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CONGENITAL HEART DISEASE

Percutaneous PDA Closure in Extremely Low Birth Weight Babies

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***Aim**: Patent Ductus Arteriosus is an important cause of morbidity and mortality in preterms. As birth weight decrease, risks increase. Main aim of our study is to emphasize the effectiveness and safety of percutaneous PDA closure even in extremely low birth infants.*
***Materials and Methods**: In our center between the dates June 2014–June 2016, PDA of 10 patients less than 1,000 gr were closed percutaneously. To the best of our knowledge this study includes the largest cohort of infants less than 1,000 g in the literature, that PDA of those were percutaneously closed.*
***Results**: Symptomatic patients, less than 1,000 gr having PDA were included in the study. All have 3 times medical therapy for PDA closure but it did not work. PDA was decided to be contributor of this medical state of them. The mean patient age was 19.5 ± 7.2 days. The median weight was 950 (842–983) gr. Mean gestational age was: 26.3 ± 0.63 weeks. Mean PDA diameter was 1.9 ± 0.41 mm. Morphology of PDA:6 of them were conical and 4 of them were tubular. In all patients ADOII-AS device were used for PDA closure via venous route. No major complications were reported. Left pulmonary arterial stenosis was detected in 1 patient who was resolved in 6 months duration.*
***Conclusion**: We want to emphasize that in experienced centers percutaneous closure of PDA can be an alternative to surgery even in the extremely low birth weight babies.* (J Interven Cardiol 2016;29:654–660)

Introduction

After birth as a part of postnatal adaptation functional closure of ductus occurs within 1–2 days in mature neonates; however, in preterms ductus arteriosus may be patent in the 3rd day depending on the gestational age.[1]

Having PDA increases the morbidity and mortality in preterms which is worse in extremely low birth weights. Patent ductus leads left to right shunt and pulmonary flow increases. It worsens respiratory distress syndrome, leads to high ventilator settings; finally ends up with bronchopulmonary dysplasia. It also increases the risk of necrotizing enterocolitis, pulmonary hypertension, and infective endocarditis.[2]

Even PDA closure is accepted in neonates to avoid these risks; there is no consensus about the timing of closure. In preterms this topic is more complicated.

Transcatheter closure of PDA of infants more than 4 kg is approved[3]; however, there is not enough data for the ones who are less than 1 kg in the literature.

Previously, surgery was the only option for the babies whose bodyweight was less than 2 kg. However, we had described a technique that allows closure of PDAs in the infants less than 2 kg.[4]

In this report, we describe our experience in 10 preterm infants with PDA. Main aim of our study is to emphasize the effectiveness and safety of percutaneous PDA closure even in extremely low birth infants (less than 1,000 gr).

Materials and Methods

The study was performed in Erciyes University Faculty of Medicine Pediatric Cardiology Department

Conflicts of interest: The authors have no conflicts of interest to declare.

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between the dates June 2014–June 2016. The study was approved by the local research ethics committee.

Patient Selection. Preterm infants weighing less than 1,000 gr were included in the study. All patients were symptomatic and hospitalized in neonatal intensive care unit. Patients were consulted for high settings of mechanical ventilation, tachycardia, murmur, worsening general condition, etc. Diagnosis of PDA was done by transthoracic echocardiography (TTE). Sizes of heart chambers, ductus size (ampulla, minimal ductus size) shape of ductus were recorded. Also the diameter of descending aorta was noted to choose appropriate device; prevent protrusion and stenosis.

The decision regarding the way of closure (whether transcatheter or surgical) was made according to the size, shape of the PDA and discussed with the family. Large window types were usually referred to surgery.

The following data for each patient were collected: age, weight, sex, non-cardiac medical problems, gestational week, birth weight, duration of hospitalization, and complications, duration of mechanical ventilation, procedure time, fluoroscopy duration, and radiation dosage and follow-up period.

Physical examination, chest radiography, electrocardiography, and TTE were done before each procedure. All the parents were informed about the procedure and its complications, and written informed consent was obtained before the procedure.

Device and Catheterization. Seldinger technique was used for vascular access to femoral artery, vein or umbilical vein. 4F sized sheath is used for venous access, 3F for arterial site. We did not have an arterial access in all patients. About 100 U/kg unfractioned heparin was given to the ones who had arterial access, the ones who had only venous site only 50 U/kg heparin was injected. If procedure took a long time we have checked activated clotting time and tried to provide it >250 seconds.

