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DIFFUSING CAPACITY IN ACUTE UNTREATED TROPICAL EOSINOPHILIA

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Single breath carbon monoxide diffusing capacity (TLCO) measurements were made in 50 acute untreated tropical eosinophilia (TE) patients. Forty-four (38%) patients had a low diffusing capacity (< 85% predicted) which was moderately severe (40-70% predicted) in 22 (44%) patients. Diffusion per lire of alveolar volume (KCO) was reduced (< 85% predicted) in 28 (56%) patients. The effective alveolar volume (VA) was reduced (< 85% predicted) in 30 (60%) patients and there. was highly signfiicant positive correlation between VA and TLCO (r=0.847, P<0.001). The reduction in TLCO, therefore, in our patients may be due to a combination of reduction in the area of membrane available for diffusion and to the involvement of pulmonary capillaries, as evidenced by low VA and KCO. The reduction in TLCO in acute TE patients may be due to acute inflammatory changes produced in the lung parenchyma by eosinophils. However, there was no correlation between peripheral blood eosinophils and diffusing capacity. Further studies are required to clarify whether locally accumulated eosinophils in the lung have any relationship with diffusing capacity.

Tropical eosinophilia (TE) is a systemic disorder involving many organs and tissues in which the pulmonary manifestations are predominent[1]. The latter are characterised by cough, dyspnoea, nocturnal wheezing and diffuse reticulonodular infiltrates on chest radiographs, and pulmonary function tests show a combination of obstructive and restrictive ventilatory defect[2-10]. There is associated with marked peripheral blood eosinophilia and elevated serum concentrations of filarial specific antibodies[4]. The histopathological observation of dense accumulation of eosinophils in the interstitial tissue; which had shown considerable thickening, suggested that there was a likelihood of diminished diffusing capacity or transfer factor in tropical eosinophilia[2]. A decrease in diffusing capacity by steady state end tidal sampling method was reported by Poh[11]. Because of rarity of published reports of studies on transfer factor for carbon monoxide (TLCO) in TE, we report our findings of single breath carbon monoxide diffusing capacity in acute tropical eosinophilia.

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As eosinophils are known to injure normal lung parenchymal cells, alveolar epithelial cells, fibroblasts, pleural mesothelial cells and bronchial epithelial cells[12-14], it may be hypothesised that the decrease in diffusing capacity in these patients is due to inflammatory changes produced in the interstitial tissues by the abnormal accumulation of eosinophils and/or its toxic mediators. Since peripheral blood eosinophilia is the hallmark of TE, the study was also utilised to find out whether there was any relationship between the eosinophils in the peripheral blood and single breath diffusing capacity.

Material and Methods

Fifty patients with recent onset of symptoms of one week to 6 months duration were investigated. They fulfilled the diagnostic criteria of TE, *i.e.* residence in the endemic area of Madras city, respiratory symptoms such as cough, dyspnoea and nocturnal wheezing, chest x-ray infiltrates, peripheral blood eosinophilia of $\geq$ 2000 cells/cmm, high serum titres of antifilarial IgG and a positive response to diethyl carbamazine therapy. Clinical evaluation of each patient included detailed history, physical examination, chest x-ray and IgG filarial antibody determinations.

The one-second forced expiratory volume (FEV_1), forced vital capacity (FVC), FEV_1/FVC per cent, total lung capacity (TLC) by helium dilution method, single breath carbon monoxide diffusing capacity (TLCO) measurements[15] were carried out on PK Morgan (U.K.) Transnfer Test Model C using Data Dec computer. A minimum of three consistent readings in the case of spirometry and two in the case of TLC measurements were obtained. The highest value obtained was used for analyses and readings were corrected to body temperature, ambient pressure and full saturation with water vapour (BTPS). Epidemiology standardisation project[16] recommendations were followed for the measurement of single breath diffusing capacity. The patients were seated comfortably and nose clips were applied. The patients were instructed to exhale completely to residual volume and on instruction to inhale a volume of test gas (Helium 14%, Carbon monoxide 0-28%, Oxygen 18% and remainder Nitrogen) rapidly and maximally to TLC, to hold the breath for 10 seconds and finally to exhale rapidly. The inspired volume and breath holding time (usually between 9-11 seconds) were noted. In ail tests, the inspired volume was adjusted to 90% of previously determined FVC. After exhalation of a preset wash out volume of at least 700 ml, the alveolar sample was collected in an empty sample bag for subsequent analysis. In all patients, the tests were performed in duplicate with an interval of at least 4 minutes. The difference between the measurements was less than 5% and the highest value was used for analysis. The effective alveolar volume (VA) corrected to BTPS was measured by helium dilution during single breath carbon monoxide diffusing capacity measurements[15] and the transfer coefficient, *i.e.* diffusion per litre of alveolar volume (KCO) was calculated from the ratio of TLCO to VA.

