



Comparison of diagnostic methods for hemodynamic treatment in unborn and preterm infants using the measurement of vena cava, lactate, and clinical criteria.

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Abstract

Introduction: There is no single criterion available to assess the hemodynamic state of newborn infants and preterm infants and the different variables in the group of newborns, such as gestational age, birth weight, and periods of birth.

Methods: This is an epidemiological, cross-sectional, descriptive observational study with two patient cohorts. Newborn-to-term and preterm neonates assisted at the Neonatal Unit of the Pablo Arturo Suarez Hospital participated during the months between November 2019 to January 2020.


Results: Ultrasound measurement of the vena cava (FVC) flow is useful for the management treatment of hemodynamically unstable neonatal patients. The sample was made up of 110 newborns treated in the Pablo Arturo Suarez Hospital's neonatology service from November 2019 to January 2020. Quito, Pichincha, Ecuador. The variables low birth weight and moderate prematurity have a statistically significant value for inotropic use. The other variables do not present statistically significant values. Heart rate, urinary output, mean blood pressure, lactic acid, capillary filling, upper vena cava flow, and lower vena cava flow had statistically significant values. FVCI and FVCS comparisons with heart rate, urinary output, mean blood pressure, lactic acid, and capillary filling had statistically significant values, except for capillary filling > 3 sec in FCVI. Multivariate analysis of categorical main components (CATPCA) was used to characterize the hemodynamic state and inotropic state, which were significant in the bivariate analysis. Dimension, one of the two-dimensional graphs, discriminates the use or not of inotropics and the categories of hemodynamic parameters TAM <35 mmHg, lactic acid, capillary filling, FVCI, and FVCS. Dimension two discriminates between the categories of urinary expenditure and HR.

Conclusion: In term and preterm infants with low weight and adequate birth weight with hemodynamic instability in general, who were evaluated with ultrasonography to measure the flow of the vena cava, the agreement between the clinical criteria and the ultrasound assessment of the flow was 0.4 cm/sec in both methods. This situation means that the measurement of venous cava flows by echo sonography is useful for assessing neonatal patients' hemodynamic status.

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Introduction

Maintaining the hemodynamic state requires adequate blood pressure, vascular resistance, and tissue perfusion [1]. These variables are influenced by gestational age, birth weight, adequate extrauterine adaptation, drugs, or adequate maternal hemodynamics; therefore, specifying normality only with clinical criteria is problematic. The normal physiological range of blood pressure is unknown in both premature and term infants [2]. Blood pressure is the product of the flow due to systemic vascular resistance, and the flow is dependent on preload, contractility, systolic volume, and afterload, so that the drop in blood pressure may be secondary to low expenditure cardiac, low vascular resistance, or both [3, 4].

Newborn hemodynamic surveillance often includes blood pressure, urine output, heart rate, capillary filling, and lactic acid, which have numerous limitations and are only variables dependent on tissue perfusion [5, 6]. The newborn can present various hemodynamic problems whose pathophysiology is complex as a variable and sometimes little predictable after clinical assessment. Therefore, the interpretation of these parameters can lead to erroneous conclusions and the adoption of incorrect therapeutic strategies in unstable patients [7]. Functional echocardiography for evaluating venous flows is a hemodynamic evaluation technique added to regular monitoring to guide the clinician in his therapeutic interventions in the neonatal intensive care unit [8, 9].

The role of echocardiography in neonatal intensive care units was intended to be performed by the pediatric cardiologist and used only for the diagnosis and control of congenital heart disease. Currently, neonatologists who have been interested in the echocardiographic evaluation of hemodynamic instability, given that it is a dynamic assessment with a noninvasive method that provides complementary information to the clinic and in real time, becomes essential for the adequate and more appropriate management of newborns in critical condition [10-12].

The first compensatory mechanism for extrauterine adaptation is the increase in chronotropism due to poor inotropism due to an immature myocardium and poorly sensitive receptors, so the use of vasoactive drugs that help maintain peripheral vascular resistance and preload is sustained to maintain adequate cardiac output accompanied by expected urine output and without lactic acid production. Under conditions of hemodynamic instability, the drop in peripheral vascular resistance promotes oliguria, and anaerobic metabolism increases the production of lactic acid, lowering the mean arterial pressure and prolonging capillary filling. As a result, these factors cause the chronotropic response to not compensate for the needs, so vasoactive drugs are needed to restore their function, an event that can be immediately identified, and respond to their treatment by measuring the flow of the vena cava [13-16].

