EXPERIMENTAL STUDIES

Double-Helix Coil for Occlusion of Large Patent Ductus Arteriosus: Evaluation in a Chronic Lamb Model

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Objectives. We sought to evaluate the efficacy and tissue reaction of a new miniature interventional device for occlusion of large patent ductus arteriosus (PDA) in a neonatal lamb model.

Background. A variety of devices are used to close PDAs by interventional measures. Spring coils found to have a high cumulative occlusion rate have thus far been limited to smaller PDAs because of the physical limitation of grip forces.

Methods. Memory-shaped double-cone stainless steel coils with enhanced stiffness of the outer rings by a double-helix configuration were mounted on a titanium/nickel core wire. A snap-in mechanism attaches the coil to the delivery wire, allowing intra-vascular coil retrieval and repositioning. The system was placed through a 4F or 5F Teflon catheter. A chronic lamb model (n = 8) of PDA (>5 mm) was used in which ductus patency was secured by a protocol of repetitive angioplasty procedures. The animals were killed after 1 to 181 days, and the ductal region was examined by inspection as well as by light and electron microscopy.

Results. Placement of the coils within the PDA was possible in all lambs. Before final detachment, the coils were retrieved or repositioned, or both, up to 12 times. In all but one animal the ductus was closed within 6 days after the procedure. The coils caused no infections or aortic and pulmonary artery obstruction. Histologic and electron microscopic studies revealed endothelial coverage of the implants but no foreign body reaction or local or systemic inflammation or erosion of the implant.

Conclusions. The device effectively closed large PDAs in our model and may overcome the previous limitations of coils. Clinical trials are indicated.

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Several percutaneous transcatheter techniques for closing the persistently patent ductus arteriosus (PDA) in older children and adults have been described (1–8). The Rashkind occluder is the only system thus far with widespread acceptance. However, size and a relatively large delivery system, as well as high costs and a late incidence of residual shunting, limit its application.

Spring coils to occlude arteries were introduced by Gian-turco et al. (9) in 1975. These coils, once delivered, are not retrievable into the delivery catheter and therefore carry the risk of improper placement or undesired embolization. Pre-formed Nitinol snares may be used to improve delivery (10).

New developments allow the retrieval of certain coils after positioning and until final release (11,12). These devices can be used with small introduction catheters but because of their physical properties (increasing the diameter of the reconfigured coil decreases its stiffness by threefold, leading to pull-through and embolization), they were found to be effective only in occluding small PDAs (13–15).

The present report focuses on the use of selectively enhanced stiffness of the outer rings of coils to allow safe positioning of the device in medium to large PDAs. The new coil on trial relies on the strong memory effect of certain metals (American National Standards Institute [ANSI] 301/4) to form biconical, “double-disk” coils in which rings inside the PDA cause its mechanical and thrombotic closure (12,16). To evaluate practicability, efficacy and medium-term biocompatibility of the new device in occluding PDAs, we used a new chronic lamb model with high shunting and a minimal inner ductal diameter >5 mm.

Methods

Occlusion device and delivery system. The PDA occlusion device consists of 1) A double-cone memory-shaped spring coil with enhanced stiffness limited to the larger distal loops by a selective double-helix configuration of the primary wire strand...
(stainless steel [DIN 1.4310, \(\approx\) ANSI 301/4] wire strand 0.20 mm in diameter, 0.80-mm primary coil, 6- to 12-mm reconfigured secondary diameter, minimal inner diameter <1.5 mm, overall number of loops 8 to 13 [pfm GmbH, Cologne, Germany]) (Fig. 1); 2) a pusher system: a) a pusher wire (a coiled stainless steel wire, 90 cm long, with a modified base to fit into hold-back mechanism of the safety handle) that is advanced over the b) core wire (nickel/titanium alloy [Nitinol], 110 cm long, 0.35 mm in diameter, a modified tip to control the coils and a modified base to fit into the hold-back mechanism of the safety handle); 3) a safety handle (stainless steel, engraved metric scale, two safety mechanisms and one distal ring on its shaft [OccluGrip, pfm, Cologne, Germany]); and 4) a Teflon introduction catheter (60-cm long, 4F or 5F in diameter [1.0/1.3 mm], including tip marker [inner gold ring]).

