suggestive evidence of ectopic pregnancy – therefore serum beta subunit hCG was tested for excluding or confirming as soon as possible the presence of an extrauterine pregnancy. A positive result of beta subunit hCG coupled with patient's condition was an indication for laparoscopic diagnostic procedure.

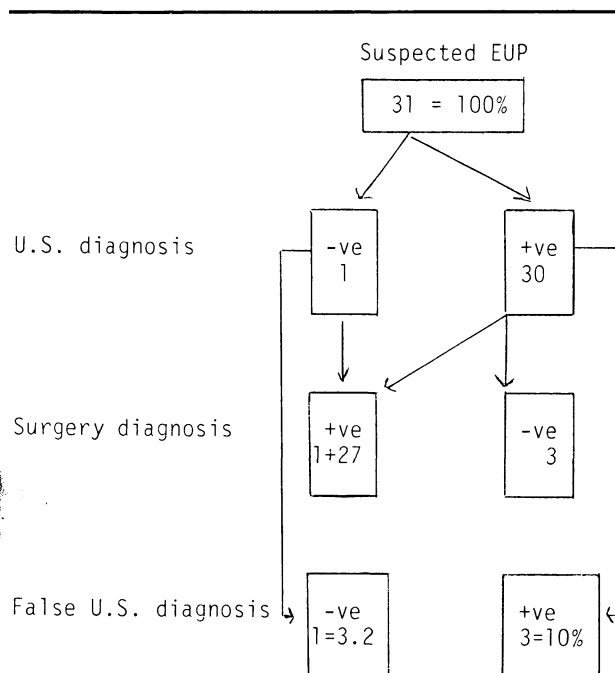
In cases of negative beta subunit hCG the diagnosis was deferred. Serum beta subunit hCG was detected by quantitative radioimmunoassay system. A result was reported negative if the serum beta subunit hCG level was less than 10 mIU/ml and positive if more.

All patients were examined by the same physicians who performed the sonography using a Picker Echoview 80-c grey scale.

Acute ectopic pregnancy was related to patients presented with acute symptoms and signs suggesting intraabdominal hemorrhage. These patients as well as patients running a temperature of 38 °C or more were excluded from the prospective study.

Comparison was made between patients of Group A and patients of Group B in order to

Table 1.



True positive U.S. diagnosis $27/31 = 87.1\%$ of all the group
 $27/28 = 96\%$ of the E.U.P.

evaluate the influence of the above mentioned protocol in the incidence of unnecessary laparoscopic procedure.

RESULTS

Group A

Among 31 women who were referred with the presumptive diagnosis of ectopic pregnancy – the diagnosis of ectopic pregnancy was confirmed by surgery in 28 women (table 1). Ultrasound as a sole diagnostic method confirmed the diagnosis in 27 patients out of 28 (96%). A false negative diagnosis of extrauterine pregnancy was made in one case (3.2%), in which a pseudogestational sac of ectopic pregnancy was erroneously interpreted as an intrauterine sac. Of the 31 women, included in the prospective study, a false

positive diagnosis was made in three cases (10%). Analysis of these cases revealed two cases of pelvic inflammatory disease that were diagnosed as ectopic pregnancy. The third one had a central sonolucent area within the uterus which mimicked a pseudogestational sac of an extrauterine pregnancy. This central lucency lacks the dense halo of echoes which is expected in a normal intrauterine gestational sac and therefore the erroneous diagnosis of pseudogestational sac was made. A negative serum beta subunit hCG in this case proved that these intrauterine echoes were probably due to hyperplastic endometrium and blood within the endometrial cavity.

Ultrasonic identification of fluid in cul de sac was presented in seven patients (25%) and a definite extrauterine gesta-

Table 2. — *Laparoscopic diagnosis in non E.U.P. patients.*

Diagnosis	No.	%
Pelvic Inflammatory Disease	12	27.9
No abdominal pathology found	10	23.3
Intrauterine missed abortion	8	18.6
Ovarian cyst	7	16.3
Early intrauterine pregnancy	4	9.3
Necrotizing myoma	1	2.3
Endometriosis	1	2.3
	43	100

tional sac was identified in three patients (10%). According to our definition all those ten cases had a positive evidence of extrauterine pregnancy and therefore immediate surgical procedure such as culdocentesis and/or laparoscopy was performed; all cases proved to have extrauterine pregnancy.

