COMBINED APPLICATION OF PLACENTAL ALPHA MICROGLOBULIN-1 (PAMG-1) AND INSULIN-LIKE GROWTH FACTOR IN THE DIAGNOSIS OF PRETERM BIRTH - OUR RESULTS

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Abstract: Placental alpha microglobulin-1 (PAMG-1) is a human protein that was first isolated in 1975 from amniotic fluid. PAMG-1 is an important biomarker for detecting premature rupture of the amniotic membrane, as the high concentration of PAMG-1 in amniotic fluid means that there is a high risk of initiating labor.
The insulin-like growth factor IGFBP-1 is a binding protein (IBP-1), also known as placental protein (PP12), is encoded in people as IGFBP-1 gene. It is a particularly important hormone in female reproductive physiology. Its presence in large quantities in amniotic fluid is used as a biochemical marker of preterm birth.
The aim of the present study was to conduct retention therapy to reduce the risk of preterm birth by detecting the presence of the specific indicator plGFBP-1 in cervicovaginal secretions in the period 24 - 34 gestational weeks using two biochemical tests and to determine their prognostic value.
Material and methods. A prospective study was performed in the maternity ward of MHAT "St. Anna" - Varna AD in the period August 2021 - December 2021, including 120 pregnant women from Varna and the region. The gestation period of the examined patients is 24-34 gestational weeks. Respondents were divided into two main groups: group 1 - 60 pregnant women with clinical symptoms of preterm birth and group 2 - 60 women without clinical symptoms of preterm birth, with a history of preterm birth and increased risk. Both groups underwent two biochemical tests (Actim Partus and Parto Sure). All with positive tests were given retention therapy with Aleract, Gynipral and Utrogestan on a 30-day schedule.
The results of a study to determine pIGFBP-1 in 120 pregnant women show that 35.8% (43 women) tested positive, with 12.5% (15 women) giving birth before 37 weeks of gestation, despite applied tocolytic therapy. In both tests, the mean gestational age of the premature fetus was 32.5 ± 2.8 gestational weeks.
Keywords: premature birth, high risk, insulin-like growth factor

1. INTRODUCTION

Placental alpha microglobulin-1 (PAMG-1) is a human protein that was first isolated in 1975 from amniotic fluid. PAMG-1 is an important biomarker for the detection of premature rupture of the amniotic membrane as a high concentration of PAMG - 1 in the amniotic fluid means that there is a high risk of the labor process starting.
Parto Sure uses monoclonal antibodies sensitive enough to detect 4pg/ml of PAMG-1 in cervical exudate.
Placental alpha microglobulin-1 (PAMG-1) has been the subject of over 20 clinical studies, the majority of which are focused on the ability of the antigen-antibody response to detect premature fetal membrane rupture (ROM) in pregnant women from 22 to 36 weeks and to evaluate the ability of PAMG-1 to assess the risk of preterm delivery in pregnant patients with symptoms of preterm birth. The results of these studies suggest that the PAMG-1 test, may be a powerful predictor of impending preterm labour (PTL).
PAMG-1 is a protein that is produced during pregnancy and acts as a biological glue by keeping the amniotic sac attached to the endometrium, it can be detected in cervicovaginal secretions up to 22 weeks and later in the late last trimester (1 to 3 weeks before delivery). This protein is absent in the secretion between 24 and 34 weeks (5½ to 8½ month).
The test is performed between 24 and 34 weeks. The presence of PAMG-1 during these weeks, along with labor symptoms, suggest that the "glue" may be breaking down prematurely and signal a possible preterm birth. Detection of PAMG-1 in the vagina of a pregnant woman up to 22 weeks is normal. In a physiologically progressing pregnancy between 22 and 35 weeks, it should not be detectable in cervicovaginal secretions. Its presence is a highly informative biological marker for risk of preterm birth.
Brinkman A., Groffen C., Korteve DJ and others in 1989 found that IGFBP-1 is a particularly important hormone in female reproductive physiology, where together with other factors enters into a complex system that regulates the menstrual cycle, ovulation, fetal implantation and fetal growth. This has implications for clinical obstetrics, particularly when there is evidence for a pathophysiological role of IGFBP-1 in preeclampsia and intrauterine fetal retardation.

