Heart Rate Variability Analysis for the Prediction of Hypotension during Spinal Anaesthesia in Programmed Cesarean Surgery and its Relation with Fetal Cord Acid-base Equilibrium

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Abstract

In this paper the ability of linear and nonlinear heart rate variability (HRV) indices to predict hypotension during spinal anaesthesia in programmed cesarean is studied, as well as their relation with fetal cord values. A database consisting of the ECG recordings of 40 pregnant women is analyzed. Recordings include the following positions: lateral decubitus (LD), supine decubitus (SD), sitting position (SP).

Classical temporal, spectral indices and non-linear HRV indices were calculated. Univariate analysis shows significant hypotension association of: maternal age, gestational age, $SampEn^{SD}$ *and* $ApEn^{SD}$, ΔTP^{SD-SP} *(p<0.05); and* ΔD_2^{LD-SD}, $\Delta SampEn^{LD-SD}$, *and* $\Delta ApEn^{LD-SD}$ *(p<0.01). Data from fetal cord study show that hypotension is associated with an increase in arterial lactic acid (p<0.05).* ΔD_2^{LD-SD}, $\Delta SampEn^{LD-SD}$ *and* $\Delta ApEn^{LD-SD}$ *are associated with venous lactic acid (p<0.05). A logistic regression model was used reaching balance accuracy in prediction of hypotension of 89.7%.*

1. Introduction

Heart rate variability (HRV) allows non-invasive assessment of autonomic nervous system (ANS) [1] although the exact contribution of its two branches (sympathetic and parasympathetic) is a matter of debate and research [2]. Several HRV indices allow the assessment of the impact that some pathologies have on ANS risk stratification, and short term response to drugs (hypotension and hemodynamical instability with general or spinal anesthesia [3]). The former applications, as well as its potential clinical use, make analysis of HRV especially interesting.

Spinal anesthesia is the elective technique in cesarean intervention, despite its high rate of hemodynamic instability and clinical hypotension (>60%) in habitual practice without pharmacological prevention [4]. Repercussion of these hypotension events on the mother and the fetus makes the prediction of this clinical situation especially relevant.

Clinical data and HRV indices have been studied in pregnant women for hypotension risk prediction after spinal anesthesia for cesarean section. Predictive value has been reported for linear (ratio between power in low and high frequency bands, LF/HF [5]) and nonlinear (peak correlation dimension [6] and approximate entropy [7]) parameters.

The objective of this work is to analyze linear and nonlinear HRV indices, obtained from women programmed for elective caesarean just before the surgery and the previous day, and their association with hypotension and with data from pH fetal cord, which is an index of placental hypoperfusion and fetal distress [8]; and to calculate, by logistic regression, a prediction model with studied indices.

2. Materials and methods

Database: The database consists of the ECGs of 40 pregnant women programmed for cesarean intervention, recorded in the University Hospital Miguel Servet, Zaragoza, Spain, after giving their informed consent. Exclusion criteria were urgent surgery, uterine contractions and maternal or fetal pathology.

Two-lead ECGs were acquired for each subject the evening before the surgery, after admission, and just before

the surgery in the Surgery Area, with a sampling frequency of 1000 Hz (Biopac Data Acquisition MP System). A protocol was designed to enhance ANS alterations. Firstly, the subject was at lateral decubitus (relaxed position, minimum stress) for 7 minutes (LD); then at supine decubitus (hemodynamic stress caused by aorto-cava compression) for other 7 minutes (SD); a sitting position for 7 minutes (SP); finally, a Valsalva maneuver of 15 s is performed, and at least one minute of recovery (RV).

HRV indices: Linear HRV indices included classical temporal and spectral indices. Time domain indices: mean heart rate (HRM), standard deviation of normal-to-normal intervals (SDNN), the squared root of the mean squared differences of successive NN intervals (RMSSD), the standard deviation of differences between adjacent NN intervals (SDSD) and the proportion of interval differences of successive NN intervals greater than 20 and 50 ms (pNN20 and pNN50, respectively), were calculated from the R-R interval series [1].

Frequency domain indices were obtained from the power spectral density of the modulating signal with information related to activity of the ANS obtained from the integral pulse frequency modulation model [9]. Then, absolute and normalized powers were computed in the following bands: very low frequency (VLF, 0.015-0.04 Hz), low frequency (LF, 0.04-0.15 Hz), high frequency (HF, 0.15-0.4 Hz.) and total power, TP, as the addition of both LF and HF bands frequency content. Besides classical bands, an extended HF band (HF_{EXT}), which ranges from 0.15 Hz to the Nyquist limit [10], is considered in order to assure the inclusion of respiratory frequency, which in pregnant women can exceed 0.4 Hz.