Adnexal mass was found by ultrasound in four patients; two of them had a positive beta subunit hCG resulting in 50% of diagnostic accuracy of this criteria.

Absence of intrauterine sac ("Empty Uterus") was found in 17 patients; 16 of them had a positive serum beta subunit hCG (250 ImU/ml or more); 8 were found to have extrauterine pregnancy on surgery.

Based on ultrasound as the sole diagnostic tool the suggestive signs of E.U.P. have a false positive rate of 14% (3/21). When the serum beta subunit hCG is coupled with these signs the accuracy of diagnosis is 100%. It is remarkable that no unnecessary laparoscopy was performed in this study group.

Group B

Among 77 patients that were evaluated in the above mentioned protocol, 34 patients (44%) were found to have ectopic pregnancy and 43 (56%) patients underwent unnecessary diagnostic laparoscopy. The

various diagnoses made on laparoscopy in non ectopic patients are listed in table 2.

DISCUSSION

A non invasive approach to the diagnosis of extrauterine pregnancy is appropriate for the hemodynamically stable patient who has mild symptoms attributable to "subacute ectopic pregnancy".

In such patients the value of the commonly used diagnostic methods is limited (¹⁷). Therefore, immediate surgical intervention is established and laparoscopy is highly reliable one but carries some risks (^{14, 15}), especially to those patients in which laparoscopy revealed no pathological condition indicating laparotomy.

According to Samuelson (¹³) 43% of his large series underwent unnecessary laparoscopic procedure while evaluating suspected ectopic pregnancy.

Recent advantages in gynecologic armamentarium are the non invasive methods such as serum beta subunit hCG and pelvic ultrasonography. These methods have a pivotal contribution in the evaluation of the stable patient suspected of ectopic pregnancy.

The ultrasound criteria (table 3) coupled with a positive pregnancy test pro-

Table 3. — *Criteria for Ultrasonic diagnosis of Ectopic Pregnancy.*

Intrauterine signs

1. Abnormal intrauterine echo pattern
2. Uterine enlargement
3. Displacement of uterus
4. Absence of intrauterine pregnancy
"Empty Uterus"

Extrauterine signs

1. Adnexal mass
Complex
Cyst
Solid
2. Fluid in cul-de-sac
3. Extrauterine gestational sac

vides the basis for the most reliable interpretation of the ultrasonogram precluding further studies and unnecessary exploratory surgery.

Considering the ultrasound scan, two problems have been encountered in applying these criteria for the diagnosis of extrauterine pregnancy. The first one is that an intrauterine sac excludes the diagnosis of ectopic pregnancy, but in some cases this intrauterine sac is indistinguishable from the pseudogestational sac that may be found in ectopic pregnancy⁽¹⁸⁾. The echogenic wall of a pseudo sac presumably represents the decidual or the sloughed endometrium cast. Similarly the echogenic free center of the sac is probably due to the free blood or secretions trapped by the cast⁽¹⁹⁾. By careful scanning, the pseudogestational sac can be differentiated from the true sac; the ring of echoes is usually incomplete or irregular and has less density than the true sac; the most important feature is the absence of fetal echoes.

Pseudogenital sac was reported in association with ovarian cysts and dysfunctional bleeding and is not pathognomonic of ectopic pregnancy⁽¹⁹⁾.

The second problem is the ability of serum radioimmunoassay for beta subunit hCG to detect intrauterine pregnancy up to two weeks earlier than ultrasonographic scan⁽²⁰⁾. Therefore, patients between 4 and 5 weeks of gestation when the beta subunit hCG is already positive and the ultrasound scan failed to show the intrauterine pregnancy, the clinician must rely on the patient history and the clinical findings. The decision either to proceed with an invasive diagnostic procedure or to wait for an extra few days can be based on repeated ultrasound examinations coupled with the trend of quantitative beta subunit hCG tests⁽²¹⁾.

In the present study an attempt was made to evaluate the diagnostic accuracy of the single ultrasonographic criteria. The study proposed that the positive signs

of E.U.P. (fluid in cul de sac and/or the appearance of an extrauterine sac) do not need to be confirmed by additional non-invasive test as serum beta subunit hCG.

