Research on the Application Value of Combinative Monitoring of Blood B-HCG and Progesterone in Treatment of Ectopic Pregnancy

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Abstract: **Objective** To investigate the value of combined detection of serum HCG and progesterone in the treatment of ectopic pregnancy (EP). **Methods** The initial value and average daily decrease within 7 days of blood β-HCG and progesterone monitored during hospitalization in 47 EP patients were retrospectively analyzed, and the correlation between them and the expectant treatment **Results** was analyzed. Results The success rate of expectant treatment decreased with the increase of initial blood β-HCG and progesterone. The group with initial blood β-HCG ≤ 1000 mIU / ml had the best expectant effect, and the difference was significant (P = 0.001 < 0.05). The group with initial progesterone ≤ 10 ng / ml had the best expectant effect, and the difference was also significant (P = 0.000 < 0.05). After 7 days expectant treatment, the greater the average daily decrease of blood β-HCG and progesterone, the higher the success rate. Among them, the average daily decease of ≥ 10 % had the highest success rate. There was significant difference in the success rate of the three groups (P < 0.05). **Conclusion** The combinative monitoring of blood β-HCG and progesterone can provide reliable data for the effective prediction of the EP expectant treatment outcome, which has a very high clinical diagnostic value.

1. Introduction

Ectopic pregnancy (EP) is one of the leading causes of death among women in early pregnancy, which accounts for 1.3% - 2.0% of all pregnancies, and the increase of induced abortion, drug abortion and corresponding pelvic inflammatory reaction can increase the incidence [1]. With the change of marriage and reproduction concept of young people in China, the EP incidence increased year by year, and the incidence tend to be younger. Combined the continuous improvement of clinical diagnosis technology and diagnostic ability in China, the early clinical diagnosis rate has been significantly improved, and the incidence and diagnosis of EP in China are increasing year by year. However, a lot of clinical data shows that a large number of EP tend to self-heal. Expectant treatment may be an important non-invasive treatment method for these people. How to identify EP with obvious self-healing tendency has become an important issue [2]. Forty-seven EP patients with

expectantly treated were included in this study from January 2018 to April 2021. During the observation procession, the correlation between the changes of serum β-HCG and progesterone and the outcome of EP expectant treatment was explored to provide reference for subsequent treatment.

2. Materials and methods

2.1. Research objects

In this study, 47 EP patients with expectantly treated who were admitted to Shaanxi Provincial People's Hospital from January 2018 to April 2021 were selected as the research objects. The patients were aged 18~35 (25.94±4.270) years old with menopause of 39-62 (49.64±5.131) days, in which 2 cases were first pregnancy (with a history of oral emergency contraceptives), 5 cases were married women who had given birth, 42 patients were with a history of one or more induced abortions, and 3 patients were secondary EP.

2.2. Inclusion criteria

All patients who were clinically diagnosed with EP after detailed medical history, symptoms, β-HCG and progesterone and vaginal ultrasonography were admitted to the inpatient department. Excluded criteria: severe abdominal pain with obvious internal bleeding and considering tubal pregnancy rupture, mass diameter >3cm measured by vaginal ultrasound or rapid enlargement and exceeding 3cm, with gestational sac and fetal heartbeat, unstable vital signs, other high-risk EP (such as abdominal pregnancy, cornual pregnancy and cervical pregnancy), other diseases not suitable for expectant treatment.

2.3. Methods

Blood β-HCG and progesterone were rechecked every 3 days, and vaginal ultrasound was rechecked every 7 days. If the results of blood β-HCG and progesterone were decreased in two consecutive reviews, and the total decrease of blood β-HCG was ≥ 20 %, then blood β-HCG and progesterone were rechecked every seven days until the blood β-HCG decreased to normal. Further, if the reexamination results of blood β-HCG and progesterone in the course of treatment rose to 1.5 times or more of the initial level for two consecutive times, or if the patients met any exclusion criteria, the expectant treatment would stop immediately and a treatment scheme suitable for the current condition would be adopted.

