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Laboratory Investigation

Use of an Intravascular Endoprosthesis (Stent) to Establish and Maintain Short-Term Patency of the Ductus Arteriosus in Newborn Lambs

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Abstract. The feasibility of stenting the ductus arteriosus with a balloon-expandable vascular endoprosthesis was tested in 8 newborn lambs. Tantalum wire and stainless steel mesh coronary stents were implanted antegrade or retrograde by percutaneous transfemoral catheterization. One lamb died during the procedure from perforation of the aorta. In 7 lambs, the ductus arteriosus was crossed using endhole catheters and wires, and stents mounted on angioplasty catheters were expanded in the ductus arteriosus. Six lambs had successful implantation and had maintained a sizeable patent ductus arteriosus at 2 h. We conclude that the feasibility of percutaneous stenting of the newborn ductus was demonstrated. By providing patency of the ductus arteriosus, stents may offer nonsurgical alternatives for palliation of cyanotic congenital heart disease and hypoplastic left heart syndrome.

Key words: Stent—Intravascular endoprosthesis—Patent ductus arteriosus

Infants with cyanotic congenital heart disease or hypoplastic left heart syndrome may depend on patency of their ductus arteriosus for survival after birth. Many such infants are palliated initially by pharmacologic dilation of their ductus using prostaglandin E1 infusion. Subsequently, palliative surgery may involve creation of a permanent artificial patent ductus arteriosus.

For several years there has been interest and research in intravascular endoprostheses (stents). These devices are implanted using percutaneous techniques and are designed to maintain blood vessel patency [1]. Human and animal studies have been performed in coronary arteries [2–4], systemic arteries [5, 6], pulmonary arteries, and systemic veins [7]. The purpose of this study was to demonstrate the feasibility of percutaneously implanting an endoprosthesis in the newborn lamb ductus arteriosus and maintain short-term patency.

Materials and Methods

Eight newborn (less than 2 days old) lambs were anesthetized with ketamine (2 mg/kg) and sodium pentobarbital (30 mg/kg). They were intubated and mechanically ventilated with room air. Arterial pressure and electrocardiogram (ECG) were monitored. Six French sheaths were placed in the femoral artery and vein using percutaneous techniques. A 5 French endhole catheter was advanced via the arterial sheath to the proximal descending thoracic aorta. Aortography was performed to determine whether the ductus arteriosus was patent and to assist in positioning the stent (Fig. 1). An attempt was made to cross the ductus from the aortic end. If the ductus could not be crossed from the aorta, a 5 French endhole catheter was advanced via the venous sheath to the main pulmonary artery. This catheter was passed across the ductus. Subsequently, a 0.016 inch coronary angioplasty wire was loaded into the catheter and placed across the ductus into the main pulmonary artery and right ventricle or into the aorta, then the catheter was removed. Six tantalum folded wire (Medtronic, Inc., Minneapolis, MN) and three stainless steel mesh (Johnson and Johnson Interventional Systems, Warren, NJ) coronary stents were loaded onto deflated and prepared 3- or 4-mm diameter coronary angioplasty balloon catheters. The catheters were advanced over the wire until the stents appeared to be centered in the ductus arteriosus according to the angiogram. The

