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Tertiary care center experience regarding the early approach to transposition of the great arteries

Büyük arter transpozisyonuna yaklaşımda üçüncü basamak merkez deneyimi

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Background: This study aims to examine the effectiveness of balloon atrial septostomy in transposition of the great arteries patients and to evaluate possible factors influencing the procedure.

Methods: Between January 2005 and January 2012, a total of 111 patients (67 boys, 44 girls; mean age 18.2±20.3 days; range 1 to 105 days) younger than four months with the diagnosis of transposition of the great arteries who had either an interventional or diagnostic catheter procedure in our clinic were included in the study. The patients were divided into two main groups including those with (n=83) and without septostomy (n=28). The septostomy group was also divided into two subgroups including before and after septostomy.

Results: The mean preoperative angiographic aortic saturation was 50.6±16.3%, while the mean postoperative angiographic aortic saturation was 75.0±11.8%. During the procedure, the mean increased saturation was 24±15.2%, indicating statistical significance ($p<0.05$). The mean preoperative and postoperative left atrial pressure in the balloon atrial septostomy group was 13.3±5.3 (5.0-24.0) mmHg and 9.5±4.5 (3.0-20.0) mmHg, respectively. The mean gradient between the right and left atria before the procedure was 6.2±5 (0-19.0) mmHg and 0.9±1.3 (0-5.0) mmHg after the procedure. The difference was statistically significant ($p<0.05$). The factor of male sex increased the possibility of septostomy by 2.6-fold, the absence of atrial septal defect by 9.6-fold, and intact ventricular septum by 3.6-fold.

Conclusion: Balloon atrial septostomy is a relatively safe and effective procedure, although the ideal treatment is the arterial switch operation in transposition of the great arteries patients in the early stages.

Keywords: Cyanosis; heart defect; transposition of the great arteries.

Amaç: Bu çalışmada, büyük arter transpozisyonu olan hastalarda balon atriyal septostominin etkinliği araştırıldı ve bu işlemi etkileyen olası faktörler değerlendirildi.

Çalışma planı: Ocak 2005 - Ocak 2012 tarihleri arasında kliniğimizde büyük arter transpozisyonu tanısı ile girişimsel veya tanısal kateter işlemi yapılan dört aylıktan daha küçük olan toplam 111 hasta (67 erkek, 44 kız; ort. yaş 18.2±20.3 gün; dağılım 1-105 gün) çalışmaya dahil edildi. Hastalar septostomi yapılan (n=83) ve yapılmayanlar (n=28) olmak üzere iki ana gruba ayrıldı. Septostomi grubu ameliyat öncesi ve sonrası olmak üzere iki alt gruba daha ayrıldı.

Bulgular: Hastaların işlem öncesi anjiyografik aort satürasyon ortalaması %50.6±16.3 iken, işlem sonrası anjiyografik aort satürasyon ortalaması %75.0±11.8 idi. İşlem sırasında ortalama satürasyon artışı %24±15.2 idi ve istatistiksel olarak anlamlı bulundu ($p<0.05$). Balon atriyal septostomi grubunda işlem öncesi ve işlem sonrası ortalama sol atriyum basıncı sırasıyla 13.3±5.3 (5.0-24.0) mmHg ve 9.5±4.5 (3.0-20.0) mmHg idi. Sağ ve sol atriyumlar arasındaki ortalama gradyan işlem öncesi 6.2±5 (0-19.0) mmHg ve işlem sonrasında 0.9±1.3 (0-5.0) mmHg idi. Bu fark istatistiksel olarak anlamlı idi ($p<0.05$). Erkek cinsiyet faktörü septostomi olasılığını 2.6 kat, atriyal septal defekt yokluğu 9.6 kat ve intakt ventriküler septum 3.6 kat artırmaktaydı.

Sonuç: Büyük arter transpozisyonu hastalarında ideal tedavi erken dönemde arteriyel switch ameliyatı olsa da, balon atriyal septostomi nispeten güvenli ve etkin bir işlemdir.

Anahtar sözcükler: Siyanoz; kalp defekti; büyük arter transpozisyonu.

