

A Case Study of the Treatment of Threatened Abortion of Twin Pregnancy and Delayed Delivery of the Second Child with Allylestrenol Tablets

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Abstract

this study aimed to explore the individual effect of allylestrenol tablets in the treatment of threatened abortion of twin pregnancy and delayed delivery of a second child. A pregnant woman with a threatened abortion of twin pregnancy and delayed delivery of a second child in our hospital was retrospectively analyzed and treated with allylestrenol tablets, and the biochemical indicators of pregnant women and the fetal situation before and after treatment were compared. The results showed that with the increase in pregnancy, the biparietal diameter (BPD) and femur length (FL) were notably increased, the amniotic fluid index (AFI) was drastically decreased ($P < 0.05$), and the white blood cell count (WBC), platelet count (PLT), and fibrinogen (FIB) were notably increased. Red blood cell count (RBC) and high sensitivity C-reactive protein (hs-CRP) was drastically decreased ($P < 0.05$). Furthermore, the levels of progesterone (P) and estradiol (E_2) in pregnant women with threatened abortion and delayed delivery of twin pregnancy were notably increased after treatment ($P < 0.05$). After treatment, the levels of interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α) in pregnant women with threatened abortion and delayed delivery of the second child in twin pregnancy were drastically decreased ($P < 0.05$). However, there was no considerable difference in fetal birth weight or fetal Apgar score ($P > 0.05$). In conclusion, allylestrenol tablets have shown positive effect in the treatment of threatened abortion and delayed delivery of twin pregnancy.

Keywords: allylestrenol tablets; twin pregnancy threatened abortion; twin pregnancy delayed delivery of the second child; individual case study; fetus condition

INTRODUCTION

Pregnancy is a process that most women go through. During pregnancy, the biochemical indicators and physiological status of pregnant women change considerably, which affects the daily life of patients.^[1,2] There are many kinds of abnormalities during pregnancy, which increases the difficulty of clinical treatment.^[3] With the change in diet and exercise habits of the female population, the incidence of threatened abortion and delayed delivery of the second child is also increasing.^[4] The number of pregnant women with threatened abortion and delayed delivery of the second child is also expanding, with an increasing number of groups occurring. Threatened abortion and delayed delivery of the second child has caused harm to the life and health of pregnant women and fetuses.^[5] Due to insufficient nutrition or incomplete growth and development, many fetuses with threatened abortion and delayed delivery of the second child

will suffer from low body weight, pulmonary dysfunction, and even death, causing great pain to the family.^[6]

In order to prevent threatened abortion and delayed delivery of the second child, drug regulation is often carried out in clinical practice to stabilize the physiological state of pregnant women and the fetal state and promote normal delivery of the fetus.^[7,8] Allylestrenol tablets are a commonly used drug in clinical practice.^[9,10] Allylestrenol tablets can improve the endocrine activity of placental trophoblasts, produce a certain stimulating effect on the placenta, maintain the normal condition of the placenta, reduce the content of oxytocin in pregnant women, resist uterine contractions, and prevent threatened abortion and habitual abortion.^[11-13] As a safe and effective drug for the

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Submitted: 09th June, 2023

Received: 21st June, 2023

Accepted: 13th July, 2023

Published: 12th August, 2023

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How to cite this article: Zhao D, Xin X, Zhang S, Miao L, Meng Y. A Case Study of the Treatment of Threatened Abortion of Twin Pregnancy and Delayed Delivery of the Second Child with Allylestrenol Tablets. J Nat Sc Biol Med 2023;14:73-80

Access this article online	
Quick Response Code: 	Website: www.jnsbm.org
	DOI: https://doi.org/10.4103/jnsbm.JNSBM_14_2_2

prevention of threatened abortion, allylestrenol tablets have a relaxation effect on uterine smooth muscle, can effectively maintain decidualized endometrium, and enable normal placental function. It has a good clinical effect and has been widely recognized by patients.^[14,15]

In this study, the individual effects of allylestrenol tablets in the treatment of threatened abortion and delayed delivery of the second child in twin pregnancy were discussed, and the B-ultrasound examination indicators and routine blood examination indicators of pregnant women with twin pregnancy at different time periods were analyzed. In addition, the hormone levels and inflammatory indicators of twin pregnant women before and after allylestrenol tablet treatment were investigated. The birth weight and Apgar score of twin-pregnant women were analyzed to improve the success rate of delivery, promote the normal delivery of pregnant women with threatened abortion and delayed delivery of the second child in twin pregnancy, and provide clinical guidance for the delivery of pregnant women.

MATERIALS AND METHODS

The research object

This study retrospectively analyzed a pregnant woman with threatened abortion of twin pregnancy and delayed delivery of a second child treated with allenestradiol tablets admitted to our hospital in April 2022 as the research objects, and conducted a study on the efficacy of drug therapy based on ultrasound examination.

Methods

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) patients with complete medical records; (2) patients older than 18 years old; (3) patients with no contraindications to ultrasound examination; (4) patients with clear consciousness and a high degree of cooperation; and (5) patients and their families who signed the informed consent.