Methods

Research design

This is a cross-sectional, epidemiological, and observational study of 2 cohort groups.

Location

Neonatology Service of the Pablo Arturo Suarez Hospital, data collection from November 2019 to January 2020.

Inclusion/exclusion criteria

All newborns of both sexes, at term and preterm born at the Pablo Arturo Suarez Hospital, with hemodynamic alteration (heart rate greater than 180 bpm or less than 100 bpm, capillary filling more generous than 3 seconds, diuresis less than 1ml/kg/h, lactate more significant than 1 mg/dL, Mean Arterial Tension less than 35 mm

Exclusion criteria were all newborns at term and preterm who were not born at the Pablo Arturo Suarez Hospital and patients without hemodynamic alteration.

Elimination criteria were newborns in the variable data that were incomplete, inconsistent, or inconsistent and newborns whose mothers did not consent to their child being part of the study.

Study Size

110 individuals, 55 to terms and 55 preterms.

Statistical method

Statistical analyses were performed with the statistical package IBM SPSS version 25, and descriptive statistics were used, using tables representing the absolute and relative frequencies of the qualitative variables. In inferential statistics, bivariate analyses were performed. For the qualitative variables where proportions were compared, the chi-square test was used. For the quantitative variables, the t-test of independent samples was used since the FVCI and FVCS variables presented a normal distribution. For the multivariate analysis, categorical main components (CMC) were used. Statistical significance to compare proportions and means was established for a P -value <0.05 .

Results

Ultrasound measurement of the Vena Cava flow (FVC) flow is useful for managing hemodynamically unstable

neonatal patients; the sample was made up of 110 newborns treated in the neonatology service Pablo Arturo Suarez Hospital from November 2019 to January 2020. Quito-Pichincha - Ecuador.

Table 1 shows that the variables low birth weight and moderate prematurity have a statistically significant value for inotropic use. The other variables do not present statistically significant values. Table 2 shows the variables heart rate, urinary output, mean blood pressure, lactic acid, capillary filling, upper vena cava flow, and lower vena cava flow, which had statistically significant values. Table 3 shows that FVCI and FVCS comparisons with heart rate, urinary output, mean blood pressure, lactic acid, and capillary filling had statistically significant values, except for capillary filling > 3 sec FCVI.

Graphic 1 shows that the multivariate analysis of categorical main components (CMC) was used to characterize hemodynamic and inotropic use, which were significant in the bivariate analysis. Dimension, one of the two-dimensional graphs, discriminates the use or not of inotropics and the categories of hemodynamic parameters TAM <35 mmHg, lactic acid, capillary filling, FVCI, and FVCS. Dimension two discriminates between the categories of urinary expenditure and HR.

Table 1 Distribution of the characteristics of neonates regarding the use of inotropics

Neonate characteristic	Total	Inotropic use		P
		Yes	No	
Sex(n (%)) ^{1/}				
Male	52 (47.27)	35 (67.31)	17 (32.69)	
Female	58 (52.73)	33 (56.90)	25 (43.10)	0.262
Gestational age (mean (SD)) ^{2/}	37 (2)	36 (3)	37 (2)	0.272
Birth weight (mean (SD)) ^{2/} gr	2.452 (509)	2.377 (510)	2.575 (488)	0.047**
Low birth weight (n (%)) ^{1/}				
Yes	65 (59.09)	42 (64.62)	23 (35.38)	
No	45 (40.91)	26 (57.78)	19 (42.22)	0.468
Preterm (n (%)) ^{1/}				
Yes	58 (52.73)	38 (65.52)	20 (34.48)	
No	52 (47.27)	30 (57.69)	22 (42.31)	0.399
Preterm category (n (%)) ^{1/}				
Mild	31 (53.45)	16 (51.61)	15 (48.39)	
Moderate	27 (46.55)	22 (81.48)	5 (18.52)	0.017*
Maternal hemodynamic changes (n (%)) ^{1/}				
Yes	71 (65.14)	48 (67.61)	23 (32.39)	
No	38 (34.86)	19 (50.00)	19 (50.00)	0.072

Note DE = Standard Deviation; 1 / based on the chi-square statistic homogeneity test * significant differences in the proportion of use of inotropic p -value <0.05 ; 2 / based on the t-test of independent samples. ** significant differences in the means between the use or not of inotropic P -value <0.05 .

