Ductal closure in infants under 6 kg including premature infants using Amplatzer™ duct occluder type two additional sizes: a single-centre experience in South Africa

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Abstract

Background: This is a report on percutaneous closure of patent ductus arteriosus (PDA) using Amplatzer Duct Occluder type two additional sizes (ADO II AS) in patients under 6 kg.

Methods: Prospective data were collected and a review of patients' records was conducted. Demographics, and angiographic and clinical outcomes are reported in this article.

Results: During the period June 2011 to June 2017, of the 92 patients who underwent closure of the PDA using the ADO II AS device, 59 were under 6 kg. The median weight of the cohort at closure was 3.6 kg (range: 900 g – 5.8 kg). The median ductal diameter was 1.9 mm (range: 1.0–3.4 mm). Three embolisations in the cohort were all retrieved percutaneously. Two PDAs were closed percutaneously and one surgically. Four premature infants required blood transfusions. The closure rate was 96.6% before discharge.

Conclusion: PDA closure using ADO II AS in small infants is feasible, effective and has few complications.

Keywords: congenital heart disease, paediatric intervention, percutaneous closure

In the term newborn, patent ductus arteriosus (PDA) accounts for about 5–10% of all congenital heart lesions. This incidence is higher in the preterm infant and may be as high as 70% in infants less than 28 weeks’ gestation, which could be due to the untoward effect of prematurity on the regulators of ductal tone.

Ductal patency in the preterm infant is associated with heart failure and pulmonary oedema, bronchopulmonary dysplasia (BPD) and necrotising enterocolitis (NEC). In addition, ductal patency may lead to intraventricular haemorrhage (IVH), prolonged ventilator or oxygen support, a long stay in hospital and increased mortality rates.

Established PDA management methods in small infants include conservative management with supportive therapy, pharmacological therapy with anti-prostaglandins, such as ibuprofen or indomethacin, and surgical ligation. However, the Rashkind device is no longer used for PDA closure, and coils are used in appropriately selected patients. The introduction of Amplatzer™ Duct Occluder type two additional sizes (ADO II AS) (Abbott Laboratories, St Jude Medical, St Marks, Minnesota) has revolutionised the management of ducts in the lower-weight infant. Routine percutaneous PDA closure in infants under 6 kg using the Amplatzer™ device as standard management is however currently not FDA approved.

There are a growing number of publications on percutaneous ductal closure in small infants, including premature infants. The introduction of Amplatzer™ Duct Occluder type two additional sizes (ADO II AS) (Abbott Laboratories, St Jude Medical, St Marks, Minnesota) has revolutionised the management of ducts in the lower-weight infant. Routine percutaneous PDA closure in infants under 6 kg using the Amplatzer™ device as standard management is however currently not FDA approved.

Challenges facing a low- and middle-income country (LMIC) such as South Africa include a shortage of congenital heart surgeons and the protracted hospital stay of patients awaiting surgery. These result in increased patient mortality and morbidity rates as well as high hospital costs. Therefore the aim of this study was to report on the experience of closing a PDA in infants under 6 kg at a single centre in a LMIC (which is usually faced with the above-mentioned challenges).
Methods
This study reports on percutaneous PDA closure using the ADO II AS device in infants less than 6 kg, including preterm infants, at the Port Elizabeth hospital complex in South Africa. This is a coastal tertiary healthcare centre offering general paediatrics, paediatric cardiology and neonatal healthcare services with fully qualified paediatric cardiologists and neonatologists. As our centre is the only referral site for the diagnosis and management of congenital heart disease in the province of the Eastern Cape, South Africa, it was used for the study, although the incidence of PDA had not been documented there. As part of the study protocol, the cohort included all those patients who were under 6 kg at ductal closure, including preterm infants, which included all those who were born before 37 weeks’ gestational age. Excluded from the study were patients with other congenital heart diseases requiring surgery and those that had severe congenital abnormalities with redirected overall clinical care.

An echocardiographically haemodynamically significant PDA (hsPDA) was defined as a PDA with a diameter of >1.4 mm/kg body weight, with or without pulmonary hypertension, and a left atrium:aortic ratio of >1.4:1.28,29 Pulmonary hypertension was defined as tricuspid regurgitation velocity of more than 3.4 m/s, with an estimated pulmonary systolic pressure of more than 50 mmHg, with or without additional echocardiographic variables suggestive of pulmonary hypertension.30

The criteria for percutaneous closure of the PDA in the premature infants involved in the study included those who were diagnosed with an echocardiographically hsPDA that had failed supportive therapy and medical treatment with anti-prostaglandins (ibuprofen or paracetamol–indomethacin is not used in our unit), and those who were ventilator-dependent and required FiO2 (fraction of inspired oxygen) of >60% after failed supportive or medical therapy.