2.4. Reagents and instruments

Human chorionic gonadotropin and β subunit assay kit (Beckman Coulter, USA).
Progesterone assay kit (Beckman Kurt, USA).
Automatic immunoluminescence analyzer DXI800 (Beckman Coulter, USA).

2.5. Criteria for recovery

After the expectant treatment, the condition was stable and β-HCG decreased to the normal range (< 3 mlU/ml).

2.6. Statistical analysis

Statistical analysis was performed with SPSS 25. The measurement data were expressed as mean

± standard deviation ($\overline{x}$ ±s), independent samples t-test was used for the comparison between two groups, and χ2 test was used for the comparison between the initial levels and the daily decline of rechecking results of blood β-HCG and progesterone in the expectant treatment process. P < 0.05 indicated that the difference was statistically significant.

3. Results

The corrplot package of R language was used to analyze the correlation between age, menopause time, initial progesterone, initial HCG, daily decline of progesterone on 4 days, daily decline of HCG on 4 days, daily decline of progesterone on 7 days, daily decline of HCG on 7 days and outcomes. The generated heatmap is shown in Figure 1. It can be seen from Figure 1 that age and menopause time have little correlation with the outcomes, the initial progesterone and initial HCG were negatively correlated with the outcome, meanwhile, HCG and progesterone decline on 4 days and 7 days were positively correlated with the outcome. Further, the daily decline of progesterone and HCG in 7 days was similar to that in 4 days, and the correlation between the outcome and the daily decline of progesterone and HCG in 7 days was significantly higher than that in 4 days. Therefore, the four parameters of initial progesterone, initial HCG, daily decline of progesterone in 7days and daily decline of HCG in 7days were selected as the key risk factors affecting the outcome.

Figure 1: Correlation between the factors and outcome.

3.1. Correlation between initial level of β-HCG and progesterone and outcome

3.1.1. Correlation between initial β-HCG level and outcome

In this study, there were 47 patients in the expectant treatment, including 19 cases (40.43 %) with initial blood β-HCG ≤ 1000 mIU / ml, 19 cases (40.43%) with 1000 mIU / ml < β-HCG < 3000 mIU / ml and 9 cases (19.14 %) with β-HCG ≥ 3000 mIU / ml. The correlation was analyzed by χ2 test. It can be seen from Figure 2 that the success rates of expectant treatment with different initial blood β-HCG levels were different, and the higher the initial blood β-HCG level, the lower the success rate. Among them, the group with blood β-HCG ≤ 1000mIU/ml had the best expected effect, and the difference was significant (P = 0.001 < 0.05), while the success rate with blood β-HCG ≥ 3000 mIU / ml was lowest.
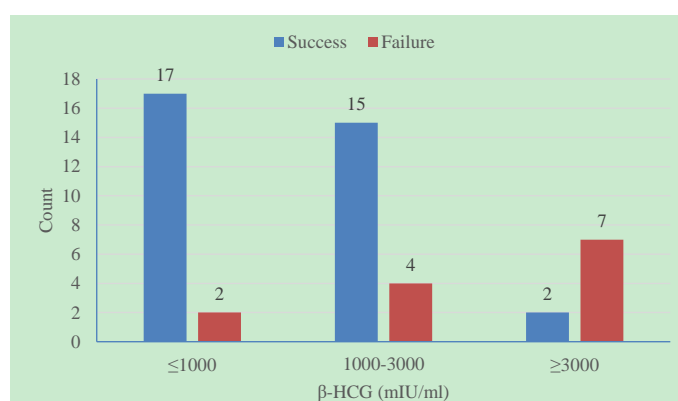
Figure 2: Strip plot of correlation between initial β-HCG level and outcom