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Transposition of the great arteries (TGA) is the most common cyanotic congenital heart disease in the neonatal period.[1] Before the balloon atrial septostomy (BAS) process was introduced to the world by Rashkind and Miller,[2] the disease had a very high morbidity and mortality. Although improvements in treatment have been seen in the last 10 years due to advancements in the arterial switch operation (ASO) in the early stages of TGA. The BAS procedure is still widely practiced.[3,4] When systemic and pulmonary circulations become parallel, the maintenance of extra-uterine life depends on intra- or extra-cardiac shunts that provide a mixture of these circulations.[1] Prostaglandin E1 (PGE1) is widely used for patency of the ductus; however, this may not provide a significant increase in the oxygen saturation (OS) of the blood to the brain because the ductal shunt follows the carotid artery. Thus, PGE1 may not be effective, especially in cases in which the interatrial septum (IAS) is restrictive.[1,5] Therefore, a septostomy seems to be one of the most viable options for reducing mortality and hypoxia, particularly for hypoxic patients.[2,6] Recently, some studies have evaluated septostomies and the risk of stroke and reported that the increase in saturation is not sufficient in some patients even when proper interatrial communication was provided via the septostomy.[5,7-9]

This study aimed to examine the clinical and demographic characteristics of patients diagnosed with TGA as well as the associated anomalies of the disease. In addition, we also discussed the complications, paucity of the BAS procedure, and factors that affect the reasons for performing this procedure.

PATIENTS AND METHODS

This study was composed of 111 infants under four months old [67 males, 44 females; mean age 18.2±20.3 days; range 1 to 105 days; mean weight 3.4±0.6 (1.8-5) kg.)] who had been diagnosed with TGA and undergone an invasive or diagnostic catheter procedure at the Dr. Sami Ulus Pediatric Research and Training Hospital between January 2005 and January 2012. Those with complex single-ventricle congenital heart disease featuring ventriculoarterial discordance as only one component and those with isomerism were excluded from the study. The patients were divided into two main groups according to whether or not they had a BAS, and the BAS group was the divided into pre and post-septostomy subgroups. The BAS procedure was performed on 81 cases (73%), and diagnostic angiography alone was applied to 28 (25%). In addition, balloon coarctation angioplasty with the BAS was performed in the same session on two (2%) other cases. Among the patients that underwent the BAS, the oldest patient was 105 days old, and the youngest was 24 hours old. Furthermore, 91 patients (81.9%) were term, 11 (9.9%) were pre-term, and nine (8.2%) were post-term.

The patients' prenatal, natal, and postnatal histories, clinical and physical examination findings, and laboratory results were retrospectively reviewed from the hospital database system, and their echocardiographic data was evaluated for the presence of an IAS, ductus arteriosus, and pulmonary hypertension (PH). In addition, we also looked for signs of any additional anomalies. Restrictive interatrial transition was noted if the gradient between the two atria was ≥8 mmHg on Doppler echocardiography.[10] Hemodynamically significant ventricular septal defect (VSD) occurred in cases in which the VSD size was at least equal to the aorta and/or the pressure difference between the two ventricles was less than 30 mmHg.[11] This was subsequently confirmed via angiography. Furthermore, hemodynamically significant stenosis was seen when the gradient of the left ventricular outflow tract (LVOT) was ≥60 mmHg on echocardiography.[12]

Catheter angiography was carried out on every patient diagnosed with TGA in order to conduct interventions associated with cardiac pathologies with an aim of collecting data to determine the type of surgery needed.

The BAS was performed in order to achieve mixing along with an increase in saturation, a reduction of left atrial pressure, and preoperative stabilization. Additionally, it was carried out particularly to reduce pulmonary congestion and heart failure, especially in patients with VSD.[6,9,13] In addition, this procedure was applied to those who no longer were suitable for the arterial switch procedure because of late presentation and a closed ductus. Moreover, the BAS was not performed in any patient for whom bedside echocardiography was performed.

All of the BAS procedures were conducted through the femoral vein. The patients' angiographic data was obtained from an angiography-based registry system, and the hemodynamic data was compared before and after treatment for patients who underwent a septostomy. Additionally, the left ventricular pressure and aorta saturations were recorded for patients who underwent diagnostic catheterization. When BAS was performed, the saturation changes were also recorded before and after treatment. The left ventricular pressures were important because they affected the treatment plans.

Table 1. Clinical and demographic characteristics of the patients

Characteristics	All patients (n=111)			BAS (n=83)			Non-BAS (n=28)			
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	*p*
Sex										
Female	44			28			16			
Male	67			55			12			<0.05
Weight (kg)			3.4±0.6			3.3±0.5			3.6±0.6	0.06
Recourse age (days)			18.2±20.3			15.6±18.5			25.4±23.7	<0.05
Age when complaints started (days)			6.3±7.1			6.1±7.2			7.0±6.8	0.6
Age at procedure (days)			19.8±21.8			16.9±19.1			28.5±27.0	<0.05
Recourse saturation*			64.4±15.7			62.0±15.7			71.3±13.7	0.02
Intubation	25	22.5		19	22.8		6	21.4		0.11

BAS: Balloon atrial septostomy; SD: Standard deviation; * With pulse oximetry.