The criteria for ductal closure in other infants included echocardiographic evidence of an hsPDA as above,31 and signs of left ventricular volume overload. In addition, the criteria included those with severe pulmonary arterial hypertension with pulmonary arterial pressures that were more than two-thirds of systemic pressures or pulmonary vascular resistances that were more than two-thirds of systemic vascular resistances, but still with a left-to-right shunt and with pulmonary vascular reactivity on vaso-reactive testing.31

The study was conducted following clearance from the Health Research and Bio-safety Committee of Walter Sisulu University regarding Research in Human Subjects and from the chief executive officer of Dora Nginza Hospital, Port Elizabeth. Moreover, informed consent from patients’ parents or guardians was obtained.

Prospective data collection and a review of records of patients who had undergone percutaneous closure of a PDA using the ADO II AS device in a single centre in South Africa was performed. Due note was taken of the manufacturer’s recommendation that this device should not be used for the percutaneous closure of the PDA in patients who weigh less than 6 kg. Moreover, the device is not FDA approved for routine use in infants under 6 kg.23 Parents were therefore informed that, even though these devices are not FDA approved for routine use in this weight group, they possess the Conformité Européenne (CE) mark. This means that they may be utilised for PDA closure in South Africa as per the South African Health Products Regulatory Authority (SAHPRA) guidelines on the use of medical devices in South Africa.31,32

The patients’ age, gender and weight at the time of closure were documented. Haemodynamic and angiographic data, ductal morphology, device type and size, radiation exposure, complications and outcomes were also recorded. The ductal shape was classified using the Kiritchenko classification,33 which classifies ductal morphology according to five types. It is type A if it is conical, B if it is tubular and less than 3 mm in length, type C if it is tubular and more than 3 mm in length, D if it is complex and has more than one constriction, and E if the duct is conical and elongated. The descending aortic diameter was measured in the thoracic aorta just distal to the PDA ampulla. A decision to close a PDA using the ADO II AS was also based on a ductal size of less than 4 mm, as per manufacturer’s guidelines. In addition, associated congenital heart defects were documented.

In this study, values are reported as median (range). There were no statistical comparisons that were required for this study.

In all treatment groups, an analysis of all complications including events related to vascular access, sedation, airway and cardiac catheterisation was done as described by Bergersen et al.34 The complications were further classified as being ‘major’ or ‘minor’.22

The ADO II AS device is made of a meshwork of self-expandable nitinol wire. A detailed account of various device sizes and guidelines regarding device selection for ductal closure is documented by Kenny et al.19 In brief, the device consists of a central ‘lobe’, which measures 3–5 mm in diameter, and a retention disk on each side of the lobe (Fig. 1). The disks are 1–1.5 mm more than the central lobe and range from 4–6.5 mm in diameter. The length of the device ranges from 2–6 mm. The devices are delivered using a TorqVue low-profile delivery system (4–5F) (Abbott Laboratories, St Jude Medical, St Marks, Minnesota). ADO II AS transcatheter (percutaneous) delivery protocol was adhered to.19

Fig. 1. Amplatzr Duct Occluder type two additional sizes: the device has two retention disks and a central lobe, and is attached to a delivery wire. Published with permission from Abbott Laboratories, St Jude Medical, St Marks, Minnesota.
During cardiac catheterisation, patients were sedated using a mixture of intravenous midazolam (at 0.2 mg/kg) and ketamine (at 2 mg/kg) as the initial dose, which was repeated as needed. Femoral arterial and/or venous access was achieved using standard 4–5F vascular access short sheaths. In the premature infants and infants where vascular access using standard vascular access set with a 0.018-inch wire was a challenge, a 0.014-inch wire and a 21- or 23-gauge scalp vein set (Butterfly set) were used. Heparin, at a dose of 50 U/kg, was given following femoral arterial access.

In premature infants, IVH was diagnosed using cranial ultrasound before cardiac catheterisation. Furthermore, in those infants with IVH, heparin was not given and only venous access was used. However, when there was difficult access through either venous or arterial access, single access was used to close the PDA, as the ADO II AS device is deliverable both anterogradely and retrogradely. Following angiographic assessment and if the PDA was amenable to percutaneous closure, a device thought to be appropriate for PDA closure was selected using the manufacturer’s device selection guidelines.

