Electrohysterogram Signals from Patients with Threatened Preterm Labor: Concentric Ring Electrode Vs Disk Electrode Recordings

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Abstract: Recording of electrohysterogram (EHG) has emerged as a non-invasive method for monitoring uterine dynamics during pregnancy. Usually EHG is picked up using conventional disk electrodes placed on the abdominal surface resulting in a limited spatial resolution due to the blurring effect of the volume conductor. In this respect, concentric ring electrodes have been proposed to pick up uterine myoelectrical activity in term patients so as to improve spatial resolution and to reduce physiological interferences embedded in these records. The aim of the present work is to check the feasibility of recording EHG signals using concentric ring electrodes (BC-EHG) in patients with threatened preterm labor and to compare their capability to discriminate true preterm labor from false alarms with that of conventional EHG bipolar recording. For this purpose, 50 sessions with simultaneous EHG recordings with conventional disk electrodes and concentric ring electrodes were conducted in 26 patients. Compared to conventional bipolar EHG recording, the BC-EHG presents smaller amplitude and similar spectral characteristics. Statistically significant differences between women who delivered preterm and those that delivered at term were found for both the average peak-peak amplitude and the dominant frequency in the frequency range 0.2-1 Hz from BC-EHG recordings. Nonetheless no EHG parameter from simultaneous conventional bipolar recording showed statistically significant differences. These results suggest superior performance of BC-EHG recordings in patients with threatened preterm labor for discriminating true preterm labor from term labor.

1 INTRODUCTION

Preterm birth (<37 weeks of gestation, WG) is one of the major cause of early neonatal mortality. The incidence of preterm birth has risen over the last decades, representing around 12% of all labors nowadays (Beck, 2010). Preterm labor also implicates around 85% of newborn deaths and 50% of newborns' neurological disorders (Beck, 2010). Currently due to the lack of specific tools, the diagnosis of preterm labor is one of the most complex problems faced by clinicians.

The gold standard for monitoring uterine dynamics is the use of an intra-uterine catheter, which provides a quantitative measure of intra-uterine pressure associated to the uterine contractions. It is an invasive technique which requires ruptured membranes and entails risks such as infection, and thus it is unsuitable for predicting preterm labor during pregnancy. In common practice, obstetricians use tocodynamometry (TOCO) for assessing uterine contractility and evaluating the risk of preterm labor. This technique measures non-invasively the uterine pressure transmitted to the abdominal surface. However, it suffers from recurrent signal failure, needing re-positioning by a midwife (Miles, 2001, Schlembach, 2009), and may also fail in obese patients (Euliano, 2013). Furthermore, TOCO is not able to distinguish effective contractions which lead to preterm delivery, from non-effective ones (Schlembach, 2009, Garfield, 2007). Recording of electrohysterom (EHG) has emerged as an alternative technique for non-invasively monitoring uterine contractility (Devedeux, 1993, Garfield, 2005, Maner, 2007). The electrohysterogram corresponds to the uterine myoelectric recordings and it is made up of action potential bursts (EHG-burst), associated to uterine contraction, and basal activity. EHG signals

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present different characteristics along the gestation and depending on the proximity of labor (Garfield, 2007, Marque, 2007), which could provide information for estimating the time horizon of labor. Some parameters extracted from EHG signals, such as those related with conduction velocity or propagation patterns, are very promising for the prediction of term and preterm delivery (Lucovnik, 2011, Euliano, 2009, Rabotti, 2009, Rabotti, 2010). Nevertheless, the estimation of conduction velocity depends on the direction of propagation of contraction in relation to the electrodes position (Rabotti, 2011). Moreover, it can also be influenced by the poor spatial resolution associated to conventional disk electrodes due to the blurring effect of the volume conductor (Ye-Lin, 2015).

