The Immediate and Intermediate Term Follow Up of Patients with Critical Pulmonary Valve Stenosis after Balloon Valvuloplasty

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ABSTRACT:

BACKGROUND:

Balloon pulmonary valvuloplasty (BPV) represents the standard of management for all patients with severe pulmonary valve stenosis (PS) irrespective of their age. Nevertheless , neonates and infants with critical PS represent an emergency and a high risk group that needs to be studied.

OBJECTIVE:

To evaluate results ,complications and follow up of BPV in neonates and infants with critical PS.

PATIENTS AND METHODS:

During the period extending from February 2010 to February 2011, 25 neonates and infant patients with critical PS were subjected to detailed history taking, full clinical examination, resting 12-lead ECG, chest x-ray and transthorasic echocardiography.BPV was attempted in all patients .Full echocardiographic evaluation was done 24 hour after the procedure as well as 3 and 6 months later.

RESULTS:

Twenty five patients with critical PS with a mean age of 32.7 ± 21.9 days were subjected to BPV .Immediately after the procedure , patients had a significant reduction of the right ventricular systolic pressure (RVSP) from a mean of 103.96 ± 24.98 mmHg to a mean of 43.6 ± 13 mmHg . The immediate success rate(defined as the drop in the RVSP to less than or equal to 50% of the baseline measurement) was achieved in 76% of cases . Throughout a follow up period of six months, there was a progressive decline in the pressure gradient (PG) across the PV by Doppler echocardiogram from a mean of 93.3 ± 18.2 mmHg to a mean of 17.4 ± 10.42 mmHg. The oxygen saturation increased from 80 ± 8% to 96 ± 2% . There was a significant increase in the mean PV annulus diameter after balloon dilatation from a mean value of 7.1 ± 1.9 mm to a mean value of 9.3 ± 1.1 mm. The incidence of pulmonary incompetence (PI) significantly increased immediately after BPV to 66.6% followed by a progressive decline over a 6 months period of follow up to 19% . Over the same period of follow up , there was a significant decrease in the incidence of tricuspid regurgitation (TR) from 32% to 9.5% . There were complications including three deaths (12%).One patient was referred to surgery (4%) and two had developed significant re stenosis (8%) .

CONCLUSION:

BPV is safe and effective procedure to relieve critical PS in neonates and infants that should be done as early as possible .

KEYWORDS: Critical Pulmonary Valve Stenosis Balloon Pulmonary Valvuloplasty

INTRODUCTION:

Pulmonary valve stenosis (PVS) , with and without other associated lesions, occur in 25-30% of all patients with congenital heart disease(CHD)[1]. , However, isolated PVS has been found in 8% to 10% of patients with CHD.[2]

Critical PVS in infants represent a special group of patients that should be treated urgently[3]. .Sex distribution is usually equal[4] or has a male prevalence.[3]

Critical PVS is defined as severe neonatal valvular PS with a pinhole opening and a "larger than normal" right to left shunt that is established in utero, systemic or supra systemic right ventricular pressure, cyanosis with signs and

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symptoms of low cardiac output and the pulmonary blood flow is highly dependent on patent ductus arteriosus (PDA) .[5]

The morphology of PV in PVS is most commonly a typical mobile, dome shaped, tricuspid valve , and less likely is an immobile dysplastic valve .

Pinpoint dome-shaped PVS in neonates is referred to as critical pulmonary stenosis[6] .

The right atrium(RA) may be thick and dilated as a result of increasing pressure necessary to fill the hypertrophied RV. In many cases, a patent foramen ovale (PFO) or less commonly a true atrial septal defect(ASD), is seen.[7] The RV pressure overload is responsible for systolic and diastolic dysfunction of the left ventricle(LV) .[8]

Infants with critical PVS are cyanotic at birth ,and the cyanosis may be severe enough to be life threatening. Symptoms of right _sided heart failure may be seen in some newborns with significant tricuspid insufficiency (dyspnea, relactance to feed , irritability with costal and subcostal retractions) or may develop in untreated infants if the atrial communication becomes inadequate with growth.[5] The ejection systolic murmur that is typically heard in severe PVS may be deceptively soft as a result of decreased flow across PV in the presence of an atrial right _ to _left shunt. A holosystolic murmur of tricuspid insufficiency may be present lower along the left sternal border , or a patent ductus murmur may be audible along the mid to upper sternal border [5] .