After percutaneous ductal closure, patients received intravenous antibiotics and would receive infective endocarditis prophylaxis for six months. Patients had clinical and echocardiographic follow up. Clinical follow up entailed a general examination, including a check-up of the vascular access site for catheterisation, pedal pulses and the rest of the cardiovascular system. This included the detection of cardiac murmurs, aortic regurgitation and features of congestive cardiac failure. These are known as complications of percutaneous PDA closure (Abbott Laboratories, St Jude Medical, St Marks, Minnesota). The clinical follow up consultations with echocardiography were scheduled in one day, one, three and six months, one year and ultimately two years following PDA occlusion, using this device as per our protocol and as suggested by the manufacturer.

Results

During the period June 2011 to June 2017, 92 patients underwent closure of a PDA using the ADO II AS device in a single centre, and 59 of these had a weight of less then 6 kg at the time of the intervention. There were 15 premature infants who had a PDA with failed medical therapy with either oral ibuprofen or intravenous paracetamol and remained with an echocardiographically hsPDA with FiO, requirements of > 60%.

Demographic, haemodynamic and angiographic data are presented in Table 1. There were 32 females and 27 males. The median age of the cohort was four months (range: 23 days to 12 months). The weight ranged from 0.9 to 5.8 kg (median: 3.6 kg) in these infants. There was significant left-to-right shunting across the PDA, with a median pulmonary-to-systemic blood flow ratio (Qp:Qs) of 2.4 in this group. Haemodynamic studies were performed on 96.6% of the patients (57 out of 59). The pulmonary artery mean range was 9–47 mmHg and that of pulmonary vascular resistance was 0.3–7.12 Wood units (Table 1).

There were 16 patients with a type A PDA (Fig. 2A, B), 15 with a type C (Fig. 2C, D), four with a type D (Fig. 2E, F), and 24 with a type E (Fig. 2G, H). There were no patients with a type B PDA. There were no patients with a ductal diameter of > 4 mm across the whole cohort, as the largest ductal diameter was 3.4 mm with the median ductal length was 8.8 mm (Table 1). The descending aortic median was 5.3 mm in the group.

The commonest devices used were the longest devices (n = 52; 88.1%), which included 03x06L (n = 12), 04x06L (n = 16) or 05x06L (n = 24) devices. These were chosen according to manufacturer guidelines.

The device was deployed through the pulmonic side in 41 patients and retrogradely in 18. Difficulty in finding either venous or arterial access dictated the delivery approach of the device since the device could be delivered either in a prograde (anterograde) or retrograde fashion.

There was immediate ductal closure in 43 patients and closure on day one in 13 patients using this device. This excludes those patients who had device embolisation following deployment (see complications below). In total, 57 patients (96.6%) had complete initial (pre-discharge) ductal closure using this device.

The dose–area product (DAP) in microgram units (µGy) × surface area/kg body weight was used to measure patient radiation absorption. The median for this was 251 µGy/kg (range: 85.5–769.4 µGy/kg) (Table 1).5

With regard to complications, there were no patients who had vascular injury, which might be because vascular access in all infants less than 3 kg was via a size 4F vascular access sheath. There were three patients with device embolisation (a major complication). Two patients had devices (03x06L ADO II AS and 04x06L ADO II AS) embolising into the right pulmonary artery (RPA) and one (04x06L ADO II AS) into the left pulmonary artery (LPA). All devices were retrieved with a size 10-mm (loop) AndraTec Exeter snare through a 4F AndraTec introducer sheath (AndraTec GmbH, Simmernster, Koblenz, Germany) (Fig. 3). It was easy to retrieve the device into the sheath as it is a softer device compared to the ADO device.

The defect was closed with a larger ADO II AS device (05x06L ADO II AS device) in one patient, closed with a 3.5 × 5-mm Oclutech duct occluder device in another patient, and surgically closed (off bypass) in the last patient. In addition, there were four patients who required blood transfusion after the procedure. Of these, three patients had haemoglobin levels of 11.7, 12.5 and 11.1 g/dl before the procedure. These levels decreased to 8.9, 9.7 and 10.1 g/dl, respectively, immediately after the procedure. The levels improved to 14.5, 14.1 and 13.6 g/dl, respectively, following blood transfusion. The fourth patient had excessive bleeding at the puncture site following cardiac catheterisation. The haemoglobin levels of this patient were 13.9 g/dl before, 8.2 g/dl immediately after the procedure, and 13.2 g/dl following blood transfusion. There were no complications after transfusion in these patients.

