European Journal of Obstetrics & Gynecology and Reproductive Biology xxx (2015) xxx–xxx

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Computerized fetal heart rate analysis in the prediction of myocardial damage in pregnancies with placental insufficiency

Q1 Mariane de Fátima Y. Maeda, Roseli M.Y. Nomura *, Juliana I. Niigaki, Rossana P.V. Francisco, Marcelo Zugaib

Department of Obstetrics and Gynecology, São Paulo University Medical School, University of Sao Paulo, São Paulo, Brazil

ARTICLE INFO

Article history:
Received 27 January 2015
Received in revised form 18 March 2015
Accepted 31 March 2015

Keywords:
Cardiotocography
Placental insufficiency
Ultrassonography, Doppler
Troponin T
Fetal hypoxia

ABSTRACT

Objective: To evaluate the reliability of fetal heart rate (FHR) parameters analyzed by computerized cardiotocography (cCTG) in predicting myocardial damage in pregnancies with placental insufficiency.
Study design: We evaluated 38 patients with placental insufficiency detected before 34 weeks of gestation. All patients underwent 30 min of cCTG (Sonicaid Fetal Care, version 2.2) and Doppler of umbilical artery, middle cerebral artery, and ductus venosus. Umbilical vein blood samples were collected at birth to determine fetal cardiac Troponin T, and a ≥0.09 ng/ml value was deemed a sign of myocardial damage.
Results: The fetuses with myocardial damage (39%) showed significantly increased values of umbilical artery pulsatility index *z*-score ($P = 0.003$), ductus venosus pulsatility index *z*-score ($P = 0.007$), basal FHR ($P = 0.033$) and periods of low episodes ($P = 0.038$). The number of small accelerations and the short-term variation (STV) were significantly reduced in the group with myocardial damage ($P = 0.013$ and $P = 0.003$, respectively). Logistic regression analysis identified STV and gestational age at delivery as independent predictors for fetal myocardial damage, with area under ROC curve of 0.91.
Conclusions: Computerized cardiotocography parameters may be useful in the management of early onset placental insufficiency, and the association of STV with gestational age could play a role in detecting myocardial injury in pregnancies with placental insufficiency.

Introduction

Q2 Intrauterine growth restriction (IUGR) due to placental insufficiency is one of the most important causes of perinatal morbidity and mortality [1,2]. The heart is a central organ in the fetal mechanisms for adaptation to placental insufficiency [3]. In fetuses with severe IUGR, an inadequate oxygen supply to the fetal heart may lead to myocardial cell destruction and an increase in circulating biochemical markers, like cardiac Troponin T (cTnT) [4].

Monitoring of changes in FHR and cardiac function is proposed as an adjunct to current methods for predicting adverse outcome and death in IUGR; however, suitable parameters are yet to be established. The use of cardiotocography (CTG) to predict acid-base status has been extensively studied [5–10] but there are no studies comparing FHR parameters with the presence of myocardial damage in pregnancies with IUGR.

The aim of this study was to verify the reliability of computerized CTG (cCTG) parameters comparing with Doppler evaluations to predict myocardial damage in pregnancies complicated by placental insufficiency.

Materials and methods

This was a cross-sectional study of 38 singleton pregnancies complicated by early onset placental insufficiency defined as estimated fetal weight <10th percentile for gestational age and umbilical artery (UA) pulsatility index (PI) >95th percentile for gestational age diagnosed before 34 weeks of pregnancy. In all women, gestational age was determined based on the last menstrual period and confirmed by first trimester ultrasound. Multiple pregnancies and fetuses with malformations or chromosomal abnormalities were excluded from our sample. The study was approved by the local medical ethics committee and all women gave their informed consent.

* Corresponding author at: Departamento de Obstetrícia e Ginecologia, Faculdade de Medicina da Universidade de São Paulo, Av. Dr. Enéas de Carvalho Aguiar 255, 10° andar, cj. 10037, São Paulo, SP CEP 05403-000, Brazil.
Tel.: +55 11 2661 6209; fax: +55 11 2661 8183.
E-mail address: roseli.nomura@hotmail.com (Roseli M.Y. Nomura).

http://dx.doi.org/10.1016/j.ejogrb.2015.03.031
0301-2115/

Fetal heart rate analysis was performed by an automated system using the Sonicaid FetalCare software version 2.2 (Huntleigh Healthcare Ltd, Cardiff, UK). The cCTG was interpreted as described elsewhere, using the traditional algorithm for satisfying the Dawes and Redman criteria [11,12]. The FHR parameters addressed in the study were the following: basal FHR in beats per minute (bpm), small acceleration (>10 bpm and <15 bpm), large acceleration (>15 bpm), short-term variation (STV; mean epoch-epoch variation of 3.75 ms), episodes of high FHR variation (defined as at least five out of six consecutive minutes in which the range of pulse interval is >32 ms), episodes of low FHR variation (defined as at least five out of six consecutive minutes in which pulse interval is <30 ms), and fetal movements (FM) assessed by maternal perception and calculated as FM/hour. As an inclusion criterion, each tracing had to be characterized by a <5% signal loss. All tracings were analyzed at 30 min.