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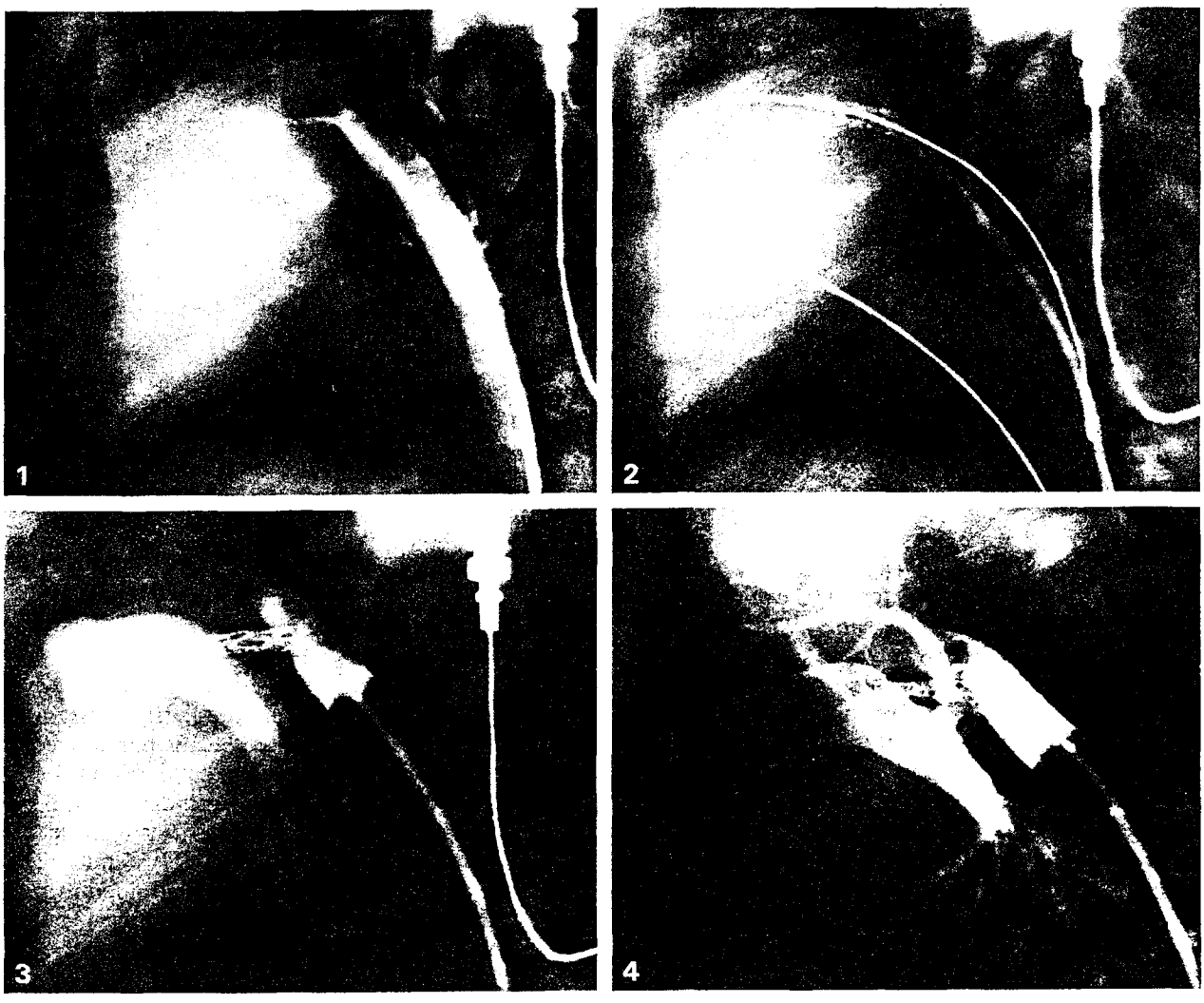

angioplasty balloons were fully inflated two times (Fig. 2), then deflated and removed together with the guidewires. Aortography was performed from the aortic side to assess patency immediately after implant and 2 h later. Two h after implant, the lambs were sacrificed and pathologic evaluation of the great arteries and the ductus arteriosus was performed.

Fig. 1. Aortogram showing tiny patent ductus arteriosus prior to implantation of stent.

Fig. 2. Implantation of a tantalum folded wire stent in the ductus arteriosus by transpulmonary approach. A 0.016 inch wire is shown crossing the ductus. The stent has been expanded by a 3 mm angioplasty balloon catheter. A catheter in the aorta marks the aortic end of the ductus.

Fig. 3. Immediate postimplantation upstream balloon occlusion aortogram showing a widely patent ductus arteriosus with shunting of contrast from aorta to pulmonary artery.

Fig. 4. Similar aortogram 2 h postimplantation showing continued significant patency of the stented ductus arteriosus.

Results

Eight lambs of average weight 3.2 kg and average age 1.5 days were studied. One lamb died of a perforated aorta caused by attempts to cross a tiny patent ductus arteriosus from the aortic end with a guidewire. Seven lambs had nine stents expanded in their ductus arteriosus. Six of 7 lambs had successful ductal implants (4 with Medtronic and 2 with Johnson and Johnson stents). One lamb (in which two stents embolized) could not have successful stent implantation because of a patent ductus arteriosus which appeared to be larger than 4 mm in diameter. Another lamb had successful implantation of a second stent after an incorrectly positioned device embolized into the left pulmonary artery. Therefore, 2 of 7 lambs had embolization of a total of three stents into the distal left pulmonary artery.

Among the 6 lambs with successful implants, 3 had a tiny patent ductus arteriosus prior to stent implants. All 6 had sizeable patent ductus arteriosi after stent implantation, as determined by immediate and 2-h postimplant angiography (Figs. 3, 4). The average pulse pressure increased from 27 to 39 mm Hg immediately postimplant.

