



Incidence of postoperative implant-related bacterial endocarditis in dogs that underwent trans-catheter embolization of a patent ductus arteriosus without intra- and post-procedural prophylactic antibiotics



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ARTICLE INFO

Keywords:

Amplatz
Coil
Congenital
Heart
Intervention

ABSTRACT

Intra- and post-procedural prophylactic antibiotics are routinely administered by veterinary cardiologists to dogs that undergo trans-catheter embolization of a patent ductus arteriosus for prevention of implant-related infective endocarditis. The hypothesis of our study was that primary antibiotic prophylaxis is not necessary to prevent bacterial endocarditis. In this retrospective case series 54 client-owned dogs that underwent trans-catheter occlusion of a patent ductus arteriosus in a single tertiary veterinary referral center between 2004 and 2016 were evaluated. Follow-up information was gained by telephone interviews with the owners or the referring veterinarians, or from the digital archives of the authors' clinic. Inclusion criteria were that at least one metal implant (a coil or an Amplatz duct occluder) had to be delivered in the ductal ampulla, no local or systemic antibiotics were given on the day of the intervention or the week thereafter, at least 3 months of postoperative follow-up information was available, and the author was performing the procedure either as the primary or as the supervising cardiology specialist. None of the 54 dogs developed infective endocarditis in the postoperative 3 months. A study describing a similar population reports 2 of the included 47 dogs having developed infective endocarditis in the postoperative period despite the administration of intra- and post-procedural prophylactic antibiotics. We conclude that intra- and post-procedural antibiotic prophylaxis is not justified in dogs that undergo trans-catheter closure of a patent ductus arteriosus. Proper surgical technique and the use of new sterile catheters and implants are sufficient to prevent infective endocarditis in these dogs.

1. Introduction

Patent ductus arteriosus (PDA) is one of the most common congenital cardiovascular anomalies in dogs. Because of the high mortality rate when left untreated, elective closure of left-to-right shunting PDAs is generally recommended at the earliest age possible (Saunders et al., 2014). Several techniques have been described for closure of a PDA (Cambell et al., 2006; Glaus et al., 2003; Goodrich et al., 2007; Singh et al., 2012). Because of its least invasiveness, high success and low complication rate, trans-catheter embolization of the PDA has become popular in veterinary cardiology in the past couple of decades (Glaus et al., 2003; Goodrich et al., 2007; Singh et al., 2012).

Bacterial endocarditis is a serious, potentially life-threatening condition that can develop spontaneously, but also after implantation of intracardiac or intravascular devices (Fine and Tobias, 2007; MacDonald, 2010).

Prophylactic antibiotics are routinely administered in a number of centers in the perioperative period to dogs that undergo therapeutic

cardiac catheterization for embolization of a PDA (Fine and Tobias, 2007; Caivano et al., 2012; Saunders et al., 2014). In the absence of canine studies or veterinary guidelines for cardiac catheterization procedures regarding antibiotic prophylaxis (Vasseur et al., 1985; Daude-Lagrave et al., 2001; Boothe and Boothe, 2015), the routine use of primary antibiotic prophylaxis is presumably based on human recommendations. Because of the rapidly growing worldwide issue of antibiotic resistance and the aim of the veterinary community to practice evidence-based (veterinary) medicine, restricting prophylactic use of antibiotics to well-established indications is desired (Laxminarayan et al., 2016).

In this retrospective case series the author investigated the following null hypothesis: intra- and post-procedural prophylactic antibiotic use is unnecessary in the prevention of bacterial endocarditis in dogs that undergo trans-catheter embolization of a PDA.

Abbreviations: PDA, patent ductus arteriosus; ACDO, Amplatz Canine Ductal Occluder
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<http://dx.doi.org/10.1016/j.vetmic.2017.05.023>

Received 21 March 2017; Received in revised form 26 May 2017; Accepted 28 May 2017
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2. Materials and methods

2.1. Animals

Case records of client-owned dogs that underwent trans-catheter embolization of a PDA at the Companion Animal Clinic of the Utrecht University between January 2004 and December 2016 were searched in the clinic's electronic database. Inclusion criteria were that (1) at least one metal implant was delivered in the PDA, (2) no local or systemic antibiotics were given on the day of the intervention, the week before and the week after the procedure, (3) at least 3 months of postoperative follow-up information was available, and (4) the author performed the procedure either as the primary or as the supervising cardiologist.

2.2. Surgical procedure

Diagnosis of the PDA was made by cardiac auscultation, based on a continuous murmur in the region of the left cardiac base, followed by an echocardiogram performed by the same cardiology specialist who carried out the surgery or a cardiology resident under the direct supervision of the cardiologist.

