Value of serum $\beta$-HCG, P, CA125, and color Doppler ultrasound in early diagnosis of ectopic pregnancy

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ABSTRACT

Objective: To explore the clinical value of serum $\beta$-HCG, P, CA125, and color Doppler ultrasound in the early diagnosis of ectopic pregnancy (EP). Methods: A total of 50 patients with EP who were admitted in our hospital from September, 2014 to September, 2015 were included in the study and served as the observation group, while 50 normal pregnant women were served as the control group. A volume of 5 mL of fasting elbow venous blood the day on admission in the two groups was extracted, and then was centrifuged for serum. The chemiluminescence immunoassay was used to detect the levels of serum $\beta$-HCG, P, and CA125. After 48h, $\beta$-HCG level was detected again. The vaginal color Doppler diasonograph was used to detect the changes of RI and PSV. The blood supply of LH was observed. Results: The levels of serum $\beta$-HCG, P, and CA125 in the observation group were significantly lower than those in the control group ($P<0.05$). When $\beta$-HCG<2000 IU/L, $\beta$-HCG level was doubled in 3 cases (6.0%) in the observation group, while in 49 cases (98.0%) in the control group, and the differences between the two groups were not statistically significant ($P<0.05$). RI in the observation group was significantly higher than that in the control group, while PSV was significantly lower than that in the control group ($P<0.05$). Blood supply in the observation group was in a half ring shape, accounting for 58.0%; in the control group was in a ring shape, accounting for 70.0%, and the difference was statistically significant ($P<0.05$). Conclusions: Determination of the levels of serum $\beta$-HCG, P, and CA125 in the pregnant women, in combined with the vaginal color Doppler ultrasound detection of RI and PSV, can contribute to distinguish the normal intrauterine pregnancy with EP and prevent the misdiagnosis, which can provide an accurate reference value for the early diagnosis and timely treatment of EP, and can be used as an ideal method for the diagnosis of EP.

1. Introduction

Ectopic pregnancy (EP) refers to that the fertilized eggs are implanted outside the uterine cavity, including the salpingocyesis, ovarian pregnancy, and abdominal pregnancy, among which salpingocyesis is the most common, accounting for 95% of EP, and is one of the most common acute abdomens in women of reproductive age[1,2]. Rupture of EP is characterized by acute onset and severe condition, and will result in massive hemorrhage, and other severe complications, and even endanger the patients’ lives with no timely treatment, with death rate accounting for 9% of pregnant women in the early pregnancy; therefore, the early diagnosis and proper treatment of EP is of great significance in reducing the mortality rate of pregnant women[3,4]. The study is aimed to explore the clinical value of serum $\beta$-HCG, P, CA125, and color Doppler ultrasound in the early diagnosis of EP in order to provide a more reliable diagnostic evidence for the early diagnosis of EP.
2. Materials and methods

2.1. General materials

A total of 50 patients with EP who were admitted in our hospital from September, 2014 to September, 2015 were included in the study and served as the observation group, aged from 22 to 45 years old, with an average age of (28.7±10.2) years old; cessation of menstruation from 35 to 50 d, with an average of (41.8±2.5) d; weight from 47.5 to 61.7 kg, with an average weight of (47.5±11.7) kg; gravidity from 1 to 3 times, with an average of (2.1±0.9) times. Moreover, a total of 50 normal pregnant women were served as the control group, aged from 22 to 44 years old, with an average age of (27.8±11.3) years old; cessation of menstruation from 35 to 51 d, with an average of (41.5±2.6) d; weight from 46.5 to 61.3 kg, with an average weight of (46.8±10.9) kg; gravidity from 1 to 3 times, with an average of (2.2±0.9) times. The comparison of the above materials between the two groups was not statistically significant (P>0.05).

2.2. Inclusion and exclusion criteria

Inclusion criteria: (1) those who had no history of habitual abortion; (2) those who had no family history of hereditary abortion; (3) those who had no exposure to chemical substances and X-rays; (4) those who had signed the informed consent were included in the study. Exclusion criteria: (1) those who had severe heart, liver, and kidney diseases; (2) those who were merged with cervical incompetence and ovarian tumor; (3) those who had multiple pregnancies were excluded from the study.

2.3. Methods

A volume of 5 mL of fasting elbow venous blood the day on admission in the two groups was extracted, and then was centrifuged for serum. The chemiluminescence immunoassay was used to detect the levels of serum β-HCG, P, and CA125. After 48 h, β -HCG level was detected again. The vaginal color Doppler diasonograph with a transducer frequency of 5-9MHz was used to detect the changes of RI and PSV. The blood supply of LH was observed.

2.4. Statistical analysis

SPSS 18.0 software was used for the statistical analysis. The measurement data were expressed as mean±SD, and t test was used. Chi-square test was used for the enumeration data. P<0.05 was regarded as statistically significant difference.