3.1.2. Correlation between Initial Progesterone Level and Outcome

Among the 47 patients in the expectant treatment, there were 34 cases (72.34 %) with initial progesterone ≤ 10 ng/ml, 10 cases (21.28%) with initial progesterone between 10 ng/ml and 15ng/ml, and 3 cases (6.4%) with initial progesterone ≥ 15 ng/ml. It can be also seen from Figure 3 that the success rates with different initial progesterone levels were different, and the higher the progesterone level, the lower the success rate. Among them, the highest success rate was in the group with progesterone ≤ 10 ng/ml, and the difference is significant (P = 0.001 < 0.05), while the lowest success rate was in the group with progesterone ≥ 15 ng/ml.
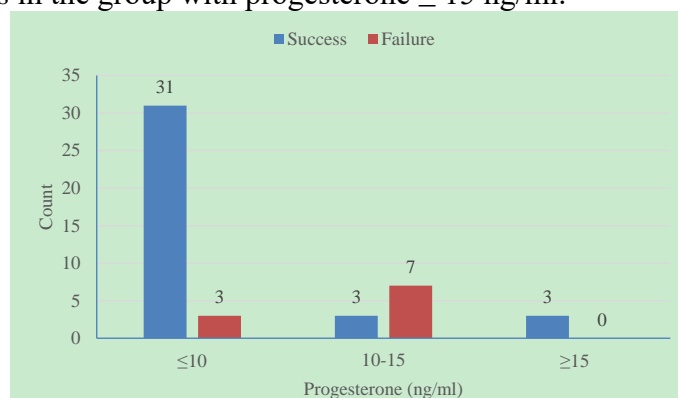

Figure 3: Strip plot of correlation between initial progesterone level and outcome

3.2. Correlation between average daily decrease of blood β-HCG and progesterone within 7 days after treatment and outcome

3.2.1. Correlation between average daily decrease of blood β-HCG within 7 days after treatment and outcome

As shown in Figure4, the patients with less than 5% of the average daily decrease of blood β-HCG within 7 days after treatment was 25 among the 47 expectant treatment cases, and 16 cases were successful. The patients with the average daily decrease between 5% and 10% was 9, and they were all successful. In addition, the women with the average daily decrease of more than 10% were 16, and only one patient was unsuccessful. Chi-square test showed that there was significant difference in the success rate of treatment among the three groups (P = 0.001 < 0.05).
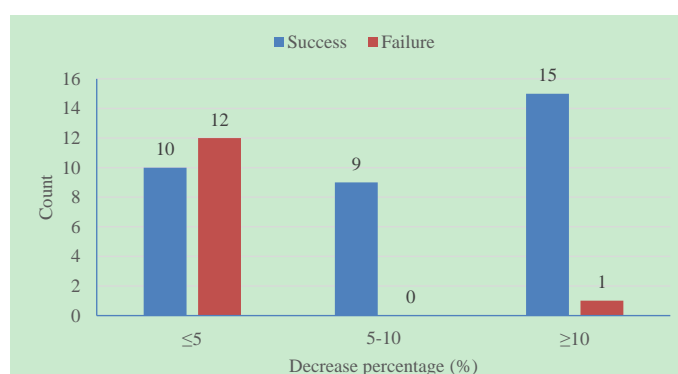
Figure 4: Strip plot of correlation between average daily decrease of blood β-HCG within 7 days and outcome

3.2.2. Correlation between average daily decrease of progesterone within 7 days after treatment and outcome

Among all the expectant treatment cases, 19 cases had an average daily decrease of ≤ 5 % in progesterone after 7 days treatment, among which 10 cases were successful. The patients with the average daily decrease between 5% and 10% was 11, and 9 cases were successful. Further, the patients with the average daily decrease between 5% and 10% was 11, and 9 cases were successful. And those with an average daily decrease of ≥ 10% were 17, among them 15 cases were successful, as shown in Figure 5. Chi-square test showed that the difference in treatment efficiency among the three groups was significant (P= 0.042 < 0.05).
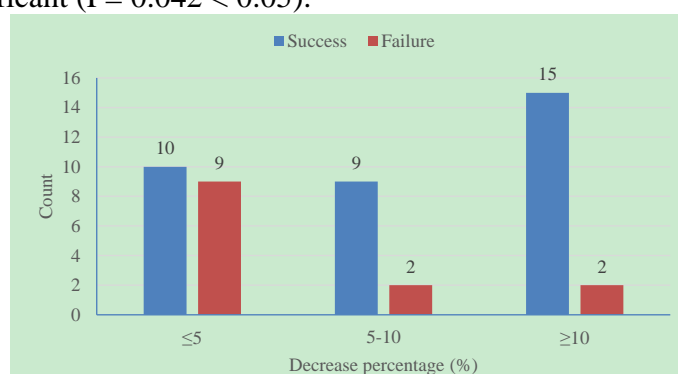