Table 1. Demographics, haemodynamic and angiographic data of patients

<table>
<thead>
<tr>
<th>Demographic, haemodynamic and angiographic data</th>
<th>Result, median (range)</th>
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</thead>
<tbody>
<tr>
<td>Age, months</td>
<td>4 (0.8–7)</td>
</tr>
<tr>
<td>Weight at catheterisation, kg</td>
<td>3.6 (0.9–5.8)</td>
</tr>
<tr>
<td>Qp:Qs</td>
<td>2.4 (1.1–5.4)</td>
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<tr>
<td>Rp, Wood units</td>
<td>1.7 (0.3–7.12)</td>
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<tr>
<td>PA mean, mmHg</td>
<td>20 (9–47)</td>
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<tr>
<td>PDA narrowest diameter, mm</td>
<td>1.9 (1.0–3.4)</td>
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<tr>
<td>Ductal ampulla, mm</td>
<td>6.1 (2.8–10.6)</td>
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<tr>
<td>PDA length, mm</td>
<td>8.8 (3.7–18.4)</td>
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<tr>
<td>Descending aortic diameter, mm</td>
<td>5.3 (3.6–10.6)</td>
</tr>
<tr>
<td>Radiation exposure, µGy/kg</td>
<td>251 (85.5–879.4)</td>
</tr>
</tbody>
</table>

Number of patients (n) and gender distribution: n = 59, F = 32, M = 27.

F: females; M: males; Qp, pulmonary blood flow; Qs, systemic blood flow; Rp, pulmonary resistance; PA, pulmonary artery; µGy/kg, microgram × square meter surface area/kilogram body weight.
Fig. 2. Descending aortograms in straight lateral views demonstrating PDAs pre- and post-closure with the Amplatzer Duct Occluder type two additional sizes device and classified as Krichenko type A (A, B), C (C, D), D (E, F) and E (G, H).
Minor complications involved two patients with bleeding at the puncture site, which was managed conservatively. One patient had catheter-induced supraventricular tachycardia before device deployment, which was treated with a single dose of adenosine at 100 µg/kg intravenously.

Concerning co-morbidity, one patient had a secundum atrial septal defect, which measured 10 mm in diameter. It was closed with a size 10.5-mm (waist) Figulla® Flex II Occlutech septal occluder (Occlutech, Helsingborg, Sweden) at the age of four years nine months and four years seven months after percutaneous PDA closure.

The duration of the follow up, with regard to our cohort ranged from 15 months to two years (median: two years). Of note, there was no device-induced coarctation of the aorta, left pulmonary artery stenosis, procedure-induced aortic regurgitation or left ventricular dysfunction. Forty-nine patients had already been discharged from follow up at the time of writing this article, as they had completed the two-year follow-up duration as per the study protocol.

Discussion

Morbidity and mortality associated with the PDA in preterm infants is well documented. In this group, failed medical therapy with ibuprofen is reported to be around 22–24%, which is comparable to failed treatment with oral paracetamol, at 18–31%. Therefore this group was subjected to percutaneous closure of the PDA in our unit.

Both medical treatment and surgery are fraught with complications. Devices other than the ADO II AS are also being explored and have been successfully utilised in percutaneous closure of the PDA in this challenging group with lower body weight. These include the Amplatzer vascular plug and the Medtronic micro vascular plug. Challenges faced by this lower-weight group include, among others, difficult vascular access, vascular access injury, excessive bleeding in relation to body mass index, haemodynamic instability, metabolic acidosis, hypothermia and death.

There have been attempts to close PDAs percutaneously using echocardiography in the neonatal unit in preterm infants who have haemodynamically significant PDAs. This approach was prompted by listed poor outcomes experienced in the cardiac catheterisation of small infants in the catheterisation laboratory. However, this bedside technique has not been translated into routine clinical practice.

In our study, there was successful closure of the PDA in 57 patients (96.6%). This is comparable with the results reported by Kang et al. in their multicentre study of 408 lower-weight patients, where there was also a 95% closure rate recorded in the last recorded patient follow up. Kenny et al. reported on the successful ductal closure in 16 of 17 patients, and there was only one embolisation in this cohort. The device was surgically retrieved with the ligation of the duct. Of note, nine patients weighed less than 6 kg, and the smallest patient was 1.7 kg in this cohort.

In another study, the ADO II AS device was used in 60 patients to close the PDA, and 26 of these patients weighed less than 6 kg. Moreover, there was successful PDA closure in 96.6% of patients without major complications, except for one embolisation.