Hemodynamic measurements of systolic, diastolic, and mean pressures of pulmonary artery and aorta also oxygen saturation obtained from the inferior, superior vena cava, right atrium, pulmonary artery, right ventricle (RV), and the aorta were done. Multipurpose, hydrophilic and pigtail catheters were used to measure the ventricle/atrium and great artery pressures. Fick principle was used to calculate the ratio of pulmonary to systemic blood flow (Qp/Qs). Hemodynamic evaluation was not done routinely for every patient. Especially in the patients who did not have a stable status; we did not perform hemodynamic measurements in order to keep the procedure time as short as possible.

Descending aorta angiograms in the right anterior oblique and lateral projections performed with a pigtail catheter; to determine the size and morphology of ductus. In patients we did not have arterial access; aortography was done with a catheter extended from the pulmonary artery to the aorta through PDA. Ducti were categorized based on their morphology, according to the classification of Kritchenko et al.[5] Device selection was done according to shape, size and relationship to adjacent structures. Consistent with our previous report[4]; Amplatzer Ductal Occluder II-Additional Size (ADOII-AS) was chosen by adding 1–1.5 mm to the narrowest point of duct.

PDA closure was done from venous site in every patient under the guidance of transthoracic echocardiography. Radiocontrast injection was done before the release of device to check the position of the device. Presence of residual shunts was evaluated with angiography done after the release of the device (Fig. 1). After implantation of the device it was checked for whether there is a pressure gradient on pullback from ascending aorta to the descending aorta to exclude the presence of obstruction on the aortic side. But the ones that we did not have arterial access pressure gradient on aortic side were checked only with transthoracic echocardiography. Follow up echocardiography was performed on the next day, 1st, 3rd, 6th months after implantation and yearly thereafter (Fig. 2). Complications related to ADO implantation were noted at each follow-up visit.

Statistical Analysis. All tests were performed using SPSS for Windows 16.0 and Sigma Stat 3.1. First, the distributions of all parameters were determined by using the Shapiro–Wilk test. The parameters with normal distribution were expressed as mean (SD), and the parameters with abnormal distribution were expressed as median (minimum–maximum). Comparisons of means were performed with Student's t-test. Comparisons of medians were performed with the Mann–Whitney U-test. Correlations were calculated with the Pearson product moment or Spearman rank order, as determined by the normalcy of data distribution. P-value <0.05 was accepted as statistically significant.

