

Title: CIRCULATORY EFFECTS OF BW33A IN THE DOG

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Introduction. BW33A is a new competitive neuromuscular blocking agent with short to intermediate duration of action. The precise information related to its cardio-hemodynamic effects, particularly those on cardiac performance, in intact subjects is not yet available. Thus, the present investigation was designed to determine the effect of BW33A upon the inotropic state and diastolic properties of the left ventricle together with those upon hemodynamic parameters in closed chest dogs under three different anesthetic agents.

Methods. Six dogs were anesthetized with an initial dose of 100 mg/kg of chloralose intravenously followed by an infusion of an equal dose over the duration of the study (approx. 2.5 hrs.). Ventilation with oxygen was controlled to maintain the PaCO₂ and pH within normal limits. Electrodes were placed to record the electrocardiogram and heart rate. Cannulae were inserted into the femoral artery, pulmonary artery and left ventricle to measure systemic arterial (ABP), pulmonary arterial (PAP), pulmonary capillary wedge (PCWP), right atrial and left ventricular pressures (LVP). Cardiac output (CO) was measured by thermodilution. Systemic (SVR) and pulmonary vascular resistances (PVR) stroke volume, and left ventricular work (LVW) were calculated. The first derivative of the LVP (LV dp/dt) to isovolemic tensile force (KP) against corresponding intraventricular pressure was continuously computed by the Siemens contractility calculator 868. The maximal value of this ratio was taken as an indicator of the contractile state of the LV. After control hemodynamic measurements 0.2 mg/kg of BW33A was injected as a bolus intravenously. Hemodynamics were measured 2, 5, and 10 minutes after injection. Following at least a forty-five minute recovery period, 0.4 mg/kg of BW33A was injected and hemodynamics measured at the same time intervals. A second group of five dogs were anesthetized initially by either halothane or isoflurane (1 MAC) in oxygen. The measurements were made using the same protocol following the administration of BW33A (0.2 and 0.4 mg/kg). Following the recovery from the first inhalation anesthetic, the other anesthetic was administered to obtain MAC level. Measurements were made before and after administration of BW33A (0.2 and 0.4 mg/kg) at the same time intervals. The end-tidal anesthetic concentration was measured by a mass spectrometer (Perkin-Elmer 1100). Data were

analyzed by Student's t-test and analysis of variance. P values less than 0.05 were considered significant.

Results. In dogs anesthetized with chloralose, there were no significant changes in CO, SV, mean ABP, mean PAP, PCWP, SVR and PVR at 2, 5, 10 minutes following administration of either dose of BW33A (values of P>0.2 in all cases). The LVW increased significantly at 2 minutes after i.v. administration of BW33A, (0.4 mg/kg). There were no changes in LV dp/dt, diastolic LV dp/dt and max. LV dp/dt/KP at any time interval following either dose of BW33A. In the second group, during halothane or isoflurane anesthesia (1 MAC), there were no significant circulatory changes at any measurement period after either dose of BW33A (P>0.5).

Discussion. Hughes and Chapple found that clinical doses of BW33A did not cause any significant circulatory changes in open chest dogs anesthetized with chloralose. Data in our study in dogs anesthetized with either chloralose, halothane, or isoflurane are consonant with those of Hughes and Chapple. Our data further demonstrated that BW33A did not cause any changes in LV dp/dt, contractile state of the LV and the early diastolic property of the LV as evidenced by unchanged diastolic LV dp/dt. In contrast to other competitive blockers, BW33A showed no evidence of cardiac autonomic effect, ganglionic blockade, or histamine release. BW33A is a short-acting, non-depolarizing neuromuscular blocking drug with rapid onset and recovery that, at least in the dog has little circulatory effect.

References.

1. Hughes R and Chapple DJ: The pharmacology of atracurium: a new competitive neuromuscular blocking agent. *Br J Anaesth* 53:31-43, 1981.