β-ADRENOCEPTOR BLOCKADE AND THE INCIDENCE OF MYOCARDIAL INFARCTION DURING TREATMENT OF SEVERE HYPERTENSION

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Introduction

In earlier studies upon 169 severe, uncomplicated, essential hypertensives followed under treatment for a mean 6.25 years I found that in the patients whose treatment included propranolol (P group) the rate of first myocardial infarction was less than one third ($P < 0.01$) of that in similar patients on hypotensive therapy that excluded β-adrenoceptor blockade (NBB group) (Stewart, 1976). I took this to imply that propranolol had 'prevented more or caused fewer infarctions'. Further observations on these patients showed that the relative risk of infarction in those whose final observed diastolic pressures, as last

Table 1 Relative risks of myocardial infarction according to FDP

FDP (mm Hg)	Number of patients	Number of infarcts	Relative risk	P
<90	18	7	5.4	<0.01
90-99	39	4	1.4	NS
100-109	42	3	1.0	—
110-119	55	13	3.3	<0.1
120+	15	2	1.9	NS

Figure 1 Comparison of matched pairs of patients (■ those with infarct, □ without infarct) whose final diastolic pressure (FDP) was in the range 80-85 mm Hg with those whose FDP was 100-109 mm Hg.

recorded before infarction or its avoidance (FDPs), had been in the range of 80–85 mm Hg (Phase IV) was more than five-fold greater than that after reduction into FDP range 100–109 mm Hg, the 'optimal' level for infarction avoidance whatever the drug treatment (Table 1, Figure 1) (Stewart, 1979).

The findings now reported are concerned with the sites of the infarctions in these same patients and the integration of this information with the earlier observations on choice of drug (P or NBB) and extent of induced pressure fall. So far as I can discover no published account has sought to assess the changing interrelationships between these three factors and their influence upon the rate of myocardial infarction in hypertensives.

Methods

The three factors were compared singly, and in combinations with each other, in terms of their effects upon the infarction rate.

Acute myocardial infarction, including sudden cardiac death within 2 days, was accepted on the strength of clinical, electrocardiographic and enzyme findings. The sites were indicated by electrocardiograms, anterior infarction by tracings that showed changes indicative of anterior (including antero-lateral and antero-septal) myocardial damage and inferior infarction by appropriate changes in leads II, III and AVF. Pathological Q waves were present in all but five of the infarction tracings. Of these, two were accepted on other electrocardiographic appearances suggestive of infarction together with positive clinical indications and significantly raised enzyme levels. Also included were three patients, long known

to have had severe ischaemic heart disease, who had died suddenly without electrocardiogram or autopsy findings.

Results

After reduction to $\text{FDP} \leq 105$ mm Hg the rate of infarction in the P group was still about one third of that in the NBB group (Figure 2). After further reduction to < 95 mm Hg it approached that of the NBB group (Figure 3).

There were 29 first infarctions, 25 of them site-known. Of these 13, with a mean FDP before infarction of 103 mm Hg, were found in the 57 patients of the NBB group (Figure 4). All were anterior, with a wide spread of FDP ($7 \geq 110$ and $4 \leq 85$ mm Hg). Among the 122 patients of the P group there were 12 infarctions, with a mean FDP of 99 mm Hg. Of these, 7 were anterior and 5 inferior. The mean FDP before the 7 anterior infarctions had been 104 mm Hg (115, 90, 110, 85, 112, 100, 115). Before the 5 inferior infarctions it was 92 mm Hg (80, 100, 85, 80, 115). Thus, of the 25 infarctions, 5 were inferior and all had occurred during severe pressure reduction under β -adrenoceptor blockade with propranolol.

Discussion

My earlier findings had suggested that hypotensive treatment with propranolol, unlike that without β -adrenoceptor blockade, was capable of conferring a measure of cardioprotection upon hypertensives that exceeded that of simple pressure reduction. Further observations then indicated that, in the presence of

Figure 2 % incidence of myocardial infarction (MI) to form of treatment and extent of pressure fall. P propranolol treatment, NBB non β -adrenoceptor blockade treatment.

Figure 3 % incidence of myocardial infarction (MI) to form of treatment and extent of pressure fall. P propranolol treatment, NBB non β -adrenoceptor blockade treatment.

Figure 4 Scheme showing number of patients in the two groups (P propranolol treatment, NBB non β -adrenoceptor blockade treatment) and the sites of infarction.

infarctions the incidence on propranolol was increased to 12/112 (10.7%). All of the 5 inferior infarctions had occurred during severe reduction under treatment with propranolol, perhaps for the reason that β -adrenoceptor blockade had imposed bradycardia and increased hypotension upon the effects of parasympathetic over-activity generated by incipient infarction itself.

Conclusion

It is concluded that β -adrenoceptor blockade, in the form of propranolol, confers considerable protection against myocardial infarction in hypertensives as compared with that from treatment without β -adrenoceptor blockade, only to lose much of this advantage largely, perhaps, through inferior infarction, if the pressure be reduced to 'normality'. Despite numbers too small for statistical significance the findings suggest an occasional causal relationship between β -adrenoceptor blockade, excess pressure reduction and inferior infarction. The implication is that less severe pressure reduction to 'optimum' levels well above 'normality', should enhance the cardioprotection already provided by β -adrenoceptor blockade against anterior infarction and should probably protect against inferior infarction as well.

References

STEWART, I.McD.G. (1976). Compared incidence of first myocardial infarction in hypertensive patients under treatment containing propranolol or excluding beta receptor blockade. *Clin. Sci. mol. Med.*, **51**, 509–511S.

STEWART, I.McD.G. (1979). Relation of reduction in pressure to first myocardial infarction in patients receiving treatment for severe hypertension. *Lancet*, **i**, 861–865.