In quadrants II and III, it was observed that the use of ino-tropics was associated with FVCI <0.40, FVCS <0.40, TAM <35 mmHg, lactic acid > 1 mmol/L, and capillary filling > 3 sec, while in quadrant I, the nonuse of

inotropics was related to FVCI > 0.40 and FVCS > 0.40 in the absence of TAM <35 mmHg and lactic acid <1 mmol/L

Table 2. Distribution of the characteristics of the hemodynamic state of neonates concerning the use or not of inotropics

Characteristics of the Hemodynamic state	Total	Inotropic use		P
		Yes	Yes	
Heart rate (n (%)) ^{1/}				
>180	86 (82.69)	48 (55.81)	38 (44.19)	<0.0001*
<100	18 (17.31)	18 (100.00)	0 (0.00)	
Urinary output (n (%)) ^{1/}				
>1ml/kg/h	96 (87.27)	54 (56.25)	42 (43.75)	<0.0001*
<1ml/kg/h	14 (12.73)	14 (100.00)	0 (0.00)	
Mean Blood Pressure < 35 mmHg (n (%)) ^{1/}				
Yes	65 (59.09)	60 (92.31)	5 (7.69)	<0.0001*
No	45 (40.91)	8 (17.78)	37 (82.22)	
Lactic acid (n (%)) ^{1/}				
<1 mmol/L	21 (19.44)	5 (23.81)	16 (76.19)	<0.0001*
>1 mmol/L	87 (80.56)	63 (72.41)	24 (27.59)	
Capillar filling >3seg (n (%)) ^{1/}				
Yes	44 (40.00)	34 (77.27)	10 (22.73)	0.006*
No	66 (60.00)	34 (51.52)	32 (48.48)	
FVCI (mean (SD)) ^{2/}	0.35 (0.14)	0.27 (0.09)	0.46 (0.13)	<0.0001**
FVCS (mean (SD)) ^{2/}	0.37 (0.17)	0.31 (0.14)	0.48 (0.17)	<0.0001**
FVCI (n (%)) ^{1/}				
<0.40	66 (60.00)	57 (86.36)	9 (13.64)	<0.0001*
≥0.40	44 (40.00)	11 (25.00)	33 (75.00)	
FVCS (n (%)) ^{1/}				
<0.40	58 (52.73)	50 (86.21)	8 (13.79)	<0.0001*
≥0.40	52 (47.27)	18 (34.62)	34 (65.38)	

Note SD = Standard Deviation; 1 / based on the chi-square statistic homogeneity test * significant differences in the proportion of use of inotropic p-value <0.05; 2 / based on the t-test of independent samples. ** significant differences in the means between the use or not of inotropic p-value <0.05. FVCI: Lower vena cava flow. FVCS: superior vena cava flow

Table 3. Comparison of FVCI and FVCS regarding the characteristics of the hemodynamic state.

Characteristics of the Hemodynamic state	FVCI		FVCS	
	Mean (SD)	P	Mean (SD)	P
Heart rate (n (%)) ^{1/}				
>180	0.36 (0.15)	<0.0001*	0.39 (0.17)	0.009*
<100	0.26 (0.07)		0.28 (0.14)	
Urinary output (n (%)) ^{1/}				
>1ml/kg/h	0.36 (0.15)	<0.0001*	0.38 (0.17)	0.024*
<1ml/kg/h	0.26 (0.07)		0.30 (0.11)	
Mean Blood Pressure < 35 mmHg (n (%)) ^{1/}				
Yes	0.28 (0.11)	<0.0001*	0.31 (0.14)	<0.0001*
No	0.43 (0.14)		0.46 (0.17)	
Lactic acid (n (%)) ^{1/}				
<1 mmol/L	0.41 (0.14)	0.011*	0.47 (0.17)	0.003*
>1 mmol/L	0.32 (0.14)		0.34 (0.16)	
Capillar filling >3seg (n (%)) ^{1/}				
Yes	0.31 (0.15)	0.054	0.32 (0.17)	0.008*
No	0.36 (0.14)		0.41 (0.16)	

Note DE = Standard Deviation; based on the t-test of independent samples. ** Significant differences in the means of FVCI or FVCS p-value <0.05. FVCI: Lower vena cava flow. FVCS: superior vena cava flow.

