Short Communication

Effect of β- Human Chorionic Gonadotropin and Progesterone Monitoring on the Treatment of Ectopic Pregnancy with Methotrexate and Mifepristone

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A B S T R A C T

The objective of this study was to observe and analyze the clinical value and nursing effect of β- human chorionic gonadotropin and progesterone monitoring on the treatment of ectopic pregnancy with methotrexate combined with mifepristone. One hundred and eighty patients with ectopic pregnancy were included in the study, all of whom were treated with methotrexate combined with mifepristone tablets. According to the treatment results, they were divided into treatment success group and the treatment failure group, each containing with 90 cases. The levels of β- human chorionic gonadotropin and progesterone in the two groups were compared. Of the 180 patients, 168 were cured successfully, 12 were failed, and the success rate and failure rate were 93.33% and 6.67%, respectively. After treatment, serum β- human chorionic gonadotropin and progesterone levels in the successful group decreased more significantly as compared with that before treatment, $p<0.05$. When the levels of β-human chorionic gonadotropin and progesterone were increased, the success rate of methotrexate combined with mifepristone tablets showed a decreasing trend, $p<0.05$. When the maximum diameter value of pelvic effusion was increased, the success rate of conservative treatment with methotrexate combined with mifepristone tablets showed a decreasing trend, $p<0.05$. The risk factors that affect the success rate of methotrexate combined with mifepristone tablets are β-human chorionic gonadotropin level and progesterone level. To conclude β- human chorionic gonadotropin and progesterone monitoring is a key step for treatment of ectopic pregnancy. Combined monitoring is of great significance in predicting the success of conservative treatment of ectopic pregnancy.

Ectopic pregnancy (EP) is one of the common acute abdominal diseases in obstetrics and gynecology. Due to oviduct lumen or surrounding inflammation, lumen patency is not good, which hinders the normal operation of pregnant eggs, makes it stay in the fallopian tube, implantation, development, leading to tubal pregnancy abortion or rupture, eventually leading to ectopic pregnancy. There are often no obvious symptoms before abortion or rupture, and there may also be menopause, abdominal pain, and a small amount of vaginal bleeding (Li *et al.*, 2019; Zhou *et al.*, 2019; Fang *et al.*, 2018). After pregnancy rupture, acute abdominal pain, recurrent attacks, vaginal bleeding, and even shock may ocurr. Examination often shows signs of intraperitoneal bleeding and periuterine mass, which can be confirmed by ultrasound. The treatment of ectopic pregnancy is mainly surgical method.

Laparotomy is performed to remove the affected side fallopian tube. In order to retain the fertility function, oviduct can also be opened to remove pregnant egg.

In clinical practice, some ectopic pregnancies with atypical symptoms are judged by intuitive indicators such as clinical symptoms and signs, showing obvious limitations. Instead, different kinds of auxiliary diagnostic methods should be used to make scientific and reasonable comprehensive judgment. Serum human chorionic gonadotropin (β-HCG) and progesterone are objective indicators for the diagnosis of ectopic pregnancy. In this study, the clinical value and nursing effect of β-HCG and progesterone monitoring in the treatment of ectopic pregnancy with methotrexate combined with mifepristone tablets were observed

Data and method

In this study, 180 patients who had been treated for ectopic pregnancy from January 2015 to May 2019 in our hospital were enrolled as research objects (First Hospotal

of Jilin University). All included patients underwent ultrasonography, serum β-HCG determination, or curettage, with a definite diagnosis of ectopic pregnancy. When entering the hospital, there were stable vital signs and no significant intraperitoneal bleeding. Patients with diseases of the blood system, abnormal liver and kidney functions, and contraindications of drug use were excluded. B-ultrasonography showed no echo of the pregnancy sac in the uterine cavity, the diameter of the tubal pregnancy mass was 4cm or less, and the urine HCG was positive or weakly positive. There was no significant increase or decrease in β-HCG, and the blood level of β-HCG on admission was between 100 and 2000U/L. Patients and their families had the right to know and signed the informed consent. The study was conducted with the approval of the hospital ethics association.

Of the 180 patients, the oldest was 43 years old and the youngest was 18 years old, with an average age of 30.2±1.3 years old. The mean gestational age was 60.2±6.21 days, and the mean time of menopause was 45.32±2.69 days. There were 100 cases of irregular vaginal bleeding and 80 cases of abdominal pain, respectively.

All patients were treated with methotrexate combined with mifepristone with intramuscular injection of methotrexate (Shanxi Pude Pharmaceutical Co., Ltd.) at dose of 0.4 mg/kg, once a day, for consecutive five days. Meanwhile, mifepristone (Beijing Zizhu Pharmaceutical Co., Ltd.) was taken at dose of 25 mg per each time, twice a day, for consecutive three days. On the fifth day of administration, if serum HCG is reduced by less than 15%, a course of methotrexate therapy was added.

For patients with conservative treatment, bed rest was advised to help patients complete daily care and reduce their activity as much as possible. The patient's vital signs and condition changes were monitored in time.

