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Research Article

Cardiovascular Risk Factors for Diagnosis of Neonatal Asphyxia

Daniel López-Arnáiz[1], José Andrés Zavala Laurel[2] and Pedro José Curi-Curi[3]*

[1]Pediatric Cardiology and Echoocardiography, Hospital Regional de Alta Especialidad Ixtapaluca (HRAEI), State of Mexico, Mexico

[2]Centro Interdisciplinario de Ciencias de la Salud – Instituto Politécnico Nacional (CICS-IPN), Mexico City, Mexico

[3]Chief of the Postgraduate Unit Hospital Regional de Alta Especialidad Ixtapaluca (HRAEI), State of Mexico, Mexico

***Corresponding Author:** Pedro José Curi-Curi, Chief of the Postgraduate Unit Hospital Regional de Alta Especialidad Ixtapaluca (HRAEI), State of Mexico, Mexico.

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Abstract

Neonatal Asphyxia (NA) is the inability of newborns to establish normal breathing after birth, which results in decreased oxygenation and perfusion of multiple organs, leading to hypercapnia and acidosis. The diagnosis is based on clinical criteria and serum parameters, which detect hypoxia or ischemia after birth. Therefore, analysis of objective echocardiography cardiovascular parameters can allow to a better recognition and diagnosis, improvement of treatment and better long-term prognosis. A case-control clinical study was designed in order to detect cardiovascular risk factors for diagnosis of Neonatal Asphyxia in a third level hospital at a 3year period of time. A total of 32 cases with neonatal asphyxia (problem group) and 20 cases without neonatal asphyxia (control group) were recruited to this study. There was no difference between the studied groups in terms of gender, type of delivery (vaginal or cesarian), and use of high-flow nasal tips. Mechanical ventilation and APGAR score below or equal 6, birth weight between 1500 and 2499 grames, and gestational age from 37 to 42 weeks were significantly higher in the problem group compared with the control group. Pulmonary and cardiovascular organic damage in neonatal asphyxia were the most frequent complications, followed by hypoxic-ischemic encephalopathy. Renal dysfunction was observed in a lesser extent. Heart rate above 120 bpm is a protective factor for neonatal asphyxia, but the use of vasoactive drugs was not a risk factor- We concluded that cardiovascular risk factors for diagnosis of Neonatal Asphyxia in order of importance were: CPK-MB above 77.5 U/L, mitral regurgitation, ventricular dyskinesia and troponin above 0.3 ng/ml.

Keywords: Neonatal Asphyxia; Cardiovascular Risk Factors; Ventricular Dyskinesia; Mitral Regurgitation; Echocardiography

Abbreviations

NA: Neonatal Asphyxia; CPK-MB: Creatine Phosphokinase-MB

Introduction

Neonatal Asphyxia (NA) is the inability of newborns to establish normal breathing after birth, which results in decreased oxygenation and perfusion of multiple organs, leading to hypercapnia and acidosis, potentially fatal conditions [1]. NA is considered one of the main causes of morbidity and mortality in the newborn, and its late sequelae are of great concern, especially in developing countries [2]. The current criteria for the diagnosis of NA include: APGAR score less than or equal to 3 at 5 minutes, pH less than 7 in umbilical cord blood gas [3], base deficit greater than -10 mmol/l, and presence of multiorgan dysfunction (cardiovascular, neurological with clinical evidence of encephalopathy, hematological and/or respiratory).

Diagnosis of NA integrates clinical criteria and serum parameters in order to detect hypoxia or ischemia after birth. However,

several criteria are not very specific because multiple neonatal pathologies lead to acidosis, hypoxia and ischemia, besides NA. Therefore analysis of objective cardiovascular parameters through echocardiography can allow to a better recognition and diagnosis of NA, for the improvement of treatment, allowing a long-term prognosis [4].

Cardiovascular alterations in NA during severe hypoxia include tricuspid or mitral regurgitation, pulmonary hypertension, and transient myocardial ischemia [5]. A 73% incidence of myocardial injury in newborns has been reported due to NA [6]. Despite several clinical manifestations of myocardial damage and the lack of specific indicators in the early stage, correct diagnosis of NA is still a goal to achieve. If myocardial injury progresses to necrosis, the prognosis is poor and mortality increases. It is important to highlight that detection of objective cardiovascular risk factors (clinical, serum and echocardiographic) may allow to guide and improve diagnosis of cardiovascular damage in newborns with NA [7].

