Insulin-like growth factor-binding protein-1 (IGFBP-1) in cervical secretions in women with symptoms of preterm delivery

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ABSTRACT

The aim of this prospective study was to investigate a value of insulin-like growth factor-binding protein-1 (IGFBP-1) in cervical secretion in women with symptoms of preterm delivery and correlate this test to the Bishop Score in prediction of a preterm delivery. The study group included 30 pregnant women with singleton pregnancy between 24 – 34 gestational weeks who were hospitalized because of a threatening preterm delivery with intact fetal membranes. A positive Actim Partus test (concentration higher than 10 µg/l) and Bishop Score higher than 4 signify a risk of the preterm delivery. The Bishop Score is a better predictor of the preterm delivery in patients with symptoms of the preterm delivery.

Key words: Insulin-like growth factor-binding protein-1 (IGFBP-1), preterm delivery, preterm rupture of the membranes (PROM)
INTRODUCTION

Preterm birth is a delivery of a baby before 37 completed weeks gestation. Over the past 20-30 years the incidence of preterm birth in the most developed countries has been about 5-7% of live births (1). Insulin-like growth factor-binding protein-1 (IGFBP-1) has been proposed to be an endometrial and decidual molecule (2). In the cases of preterm rupture of membranes (PROM), IGFBP-1 is found in cervical secretions (3). A commercial strip test has been developed for its detection which resulted in some published data on its predictive value related to preterm rupture of membranes (4). The sensitivity and specificity of the test is very high (94-100% and around 95%, respectively (4). In clinical applications 74% sensitivity has been documented (5, 6). So far there has been no convincing evidence that phosphorylated IGFBP-1 determinations in cervical secretions can predict preterm birth, especially before preterm rupture of the membranes (PROM). It has been postulated that by combining different markers (interleukin 6, fibronectin) the prediction of preterm birth could be improved (3, 7).

The aim of this study was to investigate value of insulin-like growth factor-binding protein-1 (IGFBP – 1) in cervical secretion in women with symptoms of preterm delivery and to investigate correlation of this test to the Bishop score in prediction of the preterm delivery.

MATERIALS AND METHODS

During 2006 a prospective study at the Gynaecology and Obstetrics Department of the University Clinical Centre in Tuzla was conducted. The study group included 30 pregnant women with singleton pregnancy between 24 – 34 gestational weeks who had been hospitalized because of a threatening preterm delivery with intact fetal membranes. All examinees were between 18 and 35 years old. Exclusion criteria were as follows: chronic diseases, (hypertension, diabetes, renal or cardiac diseases), genital tract anomalies of the mother, genetic or anatomical defects of the fetus, previous preterm deliveries.

Interrviews based on a template requesting information about age, number of previous births and miscarriages, previous preterm births, number of ante-natal checkups and ultrasound examinations was conducted.

The concentration of IGFBP-1 in cervical mucus was estimated by a Actim Partus test (Medix Biochemica, Finland) according manufacture’s instructions.

The test was considered positive if the concentration of IGFBP-1 in cervical mucus was higher than 10 µg/L.

The Bishop score was determined according to previously accepted scoring system published in 1964. (8).

Statistical analysis of information was done in the Data Desk Version 6.0, Wisconsin USA. Statistical importance was determined at the variation level of 5% and 1%.

RESULTS

The study group covered 30 women with symptoms of preterm delivery, 19 primiparas and 11 multiparas. The average age was 25,10 ±5,18 years. The mean gestation age of pregnancy at the time of testing in the study group was 31,17 ±1,87 gestation weeks. Twenty (66,67%) examinees in the study group had positive Actim Partus test and 15 examined women (50%) had preterm delivery.

Table 1 shows the Bishop score according to the results of Actim Partus test.

