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Prediction of preterm birth using PAMG-1 test: a single centre experience — preliminary report

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ABSTRACT

Objectives: Placental alpha microglobulin-1 (PAMG-1) is a novel biomarker detected in cervicovaginal discharge in patients threatened with preterm birth (PTB). This study aimed to show a single centre experience of assessment of imminent spontaneous PTB risk in patients with symptoms suggesting preterm labour (PTL).

Material and methods: The study group consisted of 46 women with singleton pregnancies between 24 + 0/7 and 33 + 6/7 weeks of gestation who presented with symptoms of threatened PTL, with cervical dilatation of < 3 cm, cervical length (CL) of < 30 mm and clinically intact fetal membranes. CL was measured via transvaginal ultrasound and the PAMG-1 test was performed in all of the objectives.

Results: Sensitivity (SN), specificity (SP), positive predictive value (PPV) and negative predictive value (NPV) of prediction of PTB within seven days for CL were 100%, 11.11%, 5.88% and 100%, respectively. The PAMG-1 test SN, SP, PPV and NPV of the same endpoint were 50%, 80.56%, 12.5% and 96.67%, respectively.

Conclusions: PAMG-1 is a more accurate predictor of PTB when compared to CL. Routine use of both mentioned tests could allow identification of low-risk patients and reduction of rate of unnecessary hospitalizations and treatments.

Key words: preterm birth, preterm labou; placental alpha microglobulin-1 (PAMG-1); PartoSure; cervical length (CL)

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INTRODUCTION

Preterm birth (PTB) is a delivery between 22 + 0/7 and 36 + 6/7 weeks of gestation and is one of the most frequent complications occurring during pregnancy. Preterm labour (PTL) is manifested via regular uterine contractions leading to the cervical shortening or effacement. It affects approximately 5–18% of pregnancies worldwide [1] and is a leading reason of neonatal mortality and morbidity [2, 3]. Predisposing factors of PTB are: multiple pregnancy, uterus anomaly, previous PTB, cervical insufficiency, ethnicity, low socio-economic status, maternal weight, smoking, periodontal status [4]. Accurate prediction of PTB remains a challenge, whereas more than 2/3 of symptomatic patients do not go on to deliver within seven days from the onset of symptoms [5, 6]. It leads to partly unnecessary admissions to hospital and administrations of tocolytics and antenatal corticosteroids [7], which are not devoid of its adverse consequences [8, 9].

The most widely used but also not the most accurate tool to assess likelihood of PTB is cervical length (CL) measurement via transvaginal ultrasound examination. There are several novel biomarker tests commercially available, based on fetal fibronectin (fFN), phosphorylated insulin-like growth factor-binding protein-1 (phIGFBP-1) and placental alpha microglobulin-1 (PAMG-1) concentrations in cervicovaginal discharge. The most promising test out of the mentioned three seems to be PAMG-1, with reported relatively highest values of sensitivity (SN), specificity (SP), positive predictive value (PPV) and negative predictive value (NPV) [10–15].

Objectives

This study aimed to show a single centre experience of the Clinical Department of Perinatology, Gynaecology and Obstetrics in Ruda Śląska, Poland of using PAMG-1

(the PartoSure Test) in assessment of imminent spontaneous PTB risk in patients with symptoms suggesting preterm labour.

MATERIAL AND METHODS

The prospective study was performed in the period between June 2018 and July 2019 at the Clinical Department of Perinatology, Gynaecology and Obstetrics in Ruda Śląska, Medical University of Silesia, Poland. Forty-six patients, who presented with uterine contractions, were recruited into the study. Inclusion criteria were age of 18 years and above, gestational age between 24 + 0/7 and 33 + 6/7 weeks, CL of < 30 mm in transvaginal ultrasound examination, cervical dilatation of < 3 cm, clinically intact fetal membranes and absence of vaginal bleeding at presentation. As exclusion criteria were used: previous tocolytic therapy, intercourse within the past 24 hours before examination, cervical cerclage or pessary, placenta praevia, multiple pregnancy and patient's disapproval of participation in the study.

A patient who presented to the Department with symptoms of threatened PTL was firstly screened for exclusion criteria, asked for informed consent and then recruited to the study group. A sample for the PAMG-1 test was collected accordingly to the manufacturer's instructions. Then, clinical examination and transvaginal ultrasound with CL measurement were performed as well as the patient's medical history was collected. The objectives of this study were admitted for a minimum 7-day clinical observation and possible in-patient treatment. A test-to-spontaneous-delivery interval was calculated for all patients.

RESULTS

There were 46 patients included into the study group initially. Seven were excluded from the final analysis due to lack of follow-up data on the delivery and one due to equivocal PAMG-1 test result, thus 38 objectives represented the study group. The mean age was 30.08 ± 5.37 years, the mean gestational age at presentation was 28.61 ± 2.73 weeks. A total of 15.79% (4) of the patients had a history of PTB, 28.95% (10) of miscarriage (before 22+0/7 weeks of gestation), 34.21% (13) were taking vaginal progesterone treatment.

