Effects of vasopressin on the circulation, myocardial dynamics, and left ventricular oxygen consumption in the anaesthetized dog

Effekte von Vasopressin auf das Kreislaufsystem, myokardiale Dynamik und linksventrikulären Sauerstoffverbrauch beim narkotisierten Hund

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With 8 figures

(Received February 11, 1980)

Summary

The effects of vasopressin (ADH) were tested on the cardiovascular system of 7 catheterized barbitone-anaesthetized beagle dogs.

ADH, as a constant intravenous infusion for 10 min at 0.01 and 0.1 IU/kg/min, induced a dose-dependent increase of mean arterial blood pressure (MAP). At the higher dose there was a reversal of the effect 30 min after the primary increase. Similar changes were observed for left ventricular peak pressure (LVP).

Heart rate (HR) and dP/dt\text{max} showed a significant dose-dependent decrease, while total peripheral resistance (TPR) and the contraction period t\text{-}dP/dt showed a dose-dependent increase; all reaching their maximum alterations at the end of infusion, with a slow decline thereafter.

Cardiac output index (COI) was strongly reduced with clear dose-relationship, whereas stroke volume index (SVI) remained unaffected by the low dose and only showed a slight reduction at the higher dose. The parameter V_{\text{CP}} was significantly reduced parallel to HR, while V_{\text{pm}} dropped at both doses with lesser significance.

The time index t\text{-}V_{\text{pm}} consequently was elongated at the low dose. For the high dose there were two subsequent elevations with some similarity to the time course of MAP and LVP.

Ejection time (ET) increased as did left ventricular end-diastolic pressure (LVEDP) and left ventricular end-systolic volume (LVESV). Dose-dependence was absent for the LVEDP elevation seen after discontinuing the infusion, and an inverse dose relationship occurred following the 30th min for ET and the 45th min for both LVEDP and LVESV.

Cardiac work (CW) declined in a dose-dependent manner. Left ventricular oxygen consumption (MVO\textsubscript{2}) was reduced for both doses with a lack of dose-dependence following the infusion of the hormone.

The antidiuretic hormone (ADH), a nonapeptide from the posterior pituitary with its site of action at the distal nephron, is also known as adiuretine or vasopressin. Its release can be stimulated by stress condi-
tions, e.g. during surgical intervention (11, 19), during second stage of labour in parturition (21) or by severe haemorrhage (1, 20, 21). Different anaesthetics (11, 19), histamine (6), nicotine (4) and other drugs (8) additionally stimulate ADH release. The consequent elevation of vasopressin plasma levels can exceed normal values by more than fifty-fold (18, 21) and then are assumed to provoke distinct effects on heart and circulation (7).

Because of its direct stimulatory effects on vascular smooth muscle tone, vasopressin is therapeutically used in patients for control of severe gastrointestinal and oesophageal varices’ bleeding or other dangerous haemorrhage (9, 15, 21). Pre- and perioperative systemic (intravenous) or selective (arterial) infusions in arterial bleeding proved successful and often rendered surgical intervention unnecessary (12, 15).

Some unfavourable effects on heart performance and systemic circulation (22) following such relatively high doses, however, limit its use in high risk patients: strong coronary constriction may induce severe complications (10, 21). Cardiodepressive, i.e. negative inotropic and chronotropic, effects and a reduction of cardiac output concomitant with systemic arterial blood pressure elevation are known to occur, but normally are well tolerated (9, 21, 22).

Despite numerous investigations into the multiple effects of vasopressin on different haemodynamic variables, several facts remain to be elucidated. The anaesthetized dog was used in the following experiments to measure the response of haemodynamic and myocardial parameters to intravenously infused vasopressin, in particular, the cardiac output/heart rate and heart rate/contractility relationships, cardiac work, different contraction parameters, and M\text{VO}_2, simultaneously with cardiac preload and other pressure parameters. The results obtained are compared with previous data pertaining to the mode of action of vasopressin.

Materials and Methods

The present studies were carried out in 7 adult pure-bred beagle dogs of either sex, weighing 15.8 ± 1.2 kg, under sodium pentobarbital anaesthesia (35 mg/kg BW i.p. and 5–10 mg/kg i.v. if required). The animals received endotracheal intubation and were respiring spontaneously; their body temperature was held constant at 37 °C. Blood coagulation was prevented by heparin (2 mg/kg i.v.). For registration of mean arterial blood pressure (MAP), a fluid-filled catheter was introduced into the right femoral artery connected with a strain gauge pressure transducer (Statham P 23 Db).

The measurement of stroke volume (SV) was performed by the thermodilution method. Rapid bolus injections of physiological NaCl-solution (0.4 ml/kg BW, 0 °C) were applied via a calibrated injection catheter (14) inserted into the right atrium via the V. jugularis dextra and V. cava cranialis. The temperature differences were measured in the ascending aorta (1–2 cm above the aortic valves) by a teflon® thermistor catheter (Fischer) introduced via the A. axillaris sin.

Stroke volume and cardiac output (CO) were calculated by HZV BN 2706 (Fischer/Hellige). Both were related to body weight (BW) and expressed as indices (I), i.e. (COI) [ml/min/10 kg] and (SVI) [ml/10 kg]. Total peripheral resistance (TPR) [dyn × s/cm²; kPa × s/l] and cardiac work (CW) [kpm/min; W] were calculated from mean arterial blood pressure (MAP) [kPa; mm Hg] and cardiac output.