Studies had been undertaken in 249 normal subjects, using the PK Morgan (U.K.) Transfer Test Model C, to establish regression equations for predicting normal pulmonary function values in regional subjects. The predicted values of VA, TLCO and KCO

for this study are obtained from these regression-equations (unpublished data). Transfer factor was corrected to a standard haemoglobin concentration of 14.6 G/dl, using the following equation[17].

$$\text{TLCO (corrected)} = \text{TLCO (observed)} \times \frac{14.6\ a + Hb}{(1 + a)\ Hb}$$

where Hb is the actual haemoglobin concentration in G/dl and 'a' is 0.7. The KCO (corrected) was calculated from the ratio of TLCO (corrected) to VA.

The measured values of VA, TLCO and KCO are considered normal, if they are within ± 15% of the predicted value[18].

Results

There were 45 males and 5 females in the study, 21 males and all females were non-smokers and 24 males were smokers. The mean age was 24.1 (SD 7.5) years (range 12-48 years) and the mean height was 160.8 (SD 7.6) cm and the mean weight 45.0 (SD 8.25) kg. The mean TLCO was 6.24±1.4 mmol/k.pa/mt (72±16% predicted and the mean KCO was 1.88±0.25 mmol/k.pa/mt/L (83.1±12.2% predicted).

As there was no significant difference in the mean values of transfer factor and transfer co-efficient between smokers and non-smokers, the data were pooled for analysis.

Normal TLCO was observed only in 6 (12%) patients and 22 patients (44%) had moderately severe diffusion defect (TLCO% predicted ranging between 40-70%). Twenty-eight patients (56%) had a reduction in transfer co-efficient (KCO), including 7 (14%) with moderately severe reduction (Table 1).

Table 1. *Severity of diffusion defect*

Predicted		40.0–70.0%	70.1–85.0%	>85%
Observed	TLCO	22 (44%)	22 (4%)	6 (12%)
Observed	KCO	7 (14%)	21 (42%)	22 (44%)

The mean haemoglobin concentration in 50 patients was 12.84±1.45 G/dl. When the diffusing capacity was corrected to a standard haemoglobin concentration of 14-6 G/dl. Low TLCO and KCO persisted in 37 (74%) and 19 (38%) patients. respectively even after correction of haemoglobin.

As it was observed that the effective alveolar volume (VA) was reduced (<85% predicted) in 30 patients (60%), it was assumed that one of the mechanisms of reduced TLCO in these patients may be due to reduction in the surface area of membrane available for diffusion. When VA was correlated with TLCO (Fig. 1), there was highly significant positive correlation between VA and TLCO (r= 0.847, P<0.001).

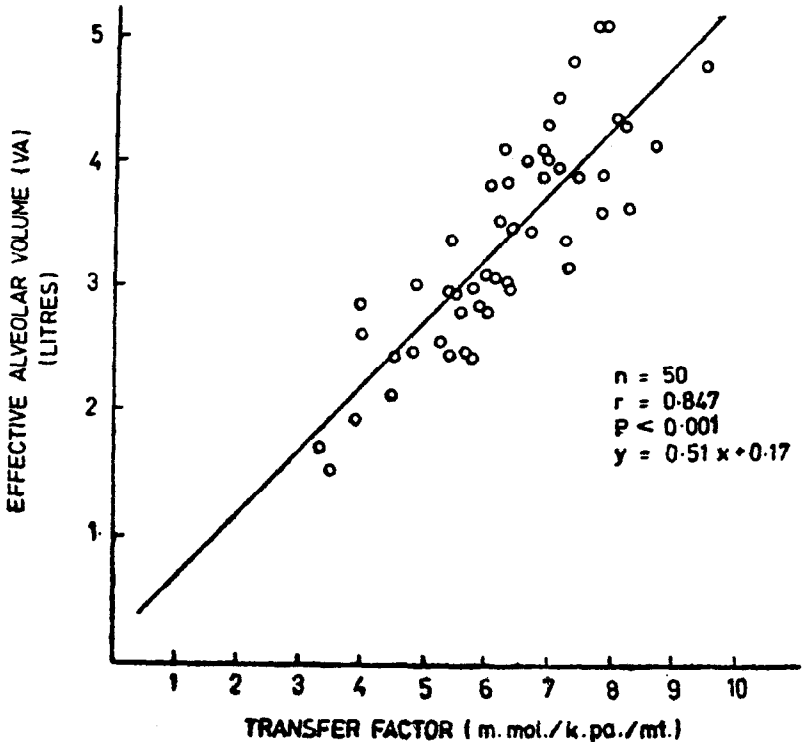

Fig. 1. Showing relationship between effective alveolar volume and transfer factor in acute tropical eosinophilia.