Doppler recordings were performed using real-time ultrasound (Envisor, Philips) equipped with a 3.5-MHz curved-array transducer. All Doppler studies were done with the patient in a semi-recumbent position and during absence of fetal body or breathing movements. The high pass filter was set at minimum and the size of the sample volume was adapted to the vessel diameter. The insonation angles were always kept below 30° and the vessel impedance was calculated when a stable signal was obtained and it lasted for at least five cardiac cycles. Pulsed Doppler examination of UA pulsatility index (PI) was performed in the umbilical cord near the placental insertion and was classified as present, absent (AEDV), or reversed (REDV). The fetal middle cerebral artery (MCA) was identified in the transverse plane across the base of the fetal skull. The sphenoid bone and the artery running along the great wing of this bone were also visualized. Pulsatility index was measured on the proximal third of the vessel. The ductus venosus (DV) was examined at the inlet portion in a transverse view of the fetal abdomen and PI for veins (PIV) was obtained. In order to adjust for gestational age, all Doppler parameters were transformed into *z*-scores (SD values from the mean) according to normative references [13,14].

In our institution, all patients with placental insufficiency are submitted to Doppler, biophysical profile score, and cCTG examinations, scheduled as routine care following already established clinical protocols, every one to three days until the day of delivery. To the present study, the analysis was made based on the last assessment carried out right before birth or administration of the antenatal steroids. All cases were examined within two days of delivery.

Immediately after delivery, a segment of 15–20 cm of umbilical cord was clamped and umbilical vein blood samples were collected for measurement of cTnT. Serum cTnT concentration was measured using a commercially available enzyme-linked immunosorbent assay kit (Enzym-test Troponin-T, Roche Diagnostics, Mannheim, Germany) according to the manufacturer's instructions. The monoclonal antibodies used are highly specific for cTnT. In adults, the decision limit for myocardial damage is 0.01 ng/ml [15] and the reported 99th percentile for cTnT in healthy term newborns is 0.89 ng/ml [16]. In our study, the presence of cTnT ≥0.09 ng/ml was set as fetal myocardial damage.

Statistical analysis

Data were analyzed using the Medcalc program, version 11.5.1.0 (Medcalc Software, Belgium). The Mann–Whitney-*U* test was used to compare the medians between the groups, according to the presence or absence of myocardial damage. Categorical data were compared using the chi-square test or the Fisher exact test when appropriate. Correlation analysis was used and the Spearman rank correlation coefficient (rho) was calculated. Logistic regression with stepwise selection was performed to identify independent variables for predicting myocardial damage at birth. The statistical significance was set at $P < 0.05$.

Results

A total of 38 high-risk pregnant women met the inclusion criteria. All cases were delivered by cesarean section. Of all newborns in the study, 15 (39%) neonates had high cTnT at birth (≥0.09 ng/ml). The maternal characteristics and neonatal data are listed in Table 1. The mean time between the last evaluation and delivery was 0.31 days (SD 0.66 days). By the time of delivery, 12 (32%) patients had severe placental insufficiency, diagnosed by AEDV ($n = 6$, 16%) or REDV ($n = 6$, 16%) flow in the UA.

In the group which presented myocardial damage, UA PI and DV PIV were significantly increased, the same as observed with their *z*-score (Table 2). With respect to cCTG parameters, the fetuses with myocardial damage showed higher basal FHR ($P = 0.033$), smaller number of small accelerations ($P = 0.013$), longer duration of low episodes ($P = 0.038$), and lower values of STV ($P = 0.003$) when compared to the group with normal levels of cTnT at birth (Table 2).

A correlation analysis was set between cTnT values at birth and all parameters with $P < 0.1$ (Table 3). We found a significant positive correlation between cTnT and basal FHR values ($P = 0.042$) and a significant negative correlation with STV ($P = 0.017$) (Fig. 1).

Logistic regression analysis was performed using cTnT ≥0.09 ng/ml as the dependent variable and including the following independent variables: gestational age at delivery, UA PI *z*-score, DV PIV *z*-score, basal FHR, number of FM/hour, number of small accelerations, and STV. The logistic regression analysis showed that STV and gestational age (GA) at delivery were independently related to myocardial damage at birth. The logistic regression model was evaluated by the ROC curve analysis (Fig. 2), defined by the following formula: $\text{logit}(p) = 18.650 - (0.509 \times \text{GA}) - (0.521 \times \text{STV})$, where p is the probability of myocardial damage. The area under the curve for predicting cTnT ≥0.09 ng/ml at birth was 0.91 (95% CI: 0.722–0.978).

Comment

Correct timing for delivery of fetuses with growth restriction is an important issue for which no uniform consensus exists. Placental insufficiency predisposes the fetus to progressive compromise of organ function and the antenatal quantification of these fetal risks is fundamental for timing delivery [17–19].

Table 1
Maternal and neonatal characteristics and Doppler velocimetry results in pregnancies with placental insufficiency ($n = 38$).

Characteristic	Value
Maternal age (years)	27.2 (6.9)
Parity 0	24 (63.5%)
Maternal disease	
Hypertension	30 (78.9%)
Preeclampsia	25 (65.8%)
Thrombophilia	5 (13.1%)
Diabetes	3 (7.9%)
Gestational age at delivery (weeks)	32.5 (3.4)
Birth weight (g)	1290.4 (530.2)
1 min Apgar score <7	11 (28.9%)
5 min Apgar score <7	3 (7.9%)
cTnT at birth (ng/ml)	0.10 (0.08)
cTnT >0.09 ng/ml	15 (39.5%)
pH at birth	7.07 (0.16)

Data expressed as *n* (%), mean (SD), or median (range).
cTnT, cardiac troponin T; AEDV, absent-end diastolic velocity; REDV, reversed-end diastolic velocity; UA, umbilical artery; MCA, middle cerebral artery; PI, pulsatility index; DV, ductus venosus; PIV, pulsatility index for veins; UV, umbilical vein.