Neonate Aortic Stenosis. Importance of Myocardial Perfusion in Prognosis

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Objective - *To analyze our experience with percutaneous aortic balloon valvuloplasty in newborn infants with aortic stenosis, emphasizing the extraordinary importance of myocardial perfusion.*

Methods - *Over a 10-year-period, 21 neonates underwent percutaneous aortic balloon valvuloplasty. Age ranged from 2 to 27 days, weight ranged from 2.2 to 4.1 kg and 19 were males. All patients presented with congestive heart failure that could not be treated clinically. The onset of symptoms in the first week of life occurred in 9 patients considered as having critical aortic stenosis. Severe aortic stenosis occurred in 12 patients with the onset of symptoms in the second week of life.*

Results - *Mortality reached 100% in the patients with critical aortic stenosis. The procedure was considered effective in the 12 patients with severe aortic stenosis. Vascular complications included the loss of pulse in 12 patients and rupture of the femoral artery in 2 patients. Cardiac complications included acute aortic regurgitation in 2 patients and myocardial perforation in one. In an 8.2±1.3-year follow-up, 5 of the 12 patients died (2 patients due to septicemia and 3 patients due to congestive heart failure). Five of the other 7 patients underwent a new procedure and 2 required surgery.*

Conclusion - *Percutaneous aortic valvuloplasty in neonates is not an effective procedure in the 1st week of life, because at this age the common presentation is cardiogenic shock. It is possible that, in those patients with critical aortic stenosis, dilation of the aortic valve during fetal life may change the prognosis of its clinical outcome.*

Key words: endocardial fibroelastosis, myocardial ischemia, valvuloplasty through balloon catheter, aortic stenosis.

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Neonate aortic stenosis is a fatal disease that, due to the obstruction of left ventricular outflow, has already presented during fetal life and is associated with myocardial dysfunction due to subendocardial ischemia or endocardial fibroelastosis [1].

The prognosis of neonate aortic stenosis has changed over the last few years, due to the possibility of alternative therapeutics, therapeutics that vary from percutaneous valvuloplasty to cardiac transplatation or the Norwood procedure [2]. In this last possibility, the right ventricle replaces the left ventricle in the control of systemic circulation. This is a situation that requires a difficult decision that must be made in the first hours of life.

Percutaneous balloon valvuloplasty has proved to be an effective method for abolishing the gradient between the left ventricle and the aorta in children with congenital aortic stenosis [3-6], with a small midterm frequency of restenosis [7-9]. Although studies concerning this pathology are increasing, the experience regarding its performance in the neonate period is still limited [10-14]. Because surgical treatment of aortic stenosis in neonates is associated with significant morbidity and mortality [15-19], even though it has become more promising in this last decade [20-23], the treatment with percutaneous balloon valvuloplasty may play an important therapeutical role in this special group of patients.

The objective of this article is to report our experience with percutaneous balloon valvuloplasty in neonate aortic stenosis emphasizing the extraordinary importance of myocardial perfusion (subendocardial coronary flow), which is already abnormal during fetal life.

These data will enable us to understand the deleterious repercussions that aortic stenosis produces on the left ventricular muscle of these patients and that seems to us as fundamental to its prognosis and therapeutics.

Methods

From January 1990 to December 1999, 25 neonate patients, 19 males, were admitted to the Instituto Nacional de Cardiologia Laranjeiras (National Institute of Cardiology

Laranjeiras), Rio de Janeiro, with the diagnosis of congenital aortic stenosis.

All patients presented with heart failure that could not be treated clinically, but with different clinical presentations. The 1st group (group I) comprised 9 patients with the onset of clinical manifestations in the 1st week of life, presenting with hypoxemia, requiring mechanical ventilation, of vasoactive amine and prostaglandin E1 (PGE1), due to a clinical picture of shock, and were designated as having critical aortic stenosis. The 2nd group (group II) presented with symptoms during the 2nd week of life, with a clinical picture of severe heart failure, without hypoxemia, not requiring mechanical ventilation, and were designated as having severe aortic stenosis. Regarding echocardiography and hemodynamic features, the groups had totally different characteristics.