The presence of IGFBP-1 in large amounts in amniotic fluid is used as a biochemical marker of preterm birth and PROM (premature rupture of the amniotic sac). Quantitative analysis of insulin-like growth factor in serum or heparinized plasma serves to detect growth-related diseases. Insulin-like growth factor contains 70 amino acid residues with a molecular mass of 7.6490 daltons, its plasma levels are barely detectable after birth, rising gradually in childhood until reaching a maximum value during puberty. During pregnancy, its levels always rise.

2. PURPOSE

The aim of the present study was to conduct retention therapy to reduce the risk of preterm birth by detecting the presence of the specific indicator plGFBP-1 in cervicovaginal secretions in the period 24 - 34 gestational weeks using two biochemical tests and to determine their prognostic value.

3. MATERIALS AND METHODS

A prospective study was performed in the maternity ward of MHAT "St. Anna" - Varna AD in the period August 2021 - December 2021, including 120 pregnant women from Varna and the region. The gestation period of the examined patients is 24-34 gestational weeks. Respondents were divided into two main groups: group 1 - 60 pregnant women with clinical symptoms of preterm birth and group 2 - 60 women without clinical symptoms of preterm birth, with a history of preterm birth and increased risk. Both groups underwent both biochemical tests (Actim Partus and Parto Sure). All with positive tests received retention therapy with Aleract, Gynipral and Utrogestan on a 30-day schedule.

4. RESULTS AND DISCUSSION

Preterm birth is the cause of 70% of neonatal mortality and 50% of long-term neurological complications in newborns. Biochemical diagnostic tests in combination with cervical biometrics allow to establish a high risk of premature birth in the period 24 - 34 g.s. and timely administration of modern tocolytic therapy with Aleract, in which in 89.6% of cases the pregnancy is preserved (3).

In the group of 120 pregnant women with positive Parto Sure test results, there were 36 women (30%) at high risk of preterm birth. Despite the implemented tocolytic therapy, 15 (12.5%) of them delivered before 37 weeks.

The results of the study conducted to determine the pIGFBP-1 in 120 pregnant women showed that 35.8% (43 women) were positive. 15 of them (12.5%), despite therapy, gave birth before 37 weeks (fig. 1 and 2).

When comparing the results we can note that there is over 90% overlap of negative results and over 97% overlap of positive ones. Between the two tests was found a strong orthogonal relationship ($r = 0.84$; $p < 0.001$), indicating that a higher percentage of negative results in one test leads to a high percentage of the same readings in the other.

Comparison of the results of the two tests in parturients with clinical symptomatology, showed that there is a difference in terms of test readings ($p < 0.001$), i.e. in case of a negative result for the Actim Partus test, all pregnant women also gave a negative result for the Parto Sure test, while in case of a positive result for the first test, we had 3 patients who gave a negative result for the Parto Sure test (fig. 3).

In the asymptomatic group, we had some discrepancy in the results ($p < 0.001$), i.e. we had 1 positive parturient for the Parto Sure test with a negative result for the Actim Partus test, and with a positive result from the last test, we observed 5 pregnant women with a negative result for the Parto Sure test (fig. 4).

Fig. 1. Result of Actim Partus test

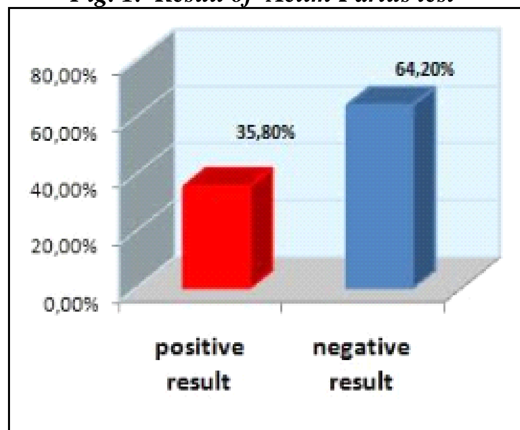


Fig. 2. Result of Parto Sure test

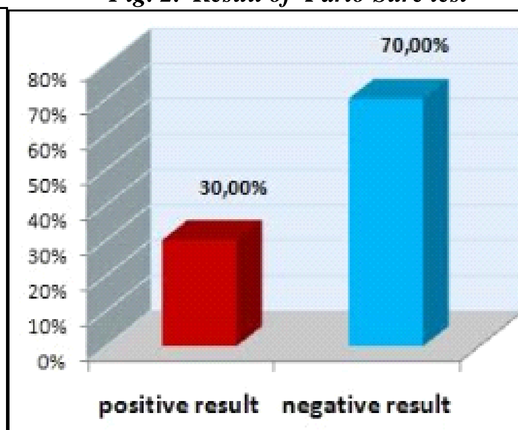


Fig. 3. Results of the Parto Sure test and Actim Partus test in clinical symptomatology