On the day of the intervention all dogs underwent a general physical examination prior to surgery. Besides their congenital heart disease, all dogs were apparently healthy and had normothermia. All procedures were performed at the fluoroscopy unit of the clinic. The catheterization procedure was carried out under general anesthesia. Intravenous methadone (0.5 mg/kg, Eurovet Animal Health, Bladel, the Netherlands) and intramuscular atropine sulfate (0.02 mg/kg, Teva Pharmachemie, Haarlem, the Netherlands) were used as premedication, and intravenous propofol (2.6–7.1 mg/kg, Abbott Laboratories, Chicago, Illinois, USA) was used for anesthetic induction. For anesthetic maintenance inhaled isoflurane (Abbott Laboratories, Chicago, Illinois, USA) vaporized in a mixture of oxygen and air (1:1) was administered by mechanical ventilation. To reduce the concentration of isoflurane, intravenous fentanyl (5 µg/kg/h in continuous rate infusion, Bipharm, Almere, the Netherlands) was administered. Blood pressure was measured during the procedure either indirectly with an oscillometric equipment or directly via the left metatarsal, femoral or the coccygeal artery. Continuous electrocardiogram, pulse-oxymetry, rectal temperature and ETCO₂ monitoring were used during anesthesia. No heparin was given to any dogs.

The dogs under general anesthesia were positioned on the fluoroscopy table in right lateral recumbency and the medial aspect of the right hind limb was surgically prepared with the hind legs spread. A surgical cut-down was performed over the right femoral artery. After identification of the femoral artery, its distal end was ligated using an absorbable multifilament suture material (polyglactin, Vicryl™ Plus 2–0, 3–0 or 4–0, ETHICON®, Johnson & Johnson International, c/o European Logistics Centre, Diegem, Belgium). Depending on the diameter of the femoral artery (more or less than 2.3 mm), either a 7- or 9-French guiding catheter with a hemostatic valve (Vistabritetip® IG introducer guide, Cordis Corporation, Miami Lakes, USA) or a 4- or 5-French multifunctional catheter (Multifunctional angiographic catheter, Cordis Corporation, Miami Lakes, USA) was introduced in the proximal part of the vessel.

After performing an aortogram by injecting iodinated contrast agent (1–1.5 ml/kg, Xenetix® 350, iobitridol 768 mg/ml, 350 mg iodine/ml, Guerbet Nederland BV, Gorinchem, the Netherlands) with the tip of the catheter at the level of the tracheal bifurcation, the diameter of the pulmonary ostium and that of the ampulla of the PDA were measured. Depending on the diameter of the femoral artery and that of the pulmonary ostium of the PDA either an Amplatzer Canine Ductal Occluder (Infiniti Medical, West Hollywood, California, USA) or a detachable coil (MR Eye embolization coil, Cook Incorporated, Boomington, USA) was chosen. The size of the implant was determined according to the manufacturer's recommendation. Once the tip of the delivery catheter

was advanced into the main pulmonary artery under fluoroscopic guidance, the correct positioning of the catheter tip was confirmed with direct blood pressure measurement. The implant was delivered in the PDA according to the manufacturer's recommendation. After the implant was released, another aortogram or a transthoracic color Doppler echocardiogram was performed. If no or only a mild residual shunting via the occluded PDA was noted, then the delivery catheter was removed and the proximal part of the femoral artery was ligated with an absorbable multifilament suture (polyglactin). If severe shunting was evident even minutes after implant release, one or more additional coils were placed in the ampulla of the PDA. After ligating the femoral artery, the surgical wound was closed in 3 layers. The fascia and the subcutis were sutured with either an absorbable multifilament (polyglactin) or an absorbable monofilament (poliglecaprone, Monocryl™ Plus 3–0 or 4–0, ETHICON®, Johnson & Johnson International, c/o European Logistics Centre, Diegem, Belgium) suture. The skin wound was closed either with an absorbable suture (polyglactin or poliglecaprone) intracutaneously in a continuous fashion, or with the same or a non-absorbable (poliamid, Ethilon®II 3–0 or 4–0, ETHICON®, Johnson & Johnson International, c/o European Logistics Centre, Diegem, Belgium) suture in an interrupted fashion. Dogs were discharged from the clinic the same day if the procedure took place in the morning, or the next morning if the surgery took place in the afternoon. Post-operative painkillers were provided for 3–4 postoperative days with oral non-steroidal anti-inflammatory agents (carprofen or meloxicam). All catheters and implants used during the procedure were sterile in their original package.