The system itself is described in detail elsewhere (12,17). Briefly, the coil is stretched and mounted on the distal end of the core wire. The proximal end of the core wire is secured into the safety grip, into which the pusher wire is screwed as well, allowing the latter to be moved independently of the core wire or vice versa. The whole system is introduced through the delivery catheter like a conventional guide wire. Advancing the pusher wire or withdrawing the core wire will deploy the ductal coil from the tip of the core wire, allowing it to regain its original shape. As long as at least 0.5 cm of coil is left on the core wire, the whole system can be withdrawn into the delivery catheter. Final release is accomplished by a positive felt action of pushing the coil from the core wire. Because the purpose of the stiffer outer loops is to avoid pull-through from the aortic side into the pulmonary artery, the loops have to be released first, characterizing the system as a transvenous device by design.

Animal studies. The animal experiments were conducted according to the guidelines of the German Animal Protection Law and were approved by the state agency supervising animal experimentation. Catheterization of the animals was performed as a sterile procedure under anesthesia with halothane (0.3% to 0.6%) and \(\text{N}_2\text{O}\) and using portable, digital, monoplane fluoroscopy (Philips, The Netherlands). A color Doppler echocardiograph (Kontron, France) was used to acquire echocardiographic data. No animal received antibiotics or antithrombotic agents, except for a heparinized flush solution (2 U/ml of normal saline solution). Before and after the investigations the lambs were cared for by the ewe.

Lamb model of persistent PDA. Eight neonatal lambs (Morino Mixed) 3 to 30 h old and weighing 3.2 to 6.4 kg (median 4.7) were anesthetized and artificially ventilated. By means of a 6F vascular sheath in the left-sided jugular vein, a pediatric valvuloplasty catheter (balloon diameter 6 to 8 mm, length 20 mm; Dr. Osypka, GmbH, Grenzach, Germany) was passed over a guide wire through the right heart across the ductus arteriosus. The ductus was dilated up to 6 to 8 mm over 10 min. On postpartum day 5 or 6, the procedure was repeated, and an angiogram 10 min after dilation demonstrated ductal patency and dimensions. If control angiography revealed circumscript narrowing on the aortic or pulmonary orifice or the minimal inner diameter of the ductus was <5 mm, the balloon angioplasty was repeated, as previously described (Fig. 2).

Coil delivery. Four to 53 days (mean 20) after the last dilation the lambs were again anesthetized and artificially ventilated. A sheath was placed into the femoral artery and jugular vein. The location and size of the PDA were again demonstrated by aortogram. By the venous route and the right heart, a 4F or 5F end-hole delivery catheter (nylon or Teflon) was placed through the PDA into the descending aorta. Two rings of the occluding coil were freed from the core wire and

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**Abbreviations and Acronyms**

ANSI = American National Standards Institute

PDA = patent ductus arteriosus

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**Figure 1.** Top, Macroscopic appearance of two coils, nearly identical in appearance, with primary strand diameter 0.2 mm, primary coil diameter 0.8 mm, reconfigured coil diameter 10 mm (in contrast to the double-cone shaped configuration of coils used in the study); the coil on the right is constructed as a double-helix coil. Bottom, Effect on stiffness is demonstrated when the coils are each pulled at 0.11 N.
extruded into the aorta, regaining their original shape and forming the distal, outer disc. The whole system was then withdrawn into the aortic ampulla of the duct, where additional loops were released. Withdrawing the system further across the PDA into the pulmonary artery, the final loops forming the proximal disk were released and, once a satisfactory position was achieved, the occlusion coil was freed from the core wire. Alternatively, the first two distal loops were primarily configured and placed into the midportion of the ductus; because of their enhanced stiffness, they were not dislocated by the shunt flow across the ductus. The softer middle and proximal loops were then deployed into this ring to occlude the ductus mechanically and through thrombus formation (Fig. 3). An additional aortogram and angiogram of the main pulmonary artery documented positioning of the coils 30 to 60 min after final placement of the device. The catheters, wires and sheath were removed, and anesthesia was discontinued. The animal was returned to the pen to be cared for by the ewe.