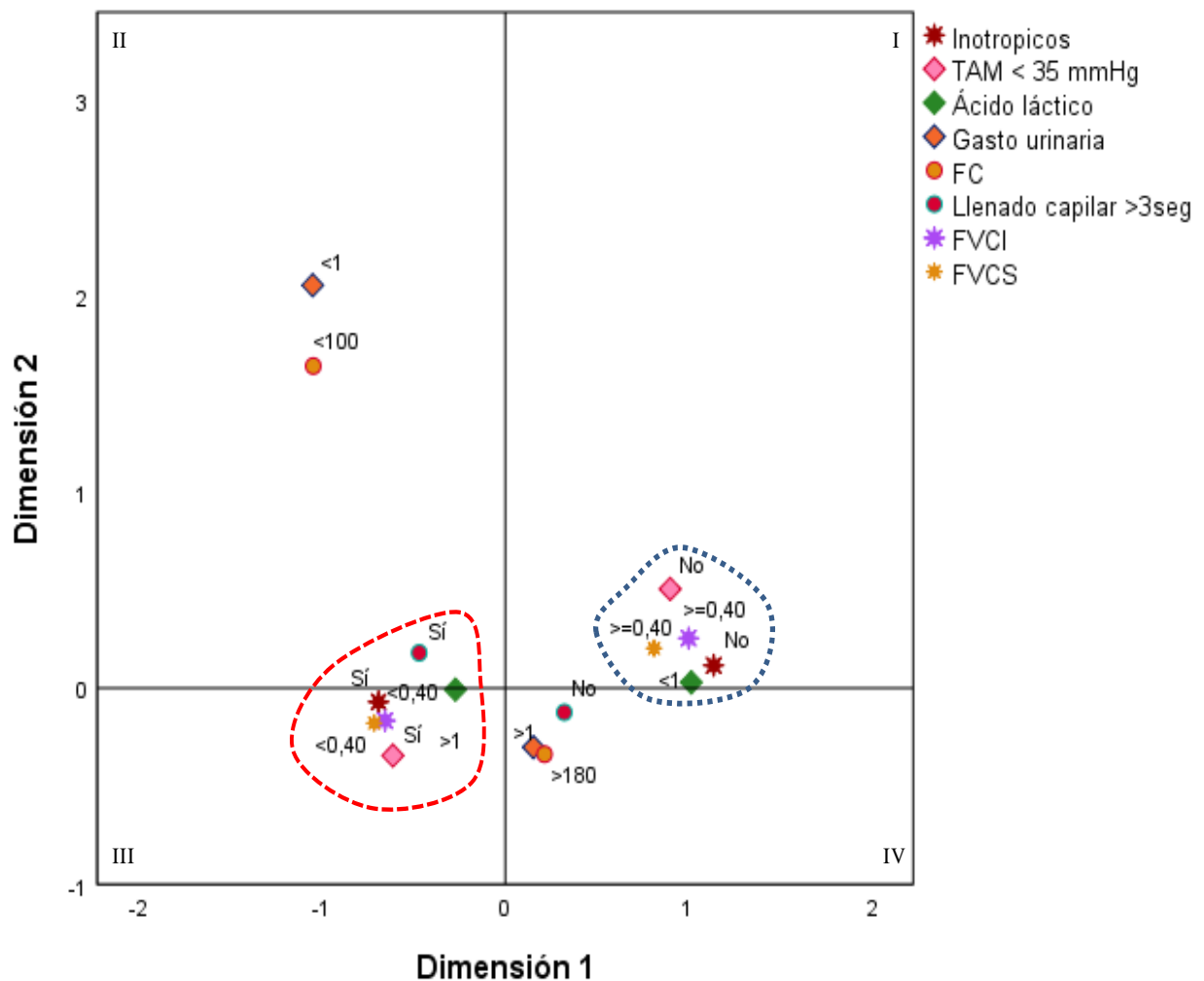


Fig. 1 Multivariate relationship of hemodynamic state parameters and inotropic use.

Note: Based on the multivariate analysis of categorical main components (CMC). FVCI: Lower vena cava flow. FVCS: superior vena cava flow

Discussion

Regarding the characteristics of neonates, it was found that low birth weight had a statistically significant value for the use of inotropics. The transition explains this from foetal to neonatal circulation, which is slower and is associated with circulatory modifications when transferring the gas exchange of the placenta to the lungs along with the slow morphological development of the receptors [4, 5]. Cardiac fetal development does not show differences

between sexes, so neonatal adaptation occurs equally. Testosterone has a more significant hypertrophic effect at an older age by developing arteries of better caliber, while progesterone and estrogens have a more significant hyperplastic effect [6, 7].

