Left ventricular pressure measurement in the telemetered dog

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1 Introduction

Cardiac contractility is defined as the intrinsic ability of cardiac muscle fibers to contract at a given fiber length. Changes in the ability to produce strong contractions result from different degrees of binding between myosin and actin filaments that depend in turn on the concentration of calcium ions in the cytoplasm of cardiac muscle cells. This is controlled by the action of noradrenaline and acetylcholine, neurotransmitters of the autonomic nervous system. The inotropic state of the heart is assessed using the Left Ventricular Pressure (LVP) signal as an indirect measure of the force of ventricular myofiber contraction. From the LVP, we can also derive useful parameters such as the maximum rate of ventricular pressure increase (dP/dt Max), the minimum rate of ventricular pressure decrease (dP/dt Min) and the Ejection Time (the duration of bleded ejection from the left ventricle, biopacing with opening of the aortic valve and ejection with closing of the aortic valve). The aim of this study was to validate a chronic model of telemetered dog, thus allowing the evaluation of cardiac contractility by the recording of LVP in conjunction with ABP and ECG (Fig. 1) after oral administration of three known inotropic compounds.

Materials and Methods

Beagle dogs (two females and two males; Harlan, France) were surgically implanted with telemetry transmitters (TELEM-070-PCRT; Data Sciences International, Saint Paul, USA). The transmitters were fixed to the abdominal musculature in the peritoneal cavity. After left thoracotomy, the LVP probe was inserted into the left ventricle cavity. The positive ECG lead was placed into the myocardiun, near the LVP catheter, whilst the negative ECG lead was subcutaneously channelled on the right side of the sternum (D1 lead position). The ABP catheter was placed in the femoral artery. After a post surgery recovery period of three weeks, the animals received, in sequence, three positive reference compounds or the vehicle (0.5% methylcellulose aqueous solution) by single oral administration (gavage), with a wash out period of at least 48 hours between each treatment.

2 Results and Discussion

Pimobendan

Pimobendan induced a rapid doserelated increase in dP/dt Max (60 min after dosing (AD): +12%; +25% and +49% at 0.1, 0.3 and 1 mg/kg respectively, when compared to the vehicle, Figs. 3 & 4), a decrease in dP/dt Min (60 mg AD: -14%, -27% and -53% at 0.1, 0.3 and 1 mg/kg) and a decrease in Ejection Time (60 min AD: -9% and -52% at 0.3 and 1 mg/kg, Fig. 5), and a decrease in Ejection Time (30 min AD: -1%, +13% and +51% at 0.1, 0.3 and 1 mg/kg, respectively, when compared to the vehicle). No effects were observed on these parameters at 4 mg/kg (Fig. 5). Similar results were reported by Markert et al (2007).

Verapamil

Treatment with Verapamil induced a rapid decrease in dP/dt Max (45 min AD: -14%, -11% and -19% at 0.1, 0.3 and 30 mg/kg, respectively, when compared to the vehicle, Fig. 4), an increase in dP/dt Min (45 min AD: +7% and +43% at 0.1 and 0.3 mg/kg, respectively, when compared to the vehicle, Fig. 5), an increase in Ejection Time (3 min AD: +3% and +14% at 0.1 and 0.3 mg/kg, respectively, when compared to the vehicle, Fig. 6) and at 30 mg/kg, a decrease in arterial pressure: SAP (45 min AD: -46%) and DAP (45 min AD: -59%). Tachycardia, followed by a sudden decrease in HR, was noted after treatment at 30 mg/kg (15 min AD: +42% to +45 min AD: -44%, Fig. 7). Similar results were reported by Geert et al (2002).

Propranolol

Propranolol at 8 mg/kg induced a decrease in dP/dt Max (30 min AD: -27% when compared to the vehicle, Fig. 4), an increase in dP/dt Min (30 min AD: +13%, Fig. 5), and an increase in Ejection Time (30 min AD: +11%, Fig. 6). No effects were observed on these parameters at 4 mg/kg (Fig. 5). No effects were noted at these doselevels on SAP and DAP. A similar depression of the left ventricular inotropic state was also shown by LeWinter et al. (2003) in the intravenous administration of Propranolol to conscious Mongrel dogs.

Discussion and Conclusion

The administration of Pimobendan, Verapamil and Propranolol induced measurable changes in cardiac contractility, which were evaluated by the measurement of LVP-derived parameters (dP/dt max, dP/dt min and Ejection Time), but effects on the hemodynamic (HR and ABP) and bromotropic (ECG) parameters were not systematically observed. These results demonstrate that the dog telemetry model, as established in our facility, can be used to characterize positive and negative inotropic actions of drugs.

Bibliography


Fig. 1: A typical recording of ECG, ABP, LVP and dP/dt signals in conscious Beagle dogs.

Fig. 2: Changes in LVP signal after administration of a positive inotropic compound (Pimobendan: 1 mg/kg PO) to conscious Beagle dogs.

Fig. 3: Dose effect of Pimobendan on dP/dt Max

Fig. 4: Variation of dP/dt Max after Pimobendan, Verapamil or Propranolol

Fig. 5: Variation of dP/dt Min after Pimobendan, Verapamil or Propranolol

Fig. 6: Variation of Ejection Time after Pimobendan, Verapamil or Propranolol

Fig. 7: Variation of HR after Pimobendan, Verapamil or Propranolol

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