Patients with a left ventricular pressure of more than 50 mmHg were evaluated for ASO while those with a left ventricular pressure of lower than 50 mmHg were evaluated for ASO. Furthermore, those with hemodynamically significantly VSD and pulmonary stenosis (PS) were evaluated for the Rastelli operation. Transfontanelle ultrasonography (USG) was conducted on all of the patients in the neonatal intensive care unit (ICU), and cranial magnetic resonance imaging (MRI) was scheduled for the patients who presented with clinical signs or for those for whom a pathology was detected via USG.

In our center, we had limited success when using PGE1 from 2009 to 2011 but have seen marked improvement since then; hence, only a small portion of the patients in this study received PGE1. Prior to surgery, PGE1 was given to those patients who might be referred for an ASO, for those referred for a septostomy before applying the BAS process, for those with arterial saturation under 75% in spite of undergoing the BAS, and for those who were unable to undergo mechanical ventilation due to acidosis.[14] The PGE1 was administered at 0.05-0.1 µg/kg/minute by continuous intravenous infusion.

Statistical analysis

The data was evaluated using the SPSS for Windows version 16 software program (SPSS Inc., Chicago, IL, USA), with the values being expressed as mean ± standard deviation (SD). The independent Student's t-test was used for averages and mean comparisons, and Pearson's Chi-square test was used to compare non-parametric variables. To identify the risk factors associated with the BAS, logistic regression were used for analysis, and a *p* value of less than 0.05 was considered to be statistically significant.

RESULTS

Our findings showed a statistically significant difference in terms of gender distribution based on whether or not the BAS procedure had been performed. The characteristics of all of the groups and subgroups at the time of admission are given in Table 1. The number one complaint of the patients at admission was bruising, and this was followed by heart failure. The complaints at admission are summarized in Table 2.

Only one patient (0.09%) was diagnosed prenatally. A family history was available for 70 patients (64.8%), and this indicated an irregular pregnancy follow-up history in 22 of the mothers (31.4%) as well as 18 (25.7%) with a history of intermarriage. For the latter group, 13 were third-degree relatives, three were fourth-degree, and two were distant relatives. Moreover, five patients (4.5%) with different diagnoses (one with hypertrophic cardiomyopathy, two with VSD, one with VSD + PS, one with double outlet right ventricle + subpulmonic VSD) were referred to our clinic for treatment.

In both the BAS and non-BAS groups, the number of patients with acidosis (pH <7.2) was not high despite the decrease in saturation. There were five (6%)

Table 2. Complaints of the patients at the time of diagnosis

Complaint	n	%
Cyanosis	63	56.7
Feeding difficulties, restlessness	14	12.6
Cyanosis + feeding difficulties + restlessness	3	2.7
Epileptic seizures	1	0.9
Pathological murmurs	7	6.4
Unavailable history	23	20.7

acidotic patients in the BAS group, and one (3.5%) in the non-BAS group. In addition, comparisons of blood gases and OS in the patients with and without BAS on admission are summarized in Table 3. Although the BAS had a positive effect on blood gas parameters, only the effect on saturation was statistically significant. A comparison of peripheral arterial blood gases before and after the procedure is given in Table 4.

The mean pressure of the left ventricle in the entire group was 62.5±14.5 mmHg. We achieved left ventricular pressure recordings during the procedure for 97 patients (87.3%), with left ventricular pressure of >50 mmHg for 83 patients (%85.5) and <50 mmHg for 14 others (14.4%). Furthermore, the left ventricular pressure values were inversely correlated with the age of the patients. Moreover, the mean left ventricular pressure was 70.2±15.6 mmHg in the patients with PH, 72.2±19.9 mmHg in the PS patients, and 59.1±12.9 mmHg in the group with an intact ventricular septum or restrictive VSD.

The mean preoperative aortic saturation (measured angiographically) was 50.6±16.3%, and the mean post-procedural angiographic aortic saturation was 75.0±11.8%. During the procedure, the mean increased saturation was 24±15.2%, with the average difference being statistically significant ($p<0.05$). The mean left atrial pressure before the operation in the septostomy group was 13.3±5.3 (5.0-24.0) mmHg and 9.5±4.5 (3.0-20.0) mmHg after surgery. Additionally, the average gradient between the right and left atria before the procedure was 6.2±5 (0-19.0) mmHg while it was 0.9±1.3 (0-5.0) mmHg afterwards, and this difference was statistically significant ($p<0.05$). We also found that the preoperative gradient between the two atria was ≥8 mmHg in 21 patients (25.3%). In 10 patients (12%), the saturation was below expectations, even after performing the procedure, and the BAS procedure was repeated in four of the patients (4.8%). Treatment for anti-pulmonary arterial hypertension (anti-PAH) was initiated for two others (2.4%) who demonstrated a right-to-left shunt from the ductus on echocardiography with reverse differentiated cyanosis, and a systemic-to-pulmonary shunt was implanted in four patients (4.8%) who demonstrated left ventricular outflow tract obstruction (LVOTO) that had settled over time on echocardiography. Thus, the expected saturation levels were achieved in all 10 cases.