The levels of serum β-HCG and progesterone in the patients were measured by time-resolved fluorescence and chemiluminescence immunoassay, respectively. The criteria for evaluation of recovery include stable vital signs, disappearance of clinical symptoms, reduction of β-HCG to the normal range, and reduction or disappearance of lesions by b-ultrasound. According to the treatment results, the patients were divided into treatment success group and treatment failure group.

Statistical analysis software SPSS21.0 was used to process data. The measurement data were expressed by mean ± average ($\overline{x}\pm s$), with t test conducted for intergroup comparison. Enumeration data were expressed by natural (n) and percentage (%), with X^2 used for inter group comparison. The intergroup difference is of statistical value when $P < 0.05$.

Results

Table I shows comparison of serum β-HCG and progesterone levels between the two groups. Of the 180 patients, 168 were cured successfully. The success rate was 93.33%. After treatment, the reduction of serum β-HCG and progesterone levels in the success treatment group was more significant (p<0.05) than before treatment and that in the failed treatment group.

Table II shows the results of multivariate logistic regression analysis. When the levels of HCG and progesterone were increased, the success rate by methotrexate combined with mifepristone tablets showed a decreasing trend, p<0.05. When the maximum diameter value of pelvic effusion was increased, the success rate of conservative treatment by methotrexate combined with mifepristone tablets showed a decreasing trend, p<0.05.

Table I. Comparison of serum β-human chorionic gonadotropin and progesterone levels between the successful and failed treatment groups ($\overline{x}\pm s$).

Group	β- Human chorionic gonadotropin (mIU/ml)		Progesterone (ng/ml)	
	Before treatment	After treatment	Before treatment	After treatment
Successful treatment group	1749.57±347.90	801.22±350.62	8.70±2.30	4.31±1.27
Failed treatment group	1778.04±350.31	1978.36±326.70	8.87±2.04	7.02±1.46
t	0.24	13.29	0.22	16.41
p	>0.05	<0.05	>0.05	<0.05

Table II. Results of multivariate logistic regression analysis.

Factor	Partial regression coefficient	Standardized regression coefficient	p	OR
β- Human chorionic gonadotropin	-0.854	-0.359	0.002	0.690
progesterone	-0.762	-0.215	0.011	0.874

The risk factors that affect the success rate of treatment method using methotrexate combined with mifepristone tablets are β-HCG and progesterone levels.

Discussion

With the continuous development of clinical medicine, the measures of diagnosis and treatment of ectopic pregnancy have been increasing. However, for ectopic pregnancy with atypical symptoms, other auxiliary diagnostic methods should be also used to make a comprehensive judgment. HCG is a glycoprotein composed of eight side chains of sugar molecules as well as α and β subunits. Therefore, β-HCG production in the blood is significantly lower than normal pregnancy. Upon abnormal rise of β-HCG or β-HCG, it is necessary to be alert for the occurrence of ectopic pregnancy (Zeng *et al*., 2018; Chen *et al*., 2018). Progesterone a sex hormone is formed by the corpus luteum of the ovary during the first eight weeks of gestation, and secreted by the placenta after the eighth week of gestation. The serum progesterone level remains at a certain level before the 12th week of gestation and does not show significant fluctuations. Progesterone is strongly associated with β-HCG, so it is another indicator for the diagnosis of ectopic pregnancy.

Methotrexate is an anti-metabolic drug as well as a competitive antagonist of folate. Methotrexate binds to dihydrofolate reductase, which blocks the conversion of dihydrofolate to tetrahydrofolate, inhibiting DNA synthesis. Methotrexate is highly sensitive to trophoblast cells and can block the growth and death of trophoblast cells (Capmas *et al*., 2016). It is widely used in conservative treatment of ectopic pregnancy. Mifepristone is a competing blocker of progesterone as well as an anti - progesterone drug with steroidal structure. Mifepristone competes with endogenous progesterone in binding receptor at molecular level, reduces local progesterone effect and forms strong anti-progesterone effect, allows granulosa cells to release relaxin, causes villi and decidua degeneration of pregnancy, and causes embryo sac exfoliation, necrosis and abortion (Cleeve *et al*., 2019; CADTH, 2017; Davenport *et al*., 2017). Ectopic pregnancy is a special form of pregnancy. The treatment effect by single application of methotrexate is not ideal. Combined application of methotrexate and mifepristone can accelerate villus tissue necrosis and produce better therapeutic effect. Ectopic pregnancy will form a certain degree of impact on pregnant women. Many ectopic pregnancy patients after the rupture of the tubal pregnancy will appear intra-abdominal bleeding, leading to severe pain. Massive bleeding can increase the risk of complications such as shock, which not only affects the patient's body, but also has psychological effects (Yong *et al*., 2019; NIHCE, 2019) Therefore, it is necessary to carry

out scientific nursing mode for patients.

Conclusion

In conclusion, serum β-HCG and progesterone are important indicators for the early diagnosis of ectopic pregnancy diseases, and monitoring these two indicators at the same time provides ideal predictive value for the success or failure of conservative treatment using methotrexate combined with mifepristone. It is also valuable to screen the high-risk group of ectopic pregnancy with the maximum diameter line of pelvic effusion, which is of great significance for timely operation and maintenance of patient safety.

Statement of conflict of interest

The authors have declared no conflict of interest.

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