In this sense, concentric ring electrodes (CRE) have been proposed to improve the spatial resolution achieved with conventional disk electrodes and to reduce physiological interferences embedded in EHG recordings (Alberola-Rubio, 2013). Specifically, these electrodes have proven to pick up uterine myoelectrical activity in patients at term ($\geq$ 37 WG), (Ye-Lin, 2015). Nonetheless, since the EHG-burst amplitude of patients at earlier WG is expected to be lower than those obtained from patients at term (Devedeux, 1993, Garfield, 2005), the utility of CRE for predicting preterm labor in patients with threatened preterm labor still needs to be proven. Therefore, the first aim of the present work was to determine if concentric ring electrodes are able to pick up the EHG in patients at early gestational age (< 37 WG). Secondly, it was aimed to explore the possibility to discriminate true preterm labor from false alarms of patients with threatened preterm labor based on BC-EHG and bipolar EHG records. Specifically, in this first approach it was studied the possible differences in EHG temporal and spectral parameters of patients who end up delivering preterm and those who did it at term.

2 MATERIALS AND METHODS

2.1 Data Acquisition

50 recording sessions were conducted in 26 patients with singleton pregnancies at the Hospital Universitario y Politécnico La Fe de Valencia. This study adheres to the Declaration of Helsinki and was approved hospitably the Institutional Review Board. The patients were informed about the nature of the study and the recording protocol and they signed an informed consent form. The criteria for inclusion in this study were: women with a gestational age between 25 and 36 weeks with symptoms of preterm labor, such as regular uterine contractions and/or cervical effacement. Patients' obstetric information was collected, as shown in Table 1, and patients were followed up to obtain the details of their final delivery. It should be highlight that cervical length shows a shortening as labor approaches, and higher values of this parameter can be observed for the term group in comparison to preterm labor group.

Term and preterm labor patients were grouped into two subgroups depending on the gestational age at recording moment: term [28, 31[WG group (6 patients and 8 records), term [31, 34[WG group (10 patients and 14 records), preterm [28, 31[WG group (4 patients and 5 records) and preterm [31, 34[WG group (6 patients and 23 records). Patients who presented threatened preterm labor but did not initiate labor spontaneously were excluded from the study. Besides the EHG registers were performed under common clinical practice conditions, this implies that most patients were under tocolytic drugs effect. For each recording session, the abdominal skin was carefully prepared using an abrasive paste in order to reduce skin-electrode impedance. Two disposable Ag/AgCl electrodes (EL501, Biopac SystemsInc, Santa Barbara, CA, USA) were placed supraumbilically, symmetrically arranged with respect to the uterine median axis being the inter-electrode distance 8 cm (see Figure 1). Furthermore, a custom-made concentric ring electrode was placed on the uterine median axis in the subumbilical zone (see Figure 1).

Table 1. Patients' obstetrical information at the recording moment.

	Term labor	*Preterm labor*
Gestations	1.59 ±1.10	1.50 ±1.10
Parity	0.23 ±0.43	0.23 ±0.43
Voluntary Interruption of Pregnancy	0.13 ±0.47	0.07 ±0.36
Abortions	0.22 ±0.68	0.20 ±0.76
Cesarean Sections	0.09 ±0.29	0.00 ± 0.00
Maternal age (years)	32.55 ± 5.70	30.47 ±5.16
Gestational Age (weeks)	31.05 ± 2.54	31.87 ±1.55
Cervical length (mm)	24.95 ± 10.17	15.37 ± 11.28

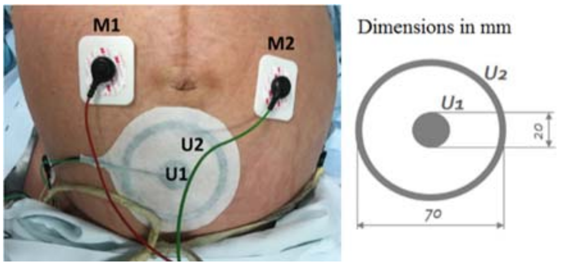

Figure 1: Scheme of the electrodes' placement on a woman's abdomen (left) and CRE dimensions (right).

Taking into account that the EHG-burst amplitude acquired using CRE with an outer ring of 36 mm was about 42 μV in patients at term (Ye-Lin, 2015), in this work it has been designed a CRE with an outer ring of 70 mm so as to facilitate picking up the uterine electrical activity during early pregnancy whose amplitude was expected to be smaller than that associated to term patients. Furthermore, two disposable Ag/AgCl electrodes were placed in each hip, as reference and ground electrodes. In this work, the bipolar recording estimated from the two monopolar raw signals from conventional disk electrodes and one bipolar concentric-EHG (BC-EHG) signal obtained by means of CRE were analysed (see Figure 1).

$$\text{Bipolar} = M1 - M2;\ \text{BC-EHG} = U2\text{-}U1; \quad (1)$$

Where M1 and M2 are the biopotentials picked up by conventional disk electrodes and U1 and U2 are the biopotentials corresponding to the central disk and external ring respectively. Two custom-made amplifiers which provide a 2059 V/V gain in the frequency band between 0.1 and 4 Hz were used for signal conditioning (Alberola-Rubio, 2015).

