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Analysis of Uterine Myoelectrical Signals Before and Immediately After Artificial Rupture of Membranes✍

Önder ÇELİK[1], Şeyma HASÇALIK[1], M. Emin TAĞLUK[2]

Malatya, Turkey

OBJECTIVE: This study was planned to compare the myoelectrical signals generated by gravid rat uterus before and immediately after artificial rupture of membranes (ROM) and the relationship between the pathological states and myoelectrical activity.

MATERIALS AND METHODS: The uterine myoelectrical signal recording was carried out on eight Wistar albino gravid rats. At 15th day of gestation bipolar electrodes were subserously implanted into the uterus. After the replacement of electrodes recording of the myoelectrical activity was conducted by the use of MP100 A-CE data acquisition system. Following the first recording, in each animal a 0.5 cm hysteroamniotomy was made in one of the amniotic sacs and subsequently myoelectrical activity was re-recorded.

RESULTS: While some of the uterine contractions were regular but some others were not, depending on the subject. After the rupture of membranes the irregularity of contractions as well as the rate of infrequent spike potentials, probably result from ROM effects and pollute the uterine signal, have increased.

CONCLUSIONS: Based on the obtained results, it seems that uterine electrical activity and thus the contractions significantly change immediately after ROM. The characterization of unusual uterine contractions following rupture of membranes can help the physicians in early diagnosis and management of ROM.

Key Words: Myoelectrical signal, Pregnancy, Rupture of membranes, MP 100 A-CE

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Introduction

Rupture of membranes (ROM) is a pathological case in which a rip spontaneously develops in the chorioamniotic membrane and causes spontaneous uterine contractions which are usually leading to a preterm labor.[1] Preterm labor is a serious clinical problem usually ends up with perinatal mortality and morbidity, and hence ROM is of interest both physiologically and clinically.[2] On one hand ROM has been assumed to result entirely from physical tearing of the membrane tissues under the stress of abnormal contractions. On the other hand, circumstances where the rupture precedes contractions in at least 10% of term labor and nearly 40% of premature labor has been reported.[1] Whatever is the case, obviously, the controllability of the uterus subjected to a premature ROM case needs to be investigated and the most trustworthy remedy to go after needs to be addressed.

Under normal circumstances, for the normal development of the fetus, during pregnancy the uterine contractility is down regulated by the physiological nature of the being.[3] In contrast, during term and preterm labor, the uterine contractions become prolonged, intense, and almost regular.[4] The basic mechanism that controls uterine contractions is the underlying myoelectrical activity which results from a collection of action potentials.[4,5] A normal myoelectrical signal is in the form of a series of prominent burst potentials generated by the whole myometrium tissue.[5]

The burst characteristics are influenced by the number of factors such as the mass of regenerative myometrial cells involved, the propagation of action potentials from one cell to another, the synchronicity of their electrical activity, and the types of currents activated[5] The most articulated hormone throughout the texts is the progesterone that exerts an overall control on uterine relaxation mechanism[6] It is possibly controlling a number of genes in the myometrium which are essential for uterine contractility, and thereby dozing off the release of proinflammatory cytokines and the availability of prostaglandins.[7]

[1]Departments of Obstetrics and Gynecology, Inonu University School of Medicine, Malatya

[2]Department of Electric and Electronic Engineering, Inonu University, Malatya

Address of Correspondence: *Önder Çelik*
Inonu University, Turgut Ozal Medical Center Department of Obstetrics and Gynecology, Malatya
oncelik@inonu.edu.tr

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The myoelectrical activity as a counterpart of the uterus contractility could change after rupture occurrence. In this perspective, a number of studies worked on pregnant rat myometrium are available in the literature.[6,8] However the factors which determine the pattern of the spontaneous activity and the changes in the myoelectrical properties immediately after rupture of membranes are not well understood yet. An increase in uterine myoelectrical activity after rupture which was ominous for pregnancy outcome has been reported.[9] However, in that text, the lack of availability of firm data regarding the effects of ROM on uterine myoelectrial activity at the time of rupture has been pointed out.