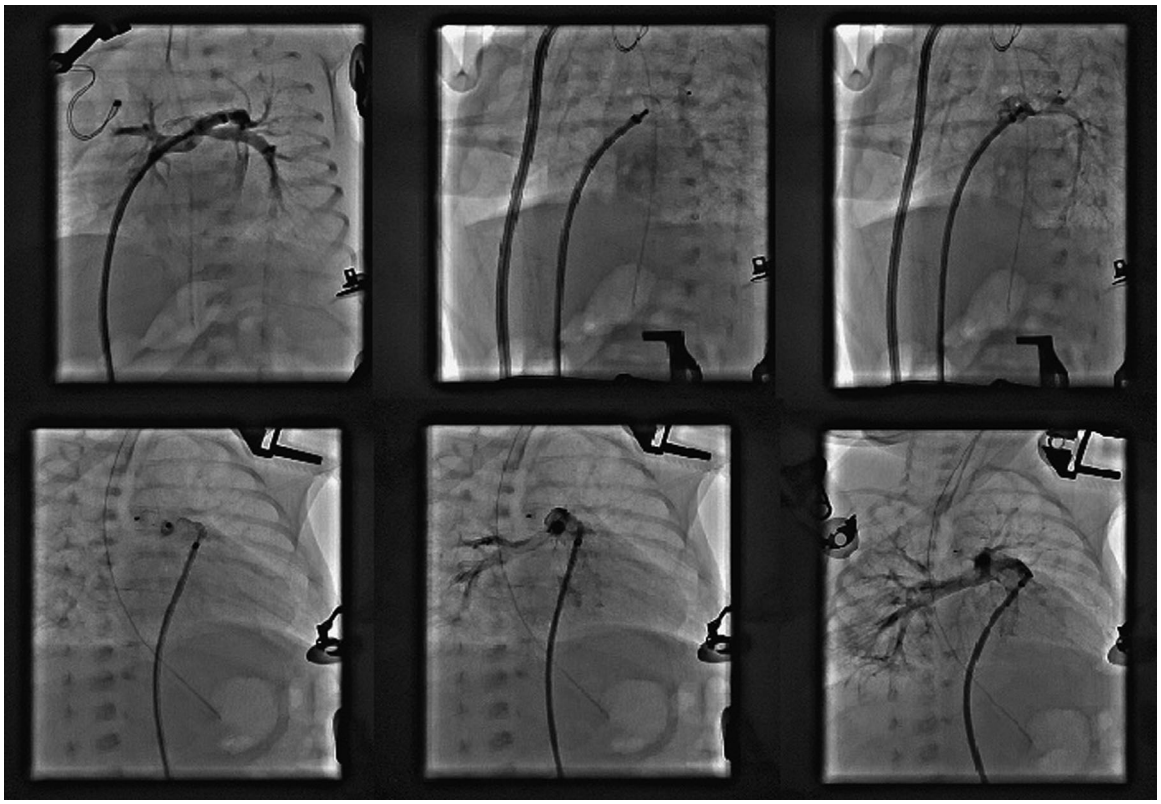


Figure 1. Angiographic views of percutaneous PDA closure via venous route.

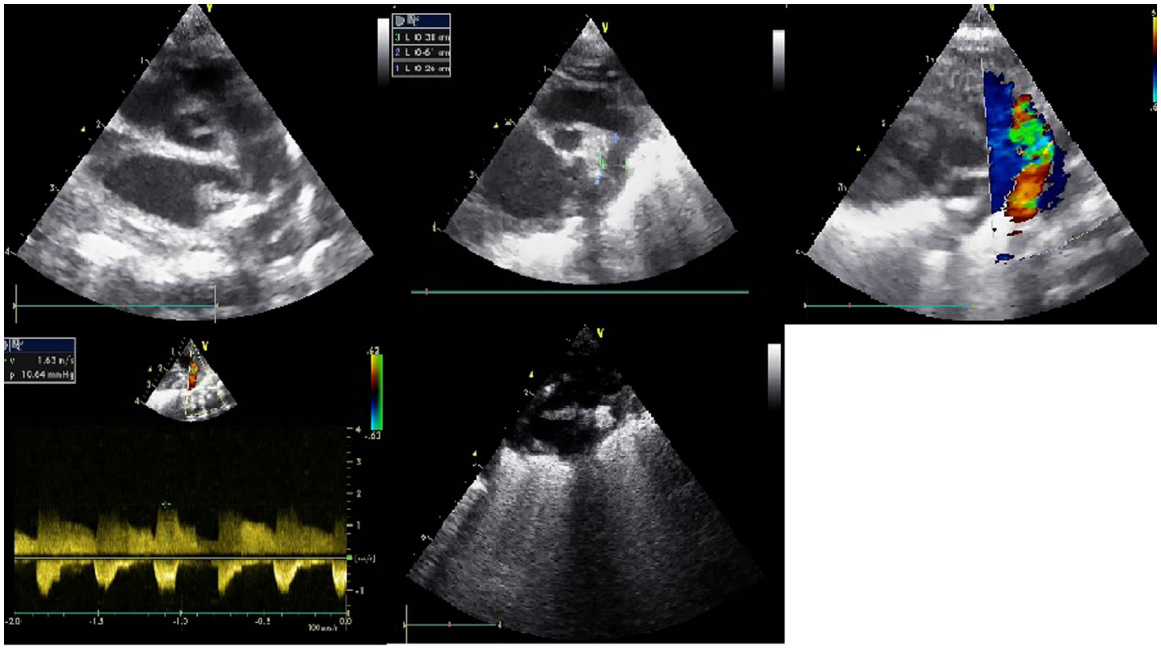


Figure 2. Echocardiographic views before and after PDA closure.

Results

Percutaneous closure of PDA of ten infants whose weight was less than 1,000 gr was done. Main characteristic features of patients like, age during the procedure, gender, gestational age, weight during the procedure, birth weight, associating disease, respiratory support type, and duration were shown in Table 1. Mean gestational age, patient age was: 26.3 ± 0.63 weeks and 19.5 ± 7.2 days, respectively. Median body weight during the procedure was 950 (842–983) gr. The weight of our smallest baby was 750 gr. Median birth weight was: 849.5 (735–958) gr. Most common associating diseases of patients were due to prematurity like Respiratory Distress Syndrome (RDS), Retinopaty of Prematures (ROP), and intraventricular Hemorrhage (IVH). Only 3 infants did not have any associating disease. The preterms that had other associating heart disease were excluded from the study.