3. Results

3.1. Levels of serum β-HCG, P, and CA125

The levels of serum β-HCG, P, and CA125 in the observation group were significantly lower than those in the control group (P<0.05) (Table 1).

Table 1

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>β-HCG</th>
<th>P</th>
<th>CA125</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>50</td>
<td>3175.68±985.45</td>
<td>19.85±3.17</td>
<td>48.65±6.85</td>
</tr>
<tr>
<td>Control group</td>
<td>50</td>
<td>10175.23±2133.51</td>
<td>38.67±6.47</td>
<td>121.65±28.47</td>
</tr>
</tbody>
</table>

P<0.05, when compared with the control group.

3.2. β-HCG multiplication after 48 h

When β-HCG<2000 IU/L, after 48 h, β-HCG level was doubled in 3 cases (6.0%) in the observation group, while in 49 cases (98.0%) in the control group, and the difference between the two groups was not statistically significant (P<0.05).

3.3. Comparison of the hemodynamics of ovarian corpus luteum between the two groups

RI in the observation group was significantly higher than that in the control group, while PSV was significantly lower than that in the control group (P<0.05) (Table 2).

Table 2

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>RI (cm/s)</th>
<th>PSV (cm/s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>50</td>
<td>0.52±0.03</td>
<td>14.22±6.5</td>
</tr>
<tr>
<td>Control group</td>
<td>50</td>
<td>0.43±0.04</td>
<td>19.31±7.55</td>
</tr>
</tbody>
</table>

P<0.05, when compared with the control group.

3.4. Blood supply distribution of corpus luteum

Blood supply in the observation group was in a half ring shape, accounting for 58.0%; in the control group was in a ring shape, accounting for 70.0%, and the difference was statistically significant (P<0.05) (Table 3).

Table 3

<table>
<thead>
<tr>
<th>Groups</th>
<th>n</th>
<th>Soft-like</th>
<th>Stripe-like</th>
<th>Ring-like</th>
<th>Half-ring like</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation group</td>
<td>50</td>
<td>2 (4.0)</td>
<td>7 (14.0)</td>
<td>12 (24.0)</td>
<td>*</td>
</tr>
<tr>
<td>Control group</td>
<td>50</td>
<td>1 (2.0)</td>
<td>6 (12.0)</td>
<td>35 (70.0)</td>
<td>8 (16.0)</td>
</tr>
</tbody>
</table>

*P<0.05, when compared with the control group.
4. Discussion

EP is an acute abdomen in the obstetrics and gynecology, with a probability of massive hemorrhage due to salpingorhexis, whose etiology is associated with intrauterine device, microbial infection, and sexual transmitted diseases. In recent years, the morbidity is gradually increasing, and more and more young women are involved[5]. The main manifestations in EP include vaginal bleeding, abdominal pain, touching the pain in the adnexa, and normal or mildly enlarged uterus. If there is a severe abdominal pain, accompanied by muscular tension and rebound tenderness, the probability of EP rupture should be taken into consideration. A timely diagnosis and emergent treatment should be performed in the clinic in order to reduce the risk[6]. The color Doppler diasonograph is a non-invasive examination method in the diagnosis of pregnancy, can reflect the gestational sac inside and outside the uterus, gestational sac location, embryo bud, and hemodynamics of corpus luteum, and is of great significance in the diagnosis of EP, while the laboratory examination is used to estimate whether there is EP or not according to the levels of biochemical indicators, characterized by simplicity and rapidness, and has been widely applied in the clinic; therefore, determination of the levels of serum \( \beta \)-HCG, P, CA125, in combined with B ultrasound are utilized by many scholars in the diagnosis of EP in that the sensitivity and accuracy are relatively high, and it can provide a forceful evidence for the diagnosis and treatment of EP[7, 8].

\( \beta \)-HCG is a main glycoprotein hormone secreted by the placenta, and is of specificity to the pregnancy. EP, the same with the normal pregnancy, needs syncytiotrophoblasts to produce HCG to maintain the growth of corpus luteum, which can increase the secretion of steroid hormones, soften and enlarge the uterine body, and induce the endometrial decidual reaction[9]. EP refers to that the fertilized eggs are implanted in the fallopian tube which is characterized by luminal stenosis, thin wall, lack of submucosal tissues, less secretion by the syncytiotrophoblasts or partial necrosis; therefore, the serum \( \beta \)-HCG level is too low in patients with EP[10]. In the early stage of normal intrauterine pregnancy, \( \beta \)-HCG level will increase by 53%–66% every 48 h. If the increased \( \beta \)-HCG level is lower than this, the probability of EP should be taken into consideration. If \( \beta \)-HCG level reaches 1 500–2 500 U/L, and no intrauterine gestational sac is detected by the vaginal ultrasound, the probability of EP should also be considered[5, 11]. The results in the study showed that the levels of serum \( \beta \)-HCG, P, and CA125 in the observation group were significantly lower than those in the control group (P<0.05); when \( \beta \)-HCG<2 000 IU/L, after 48 h, \( \beta \)-HCG level was doubled in 3 cases (6.0%) in the observation group, while in 49 cases (98.0%) in the control group, and the comparison between the two groups was not statistically significant (P<0.05), indicating that \( \beta \)-HCG is of great significance in the diagnosis of EP, but there is an intersection between 48 h level increasement and intrauterine early pregnancy, resulting in the difficult diagnosis of EP in this scope; therefore, unique determination of serum \( \beta \)-HCG can not make a confirmed diagnosis of EP.

