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Pulmonary function in tropical eosinophilia before and after treatment with diethylcarbamazine

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Nesarajah, M. S. (1975). *Thorax*, 30, 574–577. Pulmonary function in tropical eosinophilia before and after treatment with diethylcarbamazine. Spirometric and lung volume measurements were carried out before and after treatment with diethylcarbamazine in 19 patients with tropical eosinophilia. The total lung capacity and vital capacity returned to or nearly to normal while the FEV₁ and PEF₁, though improved, tended to remain below normal, indicating some residual airways obstruction especially in patients whose treatment began more than one month from the onset of symptoms. The time taken for the pulmonary function to return to normal with treatment was found to be much longer than for the clinical and haematological response.

Pulmonary function studies in patients with tropical eosinophilia have shown that during the early stages of the disease there is mild to moderate obstruction to the airways and that as the disease progresses there is, in addition, a restrictive ventilatory defect (Nesarajah, 1972). Diethylcarbamazine is the specific drug used in the treatment of patients suffering from this disease. Although there are several reports of the clinical improvement observed in such patients after treatment (Chaudhuri, 1956; Danaraj, 1958; Misra *et al.*, 1959; Edirisinghe and Weerasinghe, 1963; Narang and Jain, 1966), objective assessment of such improvement is not equally well documented (Udwadia, 1967; Azad Khan *et al.*, 1970). The present study was therefore undertaken to assess pulmonary function before and after treatment with diethylcarbamazine in patients with tropical eosinophilia in Sri Lanka.

MATERIAL AND METHODS

A group of 19 patients, 18 males and one female, was studied. All patients gave the typical clinical history, had circulating eosinophil counts of over 2000/ μ l of blood, positive filaria complement fixation tests, and elevated erythrocyte sedimentation rates, and showed a clinical and haematological response to diethylcarbamazine, thereby satisfying the criteria recommended by Donohugh (1963) for the diagnosis of tropical eosinophilia. Before their entry into the study, none of these patients had been receiving any specific therapy for tropical

eosinophilia. The duration of symptoms was less than one month in 10 patients and from one to five months in the remaining nine. The patients were accordingly divided into two groups—group A, with symptoms of less than one month's duration, and group B, with symptoms of more than one month's duration.

The lung volumes and expiratory flow rates were measured using a Godart Pulmonet, Aika spirometer, and a Wright peak flow meter, as described in a previous paper (Nesarajah, 1972). The patients were treated with diethylcarbamazine, 250 mg three times a day for 7 days, and the above measurements were repeated after the course of treatment was over. The erythrocyte sedimentation rate and the absolute eosinophil count were measured, and the filaria complement fixation test was also carried out both before and after treatment in all patients.

In 17 of the patients the measurements were repeated within two weeks to six months after completion of the course of treatment, in one subject after eight months, and in one other subject 16 months after completion of the treatment. Although it was proposed to carry out these measurements at regular intervals during the follow-up period, it was not possible to do so as the patients would not report to the laboratory for these tests once they felt better and left hospital.

For purposes of comparison, the lung function tests were also carried out on a group of 31 healthy subjects of comparable mean age and sex.

RESULTS

As in the previous communication (Nesarajah, 1972), the values obtained for the vital capacity (VC), total lung capacity (TLC), forced expired volume in one second (FEV_1), and peak expiratory flow rate (PEFR) in patients and controls were expressed as percentages of the predicted values for persons of European descent.

The changes observed in the lung volumes and expiratory flow rates before and after treatment for all patients are shown in Figs 1 and 2, and the mean values and standard deviations for the two groups of patients and the normal subjects are shown in the Table.

The mean values for the VC, FEV_1 and PEFR for both groups of patients before treatment were found to be significantly lower than for the normal subjects, while the mean values for TLC for either group was not different from that for the normal subjects. Following treatment, in both groups of patients there was a significant increase ($P < 0.01$) in the VC, FVC, FEV_1 , and PEFR. The post-treatment VC for both groups of patients and the FEV_1 for group A patients reached normal levels whereas the FEV_1 for group B patients and the PEFR for both groups were still significantly lower than for the normal subjects.

The absolute eosinophil count, erythrocyte sedimentation rate, and the filaria complement fixation test had returned to normal in all the patients at the time the pulmonary function tests were repeated.

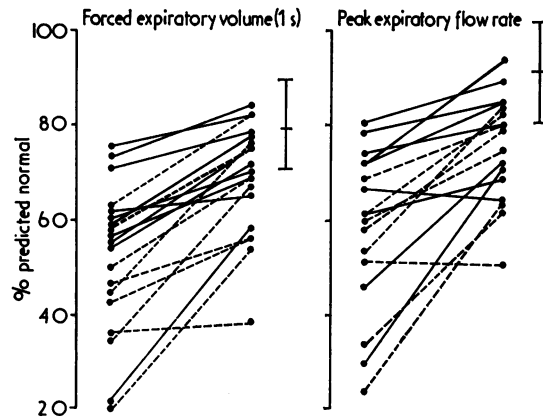


FIG. 2. Changes in expiratory flow rates with treatment in group A (unbroken lines) and group B (broken lines) patients. Mean and standard deviation of control group to right. Group A—symptoms less than 1 month; group B—symptoms more than 1 month.

DISCUSSION

Diethylcarbamazine is the specific drug used today in the management of patients with tropical pulmonary eosinophilia. It replaced the organic arsenicals as the drug of choice, because, though equally effective therapeutically, it produces none of the dangerous and sometimes fatal toxic effects commonly seen with arsenic therapy (Danaraj, 1958; Ganatra, Sheth, and Lewis, 1958; Shanker, Bhargava, and Shrivastava, 1960; Islam, 1964).

