Serum levels after everolimus-eluting stent implantation in infants with pulmonary vein stenosis

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Introduction: Everolimus-eluting stents are used in adults for interventional treatment of coronary artery disease and in small vessel disease to reduce restenosis rate. The antiproliferative substance everolimus is acting locally but is also released into the circulation. Data on their use in pediatrics concerning systemic substance levels and side effects are limited. We report systemic drug exposure after implantation of a single everolimus-eluting stent in three infants (age in months/body weight in kilograms: patient 1: 8/4.6, patient 2: 6/3.9, patient 3: 1/3.5), respectively, which were used for relief of pulmonary vein stenosis.

Methods: Xience® everolimus-eluting stents (Abbott Laboratories) were used. Each stent had different size and device drug amounts (stent diameter x stent length in mm and device drug amount in μg: patient 1: 4x18 mm, 113 μg; patient 2: 2.5x8 mm, 40 μg; patient 3: 3x8 mm, 40 μg). Everolimus levels were measured by liquid chromatography-tandem mass spectrometry (LC-MS/MS) 1 hour (except patient 1), 24, 48 and 72 hours after stent implantation.

Results: Patient 1 was exposed to a maximal calculated everolimus dose of 24.6 μg/kg, patient 2 to 10.3 μg/kg and patient 3 to 11.4 μg/kg, respectively. The highest serum everolimus level was measured 1 hour after stent implantation in the youngest and smallest child (patient 3; 2.4 ng/ml) followed by patient 2 with 1.5 ng/ml. Subsequently, serum everolimus levels decreased continuously (Figure). After 48 hours, everolimus levels were below the lower laboratory limit (<0.5 ng/ml) at our institution in each of the patients, but everolimus was still reliably detectable by repeated LC-MS/MS. At anytime, everolimus levels were below the immunosuppressive therapeutic range of 3-6 ng/ml. Complete blood count, creatinine, C-reactive protein, and liver enzymes did not change as compared to patient laboratory parameters prior to catheter intervention. Drug toxicity was not observed.

Conclusions: After everolimus-eluting stent implantation in infants we documented always subtherapeutic serum levels. Highest everolimus levels were measured in the first hour after implantation, thereafter rapidly decreasing. These data suggest that at least one everolimus-eluting stent can safely be used in small infants for therapy of pulmonary vein stenosis without systemic adverse effects.