Medical Treatment for PDA Closure Was Given to All Patients Unless Contraindicated. The angiographic data: PDA type, size, device type, size, procedure time, fluoroscopy time, radiation dosage, vascular access, closure site, sheath size were summarized in Table 2. Mean PDA diameter was 1.9 ± 0.41 mm. Mostly patients had conical type of PDA (6/10). Mean time of procedure and fluoroscopy were 44.5 ± 13.1, 13.8 ± 5.6 minutes, respectively. The mean dosage of radiation given was 223 ± 153.8 cGy/cm^2. All patients had venous; only 2 patients had both arterial and venous access. Eight patients had only venous access without arterial site. We used femoral vein in 8 patients and umbilical vein in 2 patients. All closures were done from venous route. The size of sheath was 4F in 6 patients, 5F in 2, and 3F in 2 patients. Only 2 patients had arterial access and 3F sized sheath was used.

No major complication (like death, device embolization) was reported. As a minor complication; left Pulmonary artery stenosis was seen in 2 patients that were spontaneously resolved in 6 months. We had arterial access in 2 patients. No arterial injury was reported in them. Only in one of these patients; pulses were decreased, no thrombus was seen on ultrasound and it was diagnosed as temporary arterial spasm.

Also respiratory status was checked by consultant neonatologist. Respiratory status got better in 6/10 patients. After the procedure all of them except one were extubated. One of them required CPAP ventilation after extubation but not the others. The duration of respiratory support was shown in Table 1 except for 4 patients. These 4 patients were referred to our center for PDA closure and after the procedure these patients were sent back to their hospitals. We could not get enough data about the duration of ventilation of these patients from those centers.

Patient numbered 9 shown in Tables 1 and 3 died 5 days after trancatheter closure. She was ventilated with high frequency oscillatory ventilation (HFOV) mode and high settings also had additional health

Table 1. The Demographic Features of Patients

	Gestational Week (Week)	Gender	Age (Day)	Weight (gr)	Birth Weight (gr)	Associating Diseases	Respiratory Support	Respiratory Support Duration
1	27	Male	24	850	750	RDS	Mech Vent	5
2	26	Male	24	1,000	849	ROP, Grade 2 IVH	Mech Vent	17
3	26	Female	15	960	810	Grade 2 IVH	Mech Vent	Unknown
4	26	Female	25	750	690	RDS,	Mech Vent	6
5	27	Female	10	970	985	None	Mech Vent	Unknown
6	27	Female	23	820	650	None	Mech Vent	Unknown
7	26	Male	23	1,000	925	RDS, ROP, Grade 2 IVH	Mech Vent	20
8	27	Male	10	978	950	None	Mech Vent	4-CPAP
9	26	Female	11	910	990	RDS	Mech Vent	Intubated
10	25	Female	30	940	850	ROP	Mech Vent	2

RDS, Respiratory Distress Syndrome; ROP, retinopaty of prematures; IVH, intraventricular hemorrhage; Mech Vent, mechanical ventilation.

Table 2. The Angiographic Data of Patients in the Study

	PDA Diameter (mm)	PDA Type	Device Type	Device Size	Procedure Time (min)	Floroscopy Time (min)	Radiation Dosage (cGy/cm²)	Vascular Access*	Closure Route	Size of Sheath (Fr)
1	2.00	Tubular	ADOIIAS	5 × 2	45	19	294	Venous	Venous	4
2	1.80	Conical	ADOIIAS	4 × 2	26	8	49.1	Both	Venous	3**
3	1.20	Tubular	ADOIIAS	3 × 2	50	13	115	Venous	Venous	5
4	1.80	Tubular	ADOIIAS	3 × 4	45	19	294	Venous	Venous	4
5	2.50	Conical	ADOIIAS	4 × 2	36	7	151	Venous	Venous	5
6	2.00	Conical	ADOIIAS	4 × 2	45	10	60	Venous	Venous	4
7	2.30	Conical	ADOIIAS	5 × 6	70	22	285	Umbilical	Umbilical	4
8	1.70	Conical	ADOIIAS	3 × 2	30	12	67	Venous	Venous	4
9	2.60	Conical	ADOIIAS	5 × 2	59	8	65	Umbilical	Umbilical	4
10	1.80	Tubular	ADOIIAS	4 × 2	39	20	409	Both	Venous	3**

*Venous means only femoral vein, both means both femoral arterial and venous access, umbilical means only umbilical venous access; **the ones who had both vascular access, 3 Fr was used for arterial access.

problems. Median length of hospitalization was 34 (1.4–54) days.