The cure rate with diethylcarbamazine therapy, as commonly gauged by amelioration of symptoms, disappearance of the lung signs, a clearing of the radiological picture, a return of the erythrocyte sedimentation rate to normal, and a decrease in the eosinophil count, ranges from about 80% to 100% in various series (Ganatra and Lewis, 1955; Danaraj, 1958; Ganatra *et al.*, 1958; Shanker *et al.*, 1960; Narang and Jain 1966; Azad Khan *et al.*, 1970). Udwadia (1967) observed a poor response to treatment (and so a low cure rate) in patients with a long history and with fibrosis of the lung, and there is now evidence that some of the cases which do not respond to treatment may have a non-filarial aetiology (Joshi, Udwadia, and Gadgil, 1969). The present series was selected on the basis of a cure, as judged by amelioration of symptoms, absence of lung signs, decrease of the eosinophil count to below $1000/\mu\text{l}$, return of the erythrocyte sedimentation rate to normal, and a negative filaria complement fixation test.

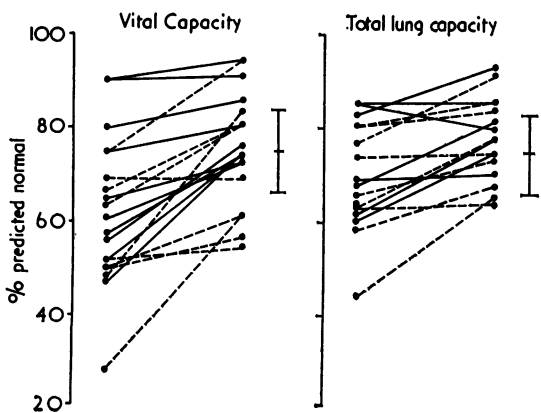


FIG. 1. Changes in lung volumes with treatment in group A (unbroken lines) and group B (broken lines) patients. Mean and standard deviation of control group to right. Group A—symptoms less than 1 month; group B—symptoms more than 1 month.

TABLE
MEAN VALUES (AND STANDARD DEVIATIONS) FOR LUNG VOLUMES AND EXPIRATORY FLOW RATES FOR NORMAL SUBJECTS AND FOR PATIENTS, BEFORE AND AFTER TREATMENT

Group	VC		TLC		FEV ₁		PEFR	
	Before	After	Before	After	Before	After	Before	After
Normal subjects	77.2 (8.7)		72.3 (7.0)		78.5 (8.5)		91.0 (11.0)	
A	66.6 (15.5) <0.01	79.3 (8.4) NS	72.8 (10.8) NS	78.9 (7.1) NS	58.1 (15.2) <0.001	72.4 (8.2) NS	63.8 (16.5) <0.001	77.9 (9.1) <0.001
B	55.3 (14.6) <0.001	70.6 (13.9) NS	65.7 (12.2) NS	73.6 (10.0) NS	43.7 (12.5) <0.001	63.1 (13.1) <0.001	50.6 (14.5) <0.001	70.9 (12.0) <0.001

The individual values from which the mean and standard deviations have been calculated have been expressed as percentages of the predicted values for Europeans (see text).

Although Danaraj (1958), using different daily dosage schedules for treatment, observed that the clinical response was better with daily doses of 18 and 30 mg/kg body weight than with the smaller dose, several workers both in India (Patwari, 1958; Viswanathan and Krishnamurthi, 1958; Baker, Rajan, and Devadatta, 1959) and in Ceylon (Edirisinghe and Weerasinghe, 1963; Attygalle, 1970) have found that diethylcarbamazine in as small a daily dose as 5 to 8 mg/kg body weight given for about a week to 10 days is effective. Shanker and Gaur (1971) used different dosage schedules and observed that the cure rate was dependent upon the total quantity of drug administered irrespective of the period of therapy. These findings confirm the earlier observations of Ganatra and Lewis (1955). Shanker and Gaur (1971) and Danaraj (1958) have also observed that with higher daily doses the clinical response was quicker than with lower daily doses. In the present series the total amount of drug administered was about 5 g in a daily dosage of about 12 mg/kg body weight.

Although clinical improvement with diethylcarbamazine therapy usually starts in two to four days after the beginning of treatment and most patients are completely free of symptoms by the end of the second week, the haematological response takes slightly longer (Danaraj, 1958; Narang and Jain, 1966; Crofton and Douglas, 1969). From the present study it seems that the time taken for pulmonary function to return to normal, if it does, is much longer than for both the clinical and the haematological response.

Even though the VC had returned to normal levels in both groups, the improvement in the airways obstruction with treatment, though significant, was still incomplete, particularly in the group B patients. These observations are consistent with the findings of Udawadia and Joshi (1964) in two patients who were submitted to lung

biopsies after a month's treatment with diethylcarbamazine. Both these patients were completely free of symptoms after seven days' therapy, yet both patients had pathological changes in the lung even after a month of treatment. They therefore concluded that relief of symptoms is not necessarily associated with a clearing of the lung lesions and also that these may exist in the absence of peripheral eosinophilia.

It has been shown that in the natural history of the disease the earliest functional defect is an obstructive ventilatory defect and that a restrictive defect is superadded as the disease progresses. So in patients who have had the disease for some time the pulmonary pathology responsible for the obstruction is of longer duration than that responsible for the restriction. It is therefore not surprising that with treatment the improvement in the VC, a decrease in which is of more recent origin, is more marked than the improvement in the FEV₁ and PEFR. In this connection it is interesting to note that Azad Khan *et al.* (1970) found that even though there was a considerable increase in the VC with treatment, it still remained below normal in most of their cases. A possible explanation would be that their patients might have had the disease for a longer period than those in the present series and therefore had a larger component of irreversible pathological changes in the lung.

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