The exclusion criteria were as follows: (1) patients complicated with diseases of other vital organs; (2) patients with other malignant tumors; (3) patients with genetic diseases; (4) patients with communication difficulties; and (5) patients who were unwilling to participate in this study.

Comparison of the patient's condition with general data

The patient was a pregnant woman with twin pregnancy and threatened abortion with delayed delivery of the second child. Her years of education were 12 years, her age was 37 years, her BIM was 29.47 kg/m², and she underwent "cervical polyp extraction" in 2014.

RESEARCH METHODS

Allylestrenol tablet treatment, B-ultrasound examination, and routine blood examination were carried out for patients with twin pregnancy. The relevant knowledge and precautions of pregnancy were introduced to the patients, and the vital signs were monitored during pregnancy. The effect of allylestrenol tablets in the treatment of threatened abortion and delayed delivery of the second child twin pregnancy was analyzed.

Examination method

Bedside ultrasound was performed to assist the patient. The device was a Mindray color portable ultrasound M7, which was performed in the middle and late pregnancy mode, with a convex array probe and a frequency of 3-5 Hz. After the puerpera emptied the bladder, they were placed in the supine position. The relationship between the fetal orbit, cerebellum, midline thalamus, and maternal pelvis was explored through the perineum to determine fetal orientation. Then, sagittal sections were taken during contractions, and images were collected when the fetal head contour and the long axis of the pubic symphysis could be clearly visualized.

Observation indicators

1. The general information of pregnant women with threatened abortion and delayed delivery of second child in twin pregnancy was compared, mainly including the years of education, age, BMI, hospitalization history, birth history, and operation history of the patients. The calculation method of BMI is shown in Equation (1).

$$BIM = \frac{Weight}{Height^2} \quad (1)$$

2. The ultrasonographic indicators of pregnant women with threatened abortion and delayed delivery of the second child in different time periods were analyzed, including biparietal diameter (BPD), femur length (FL), amniotic fluid index (AFI), fetal umbilical artery systolic blood pressure to diastolic blood pressure ratio (S/D), and cervical length.

3. Routine blood examination indicators, including red blood cell count (RBC), white blood cell count (WBC), platelet count (PLT), fibrinogen (FIB), and high-sensitivity C-reactive protein (hs-CRP), were analyzed in pregnant women with threatened abortion and pregnant women with delayed delivery of the second child of twin pregnancy at different time periods.

4. Hormonal indicators, including progesterone (P) and estradiol (E₂), were analyzed before and after allylestrenol tablet treatment in pregnant women with threatened abortion and pregnant women with delayed delivery of the second child of twin pregnancy.

5. Inflammatory indicators, including interleukin-6 (IL-6) and tumor necrosis factor- α (TNF- α), were analyzed before and after allylestrenol tablet treatment in pregnant women with threatened abortion and pregnant women with delayed delivery of the second child of twin pregnancy.

6. The fetal status of twin-pregnant women with threatened abortion and twin-pregnant women with delayed delivery of the second child were analyzed, including the birth weight and Apgar score of the fetus.

7. The secretions of pregnant women with threatened abortion and pregnant women with delayed delivery of the second child of twin pregnancy were analyzed. The cervical secretions were placental α -1 microglobulin (PAMG-1), and vaginal secretions were fetal fibronectin (fFN).

Method of statistics

Excel 2016 was used to record and summarize the data. SPSS 20.0 was used for data statistics and analysis. The mean standard deviation ($\pm s$) represents the measurement data, and a *t*-test was used. The percentage (%) was the representation

of the count data, and a statistically considerable difference was detected using the X^2 test. $P < 0.05$ indicated a statistically significant difference.

RESULTS

Pathology of the placentas of pregnant women with threatened abortion in twin pregnancy and pregnant women with delayed delivery in twin pregnancy

Figure 1A shows a pathological diagram of the placenta of a pregnant woman with threatened abortion of twin pregnancy, and Figure 1B shows a pathological diagram of the placenta of a pregnant woman with delayed delivery of a second child of twin pregnancy.

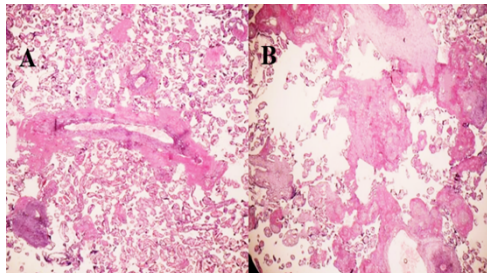


Figure. 1 Placental pathology of twin pregnancy with threatened abortion and twin pregnancy with delayed delivery of the second child.

Notes: A: patient 1, 28 years old, who was pregnant with threatened twin abortion; B: patient 2, 26 years old, twin pregnant woman with delayed delivery of her second child.

