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The assessment of selected parameters of bioelectric and mechanical activity of the uterus during pharmacologic treatment of threatening preterm delivery

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ABSTRACT

Objectives: To analyze and compare the bioelectric and mechanical activity of the uterus in pregnant women with threatening preterm delivery treated with tocolysis. Additionally, auxiliary parameters of the bioelectric signal, as registered by electrohysterography and characteristic only for this method, were measured and analyzed.

Material and methods: Forty-five women with pregnancies from 24 to 36 weeks of gestation with typical clinical symptoms of threatening preterm delivery were given tocolytic therapy. Registration and analysis of bioelectric activity with electrohysterography was performed simultaneously with registration and analysis of mechanical activity with tocography.

Results: After administration of tocolytic treatment, the presence of bioelectric activity was accompanied by the lack of or minimal occurrence of mechanical activity. All parameters of contraction recorded by electrohysterography had significantly greater values than those recorded by tocography.

Conclusions: Measurement of bioelectric activity is more sensitive than measurement of mechanical activity of the uterus. Elevated bioelectric activity of the uterine muscle was observed despite the use of tocolysis, a lack of symptoms of threatening preterm delivery, as well as a lack of contraction in tocography. The presence of bioelectric activity may precede the occurrence of mechanical activity of the uterus, but further research is required on larger groups of patients.

Key words: electrohysterography; tocography; uterine constrictions; preterm delivery; tocolysis

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INTRODUCTION

Despite huge advances in perinatal medicine, the frequency of premature deliveries is part of a continuously increasing trend. Preterm births account for 9.6% of all deliveries. Prematurity constitutes one of the most important causes of neonatal mortality and currently, it is among the most difficult health care problems worldwide [1].

The great number of factors that may cause uterine contraction activity makes prophylaxis or the creation of proper therapeutic management challenging despite the constant development of diagnostic methods. It must be noted that the physiology of contraction activity of the pregnant uterus is still poorly understood and is the subject of many scientific studies [2]. As a result, it is necessary to make a diagnosis of threatening preterm delivery before the onset of the mechanical activity of the uterus which would lead to cervical effacement and cervical dilation. Regardless of the etiologic factor leading to premature delivery, the basic mechanism responsible for the occurrence of contraction activity of the uterus tied to the 200 billion cells of smooth muscle tissue which undergo hypertrophy while adapting during pregnancy, remains unclear [3, 4]. In the process of generating a functional electrical current, each of the those 200 billion cells becomes an individual pacemaker and transmitter, and thus an action potential may be produced in any part of the uterine muscle cell in various locations. From the physiology, it appears that the uterine contraction wave originates in the uterine horns near the uterine ostium of the fallopian tubes. As the wave propagates from the ostium of the tube to the cervix, its

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intensity decreases. The magnitude of uterine muscle stimulation depends on the number of gap junction intercellular channels, which are responsible for the metabolic and functional contact between cells. The number of gap junctions increases as the pregnancy advances, with the greatest number being observed at term [5].

Classic and widely used external tocography allows obstetricians only to detect and monitor the final effect of very complicated biochemical and electrophysiological processes, such as the contractions of the uterus. It must be remembered that tocography as a diagnostic method is used in nearly all obstetric hospitals worldwide; however, it does not allow for measurement of the bioelectric signal (electrohysterogram), which is the primary source of contractile activity of the uterus. Because sensors can be placed all over the surface of the maternal abdominal wall in electrohysterography (EHG), it can determine the source and paths of propagation of separate contractions, which classic tocography (TOCO) cannot do.

EHG was introduced in two studies by Steer and Hertsch in 1950 as a method of measurement of bioelectric activity of the uterus [6]. It can be used not only to diagnose threatening preterm delivery but also as a method of monitoring uterine contraction activity during labor [7, 8]. In comparison to TOCO, EHG allows for faster and more precise registration of bioelectric activity as it covers almost the whole surface of the uterine muscle. Additionally, it can determine characteristics of the contractions such as dynamics, place of origin and propagation pattern [9]. Another important aspect in diagnosing threatening preterm delivery is that the bioelectric activity of the muscle of the uterine fundus occurs before an increase in the intrauterine pressure but at the same time as the electric activity of the cervix [10].

