

New thoughts in exploring the pathogenesis, diagnosis, and treatment of threatened abortion

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Summary

Threatened abortion is a common complication of pregnancy. Since the underlying mechanisms behind this condition are complicated, predicting and treating threatened abortion is a challenge for clinicians. Interestingly, a recent article in *Bioscience Trends* (*Biosci Trends* 2019; DOI: 10.5582/bst.2019.01111) revealed a higher, not lower, level of β -human chorionic gonadotropin (hCG) and estrogen during the first 6 weeks of pregnancy, suggesting a novel association between β -hCG, estrogen, and threatened abortion. Unfortunately, this study was limited by its small sample size, unconvincing trial design, and inadequate exploration of the underlying mechanisms. This low-quality evidence indicates that a higher level of β -hCG and estrogen is associated with threatened abortion. However, that work provided some new insights for further studies of threatened abortion.

Keywords: β -human chorionic gonadotropin, estrogen, threatened abortion

Threatened abortion is defined as vaginal bleeding, a closed cervix, and the presence of the fetal heart beat (1). It is one of the most common complications of pregnancy, with an incidence of 20-25%, and can severely affect women's physical and emotional health (2,3). However, predicting threatened abortion is difficult because predictive methods are unreliable and because its underlying mechanisms are complicated. Hormone supplements including human chorionic gonadotropin (hCG), dydrogesterone, and estrogen are common treatments for threatened abortion, but their efficiency is a subject of debate (4). Thus, predicting and preventing threatened abortion is a challenge for clinicians, and its underlying mechanisms need to be explored.

An article entitled "Higher β -human chorionic gonadotropin and estrogen levels during the first 6 weeks of pregnancy are associated with threatened

abortion" was recently published in *Bioscience Trends* (*Biosci Trends* 2019; DOI: 10.5582/bst.2019.01111), and it interestingly revealed unexpected hCG and estrogen levels in patients with threatened abortion (5). The study described in that article analyzed the association between threatened abortion and the levels of pregnancy hormones in 220 patients (80 in the study group, 140 in the control group) in Obstetrics and Gynecology as part of a cross-sectional clinical trial. In statistical analysis, logarithm (Ln)-transformed variables were used instead of the original clinical values of β -hCG, estrogen, and progesterone in blood samples. Results indicated that β -hCG and estrogen levels in the first half of the first trimester are factors associated with threatened abortion, especially at gestational age ≤ 6 weeks. Although this study yielded novel findings, it was limited by its small sample size, less convincing trial design, and inadequate exploration of the underlying mechanisms behind threatened abortion.

Major flaws of that cross-sectional study are that it failed to observe the outcomes of the enrolled patients after the first trimester and it failed to describe the tendency of levels of pregnancy hormones to

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vary. Since pregnancy is an unstable and susceptible period and there are no reliable methods with which to diagnose threatened abortion, how that study defined threatened abortion is difficult to ascertain. For instance, patients with a threatened abortion may suffer a spontaneous abortion. Thus, higher β -hCG and estrogen levels in that study cannot be proved with certainty to be associated with threatened abortion. A case-control study with a larger sample size needs to be conducted in the future to explore the fluctuation in levels of pregnancy hormones in patients with threatened abortion. Live births, miscarriages, and still births should also be included in analysis. In addition, genetic testing of embryos should be performed to rule out unhealthy embryos as a cause.

The study analyzed the correlation between β -hCG, estrogen, and threatened abortion stratified by gestational age. When patients at a gestational age ≤ 6 weeks and at a gestational age > 6 weeks were compared, a clear association between higher levels of pregnancy hormone and threatened abortion was evident in the former. Significant differences in hormonal level between a gestational age ≤ 6 and a gestational age > 6 weeks is worthy of deep reflection and discussion. Based on the study's results, the first 6 weeks are believed to be an important period in pregnancy, and whether this period has physiological significance like that of the first trimester needs to be studied further.

The authors of the article offered possible interpretations of the higher β -hCG and estrogen levels, suggesting that abnormal spatio-temporal interaction in the maternal-fetal interface and stimulation of the maternal repair system by the imbalance in pregnancy hormone may explain this phenomenon. In a future study, luteinizing hormone (LH)/hCG receptors, trophoblastic cells, decidual cells, and immune cell subsets could be studied to explain the higher β -hCG and estrogen levels and to elucidate the mechanisms of threatened abortion. Generally, low levels of hCG, estrogen, and LH are considered to be a sign of adverse pregnancy. If high-quality evidence can prove that higher levels of higher pregnancy hormones are found in threatened abortion, this may be a new way to predict threatened abortion. Moreover, an hCG receptor antagonist and an hCG inhibitor to keep hormone levels stable may represent an appropriate tocolytic therapy, but its effectiveness needs to be demonstrated.

Although this clinical trial yielded a novel finding

of a correlation between levels of pregnancy hormones and threatened abortion not seen in a normal pregnancy, more high-quality evidence is needed to verify that finding in the future. On the bright side, this study offers new insights into the pathogenesis, diagnosis, and treatment of threatened abortion and it can encourage future studies to explore the underlying mechanism of that condition.

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