A comparative analysis of B-ultrasound examination indexes of pregnant women with threatened abortion of twin pregnancy and delayed delivery of second twin pregnancy in different time periods

Figure 2 shows the comparative analysis of B-ultrasound examination indexes of pregnant women with threatened abortion of twin pregnancy and delayed delivery of second twin pregnancy at different time periods. As can be observed from the figure, the BPD, FL, AFI, S/D, and cervical length of pregnant women with threatened abortion of twin pregnancy and delayed delivery of second child of twin pregnancy were 4.6 cm, 3.2 cm, 13.2 cm, 3.2, and 3.3 cm, respectively at 20 weeks, 6.4 cm, 4.7 cm, 10.6 cm, 3.0, and 2.5 cm, respectively, at 30 weeks, and 8.0 cm, 6.2 cm, 8.8 cm, 2.8, and 2.2 cm, respectively at 34 weeks. It can be inferred that with the increase in pregnancy, the BPD and FL of pregnant women were significantly increased, and the AFI and S/D were significantly decreased ($P < 0.05$).

Table 1 Comparative analysis of B-ultrasound examination indicators of threatened abortion of twin pregnancy and delayed delivery of second twin pregnancy in different time periods

	20 weeks	30 weeks	34 weeks
BPD (cm)	4.6	6.4	8.0
FL (cm)	3.2	4.7	6.2
AFI (cm)	13.2	10.6	8.8
S/D	3.2	3.0	2.8
Length of cervix (cm)	3.3	2.5	2.2

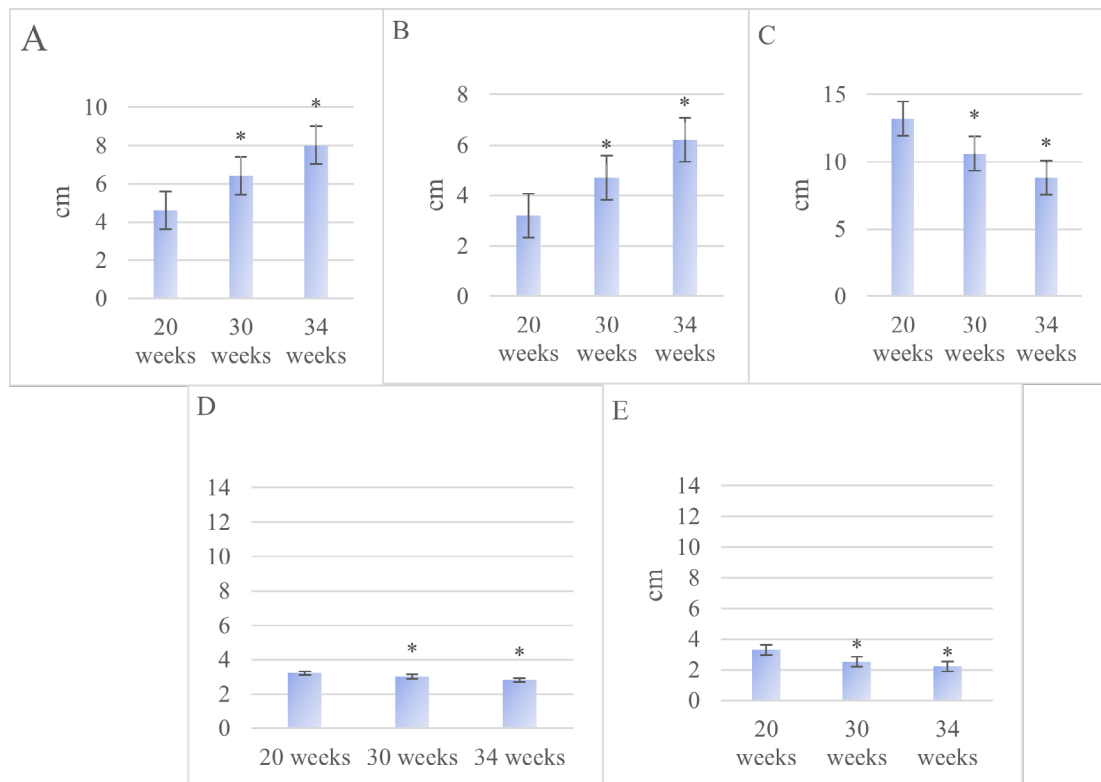


Figure 2. Comparative analysis of B-ultrasound examination indexes of pregnant women with threatened abortion of twin pregnancy and pregnant women with delayed delivery of second twin pregnancy at different time periods. (A: BPD, B: FL, C: AFI, D: S/D, E: cervical length, * meant $P < 0.05$ compared to 20 weeks)

Comparative analysis of blood routine examination indexes of pregnant women with threatened abortion of twin pregnancy and delayed delivery of second twin pregnancy in different time periods

Figure 3 shows the comparative analysis of routine blood examination indexes of pregnant women with threatened abortion of twin pregnancy and delayed delivery of the second twin pregnancy at different time periods. As can be observed from the figure, RBC, WBC, PLT, FIB, and C-reactive protein of threatened abortion of twin pregnancy and delayed delivery of

the second twin pregnancy were $3.92 \times 10^{12} /L$, $7.29 \times 10^9 /L$, $266.00 \times 10^9 /L$, 3.84 g/L , and 11.79 mg/L , respectively at 20 weeks. At 30 weeks, they were $4.48 \times 10^{12} /L$, $7.50 \times 10^9 /L$, $230.00 \times 10^9 /L$, 2.96 g/L , and 10.78 mg/L , respectively; and at 34 weeks, they were $4.50 \times 10^{12} /L$, $7.83 \times 10^9 /L$, $193.00 \times 10^9 /L$, 2.78 g/L , and 9.32 mg/L , respectively. It can be inferred that with the increase in pregnancy, the WBC, PLT, and FIB of pregnant women were significantly increased, and RBC and C-reactive protein were significantly decreased ($P < 0.05$).