Threatening preterm delivery is characterized by diversified clinical symptoms. Pregnant women may experience pain of varying intensity, which often is difficult for patients to localize. Non-specific symptoms make the decision about tocolytic treatment difficult. It should be emphasized that in many cases the diagnosis of threatening preterm delivery is completely groundless and, as a result, tocolytic therapy is being used on healthy subjects, creating a complicated clinical problem. Measuring bioelectric activity of the uterine muscle with EHG in cases of where different types of tocolytic therapy are being used (among them: beta adrenergic receptor agonists, calcium channel blockers, oxytocin receptor antagonists) might be helpful in monitoring the results of the therapy as well as determining its duration and the proper drug dosage.

In our study, we performed an analysis of the bioelectric activity of the uterine muscle during tocolytic treatment, which allowed us to evaluate the impact of tocolysis on contractile activity of the uterus, as registered on EHG recordings. Tocolytic drugs reduce intracellular calcium concentration in the myometrial cells, which activates cyclic adenosine monophosphate (cAMP), which then blocks the production of prostaglandins or the oxytocin receptor directly. The final effect of above-mentioned processes is the hampering of the actin-myosin interaction, thus making cells of the uterine muscle unresponsive to stimulation [11].

Aim of the study

The aim of the study was to analyze and compare the bioelectric and mechanical activity of the uterus in pregnant women with threatening preterm delivery treated with tocolysis. Additionally, auxiliary parameters of the bioelectric signal, as registered by EHG and characteristic only for this method, were measured and analyzed.

MATERIAL AND METHODS

The study group consisted of 45 women whose pregnancies ranged from 24 to 36 weeks of gestation who were hospitalized in the II Department of Obstetrics and Gynecology of the Wrocław Medical University. All patients had singleton pregnancy with vertex presentation of the fetus. All patients also presented clinical symptoms of threatening preterm delivery, such as lower abdominal or lower back pain, vaginal bleeding or cervical effacement. Patients presenting symptoms of threatening preterm delivery were given the following medications: beta adrenergic receptor agonists, calcium channel blockers and progesterone.

Pregnant women were simultaneously subjected to diagnosis of mechanical (TOCO) and bioelectric (EHG) contractile activity of the uterine muscle. The fetal surveillance system MONAKO (ITAM, Zabrze, Poland) and system for registration and analysis of bioelectric activity KOMPOREL (ITAM, Zabrze, Poland) were used to simultaneously register and analyze the activity of the uterus.

All the pregnant women were informed about the study procedures and gave written informed consent to participate in the study. The study was approved by the Commission of Bioethics at Wroclaw Medical University.

KOMPOREL is a measurement system using an external bioelectric signal recorder and a computer. It allows for the simultaneous registration of four signals (electrohysterograms) of electric uterine activity with measuring sensors located on the surface of the maternal abdomen. Collected bioelectric signals were processed into a digital form, transmitted to the computer system, analyzed, presented graphically on a computer screen, and stored by the KOMPOREL software. The analysis was performed based on four EHG signals and used to determine the slow frequency component of the contraction that corresponds to the TOCO signal, which then served as the basis for detecting contractions and determining their basic descriptive parameters [12]. Mechanical activity of the uterus (TOCO) was registered by the MONAKO system connected to the traditional fetal and maternal monitor Avalon FM20 (Philips, Eindhoven, Netherlands). The TOCO signal was obtained with a tensiometric sensor placed on the maternal abdomen and registered by a tocograph. Next, the signal was transmitted by a transmission system to the computer for quantitative analysis (detection of contractions and calculation of their descriptive parameters).

The analysis of registered mechanical and bioelectric activity examined the following parameters of contractile activity [12]: contraction rate (R), defined as the number of detected contractions per 10 minutes; duration of contractions (TD); duration of maximal contractile amplitude (TA); surface (S); and contraction amplitude (A). Additional analysis was performed on a contraction parameter characteristic only for bioelectric activity, contraction intensity (I), as well as on a set of parameters from the analysis of the frequency domain: power (P), median frequency (Fmed) and frequency of maximum contractile power (Fmax) [13, 14]. A model of contraction wave is presented on Figure 1.

First, the duration of mechanical and bioelectric activity of the uterine muscle was compared. Next, the mean, standard deviation, median, and maximum and minimum values were calculated for the analyzed variables. Comparative analysis of the mean values between the corresponding parameters was also performed. Normality of distribution of the contraction parameters was verified using the Shapiro-Wilk test. Before the statistical analysis, variance equality was confirmed with the F-test. For sets of data with a normal distribution, the significance of difference between mean values was analyzed with Student's t-test. In case of significant differences in variances, a modified Student's t-test called Welch's t-test was employed. For variables with a non-Gaussian distribution, the nonparametric Mann-Whitney U test was used. The criteria for statistical significance were set at $p < 0.05$ and $p < 0.001$. Statistical analysis was carried out with Statistica software v. 5.5 (StatSoft, Tulsa, OK, USA).