Of the 25 neonates, 21 underwent percutaneous balloon valvuloplasty. Four patients did not undergo the procedure: 2 weighed less than 2 kg, and 2 had an aortic annulus smaller than 5 mm. The age of these 21 neonates ranged from 2 to 27 days, and 9 underwent the procedure at less than 8 days of age. The weight of these 21 patients ranged from 2.2 to 4.1kg, with an average of 2.9 kg.

Associated malformations were present in 17 patients, ductus arteriosus in 13, coarctation of the aorta in 4, and mitral regurgitation in 9 patients. The aortic valve was considered unicommissural in 10 patients and bicommissural in 11. The ratio between the balloon diameter and the diameter of the aortic annulus in all the cases was less than 1 (0.84±0.06).

All patients underwent the procedure while under general anesthesia and endotracheal intubation and received local anesthesia and xylocaine at 1% to cannulate the femoral veins. Arteries were cannulated with a pigtail catheter 4F or 5F. In some situations, 1/3 of the pigtail catheter loop was cut to enable proper positioning of the guidewire in the ascending aorta and, consequently, reach the left ventricle through the aortic valve. Heparin was administered through the vein (100UI/kg of weight). Left cardiac catheterization included peak systolic gradient through the aortic valve, and the angiographic study included an aortography before and after the procedure, to assess aortic regurgitation and associated defects. Furthermore, 1 to 2 left ventriculographies were performed to study function.

For dilation, the aortic valve was initially passed over with an extremely flexible tipped guidewire 0.015 to 0.021 inch. Over the guidewire, the pigtail catheter was positioned near the aortic arch. Through maneuvers, the guidewire passed the aortic valve and finally reached the left ventricle. Using the guidewire as a track, the pigtail catheter was positioned in the left ventricle. At this moment, the initial guidewire was exchanged for a 0.021-0.028 inch guidewire with a preset curve in its distal end, making its positioning at ~~in~~ the tip of the left ventricle easier. Afterwards, the pigtail catheter was exchanged for a balloon catheter (Cook Inc. or Tyshak Numed) positioned over the aortic valve and inflated by hand 2 or 3 - times, until the balloon waists, caused by the valves, had disappeared. It is important to stress that small increases in the diameter of the balloon (1 mm) can be obtained by the increase in the pressure of insufflation, thus avoiding unnecessary exchanges for a balloon of greater diameter. Another important observation is that, in neonates, waists produced by the valve over the balloon do not occur. The inflation-deflation cycle was never greater than 15s.

After dilation, the gradient between the left ventricle and the aorta was assessed and then an aortography was performed. The patients were sent to the neonates intensive care unit.

Data are expressed as mean ± standard deviation (SD) and value net and were analyzed with the Kruskal-Wallis test for 2 groups. Statistical tests were performed with the computer program EPI Info, 6.04 of the CDC (Centers for Disease Control & Prevention). We used an alfa value of 0.05.

Results

Of the 21 percutaneous balloon valvuloplasties performed, only 12 procedures were successful. Thus, the gradient between the left ventricle and the aorta decreased, on average 37%, that is 72 mmHg to 45.5 mmHg.

All 9 patients with critical aortic stenosis, those who were severely ill in the 1st week of life, did not survive after the valvuloplasty. Among these, 8 had a reduced ventricular cavity (fibroelastosis), and in only 1 was the cavity enlarged. Of the 12 survivors with severe aortic stenosis, after the 2nd week of life, 11 had an enlarged ventricular cavity due to myocardial dysfunction (subendocardial ischemia) (tab. I). It is difficult to distinguish the complications due to the procedure, in this particular group of patients from those whose critical condition contributed to it. Thus, vascular complications were loss of pulse in 12 patients and femoral artery rupture in 2. Cardiac complications were acute aortic regurgitation in 2 patients and myocardial perforation in 1 patient.

