Research Paper

In a patient with tetanus we tested the hypothesis that the hyperadrenergic cardiovascular instability might be due to impairment of the baroreceptor reflex by the tetanus toxin. Baroreflex sensitivity assessed with the phenylephrine method was found to be normal. Changes in arterial pressure correlated inversely with relative changes in plasma volume but not with plasma catecholamine levels. There were both extreme hypo- and hyperadrenergic episodes. We conclude that sympathetic overactivity in tetanus temporarily overrules a functionally intact baroreflex leading to severe blood pressure instability with episodes of hypertension.

Key words: Blood pressure, Heart rate, Catecholamines

Introduction

Patients with tetanus may develop a hyperadrenergic syndrome with cardiovascular instability and episodic hypertension which has been attributed to impairment of the baroreceptor reflex by the tetanus toxin. The occurrence of hypertension has also been related to high plasma catecholamine levels found by some but not all investigators. We hypothesized earlier that the hyperadrenergic state in tetanus results in over-ruling of a functionally intact baroreflex, hypertension and reduction of the intravascular volume. Recently we had an opportunity to test this theory in a tetanus patient.

Subject and Methods

A 24-year old male heroin addict acquired tetanus from a needle-abscess and developed severe cardiovascular instability. He was sedated (lorazepam, morphine), paralysed (pancuronium) and ventilated, and treated with human tetanus immunoglobulin, penicillin and wound excision. The patient lay flat throughout the observations. During the hypertensive episodes he was not hypoxic. Since alpha-blockade was considered dangerous in the face of episodes of profound hypotension, Baclofen, a derivative of GABA with neuronal inhibitory properties, was administered intrathecally but it resulted in unconsciousness, fortunately without alleviating circulatory instability. The patient recovered after 4 weeks of artificial ventilation. This report describes the first 10 days of his stay in the intensive care unit.

Systemic arterial pressure (SAP) was monitored by a radial artery canula, pulmonary arterial pressure (PAP) by a Swan Ganz catheter which was intermittently connected to a cardiac output computer. Cardiac function was assessed by thermodilution technique (at 88, 139 and 164 h from the moment of admission) and also by echocardiography. Pulmonary and systemic arterial pressures were recorded intermittently and analysed off-line. Baroreceptor reflex sensitivity was assessed by the phenylephrine method (at 46, 67, 98 and 118 h from the moment of admission, at resting SAP levels between 152/86 and 194/100 mmHg) and was expressed by the slope of the regression line relating heart periods (RR intervals) to systolic SAP for the periods of pressure rise induced by phenylephrine. To compare the cardiovascular patterns of spontaneous and phenylephrine-induced increments in SAP, changes in beat-to-beat systemic stroke volume were computed from the arterial pressure pulse using an improved pulse contour method. Changes in cardiac output were computed as the product of heart rate (HR) and stroke volume, changes in systemic total peripheral resistance (TPR) as the ratio of mean SAP and cardiac output (expressed in arbitrary units: A.U.). Arterial plasma catecholamines were sampled from the radial artery twice daily initially, once daily later. The haematocrit (Ht) was determined on average four times daily. The relationship between changes in SAP and catecholamines was assessed by correlating noradrenaline and adrenaline plasma concentration with the corresponding hourly sampled SAP value, the relationship between changes in SAP and relative changes in plasma volume by correlating...
mean SAP values, averaging for each 6-h period, with the corresponding haematocrit values.

**Results**

**Cardiac function**: An elevated cardiac index (range 5.7–7.4 l/min/m²) at a normal total peripheral resistance index (range 370–445 dyne.s/cm²/m²) and normal left ventricular wall movement on echocardiography indicated good myocardial function.

**Beat-to-beat cardiovascular variability (Fig. 1)**: Increments in SAP evoked by phenylephrine elicited HR decrements and substantial TPR increases (Fig. 1B) irrespective of resting SAP with normal baroreceptor reflex sensitivity ranging between 7.6 and 11.6 ms/mmHg. Spontaneous shortlasting (10–60 s) rises of PAP (systolic up to 76 mmHg) and SAP (systolic up to 280 mmHg) were repeatedly observed, sometimes followed by supraventricular arrhythmias. The circulatory steady state prior to these upswings (Fig. 1A) as compared to the steady-state level before the phenylephrine test (Fig. 1B) had changed: a substantially increased heart rate, cardiac output and SAP, and a lower TPR. These pressure upswings ran parallel with, or were preceded by, a rise in HR and were accompanied by further increments in cardiac output and TPR (Fig. 1A).

**Hour-to-hour cardiovascular variability (Fig. 2)**: The SAP level was extremely variable, systolic ranging from 74 to 280 mmHg, diastolic from 34 to 150 mmHg. Hypertensive episodes were accompanied by excessive sweating and a diuresis up to 1700 ml/h (mean daily urine output 8500 ml, range 6500–12 950 ml). Mean SAP correlated well to haematocrit ($r = 0.80, p < 0.001$), but not to catecholamine level (noradrenaline range 35–3155 ng/l, $r = 0.25, p > 0.1$; adrenaline range 10–1140 ng/l; $r = 0.35, p > 0.1$) (Fig. 2).

**Discussion**

**Beat-to-beat cardiovascular variability**: The inverse relationship between the systemic blood pressure- and heart rate responses during alpha-adrenergic vasoconstriction by phenylephrine (Fig. 1B) indicates that baroreflex afferent, central and vagal efferent pathways were intact. However, the rising