HYPERTENSION TREATED WITH ACEBUTOLOL

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SYNOPSIS

Acebutolol in an open clinical trial of 22 patients with essential hypertension was found to be effective in lowering mean BP (lying) of 190/113 to 144/87, using a mean dose of 223 mg/day. There was no postural hypotension and side effects including bronchospasm were minimal. Patient tolerance and compliance was good. Acebutolol was found in this study to be an effective, safe and well tolerated beta-adrenergic blocking agent.

INTRODUCTION

The use of beta-adrenergic blocking drugs has added a new dimension in the treatment of hypertension. They may be used alone, combined with a diuretic, and also in various combinations with other hypotensive agents. The main advantages of beta blocking drugs are the low degree of side effects and they do not cause postural hypotension.

There are now a large number of beta blocking drugs available. Chemically they have certain structural elements in common but vary in their potency and biological effects. In general, there is little difference in the various beta adrenergic blocking drugs in the treatment of hypertension, but in some patients one or the other may have advantages and better tolerated.

This open clinical study was conducted to establish the efficacy and patient tolerance of a newly introduced beta-blocker, Acebutolol (Sectral, M&B 17803A) which is cardioselective like practolol, has membrane stabilising effect like propanolol and also a weak sympathomimetic action. There is a small effect on peripheral vascular dynamics, and the drug produces a fall in arterial pressure and limb blood flow. There is little or no effect on the bronchial beta$_2$ receptors.

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MATERIAL AND METHODS

The study consisted of twenty-two ambulatory hypertensive patients seen by the author over a period of 3 to 24 months. Patients with three separate blood pressure recordings greater than 150/90 mm Hg taken after 10 minutes rest were admitted to the study. All previous hypotensive agents were terminated for at least one week prior to entering the study and unless unavoidable, only a single drug Acebutolol was used.

Patients were prescribed Acebutolol 100 mg twice daily to start with and the response followed at weekly intervals initially and then monthly, increasing the dosage when necessary. The BP and pulse were taken in the lying and standing positions and questions asked for the presence of any side effects. E.C.G. and urine analysis were performed in all patients and blood chemistry was also performed in most others. Patients with heart block, cardiac failure, were excluded but not those with a history of bronchitis or obstructive airways disease to see if bronchial asthma was provoked necessitating termination of the drug.

RESULTS

Twenty-two patients of Chinese origin with essential hypertension were admitted to this study. The Male/Female proportion was 4 to 18, the age range 34 to 70 years, and the mean age 59 years.

The period of observation ranged from 3 months to 2 years for a total of 236 patient-months.

Total dosage of Acebutolol used ranged from 100 mg to 600 mg daily, the mean dose used being 223 mg/day. In only two patients was an additional hypotensive used by way of a thiazide diuretic. 11 out of the 22 patients had never been treated with hypotensive agents previously.

Patients were divided into 3 groups according to the severity of blood pressure (Table 1). In both the mild (diastolic 110 mm Hg and below), and moderate (diastolic 119 mm Hg and below) hypertensive, there was a satisfactory fall in BP at the end of treatment to below 150/100. In the severe group (diastolic over 120 mm Hg), 7 out of 9 responded. The success rate achieved was 91% in this series. The patients that did not respond despite a dose of 600 mg Acebutolol per day required addition of multiple combination drug therapy.

There was no observed difference in the lying and standing BP and pulse during the trial.

The mean lying BP prior to therapy was 190/113,

TABLE 1: Severity of hypertension and response to Acebutolol

SEVERITY	MILD	MODERATE	SEVERE	TOTAL
Diastolic B.P.	Below 110	110-119	Over 120	
Total	6	7	9	22
Satisfactory Response	6	7	7	20

TABLE 2: Progressive response of B.P. to Acebutolol

Lying B.P.	0	1 Week	4 Week	8 Week	12 Week
Mean Systolic	190	157	153	151	144
Mean Diastolic	113	97	95	91	87
Pulse	84	73	72	68	65

and pulse 84/min (Table 2). Within one week there was a substantial fall to a mean of 157/97 and pulse fell to 73/min (Fig. 1). There is a progressive but gradual fall in BP and pulse at subsequent weeks until at 12 weeks the mean BP achieved was 144/87 at a mean pulse rate of 65/minute.

SIDE EFFECTS

In one patient the drug had to be discontinued because of abdominal discomfort which was attributed to the drug (Table 3). There was no complication of heart block or cardiac failure.

Although patients with frank bronchial asthma were excluded, four patients were included who had previous history of bronchitis and bronchospasm. Two of the four had been changed over from propanolol because of persistent cough and wheezing. All four patients were able to tolerate Acebutolol with no frank asthma attacks.

There was no complication of drowsiness, giddiness, sexual dysfunction, or nightmares as reported with certain beta-blockers, and in fact there was a remarkable lack of complaints even on direct questioning for specific side effects. Nine out of the twenty-two patients gained over 2 Kg. in weight without evidence of salt retention or cardiac failure. Two patients lost weight while the remaining eleven patients showed no weight change.

Patient compliance was very satisfactory throughout the trial and no problem encountered in continuing medication after the initial three months observation. No long term side effects were detected in the patients who had completed 2 years continuous therapy and still on the drug.

