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Original Article

Effects of allylestrenol on hormone levels and delivery outcomes in threatened abortion

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Abstract: Objective: To investigate the effects of allylestrenol on sex hormone levels and delivery outcomes in women with threatened abortion. Methods: This retrospective analysis examined clinical data of patients with threatened abortion treated at Huzhou Maternity & Child Health Care Hospital from January 1, 2021, to December 31, 2022. A total of 149 eligible patients were screened and divided into two groups: a control group (n=75) treated with progesterone capsules from January to December 2021, and an observation group (n=74) treated with allylestrenol from January to December 2022. Delivery outcomes, sex hormone levels, complications, and adverse effects were compared between the two groups. Results: Successful delivery was achieved in 62 cases (83.78%) in the observation group and 61 cases (81.33%) in the control group, with no significant difference between the two groups ($P>0.05$). Both groups showed significant improvements in β-HCG and progesterone levels after treatment compared to baseline ($P<0.05$). There was no significant difference in post-treatment β-human chorionic gonadotrophin (β-HCG) levels between the two groups ($P>0.05$), while progesterone levels were significantly lower in the observation group ($P<0.05$). Among patients with successful deliveries, there were no significant differences in preterm birth, oligohydramnios, or fetal growth restriction between the two groups (all $P>0.05$). However, the observation group showed a significantly higher rate of normal vaginal deliveries compared to the control group ($P<0.05$). Neonates in the observation group had significantly higher gestational ages and birth weights (all $P<0.05$). There were no significant differences between groups in the incidence of macrosomia, low birth weight, or neonatal asphyxia (all $P>0.05$). No significant differences were observed in safety indicators between the two groups ($P>0.05$). Conclusion: Allylestrenol is comparable to progesterone in improving delivery outcomes for women with threatened abortion, with the added benefits of reducing cesarean section rates and prolonging gestational age, and without increasing safety risk.

Keywords: Allylestrenol, threatened abortion, progesterone, hormone levels, delivery outcome

Introduction

Threatened abortion, characterized by vaginal bleeding with or without abdominal pain before 28 weeks of gestation, affects approximately 25% of pregnant women [1, 2]. Among women experiencing threatened abortion, about 25% will progress to miscarriage. Those who continue their pregnancies are at a significantly higher risk of adverse outcomes, including antepartum hemorrhage, preterm birth, and low birth weight infants [3, 4]. Miscarriage can have a substantial impact on women and their families, potentially leading to long-term effects such as anxiety, depression, and heightened psychological stress in subsequent pregnancies [5, 6].

Allylestrenol is a progestogen that can enhance the endocrine function of the placental trophoblast, promoting the secretion of endogenous progesterone and human chorionic gonadotropin (hCG), thereby stabilizing poorly functioning placentas [7, 8]. Currently, there is no consensus on the efficacy of allylestrenol in treating threatened abortion. Therefore, this study aims to evaluate the effects of allylestrenol in women with threatened abortion.

Subjects and methods

Study subjects

This single-center retrospective study collected clinical data from patients with threatened abortion treated at Huzhou Maternity & Child

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Table 1. Comparison of baseline characteristics between the two groups

	Age [($\bar{X}$ ± s), years]	BMI [M_{50} (P_{25}, P_{75}), kg/m^2]	Number of pregnancies [M_{50} (P_{25}, P_{75}), times]	Number of deliveries [($\bar{X}$ ± s), times]	Gestational age [($\bar{X}$ ± s), weeks]
Observation group (n=74)	29.76±5.58	24.13 (21.51, 29.25)	3 (1, 4)	1.27±0.45	10.13±2.58
Control group (n=75)	30.12±6.20	24.10 (21.13, 28.22)	3 (2, 4)	1.25±0.44	9.67±2.86
Statistical value	-0.372	0.142	0.644	0.274	1.030
P value	0.707	0.887	0.521	0.786	0.305

Note: BMI, Body Mass Index.

Health Care Hospital between January 1, 2021, and December 31, 2022. A total of 149 eligible patients were selected and divided into two groups: a control group (n=75) treated with progesterone capsules from January to December 2021, and an observation group (n=74) treated with allylestrenol from January to December 2022. Inclusion criteria were: (1) meeting the diagnostic criteria for threatened abortion [9]; (2) singleton pregnancy; (3) intrauterine pregnancy confirmed by ultrasound; (4) first pregnancy; (5) pregnancy <28 weeks; and (6) age >18 years. Exclusion criteria were: (1) severe liver or kidney dysfunction; (2) psychiatric disorders; and (3) incomplete treatment. This study complied with the Declaration of Helsinki and was approved by the ethics committee of Huzhou Maternity & Child Health Care Hospital.