Gestational age is directly proportional to cardiac function and a slow adaptation to transition; low cardiac output is due to low peripheral vascular resistance [8].

Regarding the hemodynamic state characteristics and inotropic use, the increase in chronotropism is the

first compensatory mechanism due to poor inotropism due to an immature myocardium and poorly sensitive receptors, noting the need for inotropics [9]. Adequate cardiac output ensures adequate urinary expenditure, but in shock conditions, the fall in peripheral vascular resistance promotes oliguria by not maintaining adequate perfusion of the renal arteries needing vasoactive drugs to restore their function. In the neonatal period, high pulmonary vascular resistance falls under optimal adaptation conditions, allowing the left ventricle to have normal function. However, in any hemodynamic alteration, its persistence promotes the decrease of the mean arterial pressure mediated by inadequate response to oxygen, prostaglandins, and changes in the endothelium vascular, making clear the requirement of inotropic [10, 11].

Lactic acid is a biochemical marker of anaerobic metabolism and is an indicator of cytopathic hypoxia attributed to myocardial function's inadequate response, translated into low mean blood pressure [12, 13]. Capillary filling as an indicator of distal perfusion controlled by the vascular endothelium and peripheral vascular resistance indirectly denotes hemodynamic alteration to justify inotropic use [14, 15]. The preload is directly proportional to the systolic volume by projecting adequate cardiac output. Sonographically, the Doppler measurement of the velocity or flow through the venous veins indicates good hydrodynamics, resulting in the direct and dynamic assessment of the hemodynamic state, a fundamental contribution to the use of inotropic [16, 17].

Tachycardia is related to increased parasympathetic and beta-adrenergic activity as compensation, and increasing the minute volume increases the preload and therefore translates into the altered flow of veins [18]. The umbilical impingement produces an increase in renal blood flow due to the decrease in renal vascular resistance and the increase in systemic arterial pressure favoring glomerular filtration; if the transition due to a hemodynamic alteration is not adequate, low urinary expenditure and not increasing systemic pressure Cava flows are also altered [18, 19].

The increase in lactic acid due to anaerobic metabolism results in vasodilation with the consequent decrease in mean arterial pressure that alters vena cava flow. Venous vein flow is controlled by an

adequate preload and peripheral vascular resistances; if titular perfusion drops, capillary filling is prolonged due to the inadequate production of endothelial nitric oxide from the flow of the cava [9].

The absence of TAM less than 35 mmHg, lactic acid greater than 1 mmol/L, capillary filling greater than 3 seconds, and alteration of FVC discriminate the use of inotropics because the compensatory mechanisms are given by the autonomic nervous system, chronotropism, vascular endothelium, and peripheral vascular resistance to maintain homeostasis, allowing the flow of cava veins to be disturbed [2, 18-20].

Conclusions

In term and preterm infants with low weight and adequate birth weight with hemodynamic instability in general, who were evaluated with ultrasonography to measure the flow of the vena cava, the agreement between the clinical criteria and the ultrasound assessment of the flow was 0.4 cm/sec in both methods. This situation means that the measurement of venous cava flows by echo sonography is useful for assessing neonatal hemodynamic patients.

Abbreviations

CMC. categorical main components. FVCI: Lower vena cava flow. FVCS: superior vena cava flow.

Supplementary information

Supplementary materials are not declared.

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Authors' contributions

Geyson Deley-Muñoz: Conceptualization, Data Conservation, Fund Acquisition, Research, Resources, Software, Writing - Original Draft, Writing: Review and Editing.

Fabrizio González-Andrade: Methodology, Formal analysis, Project management, Supervision, Validation, Visualization.

Financing

The authors financed the expenses incurred in the production of this research.

Availability of data and materials

The data sets generated and / or analyzed during the current study are not publicly available due to the confidentiality of the participants, but are available through the corresponding author upon reasonable academic request.

Declarations

Ethics approval and consent to participate

This work respects all bioethical criteria and has the approval of the Ethics Committee for research in Human Beings (CEISH) -of the San Francisco de Quito University.

Consent for publication

It does not apply to studies that do not publish MRI / CT / Rx images or physical examination photographs.

Competing interests

The authors declare not to have any interest conflicts.

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