Necropsy confirmed ductus patency after sacrifice of the lambs. Furthermore, 3 of 6 had stents completely within the ductus arteriosus; the other 3 had stents protruding out of the ductus into the aorta or the main pulmonary artery. Necropsy of the lamb with two embolized stents confirmed a very large patent ductus arteriosus, with two expanded stents in the left pulmonary artery.

Discussion

This study demonstrates that intravascular endoprostheses of the types currently designed for use in human coronary arteries can be implanted in the newborn lamb ductus arteriosus. Implantation can result in sizeable ductal patency. Furthermore, implantation can be performed percutaneously by either a venous or an arterial route with currently available catheter systems. The scale of these systems is applicable without significant modifications to human infants.

There is no clinical experience in humans and no published data in animals on the use of stents in the ductus arteriosus. However, there are considerable animal data on the acute and chronic effects of a variety of stent designs in several mature vascular systems [2, 5, 7]. Mature coronary arteries have diameters similar to the newborn ductus arteriosus. Stent implants in normal animal coronary arteries studies have demonstrated excellent long-term patency and a paucity of significant complications. Data from human coronary trials show favorable long-term outcomes among patients treated with single stents and larger dilated diameters. However, patients with multiple stents and smaller dilations have shown significant loss of patency due to restenosis or thrombosis [8]. There are also data in larger human vascular systems demonstrating excellent patency and low complication rates [6].

Although data from mature vascular systems are supportive, additional animal studies are needed before clinical trials of ductal stents in human infants can be undertaken. Clearly, the ductus arteriosus has several unique features not addressed in previous animal or human studies. The anatomy and histology of the ductus are unique, and the ductus is a relatively short contractile structure. Stents may be very difficult to place without protrusion into the lumen of the aorta or the main pulmonary artery. This may predispose to thrombosis, mechanical hemolytic anemia, or distortion of the pulmonary arteries or aorta. Moreover, restenosis from muscular contraction of the ductus or intimal hyperplasia may occur. Therefore, several issues should be addressed by animal studies: optimal stent design characteristics, duration and degree of long-term patency, preferred anticoagulation regime, and effects on adjacent vascular structures.

If additional animal studies are encouraging, human applications are conceivable as palliative treatment in at least two clinical settings: cyanotic infants with tetralogy of Fallot or other lesions with insufficient pulmonary blood flow who would require an arterial approach and a stent with diameter of 4–5 mm; and infants with hypoplastic left heart syndrome who are awaiting cardiac transplantation who would require a venous approach and stents with diameters of 6–8 mm. Assuming successful human clinical applications develop, closure of a "stented" ductus could be performed percutaneously with coils, the USCI Rashkind PDA Occluder, or by surgery.

References

1. Schatz RA (1989) A view of vascular stents (editorial). Circulation 79:445–457
2. Schatz RA, Palmaz JC, Tio FO, Garcia F, Garcia O, Reuter SR (1987) Balloon-expandable intracoronary stents in the adult dog. Circulation 76:450–457
3. Sigwart U, Puel J, Mirkovitch V, Joffre F, Kappenberger L (1987) Intravascular stents to prevent occlusion and restenosis after transluminal angioplasty. N Engl J Med 316:701–706
4. Levine MJ, Leonard BM, Burke JA, Nash ID, Safian RD, Diver DJ, Baim DS (1990) Clinical and angiographic results of balloon-expandable intracoronary stents in right coronary artery stenoses. J Am Coll Cardiol 16:332–339
5. Palmaz JC, Sibbitt RR, Reuter SR, Tio FO, Rice WJ (1985) Expandable intraluminal graft: A preliminary study. Radiology 156:73–77
6. Palmaz JC, Garcia OJ, Schatz RA, Rees CR, Roerren T, Richter GM, Noeldge G, Gardiner GA, Becker GJ, Walker C, Stagg J, Katzen BT, Dake MD, Paolini RM, McLean GK, Lammer J, Schwarten DE, Tio FO, Root HD, Rogers W (1990) Placement of balloon-expandable intraluminal stents in iliac arteries: First 171 procedures. Radiology 174:969–975
7. Mullins CE, O'Laughlin MP, Vick GW, Mayer DC, Myers TJ, Kearney DL, Schatz RA, Palmaz JC (1988) Implantation of balloon-expandable intravascular grafts by catheterization in pulmonary arteries and systemic veins. Circulation 77:188–199
8. Ellis SG, Savage M, Baim D, Hirshfeld J, Cleman M, Teirstein P, Topol EJ (1990) Intracoronary stenting to prevent restenosis: Preliminary results of a multicenter study using the Palmaz-Schatz stent suggest benefit in selected high risk patients. JACC 15:118A