2.3. Follow up

If the dogs were reexamined at the author's clinic at least 3 months after the procedure or the owner contacted the clinic via telephone or email after the surgery, the clinic's digital archive was utilized to gain medical information about the dogs' health state. If this was not the case, the dogs' owners were contacted via telephone by the author between April 2015 and March 2017 to gain information about the postoperative health status of their pets. If the owners did not pick up the phone, the referring veterinarian was called and asked about the dates and reasons of the dogs' visits.

3. Results

All inclusion criteria were fulfilled by 54 dogs. None of these dogs developed clinical signs that could be compatible with bacterial endocarditis within 3 months after the PDA-occlusion.

The median age of the dogs at surgery was 4 months (range 2–95 months) and their median weight was 7.5 kg (range 1.9–35.7 kg). The implanted occlusion devices were coils in 18 dogs, ACDOs in 34 dogs, both in 1 dog and a human Amplatzer duct occluder in 1 dog. The median length of the surgery was 100 min (range 45–192 min). An immediate complete closure of the PDA was reached in 36 dogs. The median length of the follow-up was 25 months (range 3–157 months).

4. Discussion

The present study reports a case series of 54 dogs that underwent a trans-catheter embolization of a PDA in a single tertiary referral centre. None of the 54 dogs developed infective endocarditis within 3 months after surgery.

Despite the large number of dogs whose PDA is embolized with an implant worldwide, only 3 cases have been reported with device-related infective endocarditis, of which one had an ACDO and 2 had coils (Wood et al., 2006; Fine and Tobias, 2007; Saunders et al., 2014). The single study that describes the frequency of PDA-occlusion-device-related infection in dogs reported an incidence of 4.3% (2 of 47 dogs) (Fine and Tobias, 2007). Each of the 47 dogs of that study received

prophylactic antibiotics. The authors concluded that prevention of infective endocarditis can be best achieved by “proper surgical technique and appropriate use of intra- and postprocedural antibiotic prophylaxis” (Fine and Tobias, 2007). Reported incidence of infective endocarditis in dogs without intravascular/intracardiac implants in tertiary veterinary referral centers is 0.1–6.6% (MacDonald, 2010). The present study reports similar incidence (0 out of 54) without prophylactic antibiotics as the study of Fine and Tobias (2 out of 47 dogs) with prophylactic antibiotic use.

The 3 months of follow-up period was chosen based on earlier studies (Durack and Beeson, 1972; Strakebaum et al., 1977; Fine and Tobias, 2007; Peddle et al., 2009). An infective endocarditis that develops beyond the 3 months postoperative period would be very unlikely to be prevented by administering intra-procedural prophylactic antibiotics (Strakebaum et al., 1977).

The major limitation of the present study is its retrospective nature. A prospective, placebo-controlled, randomized, double-blinded study would provide stronger data. Further limitation is the relative low number of animals. Another weakness of the study is that the follow-up information was gained via telephone interview in the majority of cases. However, bacterial endocarditis is a life-threatening condition, which would not cause only mild clinical signs nor would it remain subclinical (MacDonald, 2010).

The pathogenesis of cardiovascular device-related bacterial endocarditis/arteritis in both human and veterinary medicine is not fully elucidated, but three factors are believed to play a role: device-related, patient-related and procedure-related factors (Fine and Tobias, 2007; Wilson et al., 2007; Weber et al., 2008). The presence of foreign material and a transient or sustained bacteremia are thought to play a vital role in the development of infective endocarditis (Wilson et al., 2007; Weber et al., 2008). Potential injury of the endothelium of the PDA by the device may abolish the natural microbial resistant of the endothelium. As a consequence of vascular endothelial disruption, deposition of platelet-fibrin aggregates occurs and the ultimately arising coagulum provides a susceptible nidus for microbial adhesion, colonization and biofilm formation (Wilson et al., 2007; Weber et al., 2008). The development of biofilm on the metal surface of the implant helps bacteria to hide from antibiotics and the host's immune system (Baddour et al., 2003; Fine and Tobias, 2007; Wilson et al., 2007; MacDonald, 2010). Certain microorganisms such as *Staphylococcus* and *Streptococcus spp.* possess adhesins on their surface, which enable attachment to the host's extracellular matrix proteins by binding to adhesive matrix molecules (Weber et al., 2008). The surface of the indwelling implant is coated by these proteins, which are exposed if the endothelium is disrupted by contact with the implant or adherence of the endothelium to the implant, and subsequently facilitating the microbial adherence and bacterial colonization (Baddour et al., 2003; Fine and Tobias, 2007; Wilson et al., 2007; MacDonald, 2010). Procedural-related factors, such as sterile equipment, operator experience, procedural time and meticulous aseptic technique are related to the occurrence of device infections in humans (Baddour et al., 2003; Wilson et al., 2007; Nof and Epstein, 2013). Procedural infections mostly start shortly after the surgery, typically within 30 days (Durack and Beeson, 1972; Strakebaum et al., 1977; Peddle et al., 2009; Weber et al., 2008). Routine daily activities (such as chewing) may result in transient bacteremia caused by oral microflora (Baddour et al., 2003; Wilson et al., 2007; MacDonald, 2010). Intra-cardiac-device-related infective endocarditis in humans is thought to be associated with the presence of a residual ductal flow (Baddour et al., 2003; Saint-André et al., 2012; Rushani et al., 2013). An experimental study on piglets with intravenous injection of *Streptococci* after implantation of an older PDA-closure-device confirmed this observation (Latson et al., 1994). In the present study the presence of residual shunting did not seem to have an effect on developing endocarditis.