Non-linear HRV indices included Approximate Entropy (ApEn), Sample Entropy (SampEn) and Correlation Dimension (D_2).

Statistical analysis: Hypotension was defined as a drop in mean arterial blood pressure of >20% from baseline value [11]. All data were checked for normal distribution using Kolmogorov-Smirnov (KS). Afterwards, data were analyzed with T of Student or the Mann-Whitney U-test, acording to KS. Pearson correlation was applied between HRV measures and fetal cord data. A two tailed p-value <0.05 was chosen as statistically significant. Logistic regression was performed to investigate independent factors with a significant association to hypotension within a multivariate model. A forward stepwise algorithm (inclusion criteria) was used. Statistics were performed by using the statistics program SPSS version 15.0 (SPSS, Inc., Chicago IL).

3. Results

Hypotension occurred in 26 patients (GH) (65%) and 14 not (GNH). Only both maternal and gestational age were associated with hypotension with significant differences p<0.05. Regarding non-linear parameters, both SampEn and ApEn, computed during supine decubitus position, show significance differences with lower values in GH, for the day of the surgery data. Data are shown in Table 1.

Table 1. Demographic data and HRV indices with statistically significant results (GH) and (GNH) represented as mean (μ), standard deviation (σ), p-value (p), and area under ROC curve (ROC). Sample and approximate entropy ($SampEn^{SD}$ and $ApEn^{SD}$) in supine dubitus position the surgery day.

		μ	σ	p	ROC
Age [yrs]	GNH	31.8	5.1	0.023	0.70
	GH	35.5	4.6		
G. Age [wks]	GNH	38.6	1.0	0.045	0.69
	GH	38.0	0.9		
$SampEn^{SD}$	GNH	1.1	0.3	0.012	0.72
	GH	0.8	0.3		
$ApEn^{SD}$	GNH	1.0	0.2	0.013	0.73
	GH	0.8	0.2		

Table 2. Data of the differences between lateral and supine the day of surgery of correlation dimension (ΔD_2^{LD-SD}), sample entropy ($\Delta SampEn^{LD-SD}$), approximate entropy ($\Delta ApEn^{LD-SD}$) and between supine and seated for total power (ΔTP^{SD-SP}) and extended total power (ΔTP_{EXT}^{SD-SP}) represented as mean (μ), standard deviation (σ), p-value (p), and area under ROC curve (ROC).

		μ	σ	p	ROC
ΔD_2^{LD-SD}	GNH	-0.2	0.9	0.002	0.79
	GH	1.1	0.3		
$\Delta SampEn^{LD-SD}$	GNH	-0.1	0.3	0.006	0.75
	GH	0.2	0.3		
$\Delta ApEn^{LD-SD}$	GNH	-0.06	0.18	0.006	0.76
	GH	0.1	0.2		
ΔTP^{SD-SP}	GNH	420	84	0.010	0.80
	GH	138	54		
ΔTP_{EXT}^{SD-SP}	GNH	428	240	0.033	0.77
	GH	165	295		

Differences between values for the different protocol positions and comparisons between groups were calculated. For the day of surgery data, the difference of both extended and classical total power, between SD and SP, ΔTP^{SD-SP} and ΔTP_{EXT}^{SD-SP} shows meaningful significance. For non-linear parameters, differences in D_2, SampEn and ApEn between LD and SD positions were highly significant between GH and GNH (p<0.01), data are shown in table 2. Figure 1 shows these differences expressed as mean percentage variation changes.

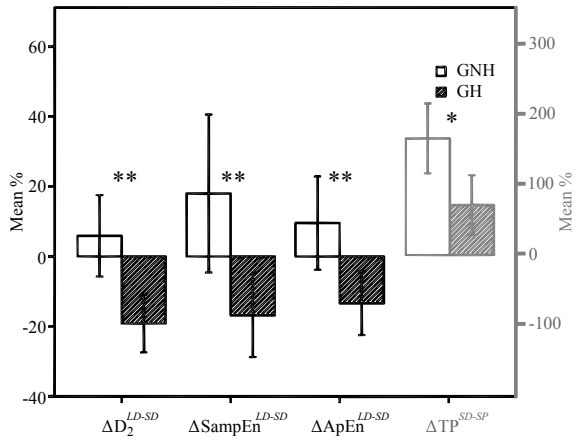

Figure 1. Mean percentage variations of the changes, expressed as mean±standard deviation, of linear and non-linear indices for position changes. $*$ means p<0.01 and $**$ means p<0.006.