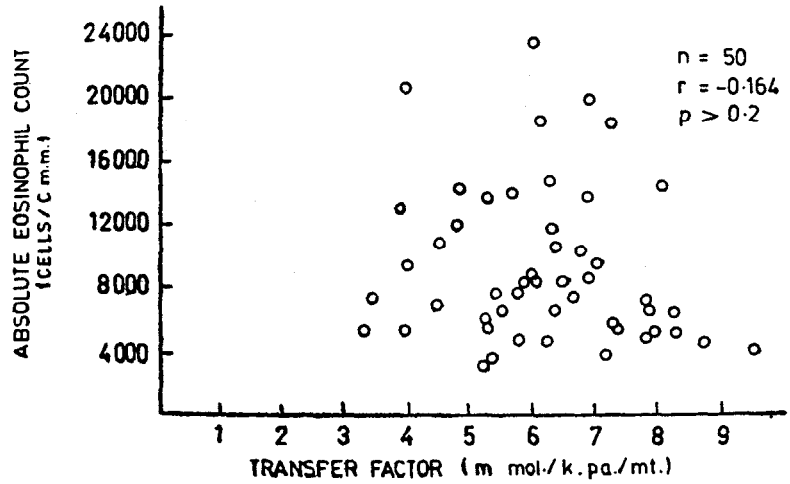

Fig. 2. Showing relationship between blood absolute eosinophil count and transfer factor in acute tropical eosinophilia.

The absolute eosinophil count in these patients varied from 3100 to 23500 cells/cumm and most of them (90%) had absolute eosinophil count of ≥ 5000 cells/cumm. As shown in Fig. 2, there was no correlation (r = – 0.164) between peripheral blood eosinophils and transfer factor (TLCO).

Discussion

The pulmonary manifestations in acute tropical eosinophilia is inflammation of the lung parenchyma in persons highly sensitised immunologically to filarial parasites[4]. The diffusing capacity is reduced in patients with diseases of the lung parenchyma[15], and reduced diffusing capacity in TE by steady state end tidal sampling method was reported by Poh[11]. Impairment of diffusion in long standing cases of TE was suggested by Udwadia[3] on the basis of histopathological evidence of dense eosinophil accumulation in lung parenchyma. Our findings of reduced transfer factor by single breath method in acute untreated tropical eosinophilia corraborates the observation that there is alveolitis in TE.

The transfer factor is the resultant of changes in the diffusing capacity of the alveolar capillary membrane (Dm) and the volume of blood in the alveolar capillaries (VC) under the conditions of measurement[15]. The reduction in diffusing capacity in most of our patients is not due to anaemia (concentration of haemoglobin range (10.1 to 15.6 G/dl). Reduction in the effective accessible gas volume (VA) and reduction in carbon monoxide transfer per litre of effective accessible gas volume *(i.e.,* transfer coefficient, KCO) are the two mechanisms of reduced diffusing capacity[18] and KCO provides some indication of the density of capillaries in the wall of the alveoli. Since we have not measured membrane diffusing capacity (Dm) and alveolar capillary blood volume (VC), specific reductions regarding these parameters cannot be made.

In interstitial lung disease of various aetiologies, there is a low TLCO and KCO, especially the membrane component, and the mechanism of this reduction is still uncertain[19]. The highly significant positive correlation of TLCO with VA shows that the reduction in transfer factor in acute TE in our patients may be mainly due to reduction in alveolar volume. As it had been shown previously[20,21] that TLCO decreases by 3% for every 8% reduction in TLC and that alveolar surface was related to $VA^{1/3}$ in the range of 40-80% TLC, the reduction in the area of membrane available for diffusion, as evidenced by low VA, may be mainly responsible for low TLCO in our patients, This may be due to acute inflammatory changes in the lung parenchyma by the abnormal accumulation of eosinophils, which reduces the membrane area for diffusion. The reduction in transfer coefficient (KCO) in 56% of our patients indirectly shows that there are changes in pulmonary capillaries as well, as it had been shown that KCO provides some indication of the density of capillaries in the wall of the alveoli[18]. Our results in TE are in agreement with the earlier morphometric studies in diffuse interstitial lung diseases[22], where it had been shown that the decreased membrane area for diffusion was the mechanism for low TLCO and also that a decrease in pulmonary capillary blood volume may be an additional contributory factor[23]. Our findings of high positive correlation of

TLCO with VA, along with reductions in VA and KCO in 60% and 56% of patients suggest that both reductions in membrane area and pulmonary capillary blood volume contribute to the reduction in transfer factor in acute TE.

There was no correlation between peripheral blood eosinophils and transfer factor (TLCO). It will be worthwhile to study whether the transfer factor is related to the abnormally accumulated eosinophils in interstitial tissue, as shown histopathologically[2]. We are continuing the study on these lines utilising bronchoalveolar lavage.

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