The neonate with pinpoint PVS and a small right ventricular cavity has an ECG that resembles pulmonary atresia with intact ventricular septum . The P waves become tall and peaked , and giant P waves appear occasionally ,especially in lead 2[9].The QRS axis is normal or left warded (in the range of +30 to +70) , with an evidence of LV hypertrophy [5]

On chest radiograph, the cardiac size is normal as long as there is no cardiac failure , otherwise, marked cardiomegaly results owning to RA enlargement, and pulmonary vascularity is severely decreased [5].

The two _ dimensional echocardiogram clearly demonstrates the typical features of the stenotic PV from the standard and high parasternal short axis and long axis views as well as the subcostal sagittal views. The valve leaflets usually appear prominent because of thickening[5].Associated features, such as poststenotic dilatation of the main and branch pulmonary artery , also is easily recognized [10] . It also detects a right _to _ left interatrial shunt via a PFO [5] .Color flow imaging determines the presence and degree of tricuspid regurgitation [10,11]

Because diagnosis and exclusion of other significant lesions can now be accomplished non invasively , the role of catheterization become largely therapeutic. Balloon pulmonary valvuloplasty has supplanted surgical valvotomy as the treatment of choice for PVS.[12] .

Percutaneous balloon pulmonary valvuloplasty is now regarded as the treatment of choice in neonates, infants and adults. Before catheterization , patients with critical PVS need stebilization and initiation of prostaglandin E1 infusion to maintain ductal patency. Several technical advances , such as the introduction of low profile balloons , has increased the safety and success of the balloon dilatation, such that its now considered the treatment of choice [12,13] .Initial dilatation with a small coronary angioplasty balloon to enlarge the orifice and subsequent dilatation with progressively larger balloons allow adequate relief of obstruction in most neonates.[14] .Risk factors for re_intervention include: younger age, lower surface area, smaller PV annular diameter Z-score, a higher PV pressure gradient at initial presentation ,and presence of Noonan syndrome .[5]

Recurrent valvular stenosis necessitating repeat valvuloplasty may occur within months of the initial procedure in about 10% of these patients and subsequently may afford long term relief of obstruction [5]. Five to fifteen percent of neonates with critical PVS ultimately require surgical intervention to relieve either valvular stenosis resistant to dilatation or associated subvavular obstruction[15] . Mortality rates due to BPV was approximately 3% ,and was due to various causes including: venous injury, myocardial dissection and development of necrotizing enterocolitis, standstill and death.

AIM OF STUDY:

To assess the results, complications and intermediate term outcome of patients with critical pulmonary valve stenosis after balloon pulmonary valvuloplasty

PATIENTS AND METHODS :

A prospective study was done on twenty five infants under the age of three months who were referred to the pediatric cardiology unit in Ibn_Albitar Centre for Cardiac surgery and were found to have a critical PVS, over 12 months time started from February 2010 to February 2011.

Inclusion criteria :

Patients who fulfilled the following criteria were selected for balloon dilatation of the PV :

Age from birth to three months (we took 3 months as a cutoff point for age rather than neonatal due to the tendency of late referral of infants in the rural areas) , Severe congenital pulmonary valvuar stenosis with systemic or suprasytemic RV pressure , All patients are cyanosed ,with oxygen saturation < 92% and No associated cardiac anomaly apart from a PFO or PDA .

Exclusion criteria :

Patients with multiple right ventricular outflow obstructions that would not benefit from balloon pulmonary valvuloplasty and Patients who didn´t come back during the follow up period were excluded.

METHODS :

All infants in this study who met the inclusion criteria were subjected to a detailed history taking and a full cardiac examination .In addition, chest x ray ,ECG, complete laboratory evaluation , transthorasic echocardiography and BPV were done in all patients .