The lambs were investigated clinically on days 1, 2 and 4 after ductal closure. Additionally, color Doppler echocardiography (transthoracic or transesophageal, or both) and clinical investigation were performed under sedation or anesthesia on day 6 to evaluate the occlusion of the duct and flow disturbances in the pulmonary artery and descending aorta. One to 181 days (mean 64) after coil implantation, a second left and

Figure 2. Angiographic appearance of the PDAs used for double-helix coil closure at day of implantation (lateral or left lateral oblique projection; anterior is left, cranial is top; in some instances, a scaling catheter in the aorta is visible, where the smaller distance between marks counts for 10 mm and the larger for 20 mm).
right heart catheterization through the jugular vein and femoral artery, including angiography, was performed under general anesthesia before the animals were killed and the ductal block removed. For gross and microscopic examination, the specimens were fixed in formalin, alcohol or glutaraldehyde. The aortic and pulmonary portions were scanned by raster electron microscopy, and the middle portion was prepared for light microscopy. Some portions were embedded in methyl methacrylate and sectioned crosswise at 1-mm intervals; the rest was submitted for routine paraffin embedding after careful coil removal to avoid damage to this section.

Results

Lamb model of the PDA. In all animals, dilation of the PDA was possible and produced persistent ductal patency. Angioplasty had to be repeated a third time in one animal and a fourth time in another. Four to 53 days (mean 19) after the last dilation at the time of coil implantation, the PDA had a tubular appearance, and the minimal inner diameter ranged between 5.2 and 7.8 mm (mean 6.3) and the overall length between 6.5 and 15 mm (mean 10).

Coil placement. Placement of coils in the PDA was possible in all lambs. To achieve complete obstruction of the PDA in the first animal, two coils had to be implanted at the same time in a crossover technique from the aorta and the pulmonary artery. This procedure was necessary to provide enough loops to obstruct the ductal flow entirely.

The whole system had to be pulled back into the delivery catheter between 1 and 12 times for repositioning or exchange. In one case the distal ring was loosened by mistake, and the coil was unintentionally freed, leading to its embolization into the left pulmonary artery. Retrieval by a snare into an 8F catheter was possible without difficulty.

Ductal occlusion and follow-up. The final aortogram 30 to 60 min after implantation revealed a complete occlusion in two cases. Clinical follow-up and color Doppler echocardiography on day 6 after implantation confirmed a complete occlusion of the ductus in four additional lambs, and no turbulent flow in the aorta or pulmonary artery was seen. One animal had to be
Figure 4. Aortic ductal orifice 101 days after coil implantation in lamb 1, demonstrating adequate ingrowth.

killed prematurely 1 day after coil placement because of recurrent arterial bleeding at the femoral puncture site. Pre-mortem angiography demonstrated a small residual shunt across the PDA. In one animal a hemodynamically insignificant shunt persisted clinically and on color Doppler echocardiography, and a standard coil was added 3 months after primary implantation, leading to subsequent complete ductal closure.

Seven to 181 days after primary implantation the final angiograms confirmed persistent ductal occlusion in all seven remaining animals. Postmortem macroscopic examination of the ductal orifices showed little if any protrusion of the outer rings of the coils into the lumen of the aorta or the pulmonary artery. Depending on the duration of implantation, the coils were partially or completely covered by thin, shiny tissue (Fig. 4). Further details are summarized in Table 1.