On the contrary, while suggestive signs of ultrasound has a diagnostic accuracy of only 86% and therefore to avoid unnecessary surgical intervention there is a strong need for beta subunit hCG.

This study indicates also, that combination of ultrasound with serum beta subunit hCG has a 100% diagnostic accuracy. Furthermore, this protocol is very useful in avoiding the unnecessary pelviscopic procedure.

It was found that among the 31 patients of Group A included in the protocol's study, no unnecessary pelviscopy was recorded. In contrast to Group B, among 77 patients, 43 unnecessary pelviscopies were performed on patients.

Bryson⁽¹⁶⁾ suggests that the initial step in the evolution of the stable suspected ectopic pregnancy patient should be beta subunit hCG. After beta-hCG screen results are obtained, patients can then be divided into two groups, those who were pregnant and those who were not. This allowed a tailoring of further investigations and subsequently more appropriate treatment.

From the practical point of view, in our center as in many others beta subunit hCG is not available 24 hours around the clock. On the other hand, ultrasound diagnostic equipment, particularly real time, is available in every gynecologic and obstetrics department.

Therefore, it seems that pelvic sonography is an essential diagnostic tool incorporated to the clinical examination. It is recommended that the scan should be performed by the clinician himself, or if not possible, then a close communication between the clinician and ultrasonographer should be established to avoid misinterpretation of the results.

In conclusion the advantages of the proposed protocol are: a) in patients pre-

senting positive signs – an unnecessary delay in treatment is avoided and in a large percentage of patients the salpinx will be conserved; b) in those patients presentin suggestive signs a delay of twenty-four hours till beta subunit hCG confirms the diagnosis will avoid unnecessary surgical intervention in patients not requiring it.

BIBLIOGRAPHY

- 1) Schneider J., Berger C. H., Cattell C.: *Obst. Gyn.*, 49, 557, 1977.
- 2) Breen J. L.: *Am. J. Obst. Gyn.*, 106, 1004, 1970.
- 3) Sivin I.: *Contraception*, 19, 151, 1979.
- 4) Landesman R., Coutinho L. M., Saxena B. B.: *Fertil Steril.*, 27, 1062, 1976.
- 5) Boyd I. E., Holt E. M.: *J. Obst. Gyn. Br. Commonw.*, 80, 142, 1973.
- 6) Chakravarti S., Sharclow J.: *Br. J. Obst. Gyn.*, 82, 58, 1975.
- 7) Barnes A. B., Wennberg C. N., Barnes B. A.: *Obst. Gyn. Survey*, 38, 345, 1983.
- 8) Sanders E. P.: *NZ Med. J.*, 87, 41, 1978.
- 9) DeCherney A. H., Kase N.: *Obst. Gyn.*, 54, 451, 1979.
- 10) Sherman D., Langer R., Sadoski *et al.*: *Fertil. Steril.*, 37, 497, 1982.
- 11) Esposito J. M.: *J. Reprod. Med.*, 25, 17, 1980.
- 12) Portuondo J. A., Remacha M. J., Llaguno M. R.: *Int. J. Gyn. Obst.*, 20, 371, 1982.
- 13) Samuelson S., Sjovala: *Acta Obst. Gyn. Scand.*, 51, 31, 1972.
- 14) Homburg R., Segal T.: *Am. J. Obst. Gyn.*, 130, 597, 1978.
- 15) Paulson G. W., DeVoe K.: *Am. J. Obst. Gyn.*, 140, 468, 1981.
- 16) Bryson P. S. C.: *Am. J. Obst. Gyn.*, 146, 163, 1983.
- 17) Hall R. E., Todd W. D.: *Am. J. Obst. Gyn.*, 37, 86, 1958.
- 18) Marks W. M., Filly R. A., Callen P. W., Laing F.: *Radiology*, 133, 451, 1979.
- 19) Mueller C. E.: *J. Clin. Ultrasound*, 7, 133, 1979.
- 20) Ghorasih B., Gottesfeld A. R.: *J. Clin. Ultrasound*, 5, 195, 1977.
- 21) Kadar N., Devore G., Romero R.: *Obst. Gyn.*, 58, 156, 1983.