Figure 5: Strip plot of correlation between average daily decrease of progesterone within 7 days and outcome

4. Discussion

EP refers to the implantation of embryos outside the uterine cavity, of which tubal pregnancy is the main type [3] and it is still one of the most common causes of death in women during early pregnancy, and the numbers dying of EP account for 2.7 % of all pregnancy-related deaths [2,4]. Expectant treatment for EP refers to the treatment of giving a period of close observation to the patient of clinically diagnosed EP, and no drug or surgical treatment is given during this period [5], which is one of the treatment methods after early diagnosis of EP. Some studies have confirmed that expectant treatment is suitable for nearly 1/3 of the tubal pregnancy [6]. It has been reported in the literature that expectant treatment for EP is a safe, reliable, simple and non-invasive program, which can not only save social medical resources, but also reduce the economic burden of patients [7,8].

The method of expectant treatment for EP is often ignored in clinical practice, the main reasons include a large population in China, high incidence, difficult follow-up, low patient coordination and so on. However, with the improvement of the education level of Chinese people and the better understanding of basic medical knowledge, the people's awareness and coordination on the dangers of EP have improved significantly. In addition, the application of early diagnostic techniques such as blood human chorionic gonadotropin (hCG) detection and transvaginal ultrasonography has created conditions for the early diagnosis and expectant treatment of EP patients. Since the progesterone level of EP patient is lower than that of normal pregnancy, which is a natural spontaneous abortion condition, and it can provide a basis and create a possibility for expectant treatment of EP [9,10]. Meanwhile, a large number of research data show that the level of blood β-HCG is the decisive factor for the success of EP expectant treatment, and with the increase of blood β-HCG, the success rate of expectant treatment is lower [9,11-14]. Based on this, this paper studies the application value of combinative monitoring of blood β-HCG and progesterone in EP treatment.

This study retrospectively analyzed the blood β-HCG and progesterone data of 47 EP patients during hospitalization. The results showed that the success rate of expectant treatment of EP was not significantly correlated with the age of onset and the time of menopause (P > 0.05), and different initial level of blood β-HCG and progesterone have different success rate of expectant treatment, which was consistent with clinical results and literature reports [15]. The group with initial blood β-HCG ≤ 1000 mIU / ml had the best expectant effect, and the difference was significant (P = 0.001 < 0.05). And the group with initial progesterone ≤ 10 ng / ml had the best expectant effect, the difference was also significant (P = 0.000 < 0.05). The greater the average daily decrease of blood β-HCG and progesterone within 7 days after the expectant treatment, the higher the success rate. The highest success rate was achieved when the average daily decrease was ≥ 10 %. Chi-square test showed that the difference in the success rate among the three groups was significant (P < 0.05). The possible reasons for this result are insufficient blood supply in the implantation sit, low vitality of trophoblast cells and poor villi developmente during ectopic pregnancy, while β-hCG can well reflect the activity of trophoblast cells, and progesterone reflects the function of trophoblast cells. During expectant treatment, regular monitoring of β-HCG and progesterone can be used to estimate the function of trophoblast histiocytes, predict the outcome of expectant treatment of EP and estimate the probability of success [5,16].

In conclusion, in the expectant treatment of EP, the combinative monitoring of blood β-HCG and progesterone levels can well estimate the function of trophoblast cells and predict the success probability of expectant treatment, which has important clinical application value.

Acknowledgement

Competing interests

The authors declare that they have no competing interests.

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