Full length article

Longitudinal progression of fetal short-term variation and average acceleration and deceleration capacity after antenatal maternal betamethasone application

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ABSTRACT

Objective: To analyze the effect of maternal betamethasone given for fetal lung maturation on fetal short-term variation (STV) and average acceleration and deceleration capacity (AAC/ADC). Both of these factors are calculated by phase-rectified signal averaging (PRSA) and represent new parameters to assess the fetal autonomic nervous system.
Study design: A longitudinal prospective study including 26 pregnant women at risk for preterm delivery was performed. Two injections of 12 mg betamethasone were administered intramuscularly at a 24 h interval for lung maturation. Cardiotocography recordings were performed at defined time intervals: day 0 (before the first injection) and days 1, 2, 4 after the first corticosteroid administration. AAC/ADC and STV were calculated.
Results: An increase of all parameters (STV, AAC and ADC) was documented between day 0 and day 1. Between day 1 and day 2, all three indices were significantly reduced ($p < 0.05$). STV declined by 19.8%, AAC by 10.1% and ADC by 14.8%. A normalization of these values was seen after 96 h.
Conclusion: Similar to STV, AAC/ADC shows significant changes after maternal betamethasone administration. The corticosteroid-induced transient decrease of the levels needs to be taken into account in the assessment of the fetal status to avoid misinterpretation of these parameters.

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Introduction

Antenatal corticosteroid administration decreases the morbidity and mortality of infants born between the 24 and 34 weeks of gestation significantly [1,2]. It reduces the risk of neonatal respiratory distress, the frequency of intraventricular hemorrhages and necrotizing enterocolitis [1,2]. Importantly, especially betamethasone and dexamethasone have been shown to induce transient but significant changes of fetal heart rate characteristics in several studies [3–7]. Besides short- and long-term variation (STV, LTV), basal heart rate, accelerations and decelerations, the average acceleration and average deceleration capacity (AAC and ADC) are two new parameters for the assessment of the fetal autonomic nervous system (ANS). These parameters are obtained

by the phase-rectified signal averaging (PRSA) method, analyzing a particular type of fetal heart rate variability (fHRV) by applying it to cardiotocography (CTG) or fetal electrocardiography (fECG) recordings. PRSA synchronizes the phase of all periodic components of the detected signal, thereby eliminating artifacts and signal perturbations. This allows not only an analysis of the heart rate variability but also a quantification of the speed of changes in fetal heart rate (FHR), described as the acceleration and deceleration capacity [8,9].

The AAC and ADC have been shown to be good parameters to assess the fetal condition in prior studies, especially for small-for-date fetuses (SFD) and during labor. Fetuses with a growth restriction caused by a limited metabolic reserve of the placenta are at significantly higher risk of perinatal mortality and morbidity. Chronic hypoxemia and malnutrition result in a central nervous system and cardiovascular adaption [10]. It has been shown in previous studies that the PRSA-method seems to identify and monitor the progressive deterioration of SFD fetuses [8,9,11–13] at least as well as STV. Regarding acute hypoxemia, Georgieva et al.

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[14] discovered a relation between PRSA results and acidemia at birth by analyzing intrapartum fetal heart rate. In this study it could be shown that the deceleration capacity appears to predict acute hypoxia more accurately than STV. Similar results could be shown in an animal model by Rivolta et al. In regards to fetal programming, PRSA additionally seems to affect the fetal ANS in pregnancies with maternal gestational diabetes [15].

This prospective longitudinal study compares the changes of fetal AAC, ADC and STV after betamethasone administration in imminent premature birth. This could help to avoid misinterpretation of these cardiac parameters after maternal betamethasone application which could lead to unwarranted delivery of preterm fetuses.

Material and methods

Patient recruitment was performed from August 2010 until May 2012 at the Department of Obstetrics and Gynecology, Technical University of Munich, Germany. All women with an indication for fetal lung maturation due to potential preterm delivery were included in the study. Two intramuscular injections of 12 mg betamethason (Celestan® solubile, MSD®) were administered 24 h apart. Inclusion criteria were singleton pregnancy of mothers aged over 18 and gestational age between 24 and 34 weeks of gestation.

