The effects of propranolol and metoprolol on skin blood flow in diabetic patients

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The effect of 2 weeks treatment with propranolol or metoprolol on skin blood flow (SBF) at rest was examined in 12 diabetic patients with essential hypertension in whom gross large vessel disease had been excluded. Neither drug significantly altered resting skin blood flow. However we cannot exclude an important difference between the two β -adrenoceptor blockers because of the great variability of SBF within subjects. A larger study and/or more accurate methods of measuring SBF are needed to determine if β_1 -selective adrenoceptor antagonists differ from non-selective β -adrenoceptor blockers with respect to skin blood flow.

Keywords β -adrenoceptor blocker skin blood flow diabetes xenon clearance

Introduction

Functional changes in skin blood flow can be detected in diabetes before clinical signs of vascular disease are apparent (Ajjam *et al.*, 1985). Non-selective β -adrenoceptor blocking drugs may reduce skin blood flow (McSorley & Warren, 1978) and hence may be hazardous in diabetic patients.

We compared the effect of propranolol (non-selective) and metoprolol (β_1 -selective) on resting skin blood flow in an observer-blind cross-over study. We studied diabetics with coexisting hypertension for whom a β -adrenoceptor blocker would be suitable treatment.

Methods

Fourteen patients (seven males, seven females; aged 34–65 years; all non-smokers) with diabetes (duration: 7 months–30 years) and hypertension (duration: 3 months–20 years) were studied. Diabetic complications present included retinopathy (6) and peripheral neuropathy (4). All patients showed standing-induced tachycardia.

Patients with clinically apparent vascular disease, those for whom β -adrenoceptor blockers would be contra-indicated, and any with Doppler flow evidence of more than 50% stenosis or a major leg vessel were excluded.

Patients were studied initially and then again 2 weeks after random allocation to receive either oral slow-release propranolol (160 mg) or oral slow-release metoprolol (200 mg) once daily. They were then crossed over for a further 2 weeks and the measurements were repeated.

Skin blood flow was measured on the lateral aspect of the leg using the clearance of ^{133}Xe (Hyer *et al.*, 1985). The ambient and skin temperatures were recorded during each measurement. Twelve patients completed the study. Two patients completed only 2 weeks treatment with metoprolol and were not included in the analysis. Skin blood flow before and after treatment with metoprolol and propranolol was calculated for each leg and the results were compared using a method appropriate for a two-period cross-over design (Hills & Armitage, 1979).

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Table 1 Skin blood flow (ml 100 g⁻¹ min⁻¹) at entry and after 2 weeks of treatment with propranolol or metoprolol

Patient	Entry	Right leg		Entry	Left leg	
		Propranolol	Metoprolol		Propranolol	Metoprolol
1	6.4	6.0	5.8	10.5	7.1	6.8
2	5.3	6.7	9.5	6.8	6.8	9.2
3	5.3	6.3	6.1	6.4	5.4	6.2
4	7.9	9.5	6.7	5.3	11.0	6.0
5	4.3	8.0	4.5	5.4	5.9	5.0
6	3.7	6.0	6.9	5.9	7.6	5.5
7	6.1	4.3	7.0	6.0	2.7	7.9
8	6.6	11.4	6.7	8.1	10.3	5.9
9	6.7	8.3	4.1	6.1	7.7	4.3
10	5.3	3.7	4.7	6.9	3.9	3.6
11	6.5	4.4	8.4	7.8	5.4	9.3
12	5.7	5.0	4.3	5.0	13.7	6.8
Mean	5.8	6.6	6.2	6.7	7.3	6.4
s.d.	1.1	2.3	1.7	1.5	3.1	1.8

Results

The results of skin blood flow (SBF) are shown in Table 1. They showed no significant carryover effect or treatment-phase interaction. Skin blood flow did not differ significantly when patients received propranolol or metoprolol. When compared with propranolol treatment, metoprolol decreased skin blood flow by a mean of 6% in the right leg and 12% in the left leg. However the 95% confidence intervals for the differences between the two β -adrenoceptor antagonists were wide. Compared with propranolol, metoprolol could decrease skin blood flow by as much as 31% (right leg) or 45% (left leg), or could increase skin blood flow by as much as 19% (right leg) or 18% (left leg).

When SBF measurements were corrected to 20° C by reference to a curve of ambient temperature vs skin perfusion (Daley & Henry, 1980) the findings were similar.

Discussion

We measured dermal blood flow at rest under conditions of relatively low sympathetic stimulation, and changes in skin blood flow may have become apparent if the patients had been exer-

cised. Some of our patients may have had sympathetic impairment so that β -adrenoceptor blockade could not influence dermal blood flow. The sympathetic nervous system may be more susceptible to impairment in diabetic patients (Watkins & Edmonds, 1983).

Other studies (White & Udwadia, 1975; Robinson & Wilson, 1968; McSorley & Warren, 1978) have shown reductions in skin blood flow with propranolol, but not with β_1 -selective adrenoceptor blockers, but these did not include diabetics. Peripheral gangrene has been reported as a complication of metoprolol treatment (Vale & Jeffreys, 1978), and Sheriff *et al.* (1978) found that cold hands were more common in patients taking β_1 -selective adrenoceptor blockers than placebo.

We have found no significant advantage for β_1 -selective adrenoceptor blocker with respect to resting skin blood flow in diabetics without overt peripheral vascular disease. However SBF measurements showed great variability within subjects and an important difference between the two β -adrenoceptor blockers cannot be excluded. Further studies with a larger number of patients or a more reproducible method of skin blood flow measurement are needed to assess the true effect of these drugs in diabetics.

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