This study was therefore planned to compare the myoelectrical signals generated by gravid rat uterus just before and immediately after an artificially introduced ROM and investigate the correlation between the pathological states and myoelectrical activity.

Material and Method

This experimental study was carried out on eight Wistar albino female rats (250-300 gr. weight) maintained in individual cages under a controlled temperature, relative humidity, and day light, and fed ad libitum. Attempts at conception were undertaken for up to 5 consecutive days. The timed conception was identified as gestational day 0 by the presence of a copulatory plug during two hours exposure with the male. The pregnant females were then housed individually throughout gestation. On the 15th day of gestation, the pregnant rats were positioned in the supine position and the abdomen was shaved, disinfected with povidone iodine and draped in a sterile manner. A liberal midline abdominal incision was made to expose the pregnant uterus and bipolar electrodes subserously implanted into the uterus with a 1 cm inter-electrode spacing as shown in Figure 1-a. The reference electrode was placed on the left leg of the rat. Immediately after the replacement of electrodes, uterine electrical activity was recorded under anesthesia. The recording of the uterine myoelectrical activity was conducted by the use of MP100 A-CE data acquisition system (model MP100; software, acknowledge, version 3.7.2) with a 1000 pre-amplifier gain (this pre-amplifier gain was compensated later through soft processing) and a sampling frequency of 500 Hz. Following the first recording, in each animal, one of the amniotic sacs was exposed to a hystero-amniotomy. The standard trauma consisted of a 0,5 cm long hysterotomy incision made with a cold knife. The incision was made on the avascular side of the uterus in which the chorion and amnion were incised and outflow of amniotic fluid was allowed as shown in Figure 1-b. The second recordings after rupture of the membranes were successfully made in all pregnant rats. Afterward each recorded biological signal is analyzed from the temporal and spectral points of view and the correlation between the electrical signals and physiological state was investigated. All surgical procedures were performed while the rats were under intraperitoneal ketamine HCL (50 mg/kg) and xylazine HCL (10 mg/kg) anesthesia. The permission for the animal tests and experiments was given by the Bioethical Board of Inonu University Medical Faculty.

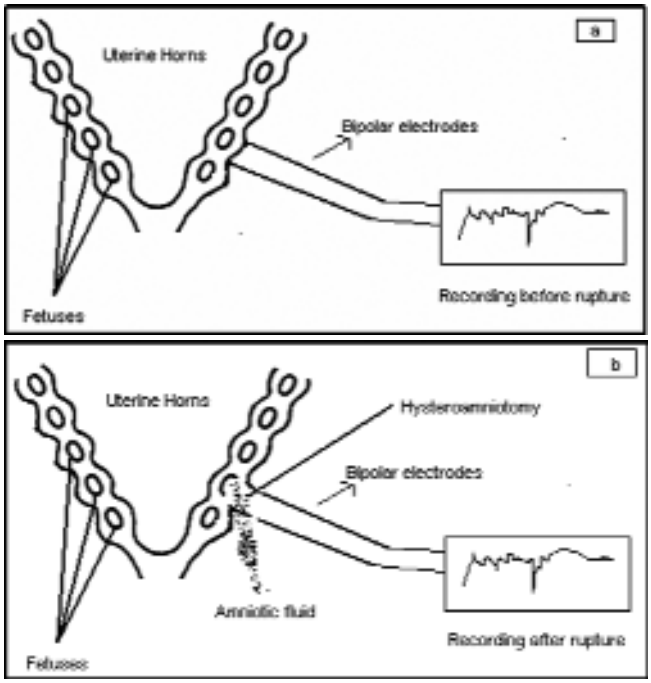

Figure 1: The diagrams show the schematic representation of in-vivo recording of the uterine myoelectrical activity (a) before and (b) and after rupture of the membranes

Results

Overall pattern of recorded myoelectrical signals was found to have a non-stationary nature. The rhythmic spontaneous electrical bursts, probably accompanied to contractions appeared as of intrauterine pressure and axial force, were observed to be fairly regular and of spike potentials. Whereas the quiescent phases between two bursts were observed to be of non-rhythmic or unformatted electrical signals. The rhythmic events were evident in general but in some of rats, both before and after the introduced artificial ROM, the periodicity of the myoelectrical activity of the uterine was not deterministic.