This division into 2 groups can be maintained with regards to echocardiography and hemodynamics in addition to the different form of clinical presentation and age at the onset of symptoms (tabs. II and III). Thus, systolic pressure developed in the left ventricle was 97.4±26.6 mmHg in those (n=9) studied in the 1st week of life and 138.6±21.7 mmHg for those (n=12) studied after this period (p=0.005). The same thing occurred regarding the pressure gradient between the left ventricle and the aorta. That is, in those patients who were less than 1 week old (n=9), the gradient was 46.1±23.6 mmHg, and in those studied after the 1st week of life (n=12), the gradient was 72±25.2 mmHg (p=0.04). Consequently, systolic pressure observed in the aorta was 51.3±7.5 mmHg

Table I – Neonate aortic stenosis – immediate results

BV	FDV decreased	FDV enlarged	Group	Total
Non survivors	8	1	I	9
Survivors	1	11	II	12

BV- balloon valvuloplasty; FDV- left ventricle final diastolic volume.

in group I (n=9) and 66.6±11mmHg in group II (p = 0.005). Regarding ejection fraction, the differences were also significant. Patients less than a week old (n=8) had ejection fractions of 23.7±5.2%, those who were older (n=10) had ejection fractions of 41.1±11.4% (p=0.003). The final diastolic volume in group I (n=7) was 38.4±2.5 mL/m² and in group II (n=10) was 51.5±25.1 mL/m² (p=0.28). The final left ventricular diastolic pressure observed was 16.3±5.5 mmHg in group I and 18.2±7.4 mmHg in group II (p=0.50).

Of the 9 patients from group I, the aortic valve was unicommissural in 5 patients and bicommissural in 4 patients. In group II, the aortic valve was unicommissural in 5 patients and bicommissural in 7 patients.

Of the 13 patients who had associated ductus arteriosus, 9 were from group I and 4 were from group II. In group I, all patients received PGE1. Coarctation of the aorta was observed in only 1 patient from group I and in 3 patients from group II. It is possible that the use of PGE1, maintaining the ductus arteriosus patent, masked the diagnosis of aortic coarctation. Mitral regurgitation was identified in 3 patients from group I and in 6 patients from group II.

The morphology of the aortic valve and the associated abnormalities are not related to the severity of the clinical picture, although they can act as predictive and cumulative factors for poor evolvement.

In an 8.2±1.3-year-follow-up, 5 of the 12 patients died: 2 due to septicemia and 3 due to heart failure. Of the 7 surviving patients, 5 underwent a new procedure and 2 were referred for surgery.

Table II - Neonate aortic stenosis – individual hemodynamic and echocardiographic findings by group of patients

Pt	LVSP (mmHg)	Pd2 (mmHg)	PAo (mmHg)	LV-Ao Gr (mmHg)	FE (%)	FDV (ml/m²)
Group I: critical aortic stenosis						
5	75	13	50	25	22	38
6	76	13	50	26	26	39
7	75	20	45	30	14	40
10	100	10	48	52	-	-
13	75	16	45	30	29	33
14	140	15	60	80	29	40
16	110	28	42	68	21	40
18	88	20	62	26	21	-
21	138	12	60	78	28	39
Mean	97.4	16.3	51.3	46.1	23.7	38.4
Group II: severe aortic stenosis						
pt	LVSP (mmHg)	Pd2 (mmHg)	PAo (mmHg)	LVAo Gr (mmHg)	FE (%)	FDV (ml/m²)
1	125	6	82	43	35	97
2	120	26	50	70	34	76
3	120	14	80	40	35	73
4	148	24	62	86	43	75
8	130	11	55	75	60	49
9	140	25	70	70	46	43
11	170	33	75	95	20	44
12	130	15	55	75	55	38
15	140	17	60	80	38	30
17	190	18	60	130	45	22
19	130	15	80	50	-	20
20	120	15	70	50	-	-
Mean	138.6	18.3	66.6	72.0	41.1	51.5

Pt - patient number; LVSP - left ventricle systolic pressure; Pd2 - final left ventricle diastolic pressure; PAo - systolic pressure in the aorta; LV-Ao Gr - left ventricle/aorta gradient; EF - left ventricle ejection fraction; FDV left ventricle final diastolic volume; mmHg - millimeters mercury; % - percentage.