Table 2 Comparative analysis of routine blood examination indexes of pregnant women with threatened abortion of twin pregnancy and delayed delivery of second twin pregnancy in different time periods

	20 weeks	30 weeks	34 weeks
RBC ($\times 10^{12}/L$)	3.92	4.48	4.50
WBC ($\times 10^9/L$)	7.29	7.50	7.83
PLT ($\times 10^9/L$)	266.00	230.00	193.00
FIB (g/L)	3.84	2.96	2.78
hs-CRP (mg/L)	11.79	10.78	9.32

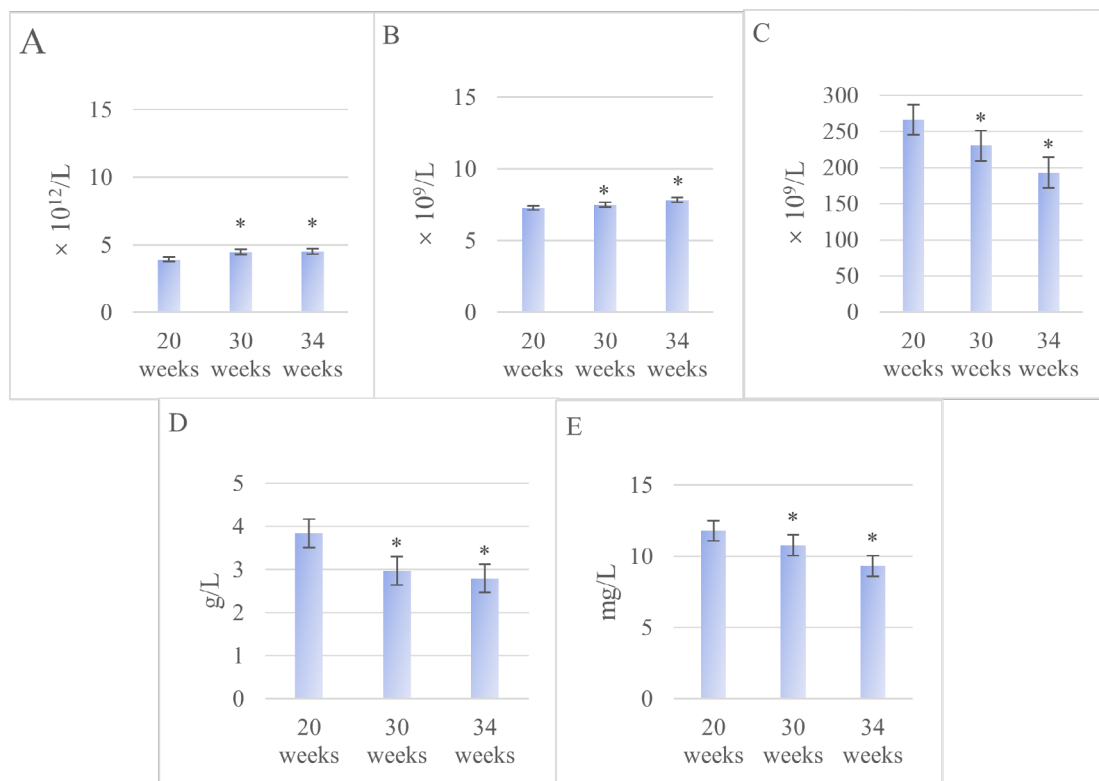


Figure 3. Comparative analysis of blood routine examination indexes of pregnant women with threatened abortion of twin pregnancy and delayed delivery of second twin pregnancy at different time periods. (A: RBC, B: WBC, C: PLT, D: FIB, E: hs-CRP, * meant compared with 20 weeks, $P < 0.05$)

Comparative analysis of hormone indexes before and after allylestrenol tablet treatment in twin pregnancy with threatened abortion and twin pregnancy with delayed delivery of the second child

Figure 4 shows the comparative analysis of P values before and after allylestrenol tablet treatment for threatened

abortion in twin pregnancy and delayed delivery of the second child in twin pregnancy. Before allylestrenol tablet treatment, the P value of threatened abortion in twin pregnancy and delayed delivery of the second child in twin pregnancy was 18.72 ng/mL . After treatment, it increased significantly to 25.37 ng/mL . ($P < 0.05$) (Table 3).

Table 3 Comparative analysis of hormone indexes before and after allylestrenol tablet treatment in pregnant women with threatened abortion and delayed delivery of a second child in twin pregnancy.

