

Abstract

The results presented in this thesis are mainly concerned with the cardiovascular and renal effects of supra-physiological and pharmacological doses of cortisol, prolactin DOCA and progesterone. In decelerate, curarized rabbits, supra-physiological doses of cortisol cause a sustained acute hypertension, when they are infused intravenously, intrarterially, intracisternally or injected intramuscular. These cardiovascular effects of cortisol are greatly reduced by ganglion-blockade, prior treatment of the animals with reserpine, anaesthesia, denial of the compound access to the carotid sinus baroreceptor regions, salt depletion and by prolactin. They are enhanced by prior treatment of the animals with pharmacological dose of progesterone, noradrenaline and salt supplementation. A semi-quantitative relationship between the dose of cortisol and the blood pressure response has been demonstrated. The time course of the cortisol effect suggests that the cardiovascular effects of cortisol are probably exerted through an alteration of the blood pressure regulatory feedback mechanisms. The suggestion is supported by the finding that the blood pressure effects of cortisol are abolished by procedures which alter or suppress this control system (e.g. anaesthesia, ganglion-blockade, depletion of catecholamines with reserpine, denial of the steroid access to the baroreceptor regions). It is suggested that the peripheral effects of cortisol (on the vasculature) are 'permissive', and are exerted through an enhancement of the vasoconstrictor effects of noradrenaline. The steroid does not facilitate release of catecholamines from the sympathetic nerve endings, but seems to enhance catecholamine-receptor combination. Myocardial effects of cortisol are minimal but not insignificant. It is concluded that the effects of cortisol on the blood vessels and the heart cannot account entirely for the hypertensive disorder of Cushing's syndrome. Baroreceptor and central effects of cortisol seem to be very important in acute hypertension caused by cortisol. It is suggested that cortisol alters baroreceptor function in such a way that they are 'reset' and hence tolerate elevated blood pressure without attempting to lower it. It is possible that primary resetting of the baroreceptors initiates the blood pressure elevation. It has been speculated that cardiovascular control centres may also be modified by high doses of cortisol. The renal effects of cortisol cannot account for the acute elevation of blood pressure. It has been suggested that the renal effects of cortisol may play a role in the maintenance of the chronic phase of the hypertensive disorder in Cushing's syndrome. The antagonism between cortisol and prolactin suggests that prolactin may be an important hormone in the regulation of blood pressure. It is speculated that prolactin may be the normal hypotensive hormone, whose function may be to counteract the hypertensive effects of cortisol, aldosterone, catecholamine etc. It is possible that prolactin is the hormone that modulates the actions of sympathetic nervous system on the blood vessels. Sodium balance may be important in determining vascular reactivity to both cortisol and catecholamine. This action may be important in the setting of peripheral resistance in the majority of hypertensive conditions. Elevated progesterone levels cause hypertension, probably through a release of aldosterone, and by sensitizing the cardiovascular system to adrenocortical steroids. This action of progesterone may be important in pre-eclampsia and contraceptive pill hypertensive conditions. Sensitization of the cardiovascular system to the effects of endogenous and exogenous adrenocortical steroids, and to cortisol by progesterone may be important in the causation of post-partum hypertension.