Four typical patterns among eight records were selected as example signals and are shown in Figure 2. The duration of signals is 1 min in which a couple of bursts (contractions) occur. The left panels illustrate for the pregnant rats before ROM, whereas the right panels illustrate for the same rats just after ROM. Here, the time domain, frequency domain and time-frequency domain (Wavelet) signal representations are respectively shown. In time domain representations each contraction is labeled by a solid line, where the thickness of the line symbolizes the degree of authenticity of the burst.

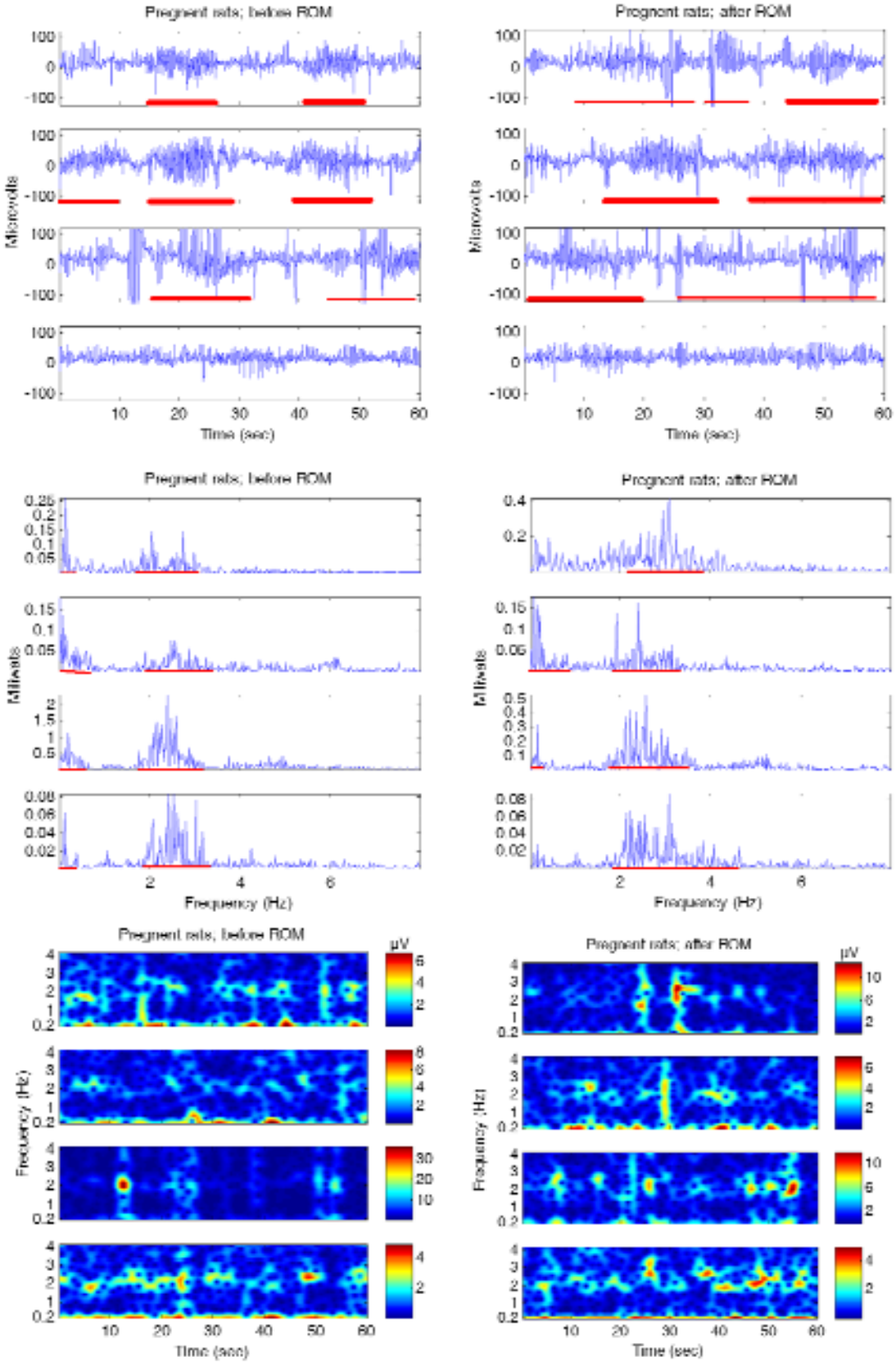

Figure 2: The representation of the myoelectrical signal of uterus of pragnent rats both before and after ROM in three domains: (I) Timeomain, the upper panels, (II) frequency domain, midway panels, and (III) time-frequency domain (Wavelets), lower panels

The dashed lines represent the patchiness of the burst whose characteristics cannot be identified. The transparency of burst potentials both before and after ROM was found to be individual; depending on the subject as clearly seen from the selected signal samples. Therefore, a direct comparison between burst potentials may not be significant at this stage. As a general observation on the whole records, however, was that most of the uterine contractions were better regular in pregnant rats whereas after the rupture of membranes the uterine contractions became somewhat irregular and masked by infrequent a few intensive spike potentials probably resulted from artificially introduced ROM effects.

From the spectral point of view, as seen from the spectral representations, the spectrum of myoelectrical signal slightly modulated to higher frequencies as ROM was introduced, in general. This observation however is valid in individual entities rather than groups. So, the post ROM case may be compared to pre ROM case for the same animal, but, to our knowledge, it is not factual if one correlates post ROM case of a subject to another's pre ROM case. The variations in the spectral peaks were also found to be inconsistent and far from being appraised at this stage.

The time-frequency representations or wavelet schemes exploited the whole characteristics of the signal in which the answers to such questions; when? at which rate? and the format of the outcome energy? is found. As seen, in both pre and post ROM case, beside the low frequency components (<0.5 Hz) non-continuous spectra occur about 2 Hz frequency range. This shows that the spectra depicted in the spectral panels are not pure synchronous, but in the form of spikes whose vigorous energy concentrated over 1.5 Hz to about 4 Hz. This representation also showed the inconsistency of spikes within burst potentials which have been spread over a vide band range of the instantaneous spectra.