	Before treatment	After treatment
P (ng/mL)	18.72	25.37
E ₂ (pg/mL)	117.49	427.34

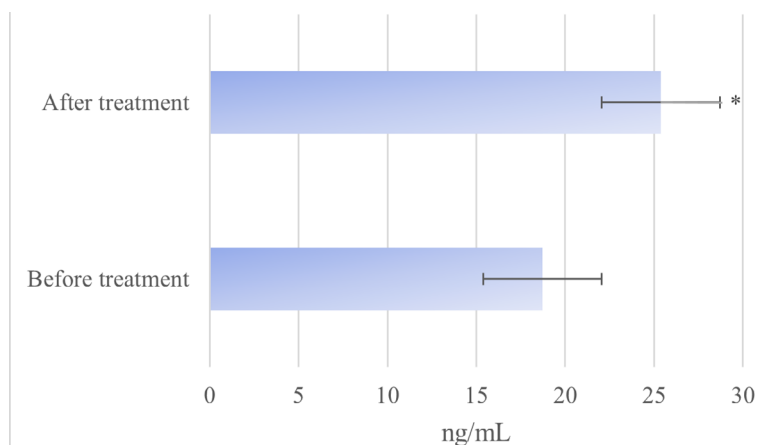


Figure. 4 Comparative analysis of P values before and after treatment for threatened abortion and delayed delivery of second child in twin pregnancy. (* indicates $P < 0.05$ compared with before treatment.)

Figure 5 shows the comparative analysis of E₂ values before and after allylestrenol tablet treatment in pregnant women with threatened abortion and delayed delivery of the second child in twin pregnancy. Before allylestrenol tablet treatment, the E₂ value of pregnant women with threatened abortion

of twin pregnancy and delayed delivery of twin pregnancy was 117.49 pg/mL. After treatment, the E₂ value was 427.34 pg/mL. After treatment, the E₂ value of pregnant women with threatened abortion and delayed delivery of the second child of a twin pregnancy increased substantially ($P < 0.05$).

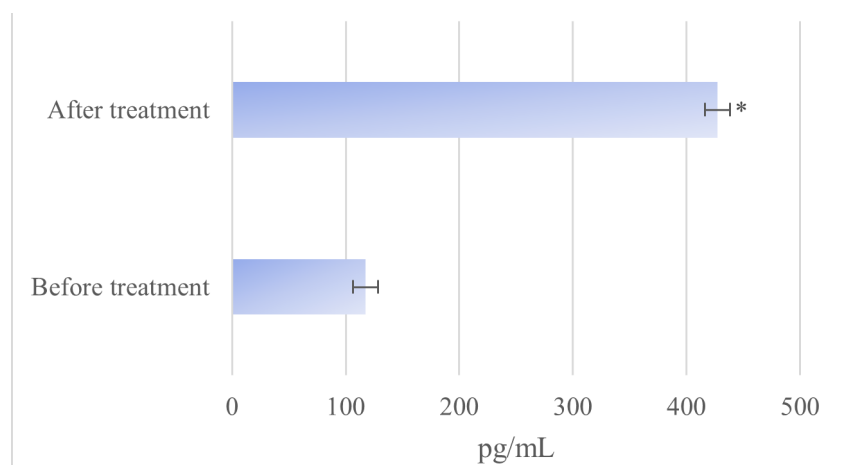


Figure. 5 Comparison and analysis of E2 values before and after allylestrenol tablet treatment in pregnant women with threatened abortion and delayed delivery of a second child in twin pregnancy. (* indicates comparison with before treatment, $P < 0.05$.)

Comparative analysis of inflammatory indicators before and after allylestrenol tablet treatment in twin pregnancy with threatened abortion and twin pregnancy with delayed delivery of the second child

Figure 6 shows the comparative analysis of IL-6 before and after allylestrenol tablet treatment in pregnant women with threatened abortion and delayed delivery of the

second child in twin pregnancy. Before allylestrenol tablet treatment, the levels of IL-6 were 159.72 pg/mL and 94.56 pg/mL in pregnant women with threatened abortion and delayed delivery of their second child, respectively. After treatment, the levels of IL-6 in pregnant women with threatened abortion and delayed delivery of the second child of a twin pregnancy were drastically decreased ($P < 0.05$) (Table 4).

Table 4 Comparative analysis of inflammatory indicators before and after allylestrenol tablet treatment in pregnant women with threatened abortion and pregnant women with delayed delivery of the second child in twin pregnancy

	Before treatment	After treatment
IL-6 (pg/mL)	159.72	94.56
TNF- α (pg/mL)	88.34	58.94