P is produced by the placenta, ovaries, and adrenal cortex, and is a key hormone for the successful implantation of blastocysts. P is mainly produced by the ovaries within 8-week gestation, and is mainly produced by the placenta after 8-week gestation. When there is an EP, the ovarian trophoblast is poorly developed, the activity of trophoblast cells is acutely reduced, the surrounding blood supply of follicles is not sufficient, and the corpus luteum is badly developed, leading to the serum P level significantly lower than that in the normal pregnancy women[12]. The results in the study showed that the serum P level in the observation group was significantly lower than that in the control group (P<0.05), suggesting that P can preferably distinguish EP with the intrauterine pregnancy. Some researches demonstrate that[13] when the serum P level is greater than 79.5 nmol/L, the probability rate of normal intrauterine pregnancy reaches 98%; but when the serum P level is less than 15.9 nmol/L, the probability rate of normal intrauterine pregnancy will reduce by 0.16%, and the serum P level is between 15.9–79.5 nmol/L in partial EP patients; therefore, there is a controversy over the appropriate critical value in the clinic.

CA125 is mainly originated from the genital tract mucosa and ovarian epithelial cell surface. The high CA125 level can be detected in the serum in pregnant women in the early pregnancy, merged with vaginal bleeding for abortion, and immediately after delivery, suggesting that the trophoblast cells are separated from the decidual cells, and the destroy of decidual cells is a main origin for the maternal serum CA125. It is reported that high CA125 level can be detected in the serum in pregnant women with or without salpingorhexis; therefore, it can be speculated that CA125 enters the blood circulation through the tubal mucosal cells, and CA125 level is associated with the destroyed degree of tubal mucosa. The results in the study showed that CA125 level in the observation group was significantly lower than those in the control group (P<0.05), indicating that CA125 is of higher diagnostic value in the diagnosis of EP.

The pregnant corpus luteum can secrete the estrogen and progestogen to maintain the growth and development of early gestational sac. After the formation of corpus luteum, the surrounding new vessels are increased, the blood perfusion is strengthened, and the vascular resistance is reduced[14, 15]. In the intrauterine pregnancy, the embryo implantation is normal, the villous tissues are favorably developed, P secretion is increased, the blood supply increasement of corpus luteum is well developed, and the corpus luteum is in a full shape; therefore, the color Doppler ultrasound shows that the blood flow is increased with a low resistance. In EP, the fertilized

\[ P \text{-HCG} \]
eggs are implanted in the fallopian tube, the villous tissues are badly
developed, the ability of decidual formation is poor, the level of $\beta$-
HCG secreted by the trophoblasts is reduced, leading to the mal-
developed hypofunction of corpus luteum; therefore, the color
Doppler ultrasound shows that the blood flow rate is reduced, and
the blood flow is in a high resistance state. It is reported that $B$
ultrasound shows no gestational sac inside the uterus, heterogenous
masses around the uterus or one-side adnexa, RI<0.4, positive urine
pregnancy, it can be deemed that a nourish blood flow exists and EP
can be confirmed[16,17]. The results in the study showed that RI in the
observation group was significantly higher than that in the control
group, while PSV was significantly lower than that in the control
observation group was significantly higher than that in the control

shape, accounting for 70.0%, and the comparison was statistically
significant ($P<0.05$); blood supply in the observation group was in a half
ring shape, accounting for 58.0%; in the control group was in a ring
shape, accounting for 70.0%, and the comparison was statistically
significant ($P<0.05$), showing that the color Doppler ultrasound can
provide a new evidence for the confirmed diagnosis of EP according
to the trophoblastic blood flow characteristics and shape.

In conclusion, determination of the levels of serum $\beta$-HCG, P,
and CA125 in the pregnant women, in combined with the vaginal
color Doppler ultrasound detection of RI and PSV, can contribute to
distinguish the normal intrauterine pregnancy with EP and prevent
the misdiagnosis, which can provide an accurate reference value for
the early diagnosis and timely treatment of EP, and can be served as
an ideal method for the diagnosis of EP.

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