Treatment and grouping

The observation group received oral allylestrenol (trade name: Duolimu, approval number: GYZZ H20113293, manufacturer: Changzhou Siyao Pharmaceutical Co., Ltd., specification: 5 mg × 20 tablets) at a dose of 5 mg three times daily for 7 days, starting from the day of admission. The control group received oral progesterone soft capsules (trade name: Qining, approval number: GYZZ H20031099, manufacturer: Zhejiang Aisheng Pharmaceutical Co., Ltd., specification: 100 mg × 12 capsules) for 10-15 days.

Data collection

All patients were followed up until delivery. Baseline characteristics were recorded, and follow-up was conducted by telephone, WeChat, or in-person visits. Data collection was performed by two physicians, with each piece of information cross-checked after collection.

Outcome measures

(1) Successful delivery and miscarriage rates in pregnant women. (2) Sex hormone levels: β-human chorionic gonadotropin (β-HCG) and progesterone levels were measured using enzyme-linked immunosorbent assay (ELISA) before and after one course of treatment. (3) Pregnancy indicators: preterm birth, threatened preterm labor, premature rupture of membranes, and antepartum hemorrhage. (4) Neonatal outcomes: fetal growth restriction, neonatal birth weight, and congenital abnormalities (including intraventricular hemorrhage, necrotizing enterocolitis, retinopathy of prematurity, respiratory distress syndrome), etc. (5) Adverse reactions, including nausea, dizziness, somnolence, breast tenderness, etc.

Statistical analysis

Data were analyzed using SPSS 28.0 and GraphPad Prism 10.0 software. Continuous variables were tested for normality using the Kolmogorov-Smirnov test. Normally distributed data were expressed as mean ± standard deviation ($\bar{x}$ ± s) and compared using a t-test, while non-normally distributed data were expressed as median (interquartile range) [M (P_{25}, P_{75})] and compared using Wilcoxon rank-sum test. Categorical variables were expressed as numbers (percentages) [n (%)], and analyzed using χ^2 test. P<0.05 was considered statistically significant.

Results

Baseline characteristics

A total of 162 cases were initially selected, with 8 excluded due to incomplete data and 5 due to loss to follow-up. The final analysis included 149 patients: 74 in the observation group and 75 in the control group. There were no significant differences between the two groups in terms of maternal age, body mass index (BMI), number of pregnancies, number of deliveries, or gestational age (all P>0.05) (**Table 1**).

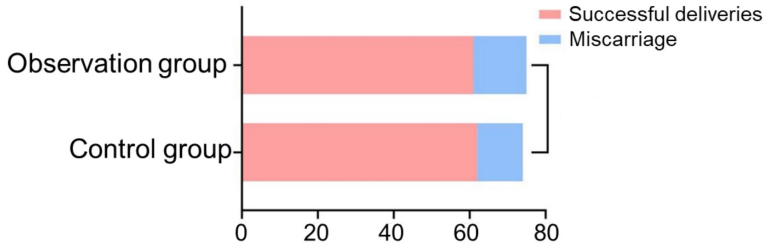

Figure 1. Comparison of main outcome indicators between the two groups.

Comparison of delivery outcomes

In the observation group, 62 cases (83.78%) had successful deliveries, while 12 cases (16.22%) experienced miscarriage. In the control group, 61 cases (81.33%) had successful deliveries, and 14 cases (18.67%) had miscarriage. There was no significant difference in delivery outcome between the two groups ($P>0.05$) (**Figure 1**). Ultrasound images from two cases of threatened abortion are shown in **Figure 2**.

Comparison of sex hormone levels before and after treatment

There were no significant differences in pretreatment β-hCG and progesterone levels between the two groups (all $P>0.05$). After treatment, β-hCG levels remained similar between the two groups ($P>0.05$), but progesterone levels were significantly lower in the observation group ($P<0.05$). Both groups showed significant improvements in β-hCG and progesterone levels after treatment compared to baseline (all $P<0.05$) (**Table 2**).

Comparison of pregnancy indicators in patients with successful deliveries

Among patients with successful deliveries, there were no significant differences in pregnancy indicators such as preterm birth, oligohydramnios, or fetal growth restriction between the two groups (all $P>0.05$). However, the observation group had a significantly higher rate of normal vaginal deliveries compared to the control group ($P<0.05$) (**Table 3**).

Comparison of neonatal outcomes

Neonates in the observation group had significantly higher gestational ages and birth weights compared to those in the control group (both $P<0.05$). There were no significant differences between the groups in the incidence of macrosomia, low birth weight, or neonatal asphyxia (all $P>0.05$) (**Table 4**).

