

## **SIMPLE TEST COMBINATION TO LOCALIZE LESIONS OF THE AUTONOMIC PATHWAY IN HYPOTENSIVE HAEMODIALYSIS PATIENTS**

**W J Brech, P Piazzolo, H R Buerkle**

*Centre of Haemodialysis, Friedrichshafen, FRG*

### **Summary**

Chronic haemodialysis patients with volume-unresponsive hypotension were studied and compared to normotensive dialysis patients using a simple test combination and the determination of plasma catecholamines. Hypotensive patients show a defect in the afferent and efferent limb of the parasympathetic and the efferent limb of the sympathetic nervous system. Plasma catecholamines were elevated. Normotensive patients showed normal results with the exception of a small lesion in the efferent parasympathetic pathway of the baroreceptor reflex. Autonomic tests may predict patient's stability on haemodialysis treatment and contribute to rational treatment.

### **Introduction**

Severe volume-unresponsive hypotension has become one of the major problems related to long-term haemodialysis treatment in chronic uraemia. It is believed to be due to abnormalities in the autonomic nervous system [1,2]. The purpose of this study was, using a simple non-invasive test combination [3,4], to define and localize those defects in severely hypotensive patients especially in comparison to patients with stable blood pressure during haemodialysis. Baroreceptors are localized in carotoid sinuses and the aortic arch. Decreased activity during a fall in blood pressure leads to activation of the vasomotor centre. An increase in sympathetic efferent activity occurs resulting in peripheral vasoconstriction and a rise in heart rate.

Afferent parasympathetic (vagal) stimulation results in a negative chronotropic response of the heart. The overall integrity of the reflex circuit may be tested by the valsalva manoeuvre. During the straining phase heart rate rises while blood pressure decreases. After release of strain there is an overshoot of blood pressure accompanied by a decrease in heart rate. Afferent parasympathetic activity is influenced by inhalation of amyl nitrite. The efferent arch of this vagal circuit affects heart rate and may be examined by cardiographic beat-to-beat variation.

Finally, the efferent sympathetic pathway is tested by blood pressure and pulse rate rise during sustained hand grip.

## Methods and Patients

These tests have been performed in 11 patients with normal blood pressure during chronic haemodialysis treatment (Group I) and compared to 11 dialysis patients with severe volume-unresponsive hypotension (Group II). Both groups were equally matched concerning age, sex, time on chronic haemodialysis treatment (4.3 vs. 4.8 years), laboratory data including PTH (1927 vs. 1719 pg/ml), nerve conduction velocity (54.1 vs 50.9 m/sec) and underlying disease. Diabetic patients were included.

*Valsalva manoeuvre* Patients were instructed to blow against a manometric pressure of 40 mmHg for 20 seconds. Blood pressure was followed by Riva-Rocci method and heart rate monitored by cardiograph. Failure of blood pressure to rise more than 5mmHg and the heart rate to fall more than five per cent after release of strain was considered as a negative response.

*Amyl nitrite inhalation* Blood pressure and heart rate were measured before and after inhalation of 0.2 per cent amyl nitrite. Normal response was indicated by a ratio greater than 0.6 for  $\Delta HR: \Delta BP$ .

*Beat-to-beat variation* Respiratory rate interval was monitored by cardiograph for 30 minutes and the standard deviation of intervals calculated while the patient was breathing deeply at a frequency of six breaths/min. This standard deviation is age-dependant and should exceed three beats/min.

*Hand grip test* Blood pressure response to sustained isometric muscular work (handgrip) lasting three to four minutes at 30 per cent of the maximum voluntary force was measured. A rise of less than 15mmHg of diastolic pressure during handgrip is abnormal.

*Plasma catecholamines* Plasma concentrations of adrenaline, noradrenaline and dopamine were determined before and after the hand grip test. For this purpose, 5ml of blood was withdrawn by an indwelling needle which had been placed 30 minutes earlier. Blood was cooled immediately in EDTA-tubes, centrifuged and plasma deep-frozen until analysis using a radio-enzymatic assay [5].

## Results

Table I gives a summary of all autonomic tests employed in normotensive (Group I) and volume-unresponsive hypotensive patients (Group II). In Group II all results were abnormal and showed a significant difference to the results obtained in normotensive patients. In Group I there was only a minor defect in beat-to-beat testing and a normal blood pressure-overshoot-reaction in Valsalva's manoeuvre, whereas bradycardia did not occur. The plasma catecholamine concentrations before and after handgrip are listed in Table II. Catecholamines

TABLE I. Results of autonomic tests in chronic haemodialysis patients

	VM bradycardia	BP-OS	AN $\Delta$ HR: $\Delta$ BO	BB standard deviation	HG $\Delta$ BP
normal	pos	pos	$\geq 0.6$	$\geq 3$	$\geq 15$
Group I	neg	pos	$1.35 \pm 0.6$	$2.8 \pm 0.5$	$18 \pm 2.6$
Group II	neg	neg	$0.30 \pm 0.1$	$1.5 \pm 0.2$	$6 \pm 1.2$
p			$< 0.001$	$< 0.001$	$< 0.001$

VM: Valsalva's manoeuvre; AN: amylnitrate inhalation; BB: beat-to-beat variation; HG: hand grip test

TABLE II. Plasma catecholamine concentration in chronic haemodialysis patients before and after hand grip test

	normal	Group I		Group II	
		before	after	before	after
noradrenaline ng/L	$230 \pm 30$	$180 \pm 63$	$261 \pm 46$	$339 \pm 78$	$340 \pm 73$
adrenaline ng/L	$75 \pm 16$	$45 \pm 11$	$62 \pm 13$	$90 \pm 31$	$92 \pm 28$
dopamine ng/L	$49 \pm 14$	$38 \pm 7$	$41 \pm 16$	$54 \pm 11$	$45 \pm 19$

were elevated in patients with volume-unresponsive hypotension ( $p < 0.01$ ) and did not change after isometric muscular work. In normotensive haemodialysis patients, in contrast, values in the lower normal range were seen with an increase after the hand grip test.

## Discussion

There is evidence that volume-unresponsive hypotension in haemodialysis patients is due to a defect in the autonomic nervous system [1,2,6]. This is not a consequence of chronic haemodialysis treatment per se, because normotensive patients on treatment for the same period of time, showed normal test results. Catecholamine values were elevated in the plasma of hypotensive patients which indicates reduced sensitivity of end-organs to autonomic stimulation and also explains the difficulties of treatment of these patients with vasoactive substances.

The defect seems to be localized in the afferent and efferent limb of the parasympathetic and the efferent limb of the sympathetic nervous system. Normotensive patients showed only a minor insignificant lesion in the efferent parasympathetic pathway.

The simple test combination applied in this study may predict patient stability on chronic haemodialysis treatment and contribute to a rational choice of modifications in blood purification methods, such as bicarbonate haemodialysis or haemofiltration, as well as to specific pharmacological treatment [4].

## References

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