Women were excluded if delivery appeared imminent in order to not delay the first administration of betamethasone for the required 40 min computerized cardiotocography (cCTG) and another 60 min for study inclusion. Multiple gestations, pregnancies with known fetal malformations or patients who had already received antenatal corticosteroids were also excluded. Study approval was obtained from the Institutional Review Board and written informed consent was obtained from all included patients.

cCTG recordings of at least 40 min were performed before the first dose of betamethasone (day 0) as well as after 24 h (day 1), 48 h (day 2) and 96 h (day 4). Measurements were performed at the same time of day. If the CTG recording was not performed at the appropriate time, the data for that day was considered as missing.

The complete 40 min cCTG signal was used for analysis. cCTGs were recorded using Sonicaid System 8002 (Oxford Instruments Medical Ltd, Surrey, UK). The STV was extracted directly using the original Dawes/Redman algorithm[16] while AAC and ADC were calculated by the PRSA method previously described by Lobmaier et al [8]. The PRSA data were analyzed off-line using the following parameters: T = 10 samples, L = 100 samples, anchor points were defined as increases (AAC) or decreases (ADC) by <5%. The CTG data does not reflect real beat-to-beat heart rates. The CTG technique works with a sample frequency of 4 Hz meaning that the fetal heart rate is sonographically detected four times per second.

Table 1
Patient characteristics and pregnancy outcomes.

Patient characteristics at time of inclusion		
patient age (years)		32.7 ± 4.6
multiparous women		25 (96.2%)
gestational age at inclusion (weeks)		29.3 ± 3.8
time of the recordings (CET)		16:15 ± 2:58
BMI (kg/m^2) pre-pregnancy		22.9 ± 5.9
BMI (kg/m^2) post-pregnancy[a]		26.0 ± 5,4
tocolysis[a]		9 (41.0%)
other treatments[b]		19 (73.1%)
pregnancy-related hypertensive disorders[a]		
	none	19 (76%)
	preeclampsia/HELLP	2 (8%)
	preexistent hypertension	2 (8%)
	Preeclampsia superimposed upon chronic/preexisting hypertension	1 (4%)
	others	1 (4%)
Smoking[a]		4 (19.0%)
Pregnancy outcome		
preterm birth (birth before 37 completed weeks)		16 (61.5%)
gestational age at birth (weeks)		35.1 ± 3.8
duration of pregnancy after the first recording (days)		40.7 ± 35.5
arterial umbilical blood pH		7.28 ± 0.7
birth weight (g)		2237 ± 923
percentile of birth weight[a]		28.8 ± 24.9
APGAR 1 min <7		5 (13.9%)
APGAR 5 min <7		0
transfer to NICU[a]		14 (56%)
neonatal resuscitation[a]		8 (33.3%)
SGA/FGR		7 (26.9%)
mode of delivery	vaginal delivery	9 (34.6%)
	Cesarean delivery	16 (61.5%)
	operative vaginal delivery	1 (3.8%)
reason for hospitalization	FGR	5 (19.2%)
	hypertensive disorders[c]	1 (3.8%)
	premature rupture of membranes	1 (3.8%)
	preterm labor	5 (19.2%)
	cervical insufficiency	5 (19.2%)
	threatened preterm delivery (combination of indications)	5 (19.2%)
	others	4 (15.4%)

values are given as mean ± SD (standard deviation).
SGA = small for gestational age; FGR = fetal growth restriction, HELLP = hemolysis, elevated liver enzymes, and low platelets.
 [a] data is missing (n differs from 26).
 [b] other treatments include: ASS, heparin, nifedipine, magnesium sulfate iv or oral, fenoterol and atosiban.
 [c] hypertensive disorders include preeclampsia, HELLP, preexistent hypertension and superimposed preeclampsia.