The procedure is performed in the cardiac catheterization laboratory .For at least 4-6 hours before the procedure, the infant s mother is instructed not to feed the baby anymore. An intravenous line is inserted, usually in the arm as a medication administration route, the patient is sedated intravenously and by inhalational anesthesia , usually without tracheal intubation. Continuous ECG monitoring was carried out as well as arterial oxygen saturation by means of a pulse oxymeter. Before starting catheterization , all drugs and equipments for resuscitation were prepared. The femoral vein is accessed using Seldinger's technique and a 5 or 6 french sheath was introduced into the vein. Arterial pressure was monitored continuously by femoral arterial line . A catheter was then placed in the RVOT(we use 5-F judkins right catheter or a less frequently 5-F multipurpose catheter) and straight lateral and frontal angiograms were performed to assess the RV and PV anatomy , and to measure the PV annulus .The catheter was manipulated into the RV with the tip directed toward the RVOT .The PV was crossed directly(less likely) or with the use of 0.021 inch, 0.018 inch ,or 0.014 inch steerable floppy tipped guide wires ,and the catheter was positioned in the lower lobe branch of either the left or the right pulmonary arteries ,sometimes in the aorta through the PDA. An exchange guide wire was placed in the peripheral pulmonary artery and the catheter was replaced with a dilatation balloon. The balloon was centered across the valve annulus in the lateral view and rapidly inflated by hand with diluted contrast material until the disappearance of the waist .

The deflated balloon was then removed while keeping the guide wire in the pulmonary artery .Constant suction on the attached syringe and counterclockwise rotation were important to deliver the deflated balloon and to avoid any possible trauma .The guide wire permitted a repositioning of an end–hole catheter in the distal pulmonary artery for pressure measurements. The inflation _ deflation cycle lasted 10 _ 15 seconds .Repeat RV angiography was routinely done .The following pressure and hemodynamic measurements were recorded before and immediately after BPV : right ventricular systolic pressure (RVSP),pulmonary artery systolic pressure (PASP) and RV to PA systolic pressure gradient(PG) .

After the procedure was completed, the patient was sent to the recovery room, and if stable, sent to the ward for removal of the sheath and close monitoring of the vital signs and pedal pulses for at least 24 hours. All patients received intravenous fluids and a broad spectrum antibiotics were administrated for at least two days

Beta – blocker therapy was started in selected patients who develop a dynamic reversible infundibular obstruction after BPV .

Success of the BPV in patients with critical PS was defined by the following criteria: 1) The patient became acyanotic. OR 2) The RVSP dropped to 50% or less of the baseline measurement. And 3)No further intervention was required .

Statistical analysis :

Continuous variables were expressed as mean ± standard deviation . Qualitative variables were expressed as percentages .A paired student t test was used for the comparison of different variables before versus immediately after BPV as well as during the follow up period ANOVA test was used to compare more than two independent means . p value < 0.05 was considered statistically significant. linear correlation was applied to determine the relation between the baseline pulmonary and tricuspid valves annuli and their measurements after dilatation.

RESULTS:

The studied group included twenty five infant patients below 3 months of age representing about 12.3% of the total number of patients referred for BPV in our institute during the given period of the study . All the 25 cases of the study were involved in the statistical analysis of follow up apart from 3 cases who died during or immediately after the catheterization procedure and one case who was referred to surgery. Patient´s age were ranged from 5 to 90 days (32.7 ± 21.9 days). Seventeen were males (68%) and 8 were females (32%) with a male : female ratio of 2.1: 1 . Weights of the patients ranged from 2.3 to 7 kg with a mean of 3.75 ± 1.2 kg. The calculated body surface area(BSA) ranged from 0.22 to 0.47 m^2 (mean 0.35m^2) .All patients were desaturated with an oxygen saturation ranged from 59% to 89%(80 ± 8%) .PFO or true small ASD(< 0.5cm) was found in 14 patients (56%), PDA in 7 patients (28%) and 4 patients(16%) had both PFO and PDA. *Table 1*. illustrates the clinical and demographic characteristics of the study group .

Table 1. Clinical and demographic characteristics of the patients:

Characteristics	***Findings***
Gender (M/F)	17/8(2.1: 1)
age (in days)	mean 32.7 ± 21.9(range 5-90)
BSA (in m^2)	mean 0.35(range 0.22-0.47)
weight (in kg)	mean 3.75 ± 1.2(range 2.3-7)
Associated anomalies PFO (56%) ,PDA (28%) ,PFO and PDA(16%)	

The echocardiography finding before performing the BPV revealed a peak PG across the PV of 65 -165 (93.3 ± 18.2) . PV annulus ranged between 4-11mm (7.1 ±1.9) .