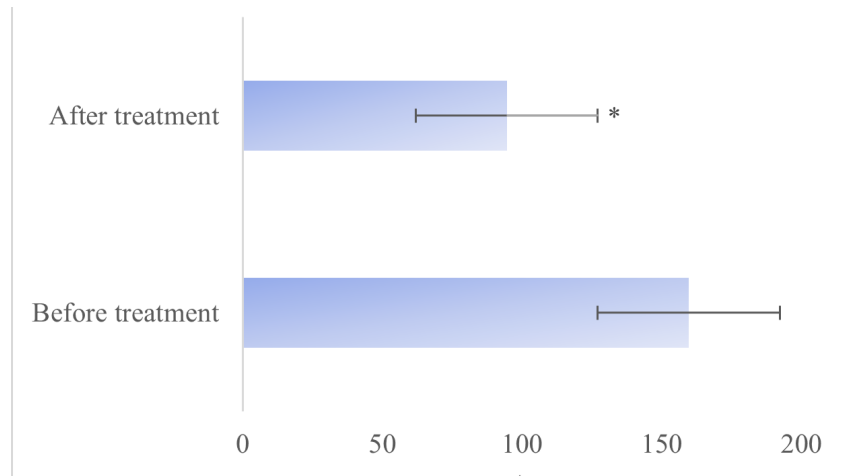


Figure. 6 Comparison of IL-6 levels before and after allylestrenol tablet treatment in pregnant women with threatened abortion and delayed delivery of a second child in twin pregnancy. (* indicates comparison with before treatment, $P < 0.05$.)

Figure 7 shows the comparative analysis of TNF- α before and after allylestrenol tablet treatment in pregnant women with threatened abortion and delayed delivery of the second child in twin pregnancy. TNF- α was 88.34 pg/mL before allylestrenol tablet treatment and 58.94

pg/mL after allylestrenol tablet treatment in pregnant women with threatened abortion and delayed delivery. After treatment, TNF- α drastically decreased in pregnant women with threatened abortion and delayed delivery of the second child in twin pregnancy ($P < 0.05$).

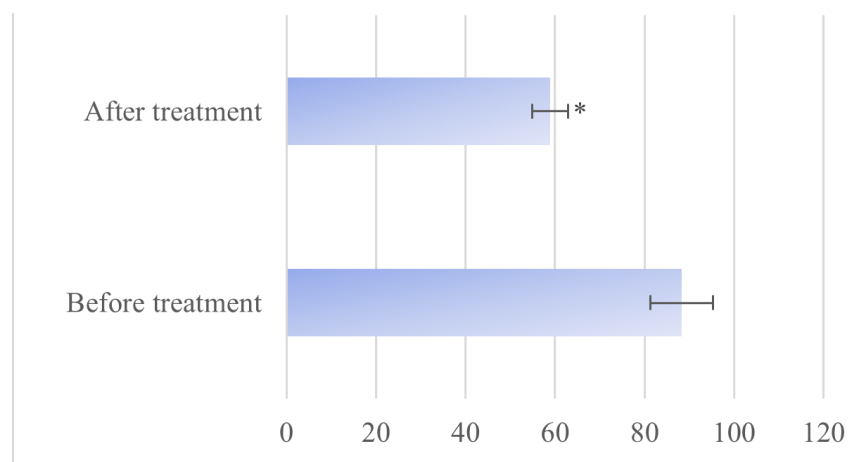


Figure. 7 Comparison of TNF- α in pregnant women with threatened abortion and delayed delivery of second child in twin pregnancy before and after allylestrenol tablets treatment. (* indicates comparison with before treatment, $P < 0.05$.)

Analysis of the fetal situation of threatened abortion and delayed delivery of a second child in twin pregnancy

The fetal birth weight was 1900 g in women with threatened abortion of twin pregnancies and delayed delivery of second twins. Pregnant women with threatened abortion and delayed delivery of a second twin pregnancy had Apgar scores of 9 for 1 minute, 9 for 5 minutes, and 9 for 10 minutes.

The secretions of pregnant women with threatened abortion of twin pregnancy and pregnant women with delayed delivery of twin pregnancy

The results of cervical secretions PAMG-1 and vaginal secretions fFN were positive in the pregnant women with twin pregnancy threatened abortion and twin pregnancy delayed delivery of the second child. Pregnant women

with twin pregnancy-threatened abortion and twin pregnancy-delayed delivery of the second child had a higher risk of preterm birth.

DISCUSSION

Abortion has a high probability among pregnant women. Studies have shown that more than 10% of pregnant women may have spontaneous abortions, and early abortion accounts for approximately 80% of them.^[16,17] As a new type of fetal protection drug, allylestrenol tablets can effectively enhance the secretory activity of the placental trophic layer, promote the secretion of human chorionic gonadotropin and endogenous progesterone, and play a positive role in the recovery of placental function with fewer adverse drug reactions and almost no impact on fetal development.^[18] The incidence of delayed delivery in twin pregnancies in Western countries is only 0.014% of births, accounting for 1% of multiple pregnancies.^[8] Allylestrenol tablets also have a positive regulating effect on delayed delivery of twin pregnancy.