The implementation details of the bioamplifier were described in a previous work (Ye-Lin, 2016). Signals were digitalized using a 24 bits ADC and sampled at 20 Hz. TOCO signal was simultaneously acquired by means of a Corometric 170 from GE Medical Systems and the digitalized data were transmitted to a PC with a sampling frequency of 4 Hz.

2.2 Data Analysis

Most studies in this field are focused on the analysis of the EHG-burst (Garfield, 2005, Maner, 2007), which usually requires manual segmentation of the EHG recordings. This process depends on the experts' subjectivity and it is a time-consuming task (Fele-Zorz, 2008). In this work, it was preferred to analyse the whole EHG recording which greatly simplifies the signal analysis process. Signal segments corresponding to motion artefacts were discarded from the analysis. Subsequently a set of temporal and spectral parameters was calculated for the EHG signals: average peak to peak amplitude, mean frequency, dominant frequency in frequency range 0.2-1 Hz (DF_1) and in frequency range 0.34-1 Hz (DF_2), normalized subband energies in frequency ranges 0.2-0.34 Hz (NE1), 0.34-0.6 Hz (NE2) and 0.6-1 Hz (NE3) and H/L ratio, which is the ratio between the energy in high frequency range (0.34-1 Hz) respect to the energy in low frequency range (0.2-0.34 Hz) (Ye-Lin, 2015). Specifically, the peak-peak amplitude was worked out over a moving window of 120 s length and 50% overlapping, and then the average value of all analysed windows was calculated. Similarly, for the estimation of the spectral parameters, the Welch periodogram was worked out in moving analysis windows of 120 s with 50% overlapping.

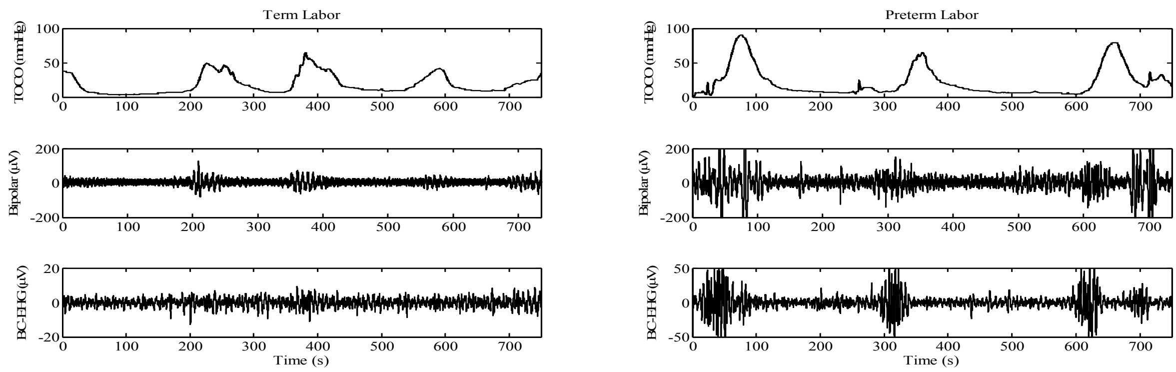

Figure 2: Simultaneous recording of TOCO, bipolar, BC-EHG performed in two patients at 33 WG. Left: recordings from a woman who delivered at term. Right: recordings from a woman who delivered preterm.

Table 2: EHG Parameters obtained from conventional bipolar recordings for both term labor and preterm labor groups, separated into two sets depending on the gestational age at the recording session. '*' indicates statistically significant differences ($p<0.05$) between term labor and preterm labor groups for the same set of WG; and '□' indicates statistically significant differences ($p<0.05$) between conventional bipolar record and BC-EHG (table 3) for each of the 4 subgroups.