Eight (32%) of our cases had TR , 84% had RVH and no case reported with PI . *Table 2*. shows the baseline echocardiographic data measured before balloon pulmonary valvuluplasty (BPV).

Table 2. Baseline echocardiographic data

Variable	Range	Mean ± SD
Peak PG mmHg	65 -165	93.3 ± 18.2
PV annulus(mm)	4-11	7.1 ± 1.9
PV annulus Z score	-3.1_0.4	-1.567 ± 0.896
Tricuspid regurgitation	32%	
RVH	84%	

The balloon sizes used ranged from 4 to 10 mm , with a mean balloon /annulus ratio of 1.23 ± 0.01(ranged from 1.1 to 1.4). Most of the patients had more than two consecutive balloon inflations (90%). The immediate success rate (defined as the drop in RVSP to less than or equal to 50% of the baseline measurement) was achieved in 19 patients (76%) of the cases. There was a significant drop in the RVSP from a mean value of 103.96 ± 24.98 mmHg to a mean value of 43.6 ± 13 mmHg(p value <0.0001) . The right ventricular / systemic pressure ratio declined from 1.1 – 2 with a mean of 1.3 ± 0.2 before balloon dilatation to 0.2–1.2 with a mean of 0.5 ± 0.3 after BPV (p value < 0.0001) which is statistically significant. The transvalvular gradient measured during the procedure dropped significantly from a mean of 82.5 ± 23.7 mmHg before performing the BPV to a mean of 21.35 ± 8.96 mmHg after the procedure (p value < 0.0001). The oxygen saturation before the procedure ranged from 59 – 89 % (mean 80 ± 8 %), which raised significantly(p value < 0.0001) after the BPV to 84 – 100 % with a mean of 96 ± 2 , and to a mean of 97 ± 1(92 – 100%) after 6 months. Table .3 shows the hemodynamic changes (mean ± SD) before and immediately after BPV.

Table .3. Hemodynamic changes (mean ± SD) before and immediately after BPV:

Variable	Before balloon dilatation		After balloon dilatation		P value
RVSP (mmHg)	103.96 ± 24.98	(70 – 160)	43.6 ± 13	(35 – 80)	< 0.0001
RV/systemic pressure ratio	1.3 ± 0.2	(1.1 – 2)	0.5 ± 0.3	(0.2 – 1.2)	< 0.0001
Transvalvular PG(mmHg)	82.5 ± 23.7	(50 – 140)	17 1 (15 – 55)		< 0.0001
Systemic oxygen saturation	80 ± 8 %	(59 – 89)	96 ± 2 %	(84 – 100)	< 0.0001

progressive drop in the PG across the PV by Doppler echocardiography throughout a follow up period of six months from a mean of 93.3 ± 18.2 mmHg to a mean of 17.4 ± 10.42 mmHg .There was a highly significant drop from a mean of 93.3 ± 18.2 mmHg before the BPV to a mean of 26.93 ± 13.26 mmHg 24 hour after BPV(p value <0.0001) , this drop in PG was maintained during the follow up at 3 months with a mean of 19.13 ± 9.91 mmHg and at 6 months with a mean value of 17.4 ± 10.42 mmHg .

There was a progressive rapid increase in the mean diameter of the PV annulus over 3 and 6 months period of follow up from a mean value of 7.1 ± 1.9 mm before BPV to a mean value of 9.1 ± 1.79mm at 3 months and 9.3 ± 1.1 at 6 months with the most rapid increment being achieved at 3 months(p value < 0.0001) .

A highly significant change has been found in the pulmonary Z score with an increase from a mean of – 1.567 ± 0.295 to a mean of - 0.650 ± 0.895 at 6 months follow up (p value < 0.0001) . There was a decrease in the mean diameter of the tricuspid valve annulus from a mean of 16.1 ± 2.3 mm before the procedure to a mean of 15.2 ± 2.1 mm 6 months after the procedure. There was no significant change in the tricuspid annulus Z score with decrease from a mean of 0.413 ± 1.22 to a 6 months post BPV mean of – 0.152 ± 1.39 (p value > 0.05).Table 4.