Some quantitative characteristic parameters of these recorded electrical activities such as signal's mean power and standard deviation (STD), as well as grand-averages of the measured powers and STDs were presented in Table 1 by which the cross-comparison might became possible. Unfortunately distinguishing characteristics were not determined in these measures. Despite that a little diminution in grand average of both mean powers and STD were detected after introduction of ROM but this is not at a significant level.

Discussion

Premature ROM has been considered as one of the major factors that initiates uterine contractions and being in charge of preterm labor (1). It has been reported that most of patients with premature ROM deliver within 48 hours of rupture phase, but the neonatal impact and general outcome depend largely on the gestational age at rupture.[10,11] In normal conditions rupture of membranes, although it is a part of and necessary for the delivery process, is likely controlled separately from uterine contractions.[12,13] To our understanding, the factors such as myometrial thickness, gestational age, endocervical length, uterine contractility have various prognostic values not only on labor but also on ROM.[14-16] Yet, any prediction of the latency interval for patients with ROM is not clear. In this context, the electrical activity of the myometrium following ROM was assessed.

Here, the myoelectrical activity of the uterus of rats before and immediately after an artificial ROM was analyzed. We searched for whether burst potentials, and consequently the contractions, of uterine are affected from acute ROM. Based on the experiments carried out, rather than insignificant irregularities and the contamination of spontaneously distributed infrequent spikes any change was not observed in the time domain signals. The minor changes and irregularity of the spikes after ROM have previously been proposed as being in a state of myometrial quiescence or incomplete myometrial activation.[14] It has been reported that only active myometrial contractility is associated with widespread thinning of the myometrium independent of ROM.[17] Therefore this effect was not considered as a distinguishing factor.

