Long-term patency of the ductus arteriosus after balloon dilatation: an experimental study

GUNNAR LUND, M.D., JOSEPH RYSAVY, B.A., ANDREW CRAGG, M.D., ERICH SALOMONOWITZ, M.D., ZEEV VLODAVER, M.D., WILFRIDO-CASTANEDA ZUNIGA, M.D., AND KURT AMPLATZ, M.D.

ABSTRACT Balloon dilatation of the ductus arteriosus was carried out in vivo in eight piglets that were 12 to 16 days old. The ductus was functionally closed in all animals before dilatation. Long-term patency for periods of up to 6 months after the procedure was demonstrated in six animals by angiography, Doppler ultrasound examination, and at autopsy. The presence of hemodynamically significant shunts was indicated by clinical development of heart failure, pulmonary infections, and left ventricular hypertrophy. These results confirm the value of this laboratory preparation to create left-to-right shunts at the ductus level. Circulation 69, No. 4, 772–774, 1984.

IN A PREVIOUS REPORT we described a technique for reopening the ductus arteriosus by balloon dilatation.1 It was suggested that the procedure could be of clinical value in the management of cyanotic congenital heart disease. As a laboratory procedure it could provide a convenient small-animal preparation for the study of left-to-right shunts without surgery. However, in the previous report the question of long-term patency was not settled.

It is the purpose of this study to report on long-term patency after balloon dilatation of the ductus arteriosus in piglets.

Materials and methods

Eight piglets weighing 4.5 to 5.5 kg were studied. The animals were 12 to 16 days old. Ketamine HCl was given intravenously for anesthesia in a dose of 100 mg and supplemented by repeat injections as required.

The femoral artery of each piglet was dissected free and a No. 4F catheter with a right-angled curved tip was introduced. The artery distal to the cutdown was flushed with heparin. After catheterization of the ductus arteriosus as described previously,1 the catheter was exchanged over a guidewire for a dilatation catheter (Olbert catheter system, Surgimed Inc.). A balloon size of 5 mm was used. The balloon was inflated twice for 5 min with a dilute contrast solution at a pressure of 6 to 8 atmospheres. The arteriotomy was repaired whenever possible (four animals).

Arteriograms were obtained before and after dilatation with the use of an injection of 10 ml Renografin 76 (Na/meglumine diatrizoate) in the descending aorta. In six animals flow-directed Doppler ultrasound examinations were also performed.

The animals were followed up by angiography, Doppler examination, and auscultation for periods ranging from 14 days to 6 months. Autopsies were performed on all animals. Specimens from the ductus arteriosus, heart, and lungs of each animal were examined by light microscopy.

Results

In all animals the ductus arteriosus was functionally closed before the dilatation, as confirmed by Doppler examination, angiography, and the absence of murmur. The ductus was patent in all animals following balloon dilatation. No animal died in the period immediately after surgery.

Four animals were killed, one at 3 weeks because of gangrene of the leg, two at 14 days because angiograms showed only minimal or no shunt flow, and one at the end of the study (after 6 months). Four animals died suddenly, one after 14 days from pulmonary embolism, one after 4 weeks during induction of anesthesia for a follow-up examination, and two within 48 hr of developing dyspnea at 6 and 8 weeks.

The ductus was widely patent at autopsy in six animals, confirming angiographic and Doppler findings during the follow-up period. In the four animals that lived more than 4 weeks, the ductus had clearly enlarged compared with the postdilatation size (figure 1). Histologic examination showed the lumen to be patent and lined by endothelium. There was evidence of intimal and medial tears at various stages of healing. Collagen tissue, ingrowth of fibroblasts, and areas of intimal hyperplasia were also observed (figure 2).
In two animals the ductus lumen was obstructed. A well-defined filling defect was seen on the arteriogram at the pulmonary end of the ductus in one animal. This was found at autopsy to be caused by a rounded mass, which histologically represented a partially organized thrombus. The other animal had no shunt that was apparent after aortic injection. However, injection of the pulmonary artery and ductus showed the pulmonary end of the ductus to be patent and the catheter could be passed into the aorta. This animal was found to have thrombosis of part of the lumen on histologic examination.

In the animals that lived longer than 4 weeks, autopsy showed the hearts to be enlarged (286 to 505 g) and the left ventricle to be thick walled (figure 3). Histologic examination revealed interstitial edema of the cardiac muscle, minimal pericardial thickening, and no evidence of infarction or myocarditis (figure 3).

One animal died of pulmonary thromboembolism with pulmonary infarctions, which were apparent on
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FIGURE 3. A, Heart specimen from animal killed after 6 months. Heart weight was 505 g. Thick-walled left ventricle. B, Enlarged and dilated heart in animal that died spontaneously at 8 weeks. C, Histologic section of myocardium showing thickened pericardium (arrows) and edema of cardiac muscle (open arrows). Hematoxylin and eosin stain, original magnification ×30.

gross and microscopic examination. Pulmonary venous congestion, alveolar fluid, and cellular infiltrates and red cells were observed in the animals that died spontaneously at 6 and 8 weeks. Signs of pulmonary arterial hypertension were noted on histologic examination in the animal killed after 6 months (figure 4). This animal also had elevated pulmonary arterial pressure at catheterization.

Discussion

This study demonstrates that in the piglet patency of the ductus arteriosus can be expected for a significant time period after balloon dilatation.

Although we made no attempt to quantify the degree of left-to-right shunting, it is indicated by the clinical course and autopsy and histologic findings that hemodynamically significant shunts resulted from the procedure. The clinical usefulness of ductus arteriosus dilatation remains unclear since benefits of the procedure must be weighed against possible risks and the benefits of established medical and surgical treatment regimens. However, the procedure does represent a simple and attractive small-animal closed-chest preparation for the study of left-to-right shunts at the ductus level. Possible applications include investigations dealing with pulmonary hypertension, cardiac hypertrophy, reliability and quantification of shunts by Doppler ultrasound, testing of occlusion devices, etc.

This study confirms the finding of a previous short-term study1 that dilatation of the ductus arteriosus in piglets results in a controlled tear of the vessel wall, with subsequent healing. In the previous study, however, most animals died shortly after dilatation of causes that were not immediately apparent. We believe that the change to intravenous ketamine as the sole anesthetizing agent, which avoids the depressant action of acepromazine and allows spontaneous respiration, was responsible for eliminating early mortality. Injection of heparin into the distal artery during surgery and repair of the arteriotomy when possible were procedures added to the protocol after the cases of pulmonary embolism and leg gangrene became apparent.

References


FIGURE 4. Medial hypertrophy and luminal narrowing of pulmonary arterioles (arrow) as evidence of pulmonary hypertension. Verhoeff-Van Gieson stain, original magnification ×480.
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