Acute and Chronic Heart Dilation Model-Induced in Goats by Carotid Jugular A-V Shunt

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Abstract

Congestive heart failure is characterized by impaired quality of life and markedly shortened life expectancy. There are currently many medical and surgical modalities that aim to treat patients with heart failure, which implies the need for an animal heart failure model for the development and testing of these therapeutic modalities. A variety of animal heart failure models have been developed, including those in which heart failure is induced via drugs, rapid ventricular pacing, genetic alteration, viral sources, idiopathic dilated cardiomyopathy, coronary arteries’ embolization, pressure overload, and volume overload by arteriovenous (A-V) shunt. The purpose of this study was to evaluate the acute and chronic effect of carotid-jugular A-V shunt in goat model of heart dilation. After cross clamping of the left carotid artery, an end-to-side anastomosis of 10 mm in diameter was performed between the free end of the vein and the side of the artery.

A dual-micromanometer transducer conductance catheter was used to determine the volume of the ventricle on-line, by measuring the time-varying electrical conductance of the segments of intraventricular blood. During and at the end of the eight weeks none of the animals showed signs of heart failure or distress. The acute and chronic hemodynamic changes were demonstrated by pressure-volume loops at baseline, immediately after the shunt, and after 8 weeks. There was an immediate rise in the LVEDV (104±27 ml) compared to the baseline volume (75±26 ml), and eight weeks later the LVEDV reached 111±22 ml. None of the eight goats demonstrated clinical signs of pulmonary congestion. The Swan-Ganz and the conductance catheters that were used to monitor the heart hemodynamic changes immediately after the creation of the A-V shunt revealed interesting results. Another advantage of the shunt model is that it is possible to evaluate the patency of the shunt by palpating blood thrill in the neck. The carotid jugular A-V shunt in goats causes significant left heart dilation without signs of heart failure, and is reproducible with low animal mortality. The study ended 8 weeks after the creation of the A-V shunt, leaving unanswered the question of possible heart failure development in this model after a longer follow up period.

Key words: animal heart failure model, arterio-venous (A-V) shunt, congestive heart failure, hemodynamic changes carotid-jugular A-V shunt.
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Methods

Experiments were performed in eight female goats, weighing 51 to 80 kg, in accordance with the Guide for the Care and Use of Laboratory Animals published by the National Institutes of Health (NIH publication 86-23, revised 1985).

Dilated cardiomyopathy was induced by a left carotid jugular A-V shunt. The acute and chronic hemodynamic changes were followed for 8 to 10 weeks by three different monitoring modalities: Swan-Ganz catheters measured cardiac output before, immediately after the creation of the A-V shunt, and 8 weeks later; conductance catheters measured left ventricle dimensions and performance before, immediately after the creation of the A-V shunt, and 8 weeks later; and echocardiography was performed before and every two weeks after the A-V shunt operation.

A-V shunt procedure

General anesthesia was induced by thiopental sodium (Pentothal, Abbott S.P.A., Italy), administered intravenously at 15 mg per kg body weight, and maintained after endotracheal intubation with oxygen/nitrous oxide (1:2) and 1.5% Fluothane (Halothane, Zeneca Ltd., Macclesfield, Cheshire, UK).

During the experiments, the lungs were ventilated with a positive pressure respirator (Harvard, Apparatus Inc., South Natick, Massachusetts) and body temperature was kept constant with a heating mattress. A single dose of 10,000 IU heparin i.v. was administered. Through a cervical incision, the left jugular vein and the left carotid artery were mobilized over a length of approximately 5 cm and ligated distally. After cross-clamping of the left carotid artery, an end-to-side anastomosis of 10 mm in diameter was performed between the free end of the vein and the side of the artery, using 6-0 polypropylene non-absorbable running sutures (Ethicon, Edinburgh, Scotland). Clamps were removed and the patency of the fistula was visually confirmed by the pulsatile filling of the jugular vein.