As a fetal protection drug, allylestrenol tablets have unique advantages, which can effectively promote smooth delivery, reduce the incidence of complications, protect pregnant women and fetuses, and have good application effects.^[19] Li *et al.*^[20] and Nwuke *et al.*^[21] studied the efficacy of allylestrenol tablets combined with lidocaine in the treatment of threatened preterm labor (TPTL) and its influence on inflammatory factors in peripheral blood. It was found that the success rate of fetal protection and average delivery time of pregnant women treated with allylestrenol tablets combined with lidocaine were notably increased. After treatment, the serum levels of IL-17, IL-10, and IL-6 in pregnant women were drastically decreased. The average neonatal weight and Apgar score were considerably better, and the incidence of postpartum hemorrhage, postpartum hospital stay, toxic side effects, neonatal death, malformation, and asphyxia were significantly reduced. Allyl progesterone combined with ritopine could considerably reduce the expression levels of IL-17, IL-10, and IL-6 in TPTL, improve adverse pregnancy status, and prolong gestation weeks, demonstrating high safety and application value. In this study, the B-ultrasound and routine blood examination indexes of pregnant women with threatened abortion and delayed delivery of twin pregnancy at different time periods were analyzed. The hormone levels and inflammatory indicators before and after allylestrenol tablet treatment in pregnant women with threatened abortion and delayed delivery of twin pregnancy were investigated. Additionally, the fetal birth of threatened abortion in twin pregnancy and delayed delivery of second child in twin pregnancy was also investigated. The results showed that with the progression of pregnancy, BPD and FL substantially increased, while AFI and S/D drastically decreased ($P < 0.05$). Furthermore, with the increase in pregnancy, the WBC, PLT and FIB of pregnant women were notably increased, whereas RBC and C-reactive protein were drastically decreased ($P < 0.05$). After treatment, the P values of threatened abortion in twin pregnancy and delayed

delivery of second child in twin pregnancy were notably increased ($P < 0.05$). After treatment, the E_2 value of twin pregnancy threatened abortion, and twin pregnancy delayed delivery of the second child increased substantially ($P < 0.05$). After treatment, the levels of IL-6 in twin-pregnancy threatened abortion and twin-pregnancy delayed delivery of the second child were drastically decreased ($P < 0.05$). After treatment, TNF- α was significantly decreased in pregnant women with threatened abortion and delayed delivery of the second child in twin pregnancy ($P < 0.05$). The fetal birth weight was 1900 g in women with threatened abortion of twin pregnancies and delayed delivery of second twins. Pregnant women with threatened abortion and delayed delivery of a second twin pregnancy had Apgar scores of 9 at 1 minute, 9 at 5 minutes, and 9 at 10 minutes. The positive results of cervical secretions PAMG-1 and vaginal secretions fFN were associated with a higher risk of preterm birth in pregnant women with threatened abortion and delayed delivery of the second child in twin pregnancy. Allylestrenol tablets have a positive application value in preventing threatened abortion of twin pregnancy and delayed delivery of the second child of twin pregnancy, which can promote the smooth progress of delivery and improve the safety of treatment.

Discussion

Allylestrenol tablets can prevent threatened abortion and delayed delivery of twin pregnancy, demonstrating high clinical application value. They effectively reduce the probability of threatened abortion and delayed delivery of the second child, providing protection to the fetus, and promoting normal delivery of pregnant women. The positive significance and guiding value for the health of both pregnant women and fetuses are evident, making them valuable in clinical practice. Nevertheless, the weakness of this study is the small sample size, necessitating further research and verification.

REFERENCES

1. Yang M, Luo J, Yang Q, Xu L. Research on the medication rules of Chinese herbal formulas on treatment of threatened abortion. *Complement Ther Clin Pract.* 2021; 43: 101371. doi: <https://doi.org/10.1016/j.ctcp.2021.101371>.
2. Zhao H, He W, Yang Z. A pairwise and network meta-analysis comparing the efficacy and safety of progestogens in threatened abortion. *Int J Gynaecol Obstet.* 2022; 156(3): 383-93. doi: <https://doi.org/10.1002/ijgo.13707>.
3. Kırıcı P, Tanrıverdi ES. Effects of Different Progesterone Doses on the Concentrations of Proinflammatory and Anti-inflammatory Cytokines in Pregnant Women With Threatened Abortion. *Cureus.* 2021; 13(11): e19333. doi: <https://doi.org/10.7759/cureus.19333>.
4. Chen X, Tao C, Wang J, He B, Xu J. Meta-analysis of therapeutic efficacy and effects of integrated traditional Chinese and Western medicine on coagulation and fibrinolysis system in patients with threatened abortion and polycystic ovary syndrome. *Am J Transl Res.* 2022; 14(5): 2768-78. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9185052>.