Table .4. measurements of PV and TV annulus before and after BPV:

Variable	*Before BPV (mean ± SD)*	*6months After BPV(mean ± SD)*	*P value*
PV annulus(mm)	7.1 ± 1.9	9.3 ± 1.1	< 0.0001
PV Z – score	_ 1.567 ± 0.295	_ 0.650 ± 0.895	<0.0001
TV annulus (mm)	16.1 ± 2.3	15.2 ± 2.1	>0.05
TV Z – score	0.413 ± 1.22	_ 0.152 ± 1.39	>0.05

The rate of pulmonary incompetence (PI) significantly increased immediately after the BPV from zero to 66.6%(14 patients). Mild PI was found in 57.1%(12 patients), moderate in 9.5%(2 patients) and no severe PI was recorded. The severity of PI was found to be correlated with the increase in the balloon/annulus ratio as seen in table 5 .However ,there was a progressive decline in PI over 6 months period of follow up from 66.6%(14 patients) to 19% (4 patients) denoting the transient nature of PI in the majority of patients.

Table.5.Relation of the degree of PI and balloon/annulus ratio :

Degree of PI	None	Mild	Moderate	Severe
Number of patients	7 (33.4%)	12(57.1%)	2(9.5%)	None(0%)
Balloon/annulus ratio	1.12 ±0.02	1.29 ±0.05	1.39 ±0.02	

The prevalence of TR was decreased significantly during the same period of follow up in patients who had TR from 32%(8 patients) before the procedure to 9.5%(2 patients) at 6 months follow up .

Six of the patients had mild to moderate TR and two had severe TR which become moderate at 6 months follow up .

Complications occurred during or immediately after the procedure included minor complications: transient bradycardia and hypotension on balloon inflation which nearly occurred in all patients(100%), transient apnea and standstill in 28.5% (6 patients) ,arrhythmias(mainly ventricular ectopics and tachycardia) in 47.6% (10 patients),vascular injury including hematoma formation at the site of insertion(the groin) in 28.5% (6 patients), and significant blood loss during cannulation in 19%(4 patients) . Major complications (death) occurred in three patients (12%) .

Two patients (8%) had a partially successful procedure in which the RVSP declined but remained above 50% of baseline .In those two patients ,the procedure was stopped due to unstablity of the patient .

Two patients (8%) developed significant restenosis of the PV during the period of follow up that required repeated valvuluplasty. They were seen after 3 months of BPV with a PG across the PV of 55 mmHg and 75mmHg with a mean of 65 mmHg. The balloon / annulus ratio used for these patients was 1.13 and 1.1 respectively .

One patient(4%) was referred to surgery due to inability to cross the severely dysplastic PV .

DISCUSSION:

Successful immediate outcome of BPV was reported in 76% of the cases. This rate is in close agreement with that reported by Moura and coworkers who reported a success rate of 78% in a similar study group.*(Moura et al 2004)* [16] The male : female ratio in our study was 2.1: 1 , and this goes with that reported by Moura [16] who found a male : female ratio of 2.3 :1. Fifty six percentage (56%) of our patients had a PFO, 28% had PDA , and 16% had both PDA and PFO . *Kovalchin et al (1998)* [17] reported 100% PFO and 71% PDA in his study .

The significant immediate reduction of both RVSP and the PG across the RVOT from

a mean of 103.96 ± 24.98 mmHg and 82.5 ± 23.7 mmHg to a mean of 43.6 ± 13 mmHg and 21.35 ± 8.96 mmHg respectively was consistent with most recent data published by *Karagoz et al (2009).* [18] who reported a decline in the RVSP from a mean of 111.3 ± 36 mmHg to a mean of 36.9 ± 22 mmHg after BPV .

The RV / Systemic pressure ratio declined from a mean of 1.3 ± 0.2 before BPV to a mean of 0.5 ± 0.3 after BPV. This finding was consistent with that reported by *Kovalchin et al (1998)* [17] where the RV/Systemic pressure ratio declined from a mean of 1.3 ± 0.5 to a mean of 0.6 ± 0.3 .