Recently, the Medtronic micro vascular plug has been used to close a PDA in eight patients weighing less than 6 kg. In fact, half of the patients in this recent study were infants weighing less than 2.5 kg. Furthermore, there was one embolisation in this cohort. The embolised device was retrieved transcutaneously and an Amplatzer type II device was successfully deployed to close the PDA.

Although, there is little data on PDA closure in premature infants weighing less than 1 000 g, the Amplatzer vascular plug II has been successfully used for ductal closure in this group. Moreover, in our cohort, we had one preterm infant weighing less than 1 000 g (900 g) at the time of ductal closure.
patient, the PDA measured 3.4 mm in diameter and was 9.3 mm long. A 05x06L device was used to close the PDA in an anterograde approach. The patient was discharged without any complications.

The ducts in preterm infants are usually large and tubular and need either medical or surgical intervention. All the patients in the study cohort had ducts that were long and the majority of these PDAs were longer than the recommended maximum length for closure using the ADO II AS. Despite this, owing to the shape of the device and the small diameter of the retention disks, it was possible to manoeuvre the device so that it was pulled into the duct, and the central lobe was snugly placed over the narrowest diameter of the PDA. However, further research is needed into ductal length and ductal closure outcomes using the ADO II AS, as there is a lack of data in the literature in this regard.

In this study, we also examined the aortic diameter and ductal closure outcomes. None of the study patients were documented to have device-induced coarctation, which has previously been defined by Kang et al. as a descending aorta catheterisation gradient of more than 10 mmHg or a velocity of > 2 m/s during echocardiography. In their cohort, there were 10 patients with device-induced coarctation of the aorta immediately following cardiac catheterisation.

On follow up, the velocity was reported to have normalised in seven patients and there was only one patient that remained with a high velocity but without a diastolic tail. In the remaining two patients, the follow-up data were incomplete. This finding may imply that device-induced coarctation of the aorta may resolve with vessel growth and somatic growth of the patient.

One advantage of this device is that it can be delivered using a delivery sheath of 4–5F. This avoids complications, such as vascular access and injury. To reduce the risk of vascular injury, we utilised a 0.014-inch wire and scalp vein needle (Butterfly) sets for vascular access, particularly in preterm infants, although this approach has not been reported in the literature. Another advantage of the ADO II AS device is that it can be delivered in both anterograde (pulmonic) and retrograde (arterial) approaches. The anterograde approach is usually the preferred approach in lower-weight infants as it eliminates femoral arterial injury if this access is avoided. Therefore the majority of our patients (about 70%) had closure of the PDA through the pulmonic route.

Regarding radiation exposure, our patients were exposed to higher doses of radiation than reported by Kobayashi et al. Their reference value at the 90th percentile was 130 μGym/kg for percutaneous PDA closure in their multicentre study. This finding suggests that in our unit, we need to be more meticulous and limit radiation exposure to the absolute minimum during cardiac catheterisation.

Complications reported in our cohort have been documented elsewhere when dealing with lower-weight infants, particularly those that are premature. The one common complication in this group was the need for blood transfusion. However, this complication was well managed in our cohort.

In addition, there were three embolisations in this cohort owing to the under-sizing of the device. Our 5% embolisation rate is comparable to that reported by Kang et al. in their study of 408 low-weight patients. With regard to embolisation of the device, the learning curve in the use of this device in our unit was a contributing factor. All the embolised devices were retrieved percutaneously, two ducts were closed with larger alternative devices, and one duct was surgically closed.

When it comes to outcomes, there were no medium- and long-term complications noted in our study. In particular, there was no LPA stenosis. To prevent LPA stenosis when using the ADO II AS device, we positioned the device in such a way that the pulmonary disk was against the roof of the main pulmonary artery, with some tenting of the disk. In addition, the central lobe and in some patients the aortic disk of the device were placed in the duct (Fig. 2B).

With regard to limitations of the study, a clinical trial comparing percutaneous PDA closure to surgical closure in lower-weight infants would be a more robust study. A recent study, which compared surgical ligation to percutaneous ductal closure using this device, has shown that percutaneous closure is feasible and safe. However, patient numbers that underwent percutaneous closure were very small in this study (25 subjects).

Conclusion

The Amplatzer Duct Occluder type two additional sizes is practical, effective and has few complications in patients less than 6 kg with a duct that is less than 4 mm in diameter, even though the infant is from a from a LMIC with reduced resources, such as South Africa. Owing to the small retention disks of the device compared to the central lobe, the device may be deployed in ducts that are longer than 8 mm, and there is a low risk for device-induced coarctation of the aorta. More studies are needed to examine the safety and efficacy of this device in ductal closure in patients weighing less than 1 000 g.

References

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