AUC of verapamil is little affected by a high protein meal a modification in dosage according to eating habits does not seem necessary.

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The effect of enalapril on baroreceptor mediated reflex function in normotensive subjects

In a recent article in the Journal, Giudicelli *et al.* (1985) reported on the influence of enalapril on baroreflexes in an attempt to explain the absence of tachycardia with blood pressure reduction, a characteristic haemodynamic feature of angiotensin converting enzyme (ACE) inhibitors. Their focus was mainly on baroreceptor reflexes, hence their article somehow obscures other possible explanations for the absence of reflex cardioacceleration including (1) a central sympatho-inhibitory action, (2) removal of the peripheral angiotensin II (AII) mediated presynaptic facilitation of noradrenaline release, (3) unchanged arterial wall tangential tension during ACE inhibition, (4) selective venodilatation or (5) parasympathetic activation. The relative merits of these propositions have been examined previously (Sturani *et al.*, 1982; Ajayi *et al.*, 1985a,b; Campbell *et al.*, 1985; Levenson *et al.*, 1985).

We would like to report on our experience with chemically diverse ACE inhibitors on baroreceptor reflex function in five separate studies. In salt replete normotensive males (24 h urine sodium 120–180 mEq) aged 18–35 years, we assessed the influence of single doses of captopril (50 mg), enalapril (10 mg), a lysine analogue of enalapril, lisinopril (10 mg), cilazapril (RO-312848) 5 mg and perindopril S-9490-3, 8 mg, on the Valsalva manoeuvre, a non-invasive test of baroreceptor reflex function (Sharpey-Shafer, 1955). The studies were of a single-blind (enalapril and lisinopril) or double-blind (captopril, perindopril, cilazapril) placebo controlled, randomised crossover design. The Valsalva manoeuvre was performed in duplicate, with on line computer analysis of R-R interval changes (Ajayi *et al.*, 1985b).

The ACE inhibitors altered neither the sym-

Table 1 The influence of angiotensin converting enzyme inhibitors on the Valsalva manoeuvre in normotensive subjects

	n	Maximum tachycardia II (ms)	Maximum bradycardia IV (ms)	Valsalva ratio	Systolic BP overshoot (mmHg)	P
Captopril	8	710 ± 150	1210 ± 100	1.87 ± 0.35	8.0 ± 6.7	NS
Placebo	8	660 ± 150	1290 ± 160	1.99 ± 0.42	8.9 ± 10.8	
Enalapril	10	580 ± 80	1130 ± 140	1.95 ± 0.32	16.3 ± 14.2	NS
Placebo	10	620 ± 90	1160 ± 160	1.92 ± 0.26	16.8 ± 17.6	
Lisinopril	10	620 ± 160	1250 ± 270	2.02 ± 0.29	8.8 ± 10.7	NS
Placebo	10	620 ± 170	1150 ± 260	1.86 ± 0.37	10.8 ± 8.4	
Perindopril (S-9490-3)	10	610 ± 90	1210 ± 180	2.01 ± 0.38	1.0 ± 7.8	NS
Placebo	10	630 ± 90	1280 ± 210	2.06 ± 0.34	5.2 ± 8.0	
Cilazapril (RO-31-2848)	10	700 ± 130	1300 ± 110	1.92 ± 0.45	5.4 ± 8.6	NS
Placebo	10	740 ± 140	1340 ± 100	1.87 ± 0.38	7.3 ± 9.4	

NS not significant.

pathetically mediated pressure overshoot nor the chronotropic responses during the manoeuvre, indicating an absence of a functionally significant impairment of baroreceptor reflex function (Table 1). Similar results were obtained in elderly normotensives receiving enalapril (10 mg) and with the angiotensin II antagonist, saralasin, in normotensive males.

Further, in 12 patients with essential hypertension, the pressor, chronotropic and nor-adrenaline response to postural stress (1 min standing) an index of baroreceptor integrity was unaltered by a single 20 mg dose of cilazapril (RO-312848).

Thus our results with chemically distinct ACE inhibitors, in salt replete normotensives in the elderly, and in essential hypertensives do not

support a functionally significant modification of baroreceptor reflex function.

The cardio-acceleration which accompanies arteriolar dilatation results largely from reflex withdrawal of vagal tone (Man in't Veld *et al.*, 1980). The release of vagal pathways from angiotensin II mediated inhibition, both centrally and peripherally may well enhance cardiac parasympathetic tone, thus blunting the reflex tachycardia (Sturani *et al.*, 1982; Ajayi *et al.*, 1985a,b; Campbell *et al.*, 1985).

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