5. Fu S, Xie H, Zhong Y, et al. Atosiban Combined with Ritodrine for Late Threatened Abortion or Threatened Premature Labor Patients with No Response to Ritodrine: A Clinical Trial. *Med Sci Monit.* 2021; 27: e929743. doi: <https://doi.org/10.12659/msm.929743>.
6. Salas A, Gastón B, Barrenetxea J, Sendino T, Jurado M, Alcázar JL. Predictive value of hyperglycosylated human chorionic gonadotropin for pregnancy outcomes in threatened abortion in first-trimester viable pregnancies. *An Sist Sanit Navar.* 2021; 44(1): 23-31. doi: <https://doi.org/10.23938/assn.0933>.
7. Zeng P, Zhou H, Guo P, Xia W, Huang J, Zeng Q. Efficacy and safety of traditional Chinese herbal medicine in the treatment of threatened abortion: A protocol for systematic review and meta-analysis. *Medicine (Baltimore).* 2021; 100(5): e23288. doi: <https://doi.org/10.1097/MD.00000000000023288>.
8. Dudukina E, Horváth-Puhó E, Sørensen HT, Ehrenstein V. Long-term risk of epilepsy, cerebral palsy and attention-deficit/hyperactivity disorder in children affected by a threatened abortion in utero. *Int J Epidemiol.* 2021; 50(5): 1540-53. doi: <https://doi.org/10.1093/ije/dyab069>.
9. Cortés-Prieto J, Bosch AO, Rocha JA. Allylestrenol: three years of experience with Gestanon in threatened abortion and premature labor. *Clin Ther.* 1980; 3(3): 200-8. Available from: <https://pubmed.ncbi.nlm.nih.gov/7459930>.
10. Czeizel A, Huiskes N. A case-control study to evaluate the risk of congenital anomalies as a result of allylestrenol therapy during pregnancy. *Clin Ther.* 1988; 10(6): 725-39. Available from: <https://pubmed.ncbi.nlm.nih.gov/3219686>.
11. Bergink EW, Loonen PB, Kloosterboer HJ. Receptor binding of allylestrenol, a progestagen of the 19-nortestosterone series without androgenic properties. *J Steroid Biochem.* 1985; 23(2): 165-8. doi: [https://doi.org/10.1016/0022-4731\(85\)90232-8](https://doi.org/10.1016/0022-4731(85)90232-8).
12. Birkenfeld A, Navot D, Ezra Y, Ron A, Schenker JG. The effect of estradiol valerate and allylestrenol on endometrial transformation in hypergonadotropic hypogonadic women. *Eur J Obstet Gynecol Reprod Biol.* 1987; 25(3): 221-9. doi: [https://doi.org/10.1016/0028-2243\(87\)90102-x](https://doi.org/10.1016/0028-2243(87)90102-x).
13. Pap E, Csaba G. Effect of neonatal allylestrenol treatment (hormonal imprinting) on the serum testosterone and progesterone concentration in adult rat. *Reprod Fertil Dev.* 1995; 7(5): 1249-51. doi: <https://doi.org/10.1071/rd9951249>.
14. Zivanovic L, Vojvodic L, Ristic P, Zecevic M, Nemcova I. Validation and application of the RP-HPLC method for the assay of allylestrenol and alpha-tocopherol in tablets. *Biomed Chromatogr.* 2000; 14(1): 56-7. doi: [https://doi.org/10.1002/\(SICI\)1099-0801\(200002\)14:1<56::AID-BMC972>3.0.CO;2-Z](https://doi.org/10.1002/(SICI)1099-0801(200002)14:1<56::AID-BMC972>3.0.CO;2-Z).
15. Karabélyos C, Horváth C, Holló I, Csaba G. Effect of perinatal synthetic steroid hormone (allylestrenol, diethylstilbestrol) treatment (hormonal imprinting) on the bone mineralization of the adult male and female rat. *Life Sci.* 1999; 64(9): P1105-10. doi: [https://doi.org/10.1016/s0024-3205\(98\)00624-9](https://doi.org/10.1016/s0024-3205(98)00624-9).
16. Dang CX, Wang D, Liu PF, Liu JX, Yu X. Network pharmacological analysis and molecular docking of Huangqin-Baizhu herb pair in the treatment of threatened abortion. *Medicine (Baltimore).* 2022; 101(36): e30417. doi: <https://doi.org/10.1097/md.00000000000030417>.
17. Battaglia C, Morotti E, Montaguti E, Mariacci G, Facchinetti F, Pilu G. Plasma and amniotic fluid concentrations of nitric oxide: Effects on uterine artery and placental vasculature in women who underwent voluntary pregnancy termination and in women with missed and threatened abortion. A pilot study. *Eur J Obstet Gynecol Reprod Biol.* 2022; 270: 105-10. doi: <https://doi.org/10.1016/j.ejogrb.2022.01.001>.
18. Yasuda N, Fujino K, Shiraji T, Nambu F, Kondo K. Effects of steroid 5alpha-reductase inhibitor ONO-9302 and anti-androgen allylestrenol on the prostatic growth, and plasma and prostatic hormone levels in rats. *Jpn J Pharmacol.* 1997; 74(3): 243-52. doi: <https://doi.org/10.1254/jjp.74.243>.
19. Shi X, Wu Y, Hang T, et al. Application of a sensitive liquid chromatographic/tandem mass spectrometric method to a pharmacokinetic study of allylestrenol in healthy Chinese female volunteers. *J Chromatogr B Analyt Technol Biomed Life Sci.* 2008; 871(1): 90-4. doi: <https://doi.org/10.1016/j.jchromb.2008.06.054>.
20. Li Q, Li C, Jin H. Efficacy of allylestrenol combined with ritodrine on threatened premature labor and its influence on inflammatory factors in peripheral blood. *Exp Ther Med.* 2020; 19(2): 907-12. doi: <https://doi.org/10.3892/etm.2019.8273>.
21. Nwuke C, Ibeh B. Antidiarrheal potential of methanol extract of *Combretum dolichopetalum* and its fractions in wistar albino rats. *Science Progress and Research (SPR).* 2021; 1(1): 11-23. doi: <https://doi.org/10.52152/spr/2021.102>.