Patients were followed with regular visits after closure. Controls were done with transthoracic echocardiography. Device position, presence of residual shunt, flow acceleration in descending aorta and left pulmonary artery were checked. In one patient (number 6 in Table 3) mild flow acceleration (1.9 m/s) in left pulmonary artery. There was no residual shunt or coarctation of aorta on the follow-up. Median follow-up interval was: 11 (6.5–20) months. Patients numbered 3, 5, 6 who were sent to other centers; did not come to follow-up visits. Therefore, we did not have data about them. But the rest of the patients came to regular visits and all had appropriate catch-up weight growth.

Discussion

Infants with a birth weight of less than 1,000 gr are defined as extremely low birth weight (ELBW). Their survival has been increased with the improvements in neonatal technologies. Therefore, we started to encounter more commonly with the problems of prematurity like bronchopulmonary dysplasia (BPD), intraventricular hemorrhage (IVH), retinopathy of prematures (ROP), and patent ductus arteriosus (PDA).[6] As gestational age and birth weight decrease, spontaneous closure rate of ductus decreases.[7] This situation explains the high frequency of PDA in ELBW infants.

Also, the decision-making process has changed over time. In earlier days, when we did not have enough experience in transcatheter closure and before the new devices came onto the market, we used to perform surgery more often. Nowadays, as we have gained more experience and with the use of improved devices, we prefer transcatheter closure in suitable cases.

It was shown that surgery also could be too risky in prematures: decrease in left ventricular output,[8] hypoperfusion, contribute to brain injury (due to the intraoperative compromise of cerebral oxygen saturation), impedes lung growth,[9] increases the risk for BPD, and severe ROP.[10]

There are some limitations of percutaneous PDA closure in preterms. Francis et al.[11] summarized these as: femoral sheath size, stiffness of delivery system, protrusion of device to LPA or aorta, and technical difficulties in the retrieval of the device when required. Arterial injury is a big problem in preterms. Femoral sheath size should be kept as small as possible also they should be taken off as soon as possible. Backes et al.[12] reported outcomes of percutaneous PDA closure in infants born preterm (<32 w) retrospectively. They concluded that: among infants born preterm, percutaneous PDA closure at weights <4 kg is generally safe and may improve respiratory health, but risk of arterial injury is noteworthy. They reported 33% complication rate due to arterial damage. We have used 4F sized sheath for venous route and 3F for arterial site. We had used arterial route only in 2 patients. PDA closure was done via venous route in all patients that decreased the risks of

Table 3. The Outcome of Percutaneous Closure: Complications, Length of Hospitalisation, Follow-up

	Major Complication	Minor Complication	Hospitalisation Duration (Day)	Sent to Other Center	Follow-Up Duration (Month)	Alive/Dead
1	None	None	3*	Yes	3	Alive
2	None	None	57	No	5	Alive
3	None	None	1*	Yes	7	Alive
4	None	None	43	No	7	Not known
5	None	None	43	No	8	Alive
6	None	LPA stenosis	1*	Yes	14	Alive
7	None	None	146	No	17	Not known
8	None	None	4*	Yes	19	Alive
9	None	None	25	No	23	Dead
10	None	None	53	No	23	Alive

*This period was the hospitalization duration in our center. These 4 babies were sent to different centers.

vascular complications related to arterial damage. As we described in our previous study[4]: the major drawback of this approach is that we could not visualize angiographically before the release of the device. However, our experience showed that good echocardiographic imaging is enough for procedure safety.

One of the possible drawback of the percutaneous approach was:the mean fluoroscopy time and radiation dose for these small children are high compared to "standard PDA closure" in older children. This was because procedure was hard and complicated in such small children. But as we got experienced we tried to do it in shorter times. Proper device selection is important. In previous studies coils,[11] arterial vascular plugs (AVP-II)[12,13] were used. In our study, we have used only Amplatzer Ductal Occluder II-Additional Size (ADO II-AS St. Jude Medical, Plymouth, MN). These are new devices with smaller angled retention disks and reduced occlusive material to allow for a smaller profile and flexibility making delivery from the aortic or pulmonary side possible.[14] Therefore, risk of protrusion to pulmonary artery and aorta decrease. As we mentioned in our previous study[4] it was used safely in babies less than 2 kg.

There is still debate on timing of PDA closure in preterms. Actually it changes depending on the clinical status of the patient and their associating problems.

But there are certain points that PDA closure had acute benefits like it improved respiratory status. Backes et al.[12] showed that pulmonary score had decreased over time after PDA closure. Also in our study 9/10 patients were extubated after PDA closure.

Conclusion

To our knowledge this study includes the largest cohort of infants less than 1,000 g in the literature, whose PDA were closed percutaneously. We want to emphasize that in experienced centers percutaneous closure of PDA can be an alternative to surgery even in the extremely low birth weight babies.

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