Materials and Methods

A case-control clinical study was designed in order to detect cardiovascular risk factors for diagnosis of NA in a third level hospital at a 3 year period of time. All hospitalized newborns of both genders, were recruited independently of the presence of NA. Lack of complete clinical, serum or echocardiographic data records and diagnosis of congenital heart disease were exclusion criteria. Patients were divided into two large groups: with NA (problem group) and without NA (control group). Base deficit > -12 mmol/l and pH in cord blood gas < 7 were the main criteria used for diagnosis of NA. Studied variables were grouped in three main categories: clinical, serum and echocardiographic (Table 1). Clinical and serum data were obtained from the institutional electronic clinical records and echocardiographical data were obtained with the use of a VIVID S9 General Electric model echocardiography equipment. Data was store in an electronic Excel spreadsheet and analyzed using SPSS V.21 statistical software. Numerical data are presented as the mean ± standard deviation with minimum and maximum ranges of variability. Categorical data are presented as the number (n) and percentage in relation to the population at risk. Comparison between groups in order to explore cardiovascular risk factor for NA, was made using the Chi square test for categorical variables and Student's T test for numerical variables. A $p < 0.05$ was considered as statistically significant. In all patients an informed consent from their parents or tutors was collected and the study was approved by the institutional research and ethics committees.

Table 1: Study variables.

Type of variable	Description
Clínic	Heart rate
	High-Flow Nasal Cannula
	Mechanic Ventilation
	Inotrope use
Serum parameters	Platelets Count
	CPK
	CPK-MB
	Troponin I
Ecochardiographic	Left ventricular Ejection Fraction
	Systolic Pulmonary Artery Pressure
	TAPSE
	Mitral Regurgitation
	Ventricular dyskinesia

Results

A total of 32 cases with NA (problem group) and 20 cases without NA (control group) were recruited to this study. Clinical and demographic data of our population are shown in Table 2. We can see no difference between the studied groups in terms of gender, type of delivery (vaginal or cesarian), and use of high-flow nasal tips. Mechanical ventilation and APGAR score ≤ 6, birth weight between 1500 and 2499 g, and gestational age from 37 to 42 weeks were significantly higher in the problem group compared with the control group. Pulmonary and cardiovascular organic damage in NA were the most frequent, followed by hypoxic-ischemic encephalopathy. Renal dysfunction was observed in a lesser extent (Table 3). Table 4 shows clinical and serum data risk factors for diagnosis of NA. Heart rate ≥ 120 bpm is a protective factor for NA. We detected that the use of vasoactive drugs was not a risk factor for NA. Risk factors for diagnosis of NA were in order of importance: CPK-MB > 77.5 U/L, mitral regurgitation, ventricular dyskinesia and troponin> 0.3 ng/ml (Table 4).

Discussion

Since 1970, cardiovascular NA alterations were described, but currently do not lead to a correct diagnosis, for a high index of suspicion is required [8]. The main circulatory change during NA is centralization of the blood flow or immersion reflex, which consists on favoring the flow to vital organs such as the brain, myocardium and adrenal glands, by reducing the flow to the less essential or-

Table 2: Baseline characteristics of the neonates with and without neonatal asphyxia.

	Without NA (n = 20)	With AN (n = 32)	
Variable	**n (%)**	**n (%)**	**p**
Masculine Gender	12 (60%)	25 (78%)	p = 0.090
Cesarean Delivery	20 (100%)	27 (84%)	p = 0.1623
Neonatal Reanimation			
High-Flow Nasal Cannula	0 (%)	5 (15%)	p = 0.1623
Mechanic Ventilation	7 (35%)	22 (70%)	p = 0.0199
None	13 (65%)	5 (15%)	p = 0.006
APGAR score (5 minutes)			
> 6	16 (80%)	15 (47%)	p = 0.0224
≤ 6	4 (20%)	17 (53%)	p = 0.0224
Birth Weight (g)			
980-1499	1 (5%)	6 (19%)	p = 0.1875
1500-2499	13 (65%)	10 (31%)	p = 0.0199
2500-3499	5 (25%)	12 (38%)	p = 0.3527
>3500	1 (5%)	4 (12%)	p = 0.3881
Gestational Age (wks)			
28 - 32	8 (40%)	8 (25%)	p = 0.2577
33 - 36	7 (35%)	6 (19%)	p = 0.1562
37 - 42	5 (25%)	18 (56%)	p = 0.031

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Table 3: Major organ involvement in the neonates with perinatal asphyxia.

Organ Ivolvement	n (%)
Cardiac Dysfunction	21 (65.6%)
Renal Dysfunction	4 (12.5%)
Hypoxic-ischemic encephalopathy	18 (56.2%)
Lungs (requiring mechanical ventilation)	22 (68%)

Table 4: Cardiovascular risk factors in newborns. Creatinfosfocinasa Miocárdica (CPK-MB).