Published guidelines for antibiotic prophylaxis in canine patients during cardiac catheterization procedures are lacking (Stauthammer,

2015), that is why veterinary cardiologists probably follow human recommendations. Publications about the short- and long term results of trans-catheter closure of canine PDAs either do not mention the use of intra-procedural prophylactic antibiotics (Achen et al., 2008; Gordon et al., 2010; Saunders et al., 2014), or they state that the use of prophylactic antibiotics is an integrated part of the institutional or personal protocol (Fine and Tobias, 2007; Caivano et al., 2012; Singh et al., 2012; Stauthammer, 2015).

Bacterial endocarditis is a very rare complication of cardiac implants in humans (Baddour et al., 2003; Agnoletti et al., 2005; Mehta et al., 2008; Roig et al., 2012; Rushani et al., 2013). Due to their rare occurrence, antimicrobial prophylaxis is not routinely recommended according to the most recent human guidelines on the prevention of cardiovascular device-related infections (Baddour et al., 2003). Up till now, scientific evidence of the benefits of perioperative antibiotic use in PDA embolization is lacking not only in dogs, but also in humans (Baddour et al., 2003; Dhoble et al., 2009; Boothe and Boothe, 2015; Gillett and Morgan, 2015). Human guidelines regarding the use of antibiotic prophylaxis are controversial (Baddour et al., 2003; Wilson et al., 2007; Weber et al., 2008; Richey et al., 2008; Shanson, 2010). Primary prophylaxis, i.e. administration of antibiotics during PDA closure, is generally not recommended in humans (Baddour et al., 2003; Richey et al., 2008). Secondary prophylaxis, i.e. when a patient, whose PDA has already been occluded, undergoes a non-sterile surgery (e.g. on the urogenital tract) antibiotic prophylaxis is only recommended if there is a residual shunting present (Baddour et al., 2003). In 2003 the American Heart Association Guidelines (Baddour et al., 2003) it is said that “In general complications from use of approved devices for these purposes are exceedingly rare, and infectious complications are even less frequent”. The primary antibiotic prophylaxis recommendations for placement of non-valvular cardiovascular devices advice that: “Because of the low incidence of infection for many of the devices, evidence-based data have not been collected that prove efficacy.” Despite these recommendations, several human cardiologists and institutions do not follow the published guidelines and do administer prophylactic antibiotics (Weber et al., 2008; Shanson, 2010; Patel et al., 2014; Behjati-Ardakani et al., 2015; Gillett et al., 2015).

In conclusion, there is no scientific evidence available showing that prophylactic antibiotic administration can prevent procedure-related infective endocarditis in dogs that undergo trans-catheter PDA-embolization. Based on the results of the present case series compared with other veterinary reports and human guidelines, no strong recommendations for routine use of primary antibiotic prophylaxis at trans-catheter embolization of a PDA in dogs can be made. In the author's center, proper surgical technique and the use of sterile catheters, guidewires and implants in their original package were sufficient to prevent procedure-related infective endocarditis, even when the implantation took place in the fluoroscopy unit and not in the operating theater of the clinic.

Competing interest

The author declares no competing interest.

Funding

Not applicable.

Acknowledgements

The authors are grateful to the anesthesiology team (among others Ies Akkerdaas, Loes van Gennip, Rob Sap and Ron van Wandelen) and the technicians of the Companion Animal Clinic of the Utrecht University for their invaluable work during the cardiac catheterization procedures. The author is grateful to Dr. Els Broens, Dr. Mark Dirven, Dr. Niek Beijerink and Prof. Dr. Erik Teske for their advice in the

manuscript preparation.

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