Bipolar	*Term labor*		*Preterm labor*	
Parameter	*[28, 31[WG*	*[31, 34[WG*	*[28, 31[WG*	*[31, 34[WG*
App (µV)	98.85 ± 35.3□	127.56 ± 31.33□	157.18 ± 41.34□	151.46 ± 77.92□
MF (Hz)	0.366 ± 0.018	0.338 ± 0.021	0.381 ± 0.034	0.353 ± 0.025
DF1 (Hz)	0.237 ± 0.023	0.234 ± 0.021	0.229 ± 0.037	0.241 ± 0.035
DF2 (Hz)	0.367 ± 0.031	0.357 ± 0.012	0.355 ± 0.012	0.366 ± 0.024
NE1	0.56 ± 0.12	0.65 ± 0.11	0.53 ± 0.1	0.63 ± 0.08
NE2	0.35 ± 0.12	0.27 ± 0.08	0.36 ± 0.07	0.28 ± 0.06
NE3	0.09 ± 0.02	0.09 ± 0.07	0.11 ± 0.04	0.09 ± 0.03
H/L Ratio	0.85 ± 0.38	0.6 ± 0.35	0.93 ± 0.34	0.6 ± 0.19

Table 3: EHG Parameters obtained from BC-EHG recordings for both term labor and preterm labor group, separated into two sets depending on the gestational week at the recording session. '*' indicates statistically significant differences between term and preterm labor groups for the same set of WG.

BC-EHG	*Term labor*		*Preterm labor*	
Parameter	*[28, 31[WG*	*[31, 34[WG*	*[28, 31[WG*	*[31, 34[WG*
App (µV)	52.72 ± 17.18	60.86 ± 37.96	97.68 ±18.49*	90.1 ± 46.16*
MF (Hz)	0.387 ± 0.017	0.358 ± 0.022	0.379 ± 0.025	0.365 ± 0.031
DF1 (Hz)	0.224 ± 0.029	0.212 ± 0.008	0.234 ± 0.028	0.237 ± 0.044*
DF2 (Hz)	0.378 ± 0.031	0.381 ± 0.026	0.391 ± 0.042	0.371 ± 0.026
NE_1	0.54 ± 0.06	0.60 ± 0.08	0.53 ± 0.05	0.58 ± 0.09
NE_2	0.33 ± 0.04	0.31 ± 0.08	0.35 ± 0.04	0.32 ± 0.07
NE_3	0.13 ± 0.03	0.09 ± 0.03	0.11 ± 0.04	0.10 ± 0.04
H/L Ratio	0.87 ± 0.17	0.70 ± 0.24	0.89 ± 0.17	0.76 ± 0.3

Wilcoxon test was performed in order to determine if there were statistically significant differences between the EHG parameters derived from preterm labor group and term labor group for both [28, 31[WG and [31, 34[WG subgroups.

3 RESULTS

Figure 2 shows 750 s of simultaneous recordings of TOCO, bipolar and BC-EHG signals performed in two patients at 33 WG, one who delivered at term and other who delivered preterm. Firstly, each uterine contraction observed in the tocographic signal was associated to an increase of signal amplitude in bipolar recording for both patients. In the case of the patient who delivered preterm, it can be clearly identified the presence of uterine contractions in BC-EHG signals. By contrast, for the patient who delivered at term, only uterine contractions around 400 s and 700 s, which are of greater intensity, can be observed in BC-EHG recording. The contractions around 200 s and 600 s are hardly noticeable, being imbedded in the basal activity. Secondly, the amplitude of EHG signals acquired with CRE was smaller than that from signals obtained using conventional disk electrodes. Finally, it can also be clearly observed that the amplitudes of the EHG-bursts of the patient whose labor was preterm is higher than those of the patient that delivered at term (false alarm), even when both records were made at the same WG.

Tables 2 and 3 show mean and standard deviation of the EHG parameters calculated from Bipolar and BC-EHG recordings respectively. Firstly, it can be noticed that BC-EHG signals presented lower peak-peak amplitude than conventional bipolar ones. In fact, the amplitude is the only parameter that shows statistically significant difference between BC-EHG signals and bipolar signals (squares) for both [28, 31[WG and [31, 34[WG groups. Comparing EHG parameters in the sets of same ranges of WG, the average amplitude of preterm labor group was higher than those of term labor group for both bipolar and BC-EHG recording. However, such difference was statistically significant only for BC-EHG. Regarding spectral parameters, it is noticeable that only DF1 for the set [31, 34 WG] presented statistically significant differences between term labor and preterm labor, and again only for BC-EHG signals.