Cardiovascular risk factors	Without NA (n = 20)	With AN(n = 32)	p	OR (95% IC)
Heart rate				
<120 lpm	0 (0%)	15 (47%)		
≥ 120	20 (100%)	17 (53%)	p = 0.0148	36.3 (2.02 - 651.81)
Vasoactive drugs	1 (5%)	8 (25%)	p = 0.0946	6.3(0.72 - 55.15)
CPK-MB				
0-77.4 UI/L	20 (100%)	7 (22%)		
> 77.5 UI/L	0 (0%)	25 (78%)	p = 0.0009	139.4 (7.50-2587.78)
Troponin I				
< 0.3 ng/ml	20 (100%)	22 (68%)		
≥ 0.3 ng/ml	0 (0%)	10 (32%)	p = 0.0460	0.0 (0.00- 0.95)
Mitral regurgitation	0 (0%)	11 (34%)	p = 0.0366	21.9 (1.21-396.73)
Ventricular Dyskinesia	0(0%)	9 (28%)	p = 0.0582	16.6 (0.91- 302.71)

gans such as the skin, kidneys and muscle. The responsible of this effect is the stimuli of carotid chemoreceptors for the releasing of catecholamines. When the severity and duration of NA are exceeded, the brain and myocardium blood flow is highly compromised. During NA oxygen deprivation, compensatory mechanisms are responsible for the redistribution of cardiac output, centralization of blood flow to vital organs and reduction of oxygen consumption. Cardiovascular response is a transient bradycardia, systemic arterial hypertension, and peripheral vasoconstriction. Furtherly, hypoxia affects myocardial contractility leading to hypotension, for the requirement of vasoactive drug support increases the risk of ischemia by means of reduction of coronary perfusion and lack of atrioventricular subvalvular irrigation which generates mitral or tricuspid regurgitation. Sehgal., *et al*. [9] reported that cardiac output redistribution fails to maintain myocardial oxygenation, there is cardiac glycogen depletion, anaerobic cycle activation and metabolic acidosis. Without a timely intervention in myocardial dysfunction at this scenario, circulatory shock, severe valvular regurgitations, hypotension and cardiac arrest may stablish [10]. Commonly, tricuspid regurgitation is the main echocardiographic alteration demonstrated, associated with a systolic murmur in the newborn. However, this tends to disappear without specific treatment due to the relationship with transient myocardial ischemia and pulmonary hypertension in the newborn.

Mitral reurgitation in NA is due to transient ischemia that leads to left ventricle dysfunction and remodeling. This mechanism generates a displacement of the papillary muscles (apical and lateral), valve immobilization, dilation and flattening of the mitral annulus, as well as reduction of valve closure forces. Because these changes depend on the phase of the cardiac cycle, secondary mitral regurgitation is dynamic and is also associated with transient myocardial ischemia and decrease left ventricular ejection function (LVEF). In our study, we found that mitral regurgitation not associated with congenital structural malformation of the valve in patients with NA criteria, represent a statistically significant risk factor. This echocardiographic marker is due to transient myocardial ischemia during the newborn hypoxia event. Likewise, the clinical correlation of

low borderline heart rate (range of 90-110 bpm) in the presence of mitral regurgitation represents a significant clinical risk factor for AN. This can be explained because heart rate is considered the gold standard indicator to evaluate the success of the transition from intrauterine to extrauterine life and is used as a guide for neonatal resuscitation and stabilization. International guidelines recommend neonatal heart rates above 100 beats per minute. Below this value, cardiopulmonary reanimation should be considered [11]. The presence of borderline low heart rates associated with echocardiographic mitral valve regurgitation are important risk factors to confirm the diagnosis of NA and initiate therapy [12]. In comparison with the adult heart, the immature newborn myocardium is more vulnerable to ischemia and reperfusion injury [13]. Understanding the cardiovascular manifestations of NA, it is easy to correlate serum changes such as the cardiac enzymes level elevation [14]. Troponin levels that correlated with a greater myocardial damage are vary from 0.3 -1.1 ng/ml [15]. This has been associated with the presence of mitral regurgitation and alteration of segmental mobility (dyskinesia or generalized hypokinesia).

Conclusion

Clinical analysis and serum changes in the patient with NA are not sufficient for the correct detection and evaluation of the hemodynamic repercussions [16]. The presence or absence of echocardiographic mitral regurgitation, alteration of segmental mobility and measurement of pulmonary systolic arterial pressure associated with the measurement of heart rates during the neonatal post-reanimation period, are important factors to considerate in the complete evaluation of cardiovascular manifestations for achieving the diagnosis of NA. Therefore, our findings suggest that clinically, the finding of borderline heart rates associated with the presence of echocardiographic mitral regurgitation are risk factors that highly confirm the diagnosis of NA.

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None.

Conflict of Interest

The authors have no financial interest to declare.

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