RESULTS

The mean duration of recordings was almost 32 minutes (1906 s) and the total duration of recordings was 24 hours and 21 minutes (87691 s). All parameters of contraction — such as the mean and maximal contractile amplitude, rate and duration of contractions, and mean surface of contractions — recorded by EHG had significantly greater values than those recorded by TOCO. Further analysis was performed for parameters such as contraction intensity, power, median frequency and frequency of maximum contractile power. The values of descriptive parameters of contractions calculated both for the bioelectric and mechanical signals, along with their comparative analysis as well as values of auxiliary parameters for contractions as assessed by measuring the bioelectric signal are presented in Table 1.

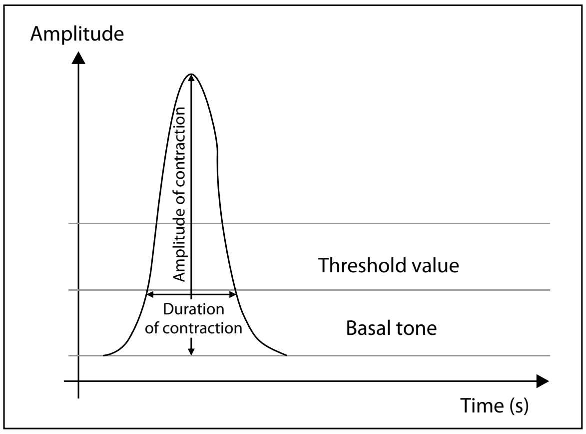

Figure 1. A model of contraction wave. The figure was adapted from Zietek J, Sikora J, Horoba K, et al. [Mechanical and electrical uterine activity. Part II. Contractions parameters. Ginekol Pol 2008; 79 (11): 798–804]

None of the pregnant women reported any side effects.

DISCUSSION

In perinatal medicine, new diagnostic tools which enable the identification of pregnancies with a high risk of preterm contractile activity of the uterus are constantly being sought. In our study, we compared two methods of detecting contractile activity of the uterus. We found that measurement of bioelectric activity is more sensitive than measurement of mechanical activity of the uterus. Additionally, the presence of bioelectric activity precedes the occurrence of mechanical activity of the uterus. We also observed the presence of bioelectric activity along with an absence of or minimal occurrence of mechanical activity in women undergoing tocolytic treatment.

As prematurity is the major cause of neonatal morbidity and mortality, tools for predicting premature labor are needed [15]. The basic diagnostic tool for the assessment of the contractile activity of the uterus is external tocography, which is a subjective examination tool. The very low sensitivity of tocography has encouraged researchers to search for more sensitive diagnostic methods. One of the alternatives is the assessment of bioelectric activity in the uterus, which can be detected starting at 19 weeks of gestation [10, 16]. Our study included only pregnant women at 24 weeks of gestation and above. In this group, a bioelectric signal was easy to detect in all patients. An additional advantage of EHG is its effective detection of contractions during labor [17, 18].

Contractions of the uterine muscle are induced by myogenic stimulation, which leads to a change in potential in muscle cell membranes. The rise in bioelectric voltage is the effect of the difference in the concentration of ions between the extracellular space and those inside myocytes. In the

Table 1. Comparison contraction parameters based on analysis of mechanical and bioelectric activity of the uterine muscle with characteristics of contractions based on analysis of bioelectric activity of the uterine muscle

Parameter	Mean	SD	Median	Min	Max	Significance
Xomparison of contraction parameters — mechanical and bioelectric activity						
R_{EHG} [l/10 min]	2.19	0.82	2.281	0.3920	4.9	$p < 0.001$
R_{TOCO} [l/10 min]	1.39	1.08	0.939	0.2560	3.9	
T_{D_EHG} [sek]	83.86	22.13	80.493	41.1000	130.3	$p < 0.05$
T_{D_TOCO} [sek]	66.38	26.14	59.632	32.5000	149.8	
T_{A_EHG} [sek]	43.99	12.11	45.247	24.3750	70.2	$p < 0.05$
T_{A_TOCO} [sek]	33.27	17.55	33.125	11.5000	107.8	
A_{EHG} [µV]	96.61	106.38	56.325	0.1590	453.1	$p < 0.001$
A_{TOCO} [–]	15.01	10.31	11.560	5.0300	50.9	
S_{EHG}	5301.38	6253.42	2603.055	11.9870	24226.4	$p < 0.001$
S_{TOCO}	656.63	549.79	458.925	134.5000	2522.5	
Descriptive statistics of auxiliary parameters — bioelectric activity						
I_{EHG} [l/1 min]	14.79	5.33	14.227	3.9290	30.5	
P_{EHG} [µV^2]	12412.06	23779.87	3240.189	0.0210	141666.6	
F_{MED_EHG} [Hz]	0.30	0.36	0.160	0.1140	1.7	
F_{MAX_EHG} [Hz]	0.22	0.29	0.118	0.0660	1.5	