4 DISCUSSION

In the present work, it was tested and confirmed the feasibility of picking up the uterine electrical activity using CRE at early gestational ages. No statistically significant differences were found between EHG parameters derived from bipolar and BC-EHG recording, apart from the peak to peak amplitude. Conventional bipolar EHG signals presented higher amplitude than BC-EHG, which may be due to the fact that CRE presented a relatively smaller interelectrode distance. This result agrees with other authors who has acquired both bipolar and BC-EHG in patients at term (> 37 weeks of gestation) (Ye-Lin, 2015). Moreover, bipolar and BC-EHG signals presented similar spectral characteristics in the target signal bandwidth.

Then it was explored the capability of bipolar and BC-EHG recordings to discriminate between women with threatened preterm labor who will deliver preterm of those who deliver at term. In comparison to term group, bipolar EHG signals from preterm group presented higher peak to peak amplitude and greater spectral content in high frequency range. This result is accordance with other authors that computed temporal and spectral parameters to characterize the EHG recording (Garfield, 2005, Maner, 2003, Marque, 2007). Nevertheless, our data did not show statistically significant differences in spectral parameters obtained from bipolar recording as reported by other authors (Maner, 2003, Maner, 2007, Fele-Zorz, 2008). Maner et al. focused on the DF2 estimated from the EHG-burst associated to uterine contractions. In that work DF2 of preterm labor group presented significantly higher values than those of term labor group. The fact that in the present work the whole EHG recording is analysed, including not only the spikes burst but also the basal activity, could mitigate the difference of EHG parameters between preterm and term labor group. On the other hand, other authors who have also analysed the whole EHG recording have found statistically significant differences in the median frequency calculated in frequency range 0.3-3 Hz (Fele-Zorz, 2008). Firstly, the target bandwidth of data analysis of our work was slightly different. Besides, EHG recordings in this work were performed under common clinical practice conditions, which implies most of them were carried on patients under tocolytic drugs effect. This can also affect the obtained results, but it is closer to real clinical conditions of patients with threatened of preterm labor after preliminary explorations in emergency rooms.

As for BC-EHG signals capability to distinguish between preterm and term group, it was found statistically significant difference in both peak to peak amplitude and DF1 parameters. This result may suggest that concentric ring electrodes not only can be used for picking up uterine electrical activity in patients with threatened preterm labor, but also could have superior performance for discriminating true preterm labor from false alarms in comparison to bipolar recordings with conventional disk electrodes. This may be associated to a higher spatial resolution of CRE that permits to discriminate better between normal local activity during pregnancy and coordinated global electrical activity as labor approaches, although this hypothesis has to be confirmed in further studies with a larger database.

The main limitation of this work is the small size of the actual database, which on one hand limits the robustness of the results and the derived conclusions, and on the other hand binds the study only for patients with gestational weeks at recording moment between [28, 34]. When the size of this database is increased, it will allow us to extend the present analysis to patients with wider ranges of gestational age [24-36] WG. It can also be considered a limitation of the study, the above mentioned use of tocolytic drugs in most patients. These drugs can modify the spectral content of EHG signals, since they are intended to alter uterine contractility in order to delay or prevent preterm labor. Despite these limitations, CRE have been proven their capability for monitoring uterine electrical activity in early gestational ages, suggesting its potential clinical use for predicting preterm labor.

5 CONCLUSIONS

In conclusion, it has been proved CREs' capability for picking up uterine electrical activity during early weeks of gestation. Moreover, BC-EHG signals present smaller amplitude but similar spectral characteristics when compared with conventional bipolar EHG recordings. Finally, average peak-peak amplitude and DF1 estimated from BC-EHG recordings showed statistically difference between preterm term and term labor group and not from bipolar EHG, suggesting better performance of the CRE to disk electrodes for predicting preterm labor based on EHG records. This prediction capability will be evaluated in future work since a more comprehensive database is needed for the implementation and testing of classifiers.

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