

## Short reports

### Transfer factor for carbon monoxide in patients with diabetes with and without microangiopathy

DC WEIR, PE JENNINGS, MS HENDY, AH BARNETT, P SHERWOOD BURGE

From the Departments of Thoracic Medicine and Diabetes, East Birmingham Hospital, Birmingham

**ABSTRACT** The transfer coefficient (KCO) was significantly lower in diabetic patients with microangiopathy than in a matched group without this complication. This may reflect microangiopathy in the pulmonary circulation.

Diabetic microangiopathy is a generalised abnormality of small blood vessels characterised by thickening of the capillary basal lamina. Postmortem studies have shown similar changes in the lungs of patients with diabetes, and its presence is associated with evidence of microangiopathy in other organs.<sup>1</sup>

Previous studies of lung function in patients with diabetes have found various abnormalities, including reduced gas transfer,<sup>2,3</sup> decreased elasticity,<sup>4</sup> and airflow obstruction.<sup>5</sup> The cause of these abnormalities is not clear. It has been suggested that the changes in elasticity and gas transfer are due in part to microangiopathy in the lungs, but they have not been shown to be associated with diabetic complications elsewhere.<sup>2</sup> We have re-examined the relation between gas transfer and microangiopathic complications in patients with diabetes mellitus.

#### Methods

Nine subjects (six male) with diabetes with either proliferative retinopathy (eight) or maculopathy (one) were matched for age, sex, height, and smoking history with nine diabetic patients without these features. None of them currently smoked or had clinical evidence of unrelated cardiorespiratory disease, and none was taking drugs known to have effects on the lungs. All patients gave written informed consent after the purpose of the study had been explained.

Spirometry was performed with a dry wedge spirometer (Vitalograph), and lung volumes were determined by a closed circuit helium dilution technique. The mean of three technically satisfactory measurements of single breath carbon monoxide gas transfer (TLCO; Morgan Transfertest machine, model C) was used in the analysis. The transfer coefficient (KCO—TLCO corrected for alveolar volume (V<sub>A</sub>)) was calculated. All patients answered the standard Medical Research Council questionnaire on respiratory symptoms and had blood samples taken for estimation of haemoglobin

Address for reprint requests: Dr D C Weir, Department of Thoracic Medicine, East Birmingham Hospital, Birmingham B9 5ST.

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Table 1 Characteristics of the two groups (mean (SD) unless otherwise specified)

	No microangiopathy (n = 9)	With microangiopathy (n = 9)
Age (y)	55 (12.6)	54 (12.8)
Duration of diabetes (y)	8.3 (4.2)	13.4 (10.4)
Insulin dependent (n)	5	6
Haemoglobin (g/dl)	13.9 (1.5)	14.4 (1.2)
Haemoglobin A <sub>1c</sub> (%)	9.3 (2.0)	10.7 (3.9)
Albuminuria (n)	0*	5*
Creatinine (μmol/l)	84 (32)	94 (18)
Lifelong non-smokers (n)	5	6
Cigarette consumption (pack years)	11.1 (14.4)	5 (10.8)
Serum thiocyanate (μmol/l)	42 (14)	46 (14)

\*p < 0.05.

and glycosylated haemoglobin concentration, and serum urea, creatinine, and thiocyanate concentrations.

TLCO measurements were corrected to a standard haemoglobin concentration (14.6 g/dl) and all lung function results were expressed as percentages of the predicted values, derived from the predictive equations of the European Community for Coal and Steel.<sup>6</sup>

The two groups were compared by the unpaired Student's *t* test and by the Wilcoxon rank sum test for variables not normally distributed.

#### Results

Details of the two groups are given in tables 1 and 2. The group with complications had a longer duration of diabetes than those free of complications; but diabetic control, as judged by glycosylated haemoglobin concentrations, was similar in the two groups. More of the patients without

Table 2 Mean (SD) lung function values (% predicted, mean (SD), unless otherwise specified)

	No microangiopathy (n = 9)	With microangiopathy (n = 9)
FEV <sub>1</sub>	107.3 (12.1)	104.5 (9.2)
Forced vital capacity	109.3 (12.4)	109.9 (12.5)
Total lung capacity	94.7 (6.4)	98.4 (9.5)†
Carbon monoxide transfer	111.7 (10.2)	103.9 (15.5)
Transfer coefficient	91.4 (10.6)*	81.0 (12.8)*
Alveolar volume (l)	5.82 (1.23)	6.27 (1.42)

\*p < 0.05.

†Two patients were unable to perform this test.

complications were ex-smokers, and the past cigarette consumption in this group was double that in the group with complications. All serum thiocyanate concentrations were within the normal laboratory non-smoking range. Serum creatinine concentrations were similar in the two groups.

The transfer coefficient (KCO) was significantly lower in the diabetic patients with complications than in those free of complications ( $p < 0.05$ ). There was no significant difference between the groups in any other lung function measurement; although TLCO measurements followed the same trend, the difference between the two groups failed to reach significance ( $0.1 < p < 0.05$ ) (table 1).

### Discussion

The transfer coefficient depends on the pulmonary capillary blood volume, the matching of ventilation and perfusion, the efficiency of the alveolar capillary membrane, and the "available" haemoglobin; it is independent of lung volume. Our results were corrected for haemoglobin. The lower values of KCO in the group with complications are likely to be accounted for by pulmonary microangiopathy, which could affect the other factors that determine KCO. Cigarette smoking is known to reduce KCO, but the subjects without complications had smoked more than those with complications. We found no correlation between the duration of diabetes and the KCO ( $r = 0.19$ ,  $p > 0.05$ ), suggesting that it was the microangiopathy rather than the diabetes itself that was the cause of the difference.

The patients with complications had evidence of diabetic microangiopathy in the retina and five had proteinuria. A postmortem study<sup>1</sup> showed a correlation between thickening of the basal lamina in the alveoli and that in other tissues, suggesting that these patients may have similar pathological changes in their lungs.

Our results are supported by a poorly controlled previous

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study,<sup>5</sup> but they contradict the findings of Sandler *et al.*<sup>2</sup> who included patients with less severe microvascular disease and considered only patients with KCO values outside the normal reference range. By directly comparing patients who had no clinical evidence of diabetic complications with patients who had fairly severe complications we have shown that systemic complications are associated with reduced carbon monoxide gas transfer, probably due to microangiopathy in the pulmonary circulation.

Systolic hypertension appears to be an important susceptibility factor for microangiopathy.<sup>7</sup> Our study, however, suggests that diabetic microangiopathy may affect the pulmonary circulation, a low pressure system.

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