A — contraction amplitude; EHG — electrohysterography; Fmax — frequency of maximum contractile power; Fmed — median frequency; I — contraction intensity; P — power; R — contraction rate; TA — duration of maximal contractile amplitude; TD — duration of contractions; TOCO — tocography; S — surface

resting state, the value of bioelectric voltage ranges from 65 to 80 mV [19]. Stimulation leads to an increase in the permeability of the cell membrane for sodium ions and thus to the flow of the sodium ion current, which results in an increase in the amount of positively charged sodium ions inside the cell and a decrease in membrane potential. When a threshold potential is reached (from –40 to –60 mV), stimulation of the cell and a further increase in the amount of intracellular positive ions occurs — this last for about 1 ms. Because potassium ions rush out of the cell, the cell membrane again becomes charged to about +20 mV, creating an action potential which stimulates contraction [16]. Action potentials initiate contractions that then propagate along the uterine muscle. The pattern, direction and speed of electrical activity change as the pregnancy advances [20].

Parameters of the bioelectric signal from the uterus itself or in comparison with other methods may help in predicting delivery but attempts to find associations among the bioelectric parameters of uterine contractions gave inconclusive results. Aviram et al. [21] found a significant difference between contraction rate and time to delivery. Kandil et al. observed significant differences in the duration of electrical bursts and the amplitude of action potentials between women in active labor and those not in labor, while other researchers found the amplitude of measurements not to be predictive for preterm labor [22–24].

We observed a different character of electric and mechanical activity of the uterine muscle in the studied women. The frequency of contractions noted using EHG was significantly greater than that resulting from mechanical activity of the uterine muscle registered in TOCO. This observation is in line with data from the literature [25]. The obtained results indicate that measurement of the bioelectric activity is more sensitive and precedes the occurrence of mechanical stimulation that results in contractile activity leading to threatening preterm delivery. In our study, in most cases, bioelectric activity of the uterine muscle persisted despite the application of a tocolytic treatment; bioelectric stimulation could be detected along with a complete lack of mechanical contraction. The tocolytic treatment had no effect on the inhibition of bioelectric activity although the studied women presented low contractile mechanical activity. In the literature, reports on the impact of tocolysis on bioelectric activity of the uterus are scarce. Aviram et al. [21] found similar electrical activity in women with imminent preterm labor who received a tocolytic treatment and those without tocolysis, while Kandil et al. [26] observed a different pattern of bioelectric activity in women who responded to tocolytic treatment than in non-responders. However, mechanical activity of the uterus was not assessed in either study.

In clinical practice, the assessment of contractile activity of the uterus is based on registration of mechanical activity in tocography and does not include an evaluation of bioelectric parameters. The presence of bioelectric activity may be evidence of contractile readiness and precedes the occurrence of uterine contractions [24]. Moreover, analysis of parameters characteristic solely for bioelectric activity such as contraction intensity, power, median frequency and frequency of maximum contractile power indicated intensified bioelectric activity preceding mechanical contractile activity [25, 27]. Another diagnostic problem revealed by our study was the lack of clinical symptoms of threatening preterm delivery in pregnant women with elevated bioelectric activity.

Registration of bioelectric activity has some advantages, including its completely noninvasive character and low cost of examination. Additionally, the lack of side effects in any of the studied women demonstrates its high safety.

Parallel registration and analysis of mechanical and bioelectric activity allows for assessment and comparison of the same descriptive parameters of contractions using both diagnostic methods. Therefore, it seems to be reasonable to conduct studies on larger populations of pregnant women, which can enable the identification of groups of women at high risk for mechanical contractile activity and eventual cervical dilation, based on intensified bioelectric activity.

CONCLUSIONS

Elevated bioelectric activity of the uterine muscle was observed despite the use of tocolytic therapy, a lack of symptoms of threatening preterm delivery, as well as a lack of contraction in tocography. The use of tocolytic therapy for threatening preterm delivery does not cease bioelectric activity of the uterus. All parameters of bioelectric activity were significantly higher than those of mechanical activity.

Conflict of interest

None.

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