Among all of the patients, seizures occurred in only one (1.2%) after the procedure, and infarction in the middle cerebral artery was observed in the MRI of this patient. In addition, four patients (4.8%) died in the early post-surgical period in spite of the medications given and invasive procedures that were performed. All of the deceased patients were male and had an early age at admission as well as an intact ventricular septum and restrictive interatrial and ductal communications. Angiographically, the left atrial pressure was 20, 22, and 24 mmHg in three patients respectively, and the pressure difference between the two atria was at least 12 mmHg in these patients. Left atrial pressure was not measured in one patient, because of hemodynamic instability.

The BAS procedure was also performed without pressure recordings on four patients, due to a severely damaged general condition, and echocardiography revealed that their ductal flow was poor or approaching poor in the early period. Moreover, there was no mortality in the early period in the non-BAS group.

When concomitant cardiac anomalies were reviewed, patent ductus arteriosus (PDA) was detected in 65 of the patients (59%), secundum atrial septal defect (ASD) in 20 (18%), and VSD in 69 (62%). The source of the VSD was at the perimembranous outlet for 24 patients and at the perimembranous inlet for six others. In addition, it was muscular in nature in 32, confluent in five, and subarterial in two others. Furthermore, mild aortic coarctation, aortic coarctation requiring invasive intervention, aortic interruption,

Table 3. Comparison of blood gas values of the groups at the time of admission

	BAS	Non-BAS	*p*
	Mean±SD	Mean±SD	
pH	7.3±0.1	7.3±0.1	0.62
pCO_2	47.4±55.8	41.0±13.3	0.62
pO_2	33.8±23.5	38.5±18.7	0.43
SaO_2	50.4±17.7	64.4±21.8	<0.05

BAS: Balloon atrial septostomy; SD: Standard deviation; pCO_2: Partial pressure of carbon dioxide; pO_2: Partial pressure of oxygen; SaO_2: Oxygen saturation.

Table 4. Comparison of peripheral arterial blood gas values before and after the procedure in the balloon atrial septostomy group

	Before BAS	After BAS	*p*
	Mean±SD	Mean±SD	
pH	7.31±0.1	7.4±0.1	<0.05
pCO_2	47.4±55.8	36.1±11.9	0.29
pO_2	33.8±23.5	53.8±47.2	0.01
SaO_2	50.4±17.7	77.0±18.3	0.01

BAS: Balloon atrial septostomy; SD: Standard deviation; pCO_2: Partial pressure of carbon dioxide; pO_2: Partial pressure of oxygen; SaO_2: Oxygen saturation.

Table 5. Extracardiac signs and symptoms

	BAS (n=83)		Non-BAS (n=28)	
	n	%	n	%
Malnutrition	4	4.8	–	–
Seizures	1*	1.2	1†	3.5
Meningomyelocele	1	1.2	–	–
Major neuroradiological findings	1‡	1.2	1¶	3.5
Minor neuroradiological findings	11#	9.9	7§	25
Pneumonia	10	12	5	17

* After balloon atrial septostomy (BAS); † At the time of diagnosis; ‡ Infarction at a.meningea media contour; ¶ Hemorrhage compressing the lateral and third ventricle; # Increased echogenicity of white and gray matter in one patient; increased echogenicity of only white matter in one patient; grade 2 subependymal hemorrhage in one patient; Chiari type 2 hydrocephalus in one patient; subependymal cysts and cystic degeneration in two patients; caudo-thalamic hemorrhage in two patients, uncertain lateral ventricle horn border in three patients; § Caudo-thalamic hemorrhage in two patients; subependymal cysts and cystic degeneration in two patients; uncertain lateral ventricle horn border in three patients.

and isthmus hypoplasia were respectively found in two patients each (1.8%). We also identified coronary anomalies in 16 patients (14.4%), static pulmonary valve stenosis in 12 more (10.8%), and dynamic pulmonary valve stenosis in five others (4.5%). Finally, 81 (72.9%) had isolated or TGA with restrictive VSD, 18 (16.2%) had TGA + hemodynamically significant VSD, and 12 (10.8%) had TGA + hemodynamically significant VSD and PS.

In addition, in an infant from a diabetic mother, significant ventricular hypertrophy was detected in the neonatal period along with signs of hypocalcemia and hypoglycemia. The hypertrophy of this patient recovered slowly in the follow-up period.