Co-existing angina pectoris in two patients and non specific chest pain in four others were substantially improved in the series (Table 3). Five of the

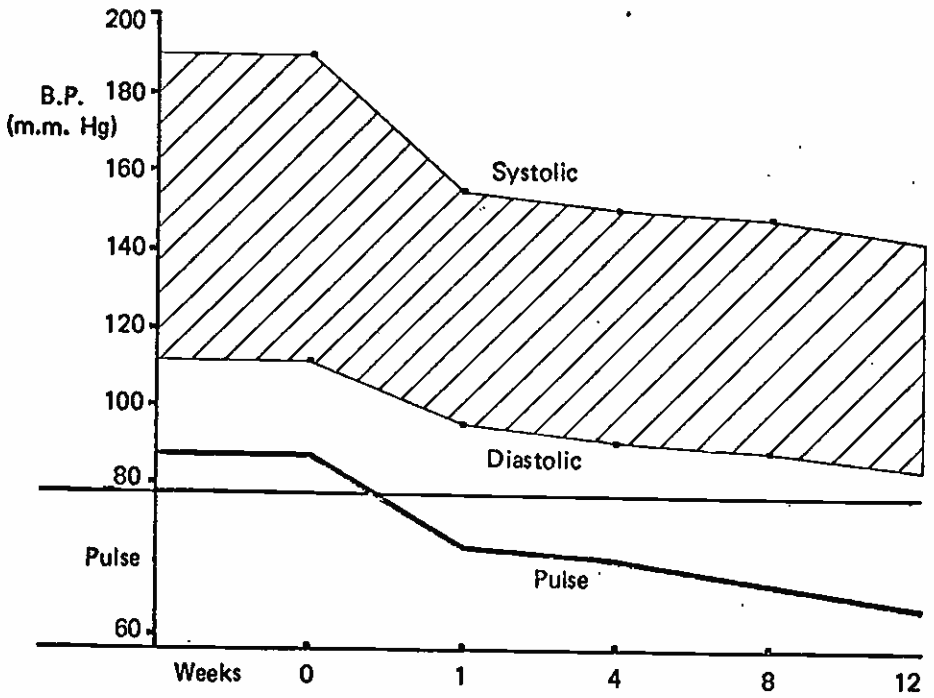

Fig. 1 Progressive Pulse & B.P. (lying) response to Acebutolol

TABLE 3: Record of favourable & unfavourable side effects

	Unfavourable Side Effects	
	Mild	Moderate/Severe
Drowsiness	2	0
Depression	0	0
Nightmares	0	0
Gastro-intest. effects	0	1
Skin Rashes	0	0
Bronchospasm	2	0
Sexual dysfunction	0	0
Others	2	0
	Favourable Side Effects	
Reduction of Chest Pain, Angina	6	
Relief of palpitations, extrasystoles	5	

patients had symptoms of palpitations with ECG evidence of intermittent atrial and ventricular extrasystoles and in all there was relief in symptoms substantiated by improvement in ECG taken during the course of treatment.

Seven patients who were continued on therapy after blood pressure had been well stablised, were switched over from twice daily dosage to a single daily dose. The BP remained satisfactorily controlled comparable to when twice daily dose was used.

DISCUSSION

There have been several studies in Caucasian patients on the effect of Acebutolol on Hypertensive patients. Lucsko et al (1975) found 74% of their patients had good or moderate hypotensive result and and the drug was well tolerated. Letac et al (1974) achieved good response in 20 out of their 24 patients with a mean effective does of 540 mg/day. Another feature of their study was the excellent tolerance to the drug throughout the trial. In the UK, similar favourable reports were achieved in two separate multi-centre trials (Ashton 1976); The General Practitioner Research Group (1976)).

Results in the present study on Chinese subjects are in accord with the European studies. Main differences are the lower mean doses of Acebutolol required to achieve control (223 mg/day) in spite of it being the sole hypotensive agent in nearly all cases. The author's observations have noted a lower dosage requirement of other beta blockers in hypertensive Asian which may be partly explained on the basis of lower average body weight.

The high success rate in reaching normotensive levels in the study could be partly explained by the fact that half of the patients had never been on hypotensive treatment before and there was only one "non-responder" in the group. Hypotensive action was gradual and smooth, with satisfactory response in one week and further progressive lowering in the following 3 months.

The minimal incidence of side effects resulted in good patient compliance in the trial. There was no postural hypotension, and troublesome central nervous system effects such as drowsiness, depression and nightmares were not seen as reported with some beta-blockers.

Because of its cardioselective property, Acebutolol was tolerated in four patients even with a past history of bronchospasm but care has to be taken to follow the response carefully and avoid its use in frank asthmatics as any beta blocker can induce serious asthma (Skinner et al, 1975; Leary et al, 1973).

The plasma half-life of Acebutolol is 1.8 hours after peak plasma levels are attained but the pharmacological half-life is more prolonged (10-12 hours). Cuthbert and Collins, (1975) and preliminary observations of seven patients in this series have suggested that once daily doses may be adequate in certain instances. Studies are being conducted to look into this further.

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REFERENCES

1. Ashton W.L: An open multicentre study of Acebutolol in hypertension. Curr. med. Res. Opin., 4: 442, 1976.
2. Cuthbert M.F., Collins R.F: Br. J. Clin. Pharmacol. 2: 49, 1975
3. General Practitioner Research Group. A new beta-adrenergic blocking drug in hypertension. Practitioner, 216: 218, 1976.
4. Leary W.P., Coleman A.J., Asmal A.C: Respiratory effects of Acebutolol hydrochloride. S. Afr. med. J., 47: 1245, 1973.
5. Letac B., Fillastre J.P., and Wolf L.M: The treatment of essential hypertension. A clinical study. Nouvelle Presse Medicale, 4: 3287, 1975.
6. Lucsko M., Chaignon M. and Guedon J: Acebutolol in the treatment of essential hypertension. A clinical study. Nouvelle Presse Medicale, 4: 3287, 1975.
7. Skinner G., Palmer K.N.V., Kerridge D.F: Comparision of the effects of Acebutolol (Sectral) and Practolol (Eraldin) on airways obstruction in asthmatics. Br. J. clin. Pharmac. 2: 417, 1975.