From the spectral point of view, a very little change in the frequency response of the uterine signals was observed. This might be linked to the frequency of uterine contractions, but individual subjects have not shown comparable characteristics to standardize some features. It seems that the intensification of uterine contractions does not occur at early stage of ROM. This can be explained as follows: it has been reported that the human fetal membranes produce more substances that inhibit myometrial contractions.[18,19] Carvayal et al.[18] have demonstrated that human chorion and amnion inhibit oxytocin stimulated myometrial contractility in vitro. Also the level of progesterone during pregnancy remains high to provide uterine quiescence.[6] Immediately after ROM such factors my not alter

Table 1: Mean power and grand-mean power as well as standard deviation of the example signals

	Subject no:	1	2	3	4	Grand Averages
Mean Power (mV)	before ROM	0.2870	0.3519	0.4277	0.2910	0.3371
	after ROM	0.1910	0.3007	0.3179	0.3129	0.3122
STD	before ROM	20.69	23.48	55.55	14.83	28.52
	after ROM	28.66	23.09	31.81	15.83	24.85

quickly. So, the occurrence of intense contractions may take longer time in which an inflammation, infection or thinning of the myometrium possibly could arise.

The absence of intensive uterine contractions on non stress test in the early stage of ROM, if it is the case, does not mean that preterm labor will not take place. Therefore patients suffering from vaginal fluid leakage need to be internalized and carefully examined for presence of ROM and bear in mind that later on uterine contractions may arise and lead to laboring. However, in the absence of clinical symptoms of preterm labor and chorioamnionitis, the management of a pregnancy with ROM is usually expectant, based on the assumption that even a minor delay in the interval to delivery will be beneficial to the fetus.[20]

The management ROM is complicated by the absence of a gold standard method to predict pathogenic processes leading to uterine contraction.[21] We found that myoelectrical activity recorded from the myometrium after ROM differs from than the activity recorded before rupture. This finding supports the clinical suspicion that preterm labor is caused by ROM related abnormal uterine myoelectrical activity. However, the myoelectrical activity delivered by animals with ROM which has been discussed here was not standardized and remained ambiguous.

On the basis of our study, it appears that myoelectrical activity measured after the ROM can provide important information and may prove to be useful in managing of patients with ROM. In addition to clinical usefulness, measurement of myoelectrical activity can be applied to a number of experimental situations, both in human subjects and in animals. The MP 100 recording technology presented in this study represents an alternative method of evaluating whether the uterus is pathologically stimulated after ROM. In human patients this method of analysis may result in better management of ROM subjects either at term or remote from term. It is clear that more studies are needed before this technology can be extrapolated for clinical use in human subjects.

Artifisyel Membran Rüptürü Öncesi ve Sonrası Uterus Elektrik Aktivitesinin Analizi

AMAÇ: Bu çalışma gebe ratlarda artifisyel membran rüptürü öncesi ve sonrası uterus myoelektrik aktivitesinin değişimini saptamak ve patolojik durumlarla aktivite değişimleri arası ilişkiyi karşılaştırmak için planlandı.

GEREÇ VE YÖNTEM: Gebeliklerinin 15. gününde olan 8 adet Wistar albino rat'ın uteruslarına bipolar elektrodlar subseröz olarak yerleştirildi ve MP100 A-CE kayıt sistemiyle miyoelektrik aktiviteleri kaydedildi. İlk kayıtları takiben her gebe rat'a 0.5 cm'lik histeroamniotomi yapıldı ve tekrar myoelektrik aktiviteler kaydedildi.

BULGULAR: Uterus kontraksiyon paternleri rüptür öncesi her hayvanda farklı paternde olup bazısında regüler bazılarında ise irregüler görünümdeydi. Rüptür sonrası kontraksiyonların irregülaritesi ve spike potansiyelleri belirgin olarak arttı.

SONUÇ: Membran rüptürü uterus elektrik aktivitesinde ve kontraksiyon paterninde belirgin değişikliklere yol açar. Bu paternin saptanması subklinik membran rüptürünün erken tanı ve yönetiminde hekime yardımcı olabilir.

Anahtar Kelimeler: Miyoelektrik sinyal, Gebelik, Membran rüptürü, MP 100 A-CE

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