In 55 of the patients (49.5%), the cranial USG results were evaluated. Cranial USG results were uncertain in the remaining 56 patients (50.5%). In 14 of 56 patients cranial USG could not have been performed due to hemodinamic instability. Unfortunately, the results of the other 42 patients (37.8%) were not accessible from the computer data because of technical issues. In 35 of the 55 patients (31.5%), the cranial USG results were normal, whereas 20 (18%) were abnormal. The neuroradiological findings are summarized in Table 5. Two patients had clinical convulsions. The seizures of one patient in the non-BAS group were attributed to disseminated intravascular coagulopathy and bleeding, and diffuse bleeding was confirmed via cranial computed tomography (CT). In the other patient, who was in the BAS group, the seizures were detected after the BAS. In this patient's cranial MRI, infarcts in the middle cerebral artery tracing were present. Other extracardiac findings were present in some of the patients, and these results are also shown in Table 5.

We also compared a number of characteristics between the BAS and non-BAS groups which we thought were likely to influence whether or not this procedure was performed, and these results are given in Table 6. According to the logistic regression analysis, there was a 2.6-fold increased in the possibility of undergoing the BAS in the male gender along with a 9.6-fold increase in the absence of ASD and a 3.6-fold increase with an intact ventricular septum.

Prostaglandin E1 was administered to 15 patients (13.5%), and three (2.7%) of these were referred for a septostomy because in spite of receiving this drug, pulmonary edema, heart failure, and signs of a worsening of the symptoms were present. Furthermore, in four patients (3.6%), the PGE1 infusion was administered due to low levels of saturation, even though they underwent the BAS procedure.

Table 6. Comparison of the group characteristics in terms of the septostomy

	BAS (n=83)		Non-BAS (n=28)		
	n	%	n	%	*p*
Sex					
Male	28		16		
Female	55		12		0.029
Ventricular septal defect‡	14	16.8	16	5.7	0.01
Atrial septal defect	7*	8.4	13	4.6	0.01
Patent ductus arteriosus	47	56.6	15	53.5	0.78
Extracardiac symptoms§	16	19.2	6	21.4	0.16
Neuroradiologic findings	12	14.4	8	28.5	0.046

BAS: Balloon atrial septostomy; ‡ Hemodynamically significant; * Restrictive; § Malnutrition; pneumonia; seizure; meningomyelocele.

DISCUSSION

The TGA is the most common cyanotic congenital heart disease in the newborn period.[1,13] Due to ventriculoarterial discordance, systemic and pulmonary circulations are parallel occurrences. In TGA, extra-uterine life depends on early surgery as well as natural or interventional shunts.[5,15] Prostaglandin E1 is commonly used for ductus patency and is crucial in terms of increased mixing and vasodilation in the pulmonary bed, leading to an increase in the return of blood into the left atrium and left-to-right shunt.[4] However, especially in cases involving a restrictive IAS, no significant increase in the amount of blood sent to the brain can be maintained because of the postcarotid localization of the ductal shunt.[5] Furthermore, the ductus of patients admitted at later periods may close, resulting in them losing their chance for an ASO.

Although undergoing an ASO is the ideal treatment in the early period, the BAS is commonly employed to increase systemic oxygenation in congenital heart diseases, especially when TGA occurs.[5,7] Because of its popularity, various studies have explored the effectiveness, reliability, associated side effects, and deficiencies of this technique,[7,8,16] and in this study, we evaluated our personal experience with this procedure in our own clinic.

In accordance with the literature,[5,12,17] our patients were predominantly male. However the number of female patients more than the other gender and the difference was statistically significant. Therefore, we concluded that simple TGA was more common in males, which was consistent with the findings of other studies.[5,17]

Similar to patients with an intact atrial septum, it is known that an intact ventricular septum increases the possibility of undergoing the BAS when the risk factors are examined. However, when a hemodynamically significant VSD is present, it does not imply that the patient will never require the BAS. For example, the BAS procedure was performed on 14 patients with a hemodynamically significant VSD in our study group. Based on this observation, one can speculate that the presence of a VSD alone is insufficient to determine the necessity for the BAS. Additional factors, including the direction of the shunt from the VSD, the ventricular compliance that determines this direction, and systemic and PH or obstruction, also must be taken into account when deciding on the need for the BAS. Some authors have chosen a septostomy in TGA patients with a right upper extremity saturation of below 60%, regardless of the intracardiac anatomy.[18] Conversely, in the non-BAS group in this study, 12 patients had an intact ventricular septum. In addition, some of our patients were ineligible for a septostomy because of their late referral to our clinic since they already had an adequate interatrial passage due to a secundum ASD. Unlike ASD and VSD, the possibility of a septostomy is likely to be independent from a PDA because it is a postcarotid shunt and cannot treat the intracerebral hypoxia effectively. A septostomy should only be used in the presence of sufficient interatrial communication.[5] Our patients showed a significant increase in OS and partial pressure of oxygen (PaO_2) on angiography, and their blood gas values were also higher after the septostomy procedure, proving that the operation was effective for hypoxic newborns.