Scanning electron microscopic and histologic studies. At higher magnification, most of the coils were covered by a monolayer of cells resembling endothelial cells, starting as early as 13 days after implantation (Fig. 5). When different intervals after implantation were compared, endothelial coverage was more pronounced at longer intervals of implantation.

A foreign body reaction was not noticeable at any time (13, 62, 80, 98 and 181 days after implantation). Segmental areas of the media showed the destruction of elastic fibers and the replacement by fibrous tissue with focal calcification that was not related to the implant (Fig. 6).

**Discussion**

Transcatheter occlusion of the PDA is now a well established method of treatment that started with the pioneering work of Porstmann et al. (18) and was continued with the Rashkind PDA occluder (7,8), probably the most extensively investigated device. High costs, size limitations, a large transvascular sheath, a late incidence of residual shunting and risks of left pulmonary artery stenosis have led to a search for alternatives in experimental models (19–21) and clinical trials (11,17,22,23). High cumulative occlusion rates have been accomplished with various coils in different protocols in PDAs of small to moderate size; however, attempts to occlude large PDAs with coils have either not succeeded (13,15,24–27) or have led to increased side effects (28).
Technical aspects. Larger and stiffer coils are needed for use in larger PDAs to withstand high flow and avoid embolization. For a given material and diameter of the primary strand, increasing the diameter of a reconfigured coil will result in a threefold decrease in its stiffness. Enlarging the diameter of the primary strand would cause a fourfold increase in the stiffness of the coil but make it very difficult to control the small-diameter loops in the center of the double-cone coil. Shaping the primary strands of the outer loops in a double-helix configuration leads to a fourfold increase in the stiffness of this selected portion of the coil because the double-helix portion will act as two coil springs at the same place.

Chronic lamb model of PDA. Dilating the ductus after a protocol of angioplasty procedures provided a chronic model of a large tubular PDA without operation (19) or implantation of stents (29), thus avoiding unwanted interactions with the device. Despite the PDA large size, we encountered no acute problems with overcirculation of the lungs, most likely due to the immediate onset of a right to left shunt on the day of birth, which allowed gradual adaptation parallel to the physiologic decrease in pulmonary resistance. Our dilated ducts are similar in shape to the long PDAs found in humans and are thought to be difficult to close because of high flow, a large minimal inner diameter and lack of tapering. Their long-term patency is at least comparable (if not superior) to other animal models of PDA (30,31).

Functional results. Appropriate placement of coils was possible in all lambs. In one animal, a coil embolized because of entrance into the pulmonary artery by mistake, but it was successfully retrieved by a snare. The overall success rate for cumulative PDA closure with appropriate follow-up rose to 100% after implantation of an additional standard coil in one animal. However, because of the small number of animals tested, the 95% confidence interval for failure still extends to 43% (32).

Histopathologic examination. No clinical, bacteriologic or histologic signs of inflammation were found in any of the lambs. Raster electron microscopy revealed endothelial cover-
The device was warranted. Coils for use in the occlusion of large PDAs. Clinical trials of available detachable coils and the Rashkind double umbrella. Will most likely range between the recently commercially obstruct the narrowest portion. The cost of the present device because despite being safely anchored on the aortic side inability. Our device may be difficult to place in very short ducts because the inner rings without loss of any of the advantages attributed to retrievable coil systems. Like other coils it is made of a ferruginous alloy, leading at least theoretically to limited nuclear magnetic resonance imaging compatibility. Our device may be difficult to place in very short ducts because despite being safely anchored on the aortic side through the enforced loops, the softer parts may pull through to the pulmonary side and not leave enough material to obstruct the narrowest portion. The cost of the present device will most likely range between the recently commercially available detachable coils and the Rashkind double umbrella. The device can be manufactured in different shapes and sizes and has the potential to overcome the previous limitations of coils for use in the occlusion of large PDAs. Clinical trials of the device are warranted.

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References