Regarding data from the fetal cord, only arterial lactic acid shows significant differences comparing groups GH and GNH (arterial lactate: 2.6±1.1 vs. 1.9±0.6 mEq/L). Studying the correlation between HRV indices and fetal cord data, differences in ΔD_2^{LD-SD}, $\Delta SampEn^{LD-SD}$ and $\Delta ApEn^{LD-SD}$ were found significant when correlated with venous lactic acid with values of with values of $r = -0.362$, $p = 0.028$; $r = -0.329$, $p = 0.047$ and $r = -0.360$, $p = 0.029$ respectively.

The logistic regression equation contains three indices variables: gestational age, ΔTP^{SD-SP} ,ΔD_2^{SD-LD}, both on the day of surgery: $p_H = 121.20 + (-0.018\Delta TP^{SD-SP}) + (3.114\Delta D_2^{LD-SD}) + (-3.023 G.Age)$. Reaching a balanced accuracy of hypotension prediction of 89,7%, a sensitivity of 90,5% and a specificity of 87,5%.

4. Discussion and conclusions

The high incidence of hypotension events and their potential risks, joined to the non-pharmacological prophylaxis limited efficiency and the possible risks of the pharmacological prevention, have led to the searching and identification of risk factors and prediction models.

Under the assumption that the main underlying mechanisms for hypotension are a decrease in both systemic vascular resistance and venous return by vena cava compression, first studies focused on the detection of induced hemodynamic changes induced by changing position from lateral to supine decubitus, called Stress supine test (SST), i.e. Dahlgren et al in [12] about 80,5%.

Global predictive value of parameters studied in literature is scarce. The highest predictive values have been shown by: increased basal systemic vascular resistances [13] with an accuracy of 80,5% and changes in heart rate from SD to LD position [14] with a 79%. Efforts to find predictive models by logistic regression using several clinical parameters associated with hypotension events have been demonstrated poor results in the ROC curve analysis: i.e. 0.68 in [15].

Our results show high correlation values between hypotension and individual parameters with large areas under the ROC curves and a predictive power of the logistic regression model about 90,5% sensitivity, 87,5% specificity and global predictive value of 89,7% being much higher than the previously reported.

None of linear and non-linear indices in all of the studied positions showed significant differences between the groups for the previous day of the surgery in agreement with the work of Hanns [5].

Ghabach in [7] found an association between ApEn and weight increment during the pregnancy. Pregnant women with less weight increment (<11 kg) presented with higher ApEn values and propensity to suffer a hypotension event after spinal anesthesia. Our results, on the contrary, show significantly lower values in patients who suffered a hypotension event, in ApEn as well as in SampEn for DS position.

Differences of LD-SD and SD-SP for each parameter were also computed and compared between GH and GNH groups, in order to study the possible qualitative differences in the reactivity to the position change stimulus. Significant differences were only observed the day of the surgery for ΔTP^{SD-SP} and ΔTP_{EXT}^{SD-SP} (p<0.05, p<0.01), with higher values in GH; while ΔD_2^{LD-SD}, $\Delta SampEn^{LD-SD}$ and $\Delta ApEn^{LD-SD}$ were significantly higher in GNH group (p<0.005). Regarding these former values it is worthy to note that the change provokes a response with opposite direction, incremented in GNH and decreased in GH

The fact that the best parameters for discriminating the groups are the responses to position change stimulus, may possibly reflect the different adaptation capability of the hemodynamic regulation system and, therefore, the response to sympathetic blockade of the spinal anesthesia. The correlation of HRV indices and the acid-base cord fetal values shows only significant correlation between venous acid lactic and $\Delta\{D_2; SampEn; ApEn\}^{LD-SD}$.

Ephedrine is the prophylaxis protocol used in the present study. It has been reported that an increment of fetal lactic acid, whose mothers were treated with ephedrine, that is a sympathicomimetic drug with betadrenergic effects responsable of the metabolic activation that produces lactic acid, is related with hypotension events [16]. Thus, HRV index correlation with lactic acid shows the relation with hypotension events, being greater in GH group.

Conclusions: Among the linear and non-linear HRV in-

dices and protocol positions, only the day of the surgery significant differences were found between GH and GNH groups in the following parameters: SampEn and ApEn in supine decubitus position. The different response observed to position changes from SD to SP position in TP (ΔTP^{SD-SP}), and from LD to SD in D_2, SampEn and ApEn ($\Delta\{D_2;SampEn;ApEn\}^{LD-SD}$), in the results obtained from the recordings of the day of the surgery, show a higher prediction power to suffer hypotension events, with a significant correlation of these parameters with the fetal venous lactic acid. The estimated prediction model by multivariable logistic regression, taken into account gestational age, ΔTP^{SD-SP} and ΔD_2^{LD-SD}, reaches a global predictive value of 89,7%, a sensibility of 90,5% and a specificity of 87,5%.

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