Applegate and Lim[7] reported that arrhythmia, subclinical cerebral ischemia, the embolization of ruptured balloon particles, valve and vessel wall injuries, and hypoxemia can be associated with the BAS, but most studies have focused on the relationship between this procedure and stroke or permanent brain damage.[5,6,16] Invasive and surgical procedures in patients with TGA may cause a cerebral embolism, damage to the cerebral vessels due to pressure, ischemia, and reperfusion injury.[9] In addition, the rate of preoperative brain injuries in patients with cyanotic congenital heart disease have been estimated to be between 25-40% in the newborn period, with the most common changes being white matter injuries, infarct, bleeding, and maturation disorders.[8] Primarily based on the appearance of infarction, McQuillen et al.[16] claimed that the rate of MR change is around 40% in patients with TGA and that this is directly related to the BAS. However, there are also many studies that have suggested that the increase in frequency of stroke may not be related to septostomies, or at least they may not be solely associated with the BAS procedure.[6-9,19] These studies emphasized that hypoxia had been present since the fetal period in patients with TGA and that their cerebral blood flow was abnormal. Therefore, some neurological structural changes can be seen in patients with TGA before any intervention takes place.[19] Finally, since the aorta derived from the ventricle in which systemic venous circulation is open, there is a risk of a cranial embolism in patients with TGA even in simple intravenous procedures. Among our patients, various neuroimaging changes were detected in 12 patients (14.4%) in the BAS group. Furthermore, our radiological findings were obtained before the septostomy in eight patients and after the BAS in four others, but it was still difficult to determine whether this procedure contributed to our findings or not. Additionally, only one patient (1.2%) had seizures,

which started at the sixth hour after the BAS. These were verified by the MRI and were consistent with an infarct of the middle cerebral artery region.

With urgent intervention requirements, the importance of fetal echocardiography has emerged in the diagnosis because it provides the opportunity for early transportation and PGE1 infusion initiation as well as the ability to maintain the potential for an ASO.[1]

As previously mentioned, only one of our patients was diagnosed prenatally, but prenatal diagnosis significantly affects mortality along with the future neurocognitive development of patients that survive. In the study by Calderon et al.,[20] the TGA group that was prenatally diagnosed and received early intervention was more successful in the executive function and social cognition tests than those who were diagnosed postnatally.

The common characteristics of the patients in this study who died in spite of undergoing the emergency BAS procedure were being male, having early symptoms (during the first hours of life), and suffering from a severe mixing problem, such as the combination of the intact ventricular septum, restrictive ductus, and restrictive atrial septum. We also observed that the ductus of those patients tended toward early closure; however, none of the common features were found to be statistically significant. Chiou et al.[1] found that patients with a restrictive or intact IAS and restrictive ductus arteriosus, even in utero, did not have a good postnatal prognosis due to the advanced stage deficiency of mixing, and they determined that the mortality rate for those patients was high. In another study by Punn et al.,[21] a hypermobile intact atrial septum and inverse ductal flow were determined to be risk factors. A restrictive ductus may be caused by a higher than normal oxygen content in the pulmonary bed, which can be explained by the fact that a high oxygen content may result in the contraction of the pulmonary end of the ductus arteriosus, thus causing a simultaneous increase in pulmonary blood flow. In other words, pulmonary congestion begins in utero in these patients; hence, early and severe PH is expected in cases of TGA with restrictive ductus, even if the restrictive ductus is reopened by PGE1 infusion.[21] Another problem is that an intact atrial septum can occur because of the change in the atrial septal configuration stemming from the elevated left atrial pressure.[22] The BAS procedure can benefit patients who have only a restrictive intact atrial septum, but a septostomy performed as adjunct therapy is required if the pulmonary vascular bed has been affected.