Table III - Neonate aortic stenosis - hemodynamic and echocardiographic findings, comparison between groups and describing level

	G I	G II	Describing level #
LVSP (mmHg)	97.4 ± 26.6 (n=9)	138.6 ± 21.7 (n=12)	p = 0.005
Pd2 (mmHg)	16.3 ± 5.5 (n=9)	18.2 ± 7.4 (n=12)	p = 0.50
PAo (mmHg)	51.3 ± 7.5 (n=9)	66.6 ± 11.0 (n=12)	p = 0.005
LV-Ao Gr (mmHg)	46.1 ± 23.6 (n=9)	72.0 ± 25.2 (n=12)	p = 0.04
FE (%)	23.7 ± 5.2 (n=8)	41.1 ± 11.4 (n=10)	p = 0.003
FDV (ml/m²)	38.4 ± 2.5 (n=7)	51.5 ± 25.1 (n=11)	p = 0.28

Kruskal-Wallis test for 2 groups; GI - critical aortic stenosis; GII - severe aortic stenosis; LVSP - left ventricle systolic pressure; Pd2 - final left ventricle diastolic pressure; PAo - systolic pressure in the aorta; LV-Ao Gr - left ventricle/aorta gradient; EF - left ventricle ejection fraction; FDV - left ventricle final diastolic volume; mmHg - millimeters mercury; % - percentage.

Discussion

Ischemic alterations, many times represented by the inversion of the T wave on the electrocardiogram of a neonate with aortic stenosis have been interpreted as a consequence of the tension on the left ventricular walls. Estimation of this parameter had been tried, using the pressures of the left ventricle and of the aorta. As already described, the supply of oxygen to the myocardium is determined not only by the coronary flow but also by the arterial oxygen content. The forces of intramyocardial compression have been interpreted as greater in the subendocardial muscle portion of the left ventricle in a situation in which they are the same or even higher than the intracavitary pressure [24-26]. Therefore, blood flow for the subendocardial musculature of the left ventricle is predominantly diastolic in normal hearts [27]; however, it should be totally diastolic in aortic stenosis where elevations of the systolic pressures of the left ventricle are present.

The increase in the need of the myocardium for oxygen at rest or with exercise may be reached from the beginning through coronary vasodilation. When maximum vasodilation is achieved, blood flow for subendocardial musculature is dependent on the low and fixed coronary vascular resistance and on the difference between coronary diastolic arterial pressure and the opponent pressure of the left ventricular subendocardial musculature or the pressure of the coronary sinus. In the absence of coronary obstruction, these determinants of the left ventricular subendocardial flow may be represented by the area between the curves of left ventricular pressure and the aorta in diastole. This area multiplied by the heart rate is referred to as the diastolic pressure time index [28, 29]. This index is the measure of the coronary

blood flow for the left ventricular subendocardial musculature, because its vases are fully dilated.

To assess the consumption of oxygen of the myocardium, the area of the pressure curve of the left ventricle and of the aorta during systole have been assessed and referred to by Sarnoff et al. [29] as the tension time index. This area per minute may be called the systolic pressure time index. With these 2 indexes, it is possible to relate the supply and the consumption of the left ventricular myocardium, as the diastolic pressure time index /systolic pressure time index ratio. However, the diastolic pressure time index is the measure of coronary flow and not the oxygen release measure. If the arterial oxygen content is decreased, then the release of oxygen for a flow band will be reduced.

For this supply/consumption index of coronary blood flow to be converted into a supply/consumption index of coronary oxygen, the diastolic pressure time index is multiplied by the arterial oxygen content (C), that is, diastolic pressure time index x C/systolic pressure time index. The values of this ratio lower than 10 would experimentally be associated with a reduction in the supply of subendocardial oxygen [29]. In some situations, this ratio cannot be determined because some patients with severe aortic stenosis have a suitable supply/consumption oxygen ratio, whereas in other patients this ratio suggests subendocardial ischemia. The explanation seems to be in the cardiac frequency because the release of subendocardial oxygen is inversely proportional to the cardiac rate. Infants with cardiac frequency above 100 bpm would all be in the ischemic group. The shortening of diastole by the tachycardia produces a large decrease in the diastolic pressure time index and, therefore, in the supply/consumption of the oxygen ratio.

This information enables us to understand that subendocardial ischemia is a present manifestation in all neonatal patients with aortic stenosis, which is responsible for heart failure that cannot be treated and for the high mortality rate in these patients.

Analysis of this group of patients seems to represent an intermediate situation between patients with aortic atresia and hypoplasia syndrome of the left heart on the one hand and those patients with a bicommissural aortic valve, whose clinical manifestations occur late, on the other hand. Different from that in patients with hypoplastic left heart syndrome, the ascending aorta in all patients who underwent aortic balloon valvuloplasty had normal dimensions or was dilated. In 8 of the 21 patients, the left ventricular cavity was smaller than normal, but in none of the patients was it rudimentary.