Table 1. Bishop score and the results of Actim Partus test for examinees with symptoms of preterm delivery

<table>
<thead>
<tr>
<th>Bishop score</th>
<th>No of positive (%)</th>
<th>No of negative (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-4</td>
<td>2 (6.67)</td>
<td>4 (13.33)</td>
<td>6 (20.00)</td>
</tr>
<tr>
<td>5-7</td>
<td>12 (40.0)</td>
<td>6 (20.00)</td>
<td>18 (60.00)</td>
</tr>
<tr>
<td>&gt;7</td>
<td>6 (20.00)</td>
<td>0 (0)</td>
<td>6 (20.00)</td>
</tr>
<tr>
<td>Total</td>
<td>20 (66.67)</td>
<td>10 (33.33)</td>
<td>30 (100.00)</td>
</tr>
</tbody>
</table>

The results of Actim Partus test point to the time of delivery ($X^2$=5.10, p=0.024). Sensitivity
of the test was 80\%, and specificity of the test 53.33\%. Positive predictive value was 65.00\% and negative predictive value 80.00\%.

Sensitivity of the Bishop score was 93.33\% and specificity was 33.33\%. Positive predictive value was 58.33\% and negative predictive value 83.33\%.

In the group of examinees sensitivity of the Bishop score in relation to the Actim Partus test was 90.00\% and specificity was 40.00\%. Positive predictive value of the Bishop score was 75.00\% and negative predictive value was 66.67\%.

In the study group correlation between the Bishop score and Actim Partus test was positive (p=0.45; p<0.05).

Multiple regression analysis between the Bishop score and Actim Partus tests has shown that the Bishop score was a better predictor of the preterm delivery with statistical significance (p=0.003)

DISCUSSION

For women with symptoms of premature delivery, sensitivity and positive predictive value of the Actim Partus test (80\% and 65\% respectively) was in accordance with information obtained from different authors: the comparison of fetal fibronectin and IGFBP-1 reliability in predicting premature deliveries has shown that sensitivity of IGFBP-1 was higher (78\%) than that of fibronectin (76\%) and positive predictive value of these tests was 66\% and 61\%, respectively (12,13). The results of other studies have shown that for pregnant women who had symptoms of premature delivery the sensitivity and specificity of these tests was 80\% and 77\%, respectively (10, 12). Similar results about reliability of determining concentration of IGFBP-1 in cervical mucus of pregnant women with symptoms of premature delivery were also found by others (13, 14). The results of this study (specificity of the Actim Partus test was 53.33\% and the negative predictive value 80\%) have proved that women who had a negative Actim partus test had little chance for premature delivery. A determination of IGFBP-1 concentration in cervical mucus (Actim Partus test) is a reliable indicator of premature delivery for women who have symptoms of premature delivery which obliges us to take all therapeutic measures in order to prevent or postpone premature delivery. Using the Actim Partus test we would be able to significantly avoid unnecessary interventions and reduce the costs of treatment (9-11).

Sensitivity of the Bishop score and positive predictive value (90\% and 75\%, respectively) in the group of women with symptoms of premature delivery in our study indicated that the Bishop score was a reliable indicator of premature delivery in this group. But, low specificity and negative predictive value (66.67\%) indicated that the low Bishop score was not reliable in giving prediction, i.e. we cannot rule out the possibility of premature delivery. In the group of women with symptoms of premature delivery, correlation between the two tests was positive (statistically significant) which means that the positive Actim Partus test and high Bishop score have shown a high risk of premature delivery. Some authors have noted a value of these tests in order to predict of premature delivery (15-18) which is in accordance with the results of our study.

In conclusion, IGFBP – 1 in cervical secretion (concentration greater than 10 µg/l) can be used as a predictor of preterm delivery, but the Bishop score greater than 4 is a better predictor of preterm delivery in symptomatic pregnant women.

We are aware of limitations of our study. We did not compare predictive value of IGFBP-1 with predictive values of other markers (fetal fibronectin, interleukin-6, somatomedin) in prediction of preterm delivery. But, this is the first prospective study in Bosnia and Herzegovina about a role of IGFBP-1 in prediction of preterm delivery and further studies should be done in order to better define a connection of other markers in the prediction of preterm delivery.
REFERENCES