The success of the BAS depends on many factors, including the parallel circulation mix, local pressure gradient, compliance of the heart chambers, heart rate, effective blood volume, and circulating resistance of both systems. In addition, some of our cases showed a moderate but lower than expected increase in saturation following the procedure. Despite successful treatment, a persistent decrease in OS has been reported in several studies in the literature.[23,24] One of the most important causes of this condition is persistent pulmonary hypertension (PPHN), with a frequency in patients with TGA of between 1 and 3%.[13] Furthermore, PPHN increases mortality by up to 30%.[23,24] Typically, a systemic-to-pulmonary shunt at the ductus level with a decrease in pulmonary vascular resistance is used in these cases, but when there is pulmonary vascular resistance, it should not decrease but be bidirectional so that a reduction in the pulmonary venous return occurs. Therefore, although the BAS provides a sufficient range of the IAS, it is not sufficiently effective in patients in which pulmonary vascular resistance does not decrease through various means.[14] El Seagier et al.[23] reported that PPHN can be caused by acidosis, hypoxemia, polycythemia, and increased pulmonary artery pressure (PAP) due to circulating vasoactive substances in patients with TGA. However, they found that this effect was more pronounced in some patients and that it prevented an increase in saturation, even when the appropriate mixture was provided. If there are physical examination findings, such as echocardiographic or reverse differential cyanosis, which are suggestive of severe PH in patients after a septostomy, anti-PAH drugs can also be used effectively as well as volume, inotropic support, and PGE1 infusion in these patients. For example, two patients in this study group had positive results with anti-PAH treatment. Nitric oxide (NO) was administered to these patients, and this was followed by a drop in PAP and higher saturation levels. However, there may be a need to improve the myocardial dysfunction and failure influenced by deep hypoxemia and acidosis in patients who do not respond to anti-PAH treatment. Jaillard et al.[18] applied extracorporeal membrane oxygenation (ECMO) to a patient with no improvement in ventricular function, and this occurred in spite of the BAS, inhaled NO, and PGE-1 infusion treatments. After six days of ECMO support, an ASO was performed on this patient which achieved good results. Another treatment option is leaving the VSD open and conducting a palliative ASO.[24] Patients with a severe LVOTO also response poorly to the BAS procedure. In these cases, systemic-to-pulmonary shunts should be also

be applied afterwards to ensure a better prognosis. In our patient group, improved saturation was observed in four patients (4.8%) when this was done. However, the outflow obstruction became more prominent in these cases over a period of time due to the anatomy. Although researchers have observed that some patients have had mild hypoplasia of the left pulmonary artery because of the tendency for the blood to flow into the right pulmonary artery in TGA, there were no clinically affected cases in our study group. In some cases, the PGE1 was stopped after successfully performing the BAS. Afterwards, we observed a modest reduction in saturation that did not adversely affect the patients' clinical status and we concluded that this was because of the reduction in the amount of blood returning to the heart from the left lung with the closure of the ductus, and the reduction of the left-to-right shunt at the IAS. Hiremath et al.[6] emphasized that the vasodilation effects of prostaglandins on the pulmonary vascular bed also provided patency of the ductus.

Finally, although some authors accept that the BAS procedure under transthoracic echocardiography (TTE) is safe and effective, the fluoroscopic BAS procedure is preferred in our clinic because it provides the opportunity to collect detailed anatomic and hemodynamic data.[25]

This study had several limitations. Firstly, it was based on a retrospective screening of the patient files; therefore, some incomplete or inaccurate data may have been obtained. For example, there were a certain number of patients with VSD, and classifying some of the cases was difficult in terms of hemodynamic data. In addition, the BAS procedure rate was higher than usual because of the difficulty accessing the PGE1 and also the late admission of some of the patients to the hospital. Furthermore, although transfontanelle USG was conducted on all patients, a cranial MRI was performed only on the patients with clinical manifestations and/or pathology detected via USG. Another limitation was that the preductal/postductal distinction, in terms of specified saturations, could not be determined for each case. Lastly, only the short-term follow-up results of the patients were collected; hence, long-term morbidity (such as neurocognitive function) was not evaluated.

Conclusion

Despite a rapid decline in mortality rates and common developments in surgical techniques, the BAS is a safe and efficient procedure that is still widely used. Balloon atrial septostomies in TGA patients are not only vital for maintaining intra-atrial mixing, but they are also beneficial for decreasing the left atrium pressure, preoperatively stabilizing the patients, and facilitating the operation.[6,9] Although there have been some discussions concerning the fact that the BAS increases the incidence of stroke, it is still considered to be a life-saving procedure. An early or prenatal diagnosis can reduce morbidity and mortality because of the possibility for emergency intervention. After the BAS, if the expected increase in saturation levels does not occur, various other treatment methods specific to the patients' hemodynamic characteristics can be attempted.