Because these patients were critically ill, immediately after birth, it was fundamental to know their fetal and postnatal hemodynamic history. Experimental studies of sheep fetuses showed that in normal fetuses the right ventricle ejects around 66.6% (300 mL/kg/min) of the combined left and right cardiac output and the volume of 265 mL/kg/min crosses the ductus arteriosus for the descending aorta [30]. The placental flow was 200 mL/kg/min (44.0% of the combined ventricular output), most of it derived from the right ventricular output. The left ventricle ejects around 33.3% of the combined ventricular output (150 mL/kg/min) of which most (around 26% of the combined ventricular output) is deviated from the inferior vena cava that crosses the foramen ovale to the left atrium and reaches the left ventricle [30]. Without this contribution of the left-side flow, the stimulus of the volume for the normal development of the atrial cavities and left ventricle may fail, possibly, resulting in a left heart hypoplasia [31,32]. Therefore, the lower the obstruction level of the foramen ovale, the greater the development of the left heart, with a large spectrum of ventricular dimensions. The primary involvement of the aortic valve during fetal life may explain these morphological findings.

The severity of aortic valve obstruction and the gestational period in which it develops may influence the development of the left ventricle. Experimentally, during fetal life, in sheep of 90 to 115 days of gestation, the mildly severe supravalvar obstruction, produced by the constriction of the aorta, resulted in a great decrease in left ventricular output [33]. Furthermore, mean ventricular volumes are less than half of those used as controls. The increase in muscle mass developed as a response to the obstruction would result in a decrease in left ventricular compliance, interfering with left ventricular filling. Left atrial pressure and final left ventricular diastolic pressure increase; however, left atrial flow through the foramen ovale decreases.

Based on these observations, the severe aortic obstruction produced early in fetal life may result in left ventricular wall thickening with a reduction in ventricular cavity size, leading to endocardial fibroelastosis and, in extreme cases, in a real left heart hypoplasia. In this study left heart hypoplasia was not observed, although in 9 patients (1 with an enlarged cavity) the form and the age of the onset, clinical behavior, hemodynamics and prognosis-were completely different from the other 12 patients. If aortic valve obstruction is less severe and occurs in a late phase of gestation, the left ventricular wall will also be thicker; however, the size of the cavity may be normal or may be enlarged. The anatomicopathological substrate will be subendocardial ischemia, with a better prognosis, and with the development and later age of onset with a completely different clinical and hemodynamic picture.

After birth, survival of the patients with critical aortic stenosis will depend on the capacity of the left ventricle to maintain systemic output. If the left ventricle is not able to maintain it, the ductus arteriosus may play an important role in the maintenance of systemic output.

Short-term results in this sample are discouraging. Good surgical results are also rare. Certainly, myocardial dysfunction due to abnormal myocardial perfusion disables the left ventricle preventing it from maintaining normal cardiac output.

As we observed, myocardial dysfunction is one of the main variables in the prognosis of patients with aortic stenosis in the neonate period. It is not an isolated factor; however, it is the final product of a complex process that started during fetal life and that, depending on the gestational phase in

which the disturbance occurred, and on the severity of the obstructive phenomena, will have a real morpho-functional spectrum that goes from left heart hypoplasia to a congenitally malformed valve in an asymptomatic adolescent.

Another important finding in these patients was the age of onset of symptoms. None of the patients who presented with it in the 1st week of life survived to receive the balloon catheter treatment. On the other hand, those whose presentation occurred during the 2nd week of life, had a better prognosis. Associated abnormalities and the morphologic characteristics of the left ventricle may be predictive factors and cumulative data of a poor evolution.

Then, how can the natural history of neonate critical aortic stenosis be altered? Certainly the first step would be dilation of the aortic valve as early as possible, during fetal life [1]. With this, the left ventricle would be spared from irreversible and fatal lesions from the obstructive phenomenon. To that end, greater use of fetal echocardiography is necessary as is an improvement in the techniques used to perform procedures during intrauterine life.

Finally, we must bear in mind that the success of valvuloplasty may help the survival of those patients, even with unfavorable anatomical characteristics. In this sense, we may identify patients whose survival is greater using, for example, the Norwood procedure rather than valvuloplasty, even when the ventricular volume has values close to normal.

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