β -ADRENOCEPTOR BLOCKING DRUGS AND DIURETICS IN HYPERTENSION

We have read with considerable interest the paper by Neuvonen, Pentikainen & Jounela (1978) entitled 'Effect of diuretic, β -adrenoceptor blocking agent and their combination on elevated blood pressure and serum potassium: a cross-over study'.

We should like to make two points which arise from the discussion section. Dr Neuvonen and his colleagues mention that for treatment with propranolol plus a thiazide diuretic, the reduction in diastolic blood pressure was less than the sum of the effect when both drugs were used alone. The authors cite some unpublished preliminary data quoted in a review by Conway (1975). When this study was completed in 19 patients, there were no differences between the effects of simultaneous treatment with propranolol and bendrofluazide, and summation of the effects of treatment with the individual drugs (Turner & Lishman, unpublished observations). The final results are shown in Table 1.

More recently we have obtained data (Table 2) in 101 hypertensive patients in six separate double-blind, randomised clinical trials with propranolol (80 mg twice daily) and bendrofluazide (2.5 mg twice daily) administered separately and in combination ('Inderetic'). There was no significant difference ($P > 0.05$ by paired *t*-test) between the sum of the falls in systolic or diastolic blood pressure responses to propranolol and bendrofluazide alone and the effect of 'Inderetic' (George, Agrawal, Alliot, Gomez, Lishman, Turner, Trafford & Baber, 1978). However, the percentage of patients responding to such drugs alone or in combination is known to vary according to the patients' age and renin status (Buhler, Bertel & Lutold, 1978).

The second point relates to patients who fail to respond well to either propranolol or bendrofluazide or both drugs when given alone. Such patients often respond adequately when both drugs are given

Table 1 Blood pressure in 19 hypertensive patients receiving propranolol alone (360 mg/day), bendrofluazide alone (15 mg/day) or both drugs together

		Treatment sequence				
	Control 1	Propranolol alone (4 weeks)	Propranolol + diuretic (2 weeks)	Control 4 (2 weeks)	Diuretic alone (2 weeks)	Diuretic + propranolol (4 weeks)
Systolic (mmHg)	199.4	171.5	158.8	190.0	174.5	149.4
Diastolic (mmHg)	120.1	97.8	92.6	114.2	107.6	90.4
				Change from control		
Systolic (mmHg)		−27.9	−40.6		−16.4	−41.5
Diastolic (mmHg)		−22.3	−27.5		−6.6	−23.8

The sum of the effects of propranolol alone and bendrofluazide alone (-44.3/-28.9 mmHg) is clearly similar to the results of combined treatment.

Table 2 Mean blood pressure in 101 patients treated with propranolol (80 mg twice daily), bendrofluazide (2.5 mg twice daily) or a combination of both drugs

	Control	Propranolol alone	Bendrofluazide alone	'Inderetic'
Systolic (mmHg)	178.9	157.8	157.4	144.6
Diastolic (mmHg)	109.0	97.2	98.3	90.4
<i>Change in blood pressure</i>				
Systolic (mmHg)		-21.1	-21.5	-34.3
Diastolic (mmHg)		-11.8	-10.7	-18.6

Figure 1 Change in resting diastolic blood pressure in six patients in response to a) propranolol alone (160 mg/day), b) bendrofluazide alone (5 mg/day) and c) to a combination of propranolol and bendrofluazide (160 mg and 5 mg/day, respectively).

concurrently (Figure 1). For example, the six patients identified as non-responders to both drugs when given alone (mean response to bendrofluazide alone and propranolol alone: -0.5 mmHg, and -0.6 mmHg, respectively) responded well to the combined treatment with a reduction in sitting diastolic blood pressure of 19.3 ± 2.8 mmHg (mean $\pm$ s.e. mean). In these patients the β -adrenoceptor blocker may be preventing the rise in renin which accompanies diuretic treatment and which may offset any potential hypotensive effect.

It would seem that there may be a sub-group of patients in whom the presence of either a β -

adrenoceptor blocking agent or a diuretic alters the response to the introduction of the other drug. This could be important when considering when to use a combination of a β -adrenoceptor blocker and a diuretic in contrast to either drug alone.

N. S. BABER & P. M. DAWES

Medical Department, ICI Pharmaceuticals, Mereside, Alderley Park, Macclesfield, Cheshire

Received December 27, 1978

References

- BUHLER, F.R., BERTEL, O. & LUTOLD, B.P. (1978). Simplified and age stratified antihypertensive therapy based on beta blockers. *Cardiovascular Med.*, **3**, 135–148.
- CONWAY, J. (1975). Beta adrenergic blockade and hypertension. In *Modern Trends in Cardiology*, Ed Oliver, M.F., **3**, 376–403.
- GEORGE, M., AGRAWAL, R., ALLIOTT, R., GOMEZ, G., LISHMAN, J., TURNER, J., TRAFFORD, A. & BABER, N. (1978). Propranolol and bendrofluazide in the treatment of hypertension: a study in six centres. *Proc. 8th World Congress of Cardiology, Abst. 1088*.
- NEUVONEN, P.J., PENTIKAINEN, P.J. & JOUNELA, A.J. (1978). Effect of diuretic, β -adrenoceptor blocking agent and their combination on elevated blood pressure and serum potassium: A cross-over study. *Br. J. clin. Pharmac.*, **6**, 363–367.

INEFFICIENCY OF HAEMODIALYSIS IN ACUTE PHENYTOIN INTOXICATION

In the last ten years, controversial reports have appeared regarding the efficiency of dialysis in acute phenytoin poisoning.

On theoretical grounds, ineffective dialysis of

phenytoin was expected due to the high (90%) binding of the drug to serum protein albumin (Reidenberg, Odar Cederlof, von Bahr, Borga & Sjoqvist, 1971). On the other hand, clinical recovery was reported