IMPLANTATION OF VALVULAR COLLAGEN BIOMATERIALS SEEDED WITH AUTOLOGOUS STEM CELLS – INTRAOPERATIVE HEMODYNAMIC MEASUREMENTS IN AN ANIMAL MODEL

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Abstract: *Objective: achieving a pulmonary valve xenograft with no hemodynamic impact. Methods: In the Tissue Engineering and Regenerative Medicine Laboratory at the University of Medicine and Pharmacy Tîrgu-Mureș, acellular scaffolds were created from decellularized porcine pulmonary valves using mechanical, chemical and enzymatic methods. Those were included in a decellularized bovine pericardium conduct and placed in extra-anatomic position between the right ventricle outflow tract and the pulmonary trunk. 7 juvenile sheep about 4-5 months (22-25 kg) were selected as animal model. Right ventricle and pulmonary artery invasive pressures were measured intra-operatorily, before and after the ligature of the native pulmonary trunk. Systemic blood pressure, heart rate and oxygen saturation were also monitored. Results: The physiologic average of the right ventricle mean pressure was 20.14 mmHg (interval between 17 and 22) and in the pulmonary artery, it was 23.42 mmHg (interval between 21 and 26). Redirecting the blood flow through the valvular conduit, by ligating the pulmonary trunk origin produced similar values: 21.42 mmHg (19 to 23) in the right ventricle and 23.14 mmHg (21 to 26) in the pulmonary artery. The new means were not significantly different from the native values, as shown by the two-tailed p values of the paired t-test (p = 0.06, respectively 0.77, at a 95% confidence level). Arterial blood pressures were maintained between 110-130/70-80 mmHg, heart rate below 100/min and oxygen saturation above 94%. Conclusions: Our pulmonary valve xenograft implantation technique did not modify intraventricular and pulmonary pressures. Systemic blood pressure, heart rate and oxygen saturation were also stable. Long term follow-up is necessary to evaluate the xenograft performance.*

INTRODUCTION

The limitations of the current valvular alternatives are well known. The bleeding risks because of the mandatory anticoagulant therapy for mechanical valves and the risks of reoperation for biological prosthesis (1), demand finding a new valvular substitute. Currently, the medical research is focusing to obtain a cardiac valve that overcomes these disadvantages by tissue engineering. Design criteria for a tissue engineering heart valve (TEHV) include extended durability, minimal or no regurgitation, the ability to withstand physiological pressure differences, and the capacity to grow and adapt to the patient. The TEHV must also be non-thrombogenic and non-immunogenic to prevent clot formation and immune rejection, respectively.(2) A TEHV requires a scaffold, polymeric or decellularized allo- or xenogenic extracellular matrix, seeded or not with cells.

MATERIALS AND METHODS

This study was approved by the Ethical Committee within the University of Medicine and Pharmacy of Tîrgu-Mureș.

Valve preparation

In the Tissue Engineering and Regenerative Medicine Laboratory (University of Medicine and Pharmacy of Tîrgu-Mureș, Romania), porcine pulmonary trunks were harvested, preserving 4 mm muscular tissue under the cusps basis and up to 2 mm above the sinotubular junction of the pulmonary valve (figure no. 1).

Figure no. 1. Fresh pulmonary trunk

Figure no. 2. Decellularized pulmonary valve

Acellular scaffolds were obtained with a six-day decellularizing protocol, using mechanical, chemical and

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enzymatic methods. A valvulated conduct was designed by interposing the valve in a decellularized bovine pericardium tube. Before in vivo implantation, the scaffold was internally seeded with autologous adipose derived stem cells (figure no. 3).

Figure no. 3. Internal seeding

Implantation of TEHV

TEHVs were implanted in 7 juvenile sheep of about 4-5 months (22-25 kg). Under general anesthesia and mechanical ventilation, a left antero-lateral thoracotomy in the 3rd intercostal space was performed to expose the pulmonary artery and the right ventricle outflow tract. After systemic heparinisation, 3 cm right ventriculotomy was made by lateral clamping and the valvular conduit proximal end was anastomosed with 4.0 Prolene Surjet suture. In the same manner, the distal end was anastomosed to the main pulmonary artery. By ligating the pulmonary artery origin, the right ventricular blood flow was bypassed through the valvular conduit (figure no. 4).

Figure no. 4. Native pulmonary artery ligature

Intraoperatory measurements

Right ventricle and pulmonary artery invasive pressures were measured (figure no. 5) intraoperatorily, before and after the ligature of the native pulmonary trunk. Systemic blood pressure, heart rate and oxygen saturation were also monitored.

Figure no. 5. Invasive pressure measurement

RESULTS AND DISCUSSIONS

The physiologic average of the right ventricle mean pressure was 20.14 mmHg (interval between 17 and 22) and in the pulmonary artery, it was 23.42 mmHg (interval between 21 and 26). Redirecting the blood flow through the valvular conduit, by ligating the pulmonary trunk origin, produced similar means: 21.42 mmHg (19 to 23) in the right ventricle and 23.14 mmHg (21 to 26) into the pulmonary artery. The new means are not significantly different from the native values, as shown by the two-tailed p values of the paired t-test ($p = 0.06$, respectively 0.77, at a 95% confidence level) (table no. 1). Arterial blood pressure has been maintained between 110-130/70-80 mmHg, heart rate below 100/min and oxygen saturation above 94% (figure no. 6).

Postoperatorily, transthoracic echo-cardiography was performed. Cusps mobility and coaptation, and low transvalvular gradients provide a physiological functionality (figure no. 7).

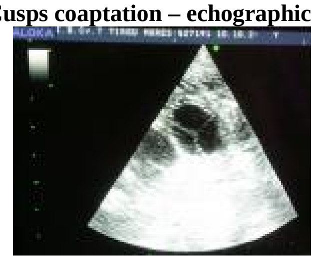
Figure no. 6. Intraoperative monitoring

Table no. 1. Intraoperative measurements (mmHg)

Nr.	RVMPb	RVMPa	PAMPb	PAMPa
1.	22	22	24	24
2.	21	21	26	23
3.	21	23	23	26
4.	19	23	23	22
5.	20	20	23	23
6.	21	22	25	23
7.	17	19	20	21

RVMPb – Right Ventricle Mean Pressure before ligation; RVMPa – Right Ventricle Mean Pressure after ligation; PAMPb – Pulmonary Artery Mean Pressure before ligation; PAMPa – Pulmonary Artery Mean Pressure after ligation

Figure no. 7. Cusps coaptation – echographic aspect



CONCLUSIONS

Our pulmonary valve xenograft implantation did not modify intraoperative intraventricular or pulmonary pressures. Choosing the right valve diameter, in accordance with the native pulmonary valve, will ensure an appropriate pulmonary blood flow. The clinical expression of good hemodynamics is the oxygen saturation, heart rate and systemic blood pressure, which were all registered in physiological ranges. The main conclusion is that our implantation surgical technique is an excellent pulmonary valve testing model without using the extracorporeal circulation. Long term follow-up is necessary to evaluate the xenograft performance.

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