DESCRIPTION OF AN ANIMAL MODEL OF ACUTE CARDIAC FAILURE: IN VIVO EXPERIMENTS IN SHEEP

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Abstract: The purposes of this work were to, a) describe an acute animal model of severe cardiac failure induced by high doses of halothane, b) analyze the effects of these overdoses of halothane on arterial wall dynamics and c) characterize the cardiovascular effects of halothane through the autonomic nervous system. Measurements were performed in six sheep before and after halothane administration (4%). A significant decrease was observed in mean aortic flow (P<0.05) and diameter (P<0.01) in heart failure with respect to control state (from 2.64±0.95 L.min⁻¹ and 17.32±1.86 mm to 1.69±0.58 L.min⁻¹ and 15.33±1.71 mm; respectively). A significantly decrease was observed in mean (P<0.005), systolic (P<0.01) and diastolic (P<0.005) aortic pressure in heart failure (from 85.90±19.49 mmHg, 93.52±18.07 mmHg and 78.86±20.12 mmHg to 49.12±21.77 mmHg, 55.54±20.71 mmHg and 43.48±21.21 mmHg; respectively). Heart rate in control group (127.73±11.20 bpm) was significantly (P<0.05) higher than that observed in heart failure (107.15±13.53 bpm).

Keywords: cardiac failure, halothane, left ventricular dysfunction.

I. INTRODUCTION

Despite the use of new drugs and modern circulatory assist devices to treat left ventricular dysfunction, heart failure mortality and the number of hospitalizations have shown a progressive and dramatic increase of epidemic proportions (Fang et al., 2008). In this sense, new pharmacological options should be incorporated, and the development of new circulatory assistance devices is a technological area in continuous development in the treatment of left ventricular dysfunction. Consequently, a great number of animal models of heart failure have been developed in order to study both, the modifications induced by new drugs and the effects produced by modern devices and techniques thought to improve the deteriorated hemodynamic state of these patients (Hongo et al., 1997; Doggrell and Brown, 1998; Muders and Elsner, 2000).

Each animal model has its own advantages and disadvantages depending on the animal utilized and the technique employed to induce heart failure. The ideal model should mimic, as closely as possible the human syndrome, be easy to reproduce in the same or different species, inexpensive and capable of exhibiting prolonged steady states that allow cardiac function measurements (Hongo et al., 1997). The mentioned characteristics and others more specific are originated from the fact that these experimental treatments are numerous and have many requirements.

Cardiac failure is the last stage of almost all cardiopathies, consequently the animal models available have different etiologies and levels of hemodynamic impairment. Some of them have acute evolution, while others have chronic features. For instance, animal models of right ventricular failure have been developed showing both, acute (Jett et al., 1983; Cabrera Fischer et al., 1985) and chronic characteristics (Doggrell and Brown, 1998; Hasenfuss, 1998; Muders and Elsner, 2000; Vanoli et al., 2004).

Halothane is a volatile liquid used to maintain the anaesthesia during a surgical procedure. Since it has a relatively high blood/gas coefficient, the induction is relatively low. Besides it is very soluble in lipids and other biological tissues, therefore, the recovery from this type of anaesthetic agent depends on the duration of administration (Zhou and Liu, 2001; Bergadano et al., 2003). Furthermore, halothane has a very strong negative inotropic compound effect, as was reported in the last decades in studies were cardiac function during anaesthesia was analyzed (Hamilton et al., 1966; Sinnet et al., 1981; Schotten et al., 2001).

In previous works, the authors have used high doses of halothane (3% and 4%) in mongrel dogs and in sheep obtaining severe left ventricular dysfunction that was used to test experimental circulatory assistance devices (Cabrera Fischer et al., 1991; Cabrera Fischer et al., 2002; Cabrera Fischer et al., 2004; Risk et al., 2004). However a complete description of the acute left ventricular failure induced by halothane 4% including hemodynamic changes, arterial wall function and heart rate variability have never been reported. In our published works we used different models of acute heart failure including those surgically induced (Cabrera Fischer et al., 1985) or pharmacologically obtained such as the administration of beta blockers (Cabrera Fischer et al., 1999). Nevertheless, we considered that the analysis of the characteristics that define a reliable model of acute heart failure exposed in experiments performed in a group of sheep using high doses of halothane could contribute to the knowledge of the halothane induced animal model of heart failure that we propose.