Heart catheterization

A dual-micromanometer transducer conductance catheter (7F, Sentron, The Netherlands) was used to determine the volume of the ventricle on-line, by measuring the time-varying electrical conductance of the segments of intraventricular blood [8]. The catheter’s position along the long axis of the left ventricular cavity via the left femoral artery was set under fluoroscopic guidance and verified by inspection of the segmental conductance signals: a correct position was assumed if the signals of at least the four most distal segments displayed a typical phasic LV volume tracing. A Leycom Sigma-5DF signal conditioner-processor (Cardiodynamics, Zoetermeer, The Netherlands) provided the current source and processed the segmental conductance, producing an on-line display of the LV contours, as well as continuous and instantaneous volume signals. The volume signals were combined with the pressure signals on an X-Y oscilloscope to provide an instantaneous and uninterrupted display of pressure-volume loops.

Readings of the volume signal were corrected to account for the parallel conductance caused by tissues surrounding the ventricular cavities. A bolus of 7.5 ml of hypertonic NaCl (9%) was injected into the central venous compartment via the Swan-Ganz catheter. As the bolus mixed with the fluid in the ventricular cavity, its conductivity increased, causing the overall conductance signal to increase while the parallel component remained constant. End-systolic overall conductance was then plotted as a function of end-diastolic overall conductance during the mixing of the bolus; the conductance was equal to the intersection point between the regression line of these values and the line of identity.

Results

During and at the end of the eight weeks none of the animals showed signs of heart failure or distress.

One animal died three weeks after the A-V shunt operation most probably due to lung infection.

The carotid-jugular A-V-shunt induced both immediate and long-term hemodynamic changes. The immediate effect of the shunt, an abrupt rise in cardiac output, was observed within 30 minutes after opening of the shunt and measured by Swan-Ganz thermodilution technique: 7.9±1.9 l/min compared to the baseline cardiac output of 4.9±1.3 l/min. Eight weeks after the shunt procedure, an increase in cardiac output was observed in comparison not only to the baseline value but also to the measurements obtained immediately after opening of the shunt, measuring 9.9±2.7 l/min.

Echocardiography tests revealed a gradual increase in left ventricular end-diastolic diameter, reaching the maximal left ventricle dilation at 8 weeks (Fig. 1).

The acute and chronic hemodynamic changes were demonstrated by pressure-volume loops at baseline, immediately after the shunt, and after 8 weeks (Fig. 2). There was an immediate rise in the LVEDV (104±27 ml) compared to the baseline volume (75±26 ml), and eight weeks later the LVEDV reached 111±22 ml.

Discussion

This study demonstrates that the A-V shunt heart failure model is capable of producing stable, immediate and long-term high cardiac output (overload) dilation. None of the eight goats demonstrated clinical signs of pulmonary congestion. Fortunately, these results are in contrast with the high mortality rates (77%) and signs of
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pulmonary congestion that commonly occur within 24 hours of performing the A-V shunt in small animals, as reported by Flaim and coworkers [10]. This discrepancy is probably due to the relatively small A-V shunt of approximately 10mm, used in our study (in goats weighing 51 to 80 kg). Moreover, in the present study the animals presented neither clinical nor hemodynamic signs of heart failure, such as tachycardia or an increase in LVEDP, as was observed with inferior vena cava aortic A-V shunt applied in mongrel dogs [7]. Strangely, no changes in heart rate were observed. We observed a moderate rise in the dPdt max (from 1361 mmHg/s to 1423 mmHg/s), as well as a significant rise in peak ejection rate (PER) from 280 (ml/s) before the shunt to 446 (ml/s) immediately afterward. All these dramatic changes were reversible at this point in time, by closure of the shunt. These results suggest that the wide changes in left ventricle model are within the efficient part on Starling’s curve.

Another advantage of the shunt model is that it is possible to evaluate the patency of the shunt by palpating the blood thrill in the neck. The shunt’s location facilitates access to ultrasonic measures for a more precise evaluation, as well as temporary closure, obtained by applying manual pressure at the animal’s neck.

Our study ended 8 weeks after the creation of the A-V shunt, leaving unanswered the question of possible heart failure development in this model after a longer follow up period.

In conclusion, the carotid jugular A-V shunt in goats causes significant left heart dilation without signs of heart failure, and is reproducible with low animal mortality.

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