Comparison of safety indicators

There were no significant differences in safety indicators between the two groups ($P>0.05$) (**Table 5**).

Discussion

With improvements in social living standards, threats to food safety, and the impacts of environmental pollution, the incidence of threatened abortion among pregnant women has gradually increased. While most pregnant women can continue their pregnancies after rest and symptomatic treatment, some still experience miscarriage, which can elevate the risk of infection and shock, posing serious threats to maternal health [10, 11]. Currently, the main treatment approach is to supplement with progestogens. Progesterone is a progestogen that plays a crucial role in establishing and maintaining pregnancy. It can induce changes in endometrial secretion critical for embryo implantation [12, 13] and helps regulate maternal immune responses, prevent embryo rejection, stabilize the uterus, and inhibit uterine contractions [14]. Clinical studies have confirmed the effectiveness of progesterone in treating threatened abortion and its role in improving pregnancy continuation rates [15-17].

Allylestrenol is a synthetic hormone without sex hormone effects, and does not affect the patient's adrenal and gonadal functions. Allylestrenol can enhance the activity of chorionic phosphate dehydrogenase in pregnant women, thereby elevating β-hCG and progesterone levels in the body [18, 19]. At the same time, allylestrenol can stabilize placental function and reduce oxytocin levels in pregnant women.

Our study compared the efficacy of allylestrenol and progesterone in treating threatened abortion. The results showed comparable successful delivery rates of the two treatments (83.78%

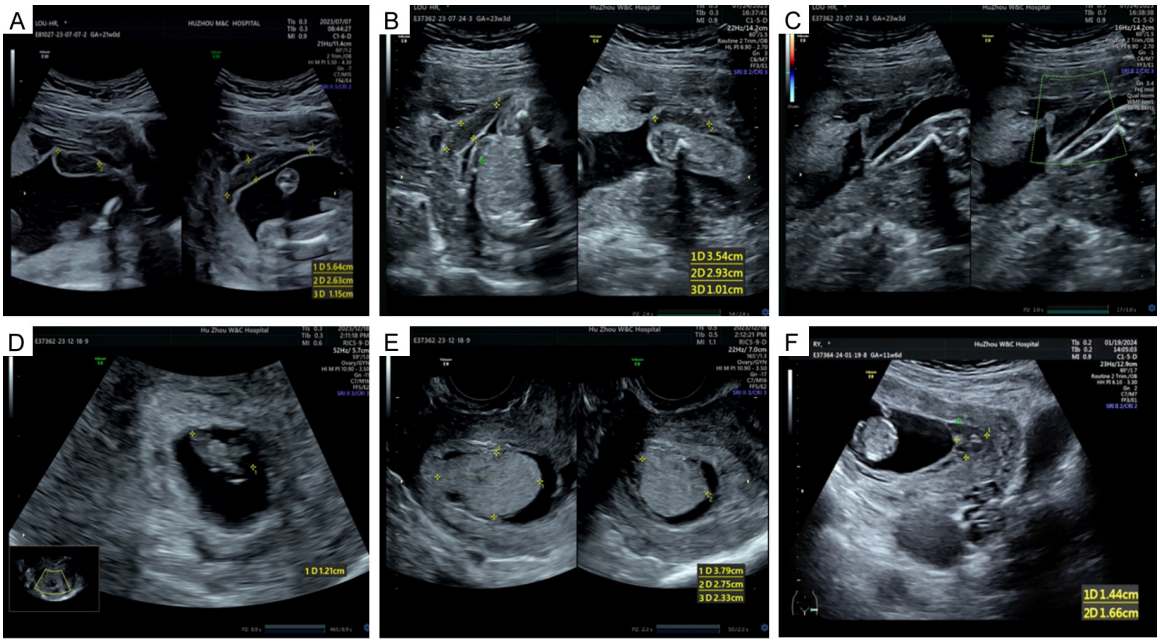

Figure 2. Ultrasound images of two cases of threatened abortion. A. Case 1, 21 weeks of gestation, initial discovery of subchorionic hematoma at the lower edge of the placenta, size 56.4*26.3*11.5 mm; B. Case 1, follow-up at 23 weeks + 3 days, subchorionic hematoma size 35.4*29.3*10.1 mm; C. Case 1, CDFI showing no blood flow signal; D. Case 2, 50 days + of gestation, germ length 12 mm; E. Case 2, 50 days + of gestation, initial discovery of homogeneous hyperechoic area within the gestational sac, size 37.9*27.5*23.3 mm, considered as subchorionic hematoma; F. Case 2, follow-up at 11 weeks + 6 days, subchorionic hematoma size 16.6*14.4 mm.

