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Electrohysterographic characterization of the uterine myoelectrical response to labor induction drugs

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A B S T R A C T

Labor induction is a common practice to promote uterine contractions and labor onset. Uterine electrohysterogram (EHG) has proved its suitability for characterizing the uterus electrophysiological condition in women with spontaneous labor. The aim of this study was to characterize and compare uterine myoelectrical activity during the first 4 h in response to labor induction drugs, Misoprostol (G1) and Dinoprostone (G2), by analyzing the differences between women who achieved active phase of labor and those who did not (successful and failed inductions). A set of temporal, spectral and complexity parameters were computed from the EHG-bursts. As for successful inductions, statistical significant and sustained increases with respect to basal period were obtained for EHG amplitude, mean frequency, uterine activity index (UAI) and Teager, after 60′ for the G1 group; duration, amplitude, number of contractions and UAI for the G2 group, after 120′. Moreover, Teager showed statistical significant and sustained differences between successful and failed inductions (1.43 ± 1.45 $\mu V^2 \cdot Hz^2 \cdot 10^5$ vs. 0.40 ± 0.26 $\mu V^2 \cdot Hz^2 \cdot 10^5$ after 240′) for the G1 group, but not in the G2 group, probably due to the slower pharmacokinetics of this drug. These results revealed that EHG could be useful for successful induction prediction in the early stages of induction, especially when using Misoprostol.

1. Introduction

Labor induction is now a daily obstetric routine and is performed in an ever-increasing number of cases. It is indicated when the risk to mother and fetus of continuing the pregnancy outweighs that of terminating it. The goal is to achieve vaginal delivery by stimulating uterine contractions before the spontaneous onset of labor by promoting uterine contractions. Its use has increased significantly in recent years, from 9.0% of all births in 1989 to 23% in 2012 in the United States [1]. Labor induction can last for many hours (approximately 17–20 [2]), sometimes more than 36 h, and in most cases does not ensure vaginal delivery. Indeed, almost 20% of all labor induction cases end in caesarean sections [3]. Predicting the success of induction is a key aspect in improving maternal and fetal well-being and reducing healthcare costs. The most common method of predicting success is based on cervix assessment by the Bishop score [4], although this method is subjective with poor reproducibility [5]. Other obstetric variables have been used for this purpose, such as cervical length, maternal age, height, weight, parity, and birth weight [6–10]. Some of the predictive capacity values given in the literature are in the area under the curve (AUC) of the receiver operating characteristic (ROC) curves (0.689 for cervical length and 0.72 for cervical dilatation [8]). The Bishop score and cervical length were found to achieve an AUC of 0.39 and 0.69, respectively in [7] and Prado et al. (2016) found an AUC = 0.60 for fetal weight. Consequently, no reliable models are available to predict the outcome of labor induction in clinical practice with common obstetric data.

Monitoring uterine activity is also fundamental to determining the uterine response to induction drugs, assessing maternal and fetal wellbeing and estimating the success of labor induction. In clinical settings, evaluating uterine dynamics can help clinicians to estimate the progress of labor and its outcome. Measuring intrauterine pressure (IUP) is the gold standard of uterine dynamics monitoring. Although this technique provides a reliable measure, it is somewhat limited due to its invasiveness, requiring the rupture of membranes [11]. The most commonly used method of noninvasively monitoring uterine activity consists of placing a tocody-

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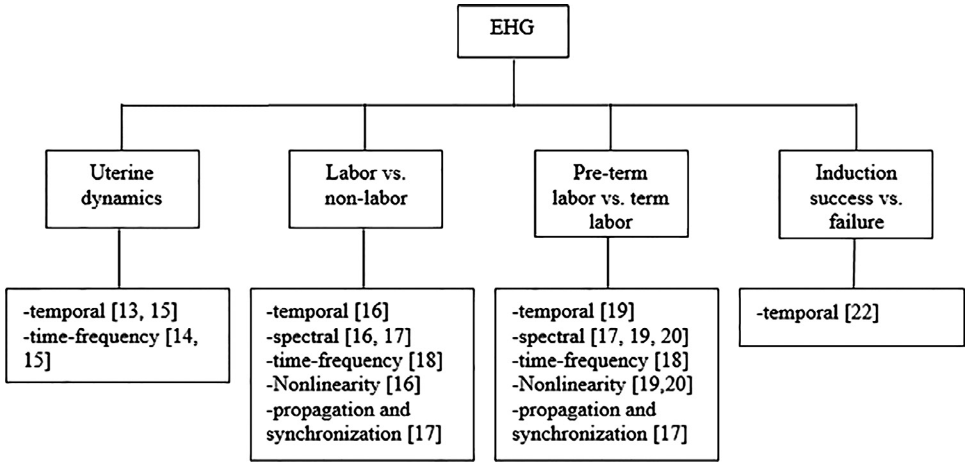

Fig. 1. Applications of EHG analysis and types of parameters used for signal characterization.

Table 1
Obstetric data of induced women and outcomes of labor induction.

Obstetric variables	Misoprostol ($N=35$)	Dinoprostone ($N=37$)	*P-value*
Maternal age (years)	31.3 ± 4.2	32.0 ± 5.0	0.419
BMI (kg/m^2)	29.8 ± 4.6	28.01 ± 3.5	0.066
Parity	1.4 ± 0.6	1.46 ± 0.7	0.946
Gestation	0.11 ± 0.40	0.11 ± 0.31	0.792
Bishop	1.5 ± 1.1	2.2 ± 1.04	**0.011**
Vaginal delivery	23 (66%)	23 (62%)	0.754
>24 h	12/23 (52%)	11/23 (48%)	0.768
<=24 h	11/23 (48%)	12/23 (52%)	
Active labor period	31 (89%)	32 (86%)	0.789
Time to achieve active labor period (hours)	15.8 ± 9.13	18.0 ± 12.44	0.657
Cesareans	12	14	0.754
Arterial pH	7.26 ± 0.06	7.26 ± 0.07	0.85
Vein pH	7.29 ± 0.06	7.30 ± 0.07	0.17

namometer (TOCO) on the mother's abdomen [12]. However, this method does not provide reliable information, often experiences loss of contractions [12], repositioning the sensor may be required and its interpretation is highly dependent on the examiner's subjectivity.

Electrohysterography (EHG), the recording of uterine muscle electrical activity at the abdominal surface, has emerged as an alternative technique for non-invasive monitoring of uterine dynamics. EHG consists of intermittent bursts of action potentials associated with uterine contractions and basal activity when the uterus is at rest. In the literature, EHG has been widely used for monitoring uterine dynamics by generating TOCO-like and IUP-like signals [13–15], to differentiate between labor and non-labor contractions [16–18] and term vs preterm deliveries during pregnancy [17,19,20]. Fig. 1 shows the main applications of EHG, at the research level, and the different type of parameters employed in each case. However, few studies focus on the uterine myoelectrical activity response to labor induction drugs [21,22]. In these latter, the uterine EMG signal characterization is based mainly on signal amplitude and only Toth et al. [22] examined the possibility of predicting the success of labor induction. The question is still unclear of whether or not the distribution of spectral content and complexity parameters from the EHG signal undergo changes throughout labor induction by drugs (prostaglandins), and if these parameters –derived from the EHG-burst -might also be used to develop tools to predict successful induction.

The aim of the present work was thus to characterize and compare the uterine myoelectrical response of mothers administered Misoprostol and Dinoprostone, two commonly used labor induction drugs, by analyzing the modifications to uterine dynamics in the first hours of the induction process. For this, temporal, spectral and complexity parameters from EHG-burst were calculated and a set of parameters was identified capable of distinguishing between successful and unsuccessful inductions.

2. Materials and methods

2.1. Signal acquisition

Seventy-two recording sessions were conducted on expectant mothers with late term pregnancies admitted for cervical ripening and labor induction at the *Hospital Universitario y Politécnico La Fe*, in Valencia, Spain. The study adhered to the Declaration of Helsinki and was approved by the local medical ethical board. The subjects were informed of the nature of the study and provided written informed consent. The collected obstetric data included maternal age, body mass index (BMI), parity, gestations, pre-induction Bishop score and time to achieve active labor period (Table 1).

The recording sessions were divided into two groups according to the drug administered for labor induction: Group 1 (G1) were given a vaginal insert of 25 µg of Misoprostol (Misofar, Bial, Coronado, Portugal) with repeated doses of up to four administrations every 4 h. Group 2 (G2) was given a 10 mg vaginal Dinoprostone insert (Propess, Ferring, Germany) in a single dose. The success of induction has been defined in the bibliography in different ways: vaginal delivery within 24 h of induction [23,24], vaginal delivery within 48 h of induction [25] and vaginal delivery at any time after induction [26]. However, when it is intended to assess the drug's success in activating uterine dynamics, regardless of whether or not the induction ended in a vaginal delivery, it can