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REFERENCES

1. Chiou HL, Moon-Grady A, Rodriguez R, Konia T, Parrish M, Milstein J. A rare lethal combination of premature closure of the foramen ovale and d-transposition of the great arteries with intact ventricular septum. Int J Cardiol 2008;130:e57-9.
2. Rashkind WJ, Miller WW. Creation of an atrial septal defect without thoracotomy. A palliative approach to complete transposition of the great arteries. JAMA 1966;196:991-2.
3. Jatene AD, Fontes VF, Paulista PP, de Souza LC, Neger F, Galantier M, et al. Successful anatomic correction of transposition of the great vessels. A preliminary report. Arq Bras Cardiol 1975;28:461-64.
4. Galal MO, El-Naggar WI, Sharfi MH. Phentolamine as a treatment for poor mixing in transposition of the great arteries with adequate intraatrial communication. Pediatr Cardiol 2005;26:444-5.
5. Mukherjee D, Lindsay M, Zhang Y, Lardaro T, Osen H, Chang DC, et al. Analysis of 8681 neonates with transposition of the great arteries: outcomes with and without Rashkind balloon atrial septostomy. Cardiol Young 2010;20:373-80.
6. Hiremath G, Natarajan G, Math D, Aggarwal S. Impact of balloon atrial septostomy in neonates with transposition of great arteries. J Perinatol 2011;31:494-9.
7. Applegate SE, Lim DS. Incidence of stroke in patients with d-transposition of the great arteries that undergo balloon atrial septostomy in the University Healthsystem Consortium Clinical Data Base/Resource Manager. Catheter Cardiovasc Interv 2010;76:129-31.
8. Beca J, Gunn J, Coleman L, Hope A, Whelan LC, Gentles T, et al. Pre-operative brain injury in newborn infants with transposition of the great arteries occurs at rates similar to other complex congenital heart disease and is not related to balloon atrial septostomy. J Am Coll Cardiol 2009;53:1807-11.

9. Mosca R. Balloon atrial septostomy let's take a closer look. J Am Coll Cardiol 2009;53:1812-3.
10. Graziano JN, Heidelberger KP, Ensing GJ, Gomez CA, Ludomirsky A. The influence of a restrictive atrial septal defect on pulmonary vascular morphology in patients with hypoplastic left heart syndrome. Pediatr Cardiol 2002;23:146-51.
11. Chaudhry TA, Younas M, Baig A. Ventricular septal defect and associated complications. J Pak Med Assoc 2011;61:1001-4.
12. Prieto LR, Latson LA. Pulmonary stenosis. In: Allen HD, Driscoll DJ, Shaddy RE, Feltes TF, editors. Moss and Adams' heart disease in infants, children, and adolescents: including the fetus and young adults. 7th ed. Baltimore: Lippincott Williams & Wilkins; 2008. p. 835-59.
13. Rao PS. Diagnosis and management of cyanotic congenital heart disease: part I. Indian J Pediatr 2009;76:57-70.
14. Hartas GA, Tsounias E, Gupta-Malhotra M. Approach to diagnosing congenital cardiac disorders. Crit Care Nurs Clin North Am 2009;21:27-36.
15. Şaşmazel A, Özkökeli M, Büyükbayrak F, Baysal A, Erdem H, Tuncer A, et al. Our surgical experience and mid-term results with the Senning procedure Turk Gogus Kalp Dama 2011;19:157-62.
16. McQuillen PS, Hamrick SE, Perez MJ, Barkovich AJ, Glidden DV, Karl TR, et al. Balloon atrial septostomy is associated with preoperative stroke in neonates with transposition of the great arteries. Circulation 2006;113:280-5.
17. Gabriel J, Scheld HH, Tjan TD, Osada N, Krasemann T. Is the function of all cardiac valves after the arterial switch operation influenced by an associated ventricular septal defect? Cardiol Young 2011;21:383-91.
18. Jaillard S, Belli E, Rakza T, Larrue B, Magnenant E, Rey C, et al. Preoperative ECMO in transposition of the great arteries with persistent pulmonary hypertension. Ann Thorac Surg 2005;79:2155-8.
19. Petit CJ, Rome JJ, Wernovsky G, Mason SE, Shera DM, Nicolson SC, et al. Preoperative brain injury in transposition of the great arteries is associated with oxygenation and time to surgery, not balloon atrial septostomy. Circulation 2009;119:709-16.
20. Calderon J, Angeard N, Moutier S, Plumet MH, Jambaqué I, Bonnet D. Impact of prenatal diagnosis on neurocognitive outcomes in children with transposition of the great arteries. J Pediatr 2012;161:94-8.e1.
21. Punn R, Silverman NH. Fetal predictors of urgent balloon atrial septostomy in neonates with complete transposition. J Am Soc Echocardiogr 2011;24:425-30.
22. Maeno YV, Kamenir SA, Sinclair B, van der Velde ME, Smallhorn JF, Hornberger LK. Prenatal features of ductus arteriosus constriction and restrictive foramen ovale in d-transposition of the great arteries. Circulation 1999;99:1209-14.
23. El-Segaier M, Hellström-Westas L, Wettrell G. Nitric oxide in neonatal transposition of the great arteries. Acta Paediatr 2005;94:912-6.
24. Kumar A, Taylor GP, Sandor GG, Patterson MW. Pulmonary vascular disease in neonates with transposition of the great arteries and intact ventricular septum. Br Heart J 1993;69:442-5.
25. Lopes LM, Kawano C, Cristóvão SA, Nagamatsu CT, Fonseca Ld, Furlanetto BH, et al. Balloon atrial septostomy guided by echocardiography in a neonatal intensive care unit. Arq Bras Cardiol 2010;95:153-8.