Oxygen saturations raised after BPV from 80 ± 8% to 96 ± 2% which is consistent with *Abdul Aziz Bilkis (1999)* [19] who reported an increase in the oxygen saturation after BPV from 84 ± 8% to 98 ±2%. There was a progressive decrease in the PG across the RVOT throughout the follow up period by echocardiography from a mean of 93.3 ± 18.2 mmHg before performing the BPV to a mean of 26.93 ± 13.26 mmHg immediately after BPV and to a mean of 17.4 ± 10.42 mmHg after 6 months. This was consistent with the data published in other studies like that of *Sharieff et al (2003)* [20] who reported a decrease in the PG from a mean of 99.2 ± 11.5 mmHg before the procedure to a mean of 33.5 ± 9.7 mmHg immediately after the BPV and to 18.6 ± 3.4 mmHg at a follow up .This finding might be explained by the gradual regression of the infundibular hypertrophy.

Immediately after the BPV ,we documented a sharp increase in the incidence of PI that reached 66.6% of the patients . This data was consistent with the data published by *Poon and Menahem (2003)* [21] who reported a 61% incidence of PI the day after the procedure. *Werynski et al (2009)* [22] reported PI in 39.5% of infants with critical PS immediately after the BPV. All the patients of *Kovalchin(1998)*[17] developed PI after successful BPV of 22 neonates with critical PS . However , unlike the data published by *Fedderly et al and others* [11,15] , who reported a progressive increase in the incidence of PI from 22% to 40% at a mean follow up period of 11.9 years which was attributed to the use of high balloon / annulus ratio (>1.5) ,we reported a gradual decline in the incidence of PI to about 19% at 6 months follow up.

The current study showed a significant increase in the PV annulus and PV annulus Z score from a mean value of 7.1 ± 1.9mm and - 1.567 ± 0.295 to a 6 months post BPV mean of 9.3 ± 1.1 mm and – 0.650 ± 0.895 respectively. *Tabatabaei et al (1996)* [13] showed an increase in the pulmonary annulus diameter Z score from – 3 ±1.0 to 0 ± 0.1 . *Cazzaniga et al (2000)* [23] also reported that the RV – PA junction Z value grew from – 1.25 ± 0.9 before BPV to – 0.51 ± 0.7 at follow up .This increase in the pulmonary valve annulus towards the normal values was also consistent with the most recent data published by *Karagoz et al (2009).* [18]

There was a significant decrease in the number of patients with TR from 8 (32%) to 2 (9.5%) at 6 months follow up.This data was consistent with the data published by *Fawzy et al (2007)* [24] who showed that severe TR in seven patients with critical PS either regressed or totally disappeared at follow up .

There was no significant change in the tricuspid annulus Z score with decrease from a mean of 0.413 ± 1.22 to a 6 months post BPV mean of -0.152 ± 1.39 . This result was similar to that obtained by *Cazzaniga et al (2000)* [23].

The mortality rate was 12 % compared to 8% of the patients as reported by *Tabatabaei et al (1996)*[13] and a 14% mortality rate as reported by *Karagoz et al (2009)* [18] . *Abdul Aziz Bilkis et al (1999)* [19] reported a mortality rate of 5% and was due to the use of oversized balloon .

We have one patient (4%) who was referred to surgery due to inability to cross the PV because of severely dysplastic PV .*Abdul Aziz Bilkis et al* [19] were reported 9% required surgery due to severely dysplastic and immobile PV with severe RV hypoplasia .

Two patients (8%) required repeated BPV due to restenosis of the PV .The balloon/annulus ratio used for those patients was 1.13 and 1.1 . *M.Talsma et al(1993)* [25] reported a restenosis incidence of 9% in his study with a mean balloon/annulus ratio used 1.2 .

CONCLUSIONS:

BPV is safe and effective for both immediate and intermediate term relief of obstruction in infants with critical PS that should be done as early as possible and it is the procedure of choice. The balloon promotes advantageous changes in both pulmonary annulus and PG across the RVOT , with growth of the right heart structures in parallel to somatic growth. In addition , the Doppler gradient observations during the follow up support the expectations that BPV is a curative therapy. PI is common after BPV that regressed during follow up period denoting the transient nature of the PI. Good preparation of the patient and the choice of appropriate size balloon of low profile is crucial to increase the safety and success of the balloon dilatation and reduce the risk of complications.

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