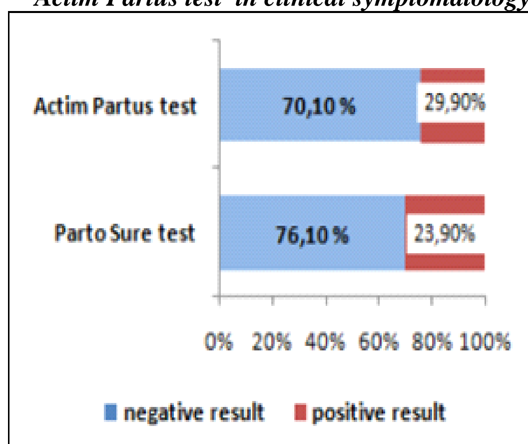
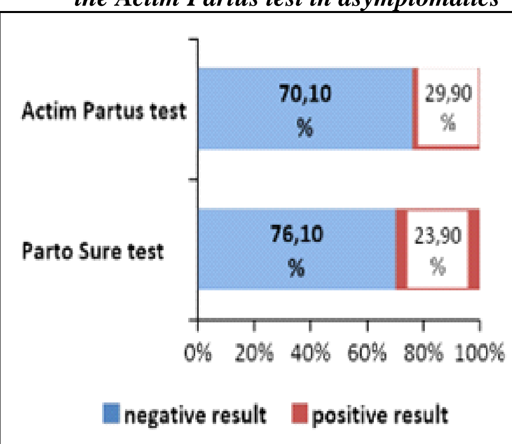


Fig. 4. Results of the Parto Sure test and the Actim Partus test in asymptomatics



Patients who had positive results of both tests showed a significant difference in newborn weight in the presence of clinical symptomatology ($p < 0.001$), i.e. pregnant women with clinical symptoms of preterm birth gave birth to approximately 500 g lower birth weight infants (mean infant weight in patients without symptoms was 2 800 g and mean infant weight in women with symptoms was 2 300 g).
There was also a difference in the gestational age of the fetus ($p < 0.001$); pregnant women with positive test results and the presence of symptoms gave birth approximately 3 weeks earlier, which puts them in the group of preterm births (mean gestational age in patients without symptoms was 37 weeks and in women with symptoms 34 weeks).
In contrast to the Parto Sure test in Actim Partus, we had a categorical sensitivity rate for the risk of preterm birth by day 14 in all three groups of pregnant women, indicating that a positive test result guarantees the occurrence of preterm birth (tab. 1).

Tab. 1. Specificity and sensitivity of the Actim Partus test

Indicator	Up to 7th day		Until the 14th day	
	Sensitivity	Specificity	Sensitivity	Specificity
Total all parturients	100	67	100	71
Pregnant women with clinical symptomatology for IP	100	63	100	69
Asymptomatic pregnant	30	70	100	71

In the results for the occurrence of preterm birth by day 7, as in the Parto Sure test, we had a low probability of the risk of preterm birth. That gave us reason to believe that in the interval up to 7 days the two tests gave us overlapping information on the occurrence of preterm birth.

5. CONCLUSION

In clinical practice, we often encounter pregnant women with clinical symptoms of preterm birth when we need to predict the onset of labour and need to assess the possibility of delaying or postponing labour until the maximum favourable gestational week is reached.
The application of rapid immunochromatographic tests in the period from 24 to 34 weeks, complemented by cervical biometry, allows us to differentiate high-risk parturients and take the necessary therapeutic measures to prevent preterm birth in an extremely short period of time - 10 to 15 min.
The results of the analysis of the two tests show that there is an overlap of values, which gives us reason to believe that they have a high predictive value for determining the risk of the occurrence of preterm birth.

When comparing our test data with those from international studies, we concluded that both tests are characterized by high sensitivity and specificity, which gives us reason to believe that the positive and negative values are sufficient grounds to accept or reject the risk of the occurrence of preterm birth.
Using biochemical diagnostic tests in combination with cervical biometry, we can determine with certainty in more than 95% of cases the presence of risk of preterm birth and the appointment of appropriate tocolytic therapy.

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