Table 1. Summary of CL measurements and deliveries within 7 and 14 days of presentation

CL < 25 mm	Delivery ≤ 7 days		Delivery ≤ 14 days	
	+	−	+	−
+	2 (5.26%)	32 (84.21%)	3 (7.89%)	31 (81.58%)
−	0	4 (10.53%)	0	4 (10.53%)

Table 2. Summary of the PAMG-1 test results and deliveries within 7 and 14 days of presentation

PAMG-1	Delivery ≤ 7 days		Delivery ≤ 14 days	
	+	−	+	−
+	1 (2.63%)	7 (18.42%)	1 (2.63%)	7 (18.42%)
−	1 (2.63%)	29 (76.32%)	2 (5.26%)	28 (73.68%)

In total 5.26% (2) of the patients delivered within seven days of presentation and 7.89% (3) within 14 days. The mean value of CL was 16.39 ± 6.44 mm. 92.11% (34) of the objectives were evaluated as those with a short cervix (CL < 25 mm), while only two delivered within 7 days and three delivered within 14 days of presentation (Tab. 1). In total, 21.05% (8) of the study group had a positive result of the PAMG-1 test, out of which one delivered within 7 days of presentation (Tab. 2).

Prediction of delivery within 7 days of testing using CL measurement had sensitivity (SN) of 100%, specificity (SP) of 11.11%, positive predictive value (PPV) of 5.88% and negative predictive value (NPV) of 100%. SN, SP, PPV and NPV of CL measurement for prediction of delivery within 14 days of testing were 100%, 11.43%, 8.82% and 100%, respectively. The PAMG-1 test had SN of 50%, SP of 80.56%, PPV of 12.5% and NPV of 96.67% of prediction of delivery within 7 days of testing. Its SN, SP, PPV and NPV of prediction of delivery within 14 days of testing were 33.33%, 80%, 12.5% and 93.33%, respectively (Tab. 3).

A test-to-spontaneous-delivery interval ranged from 0 to 109 days, with a mean value of 58.79 ± 28.32 days.

Table 3. Performance of CL measurement and the PAMG-1 test of prediction of spontaneous preterm delivery within 7 and 14 days

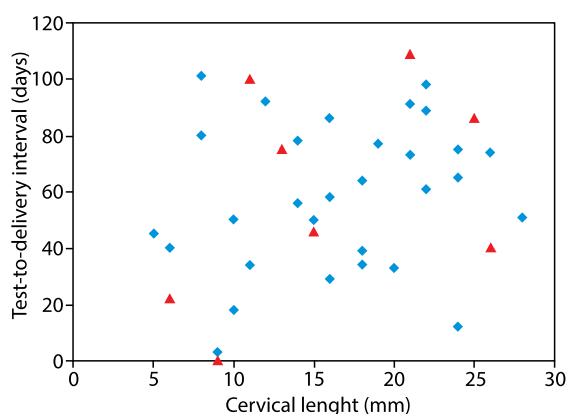|	Sensitivity	Specificity	Positive predictive value	Negative predictive value
Delivery ≤ 7 days				
CL < 25 mm (95% CI)	100% (15.81–100%)	11.11% (3.11–26.06%)	5.88% (5.28–6.56%)	100%
PAMG-1 (95% CI)	50% (1.26–98.74%)	80.56% (63.98–91.81%)	12.5% (2.98–39.92%)	96.67% (87.78–99.15%)
Delivery ≤ 14 days				
CL < 25 mm (95% CI)	100% (29.24–100%)	11.43% (3.2–26.74%)	8.82% (7.91–9.83%)	100%
PAMG-1 (95% CI)	33.33% (0.84–90.57%)	80% (63.06–91.56%)	12.5% (2,47–44.68%)	93.33% (86.08–96.94%)

Figure 1. Cervical length (mm) and test-to-spontaneous-delivery interval in the study group. ▲ — positive result of PAMG-1 test; ◆ — negative result of PAMG-1 test

Additionally, there was found no statistically significant correlation between CL and the test-to-spontaneous-delivery interval (p = 0,1253) (Fig. 1).

DISCUSSION

In the study group only 5.26% of patients presenting with symptoms suggesting PTL went on to deliver within 7 days. According to the literature, rate of PTB within 7 days of presentation in symptomatic patients ranges from 1.8 to 29.7% [5, 6]. It shows that screening for patients truly endangered with PTB is still very poor and leads to partially unnecessary admissions to hospital and treatments [16]. Empana et al. [7], revealed that 85% of European centres administer multiple courses of antenatal corticosteroids. Although it is proven to be a treatment that promotes neonatal lung maturation, uncontrolled use of corticosteroids may lead to several neonatal adverse consequences, such as respiratory distress syndrome [8] or delay in myelination in the central nervous system [9].

Assessment of likelihood of PTB within 7 days with CL measurement via transvaginal ultrasound in the study group is characterized by high SN and NPV but also very low SP and PPV. Performance of CL measurement in the literature is also unsatisfactory, with SN, SP, PPV, and NPV values of 57%, 73%, 89% and 30%, respectively [11] and proves CL to be an inaccurate tool in prediction of imminent PTB.

As expected, the PAMG-1 test in the study group obtained a much higher value of SP and similar value of NPV of PTB prediction within 7 days when compared to CL. SN and PPV values of the PAMG-1 test in the study group were not consistent with the literature [17], most likely due to a small size of the group. Nevertheless, obtained data show that PAMG-1 is a superior predictor of imminent PTB than CL.

Since the prediction of PTB in symptomatic patients is still a challenge for clinicians, it needs to provide focus on more efficient screening for patients truly threatened with PTL. Combination of routine CL measurement and the PAMG-1 test could allow identification of patients at low risk of imminent PTL and reduction of rate of unnecessary hospitalizations and antenatal corticosteroids administrations. It would be beneficial not only for patients but also for the healthcare system budget.

CONCLUSIONS

Our centre experience of predicting imminent spontaneous PTB using the PAMG-1 test is consistent with currently available literature. It shows that the PAMG-1 test is more accurate in assessment of likelihood of PTB than CL measurement. Therefore, routine use of this test should be recommended in order to identify low-risk patients.

Conflict of interest
All authors declare no conflict of interest.

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