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SHORT COMMUNICATION

HLA Antigen and Ventilatory Drive in Thais with Chronic Obstructive Pulmonary Disease

Nanta Maranetra,* Dasnayanee Chandanayingyong, and Somchai Bovornkitti***

SUMMARY **Studies of HLA antigens in 15 Thai patients with chronic obstructive pulmonary disease revealed a significant increase in HLA-Bw 60 frequency in the group with low ventilatory drive to carbondioxide using unstimulated airway pressure. The finding suggests an immunogenetic role of HLA-Bw 60 on the control of ventilation in COPD.**

Clinically, patients with chronic obstructive pulmonary disease (COPD), based on as yet unclear mechanism(s), can be divided into two groups having the same degree of airways obstruction: viz, (a) hypoventilating patients with decreased or normal ventilatory drive and low ventilatory response to hypercapnia and (b) normally ventilating patients with higher ventilatory drive and response.[1-4] A study carried out on the offspring of two groups of COPD patients, with an equal degree of airways obstruction but different ranges of ventilating performance, yielded results suggesting that familial factors in the control of breathing may comprise an important determinant of ventilation in chronic obstructive pulmonary disease.[5] Previously, we reported a lower frequency of HLA-DR 7 in Thai COPD patients when compared with a matched control population.[6] The present communication describes the result of a recent investigation on HLA-phenotype distribution among COPD patients with different gradings of ventilatory drive, aimed at elucidating the possible role that any special HLA antigen may