Table 2. Comparison of sex hormone levels before and after treatment between the two groups

	β-hCG (U/L)		Progesterone (mmol/L)	
	Before treatment	After treatment	Before treatment	After treatment
Observation group (n=74)	1839.44±382.19	8873.69±887.37*	86.79±10.83	166.72±25.27*
Control group (n=75)	1779.03±375.22	8939.30±869.36*	88.37±12.39	189.37±28.70*
Statistical value	0.974	-0.456	-0.828	-5.110
P value	0.332	0.649	0.409	<0.001

Note: Compared with before treatment within the group, *P<0.01. β-hCG, β-human chorionic gonadotrophin.

Table 3. Comparison of pregnancy indicators in patients with successful deliveries between the two groups [n (%)]

	Preterm birth	Oligohydramnios	Fetal growth restriction	Delivery mode	
				Normal vaginal delivery	Cesarean section
Observation group (n=61)	6 (9.84)	1 (1.64)	2 (3.28)	38 (62.30)	23 (37.70)
Control group (n=62)	9 (14.52)	3 (4.84)	3 (4.84)	27 (43.55)	35 (56.45)
χ^2 value	0.629	1.000	0.192	4.336	
P value	0.428	0.317	0.661	0.037	

vs 81.33%). This indicates that both medications are effective in treating threatened abortion and have comparable efficacy. Pang et al. [20] reported a total effective rate of 83.46% when using magnesium sulfate combined with allylestrenol for threatened abortion in pregnancies achieved through assisted reproductive technology. McLindon et al. [21] conducted a placebo-controlled trial of progesterone for threatened miscarriage, reporting successful

Table 4. Comparison of neonatal outcomes between the two groups

	Gestational age [($\bar{x} \pm s$), weeks]	Birth weight [($\bar{x} \pm s$), kg]	Macrosomia [*n* (%)]	Low birth weight [*n* (%)]	Neonatal asphyxia [*n* (%)]
Observation group (n=61)	38.93±3.48	3.65±0.63	1 (1.64)	2 (3.28)	1 (1.64)
Control group (n=62)	37.16±4.27	3.37±0.71	1 (1.61)	1 (1.61)	0 (0.00)
Statistical value	2.520	2.313	0.000	0.359	1.025
P value	0.013	0.022	0.991	0.549	0.311

Table 5. Comparison of safety indicators between the two groups [n (%)]

	Nausea and vomiting	Headache	Tachycardia	Tachycardia	Tachycardia	Tachycardia	Tachycardia
Observation group (n=74)	2 (2.70)	2 (2.70)	0 (0.00)	1 (1.35)	0 (0.00)	2 (2.70)	7 (9.46)
Control group (n=75)	1 (1.33)	1 (1.33)	1 (1.33)	2 (2.67)	2 (2.67)	2 (2.67)	9 (12.00)
χ^2 value	0.354	0.354	0.993	0.327	2.000	0.000	0.251
P value	0.552	0.552	0.319	0.568	0.157	0.989	0.616

delivery rates of 82.4% for progesterone and 84.2% for placebo. These findings support our results.

Regarding sex hormone levels, both groups experienced significant post-treatment improvements compared to baseline. Inter-group comparison after treatment revealed no significant difference in β-hCG levels, but progesterone levels were lower in the allylestrenol group. This suggests that while both medications improve sex hormone levels, progesterone has a more pronounced effect on progesterone levels. The mechanism may involve both drugs stabilizing placental function and promoting fetal development by regulating body hormone levels, with progesterone exerting a stronger effect on progesterone levels. Huang et al. [22] reported that progesterone and β-hCG levels are associated with the risk of threatened abortion. Chen et al. [23] found that combined treatment with progesterone and allylestrenol in older women with threatened abortion resulted in greater improvements in β-hCG and progesterone levels compared to progesterone alone, with both treatments showing significant improvements from baseline.

In terms of pregnancy indicators and neonatal outcomes, allylestrenol treatment was associated with higher rates of normal vaginal delivery, longer gestational ages, and higher birth weights compared to progesterone. No significant differences were observed in other indicators. This suggests that allylestrenol may be superior to progesterone in promoting fetal development and maintaining placental stability in women with threatened abortion. Safety indicators were comparable between the two treatments, indicating that allylestrenol does not increase the risk of adverse effects in women with threatened abortion.

Conclusion

Allylestrenol is comparable to progesterone in improving delivery outcomes for women with threatened abortion, with the added benefits of reducing cesarean section rates and prolonging gestational age, without increasing safety risks. This was a single-center study with a limited sample size. Further multi-center research is needed to validate these findings.

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Disclosure of conflict of interest

None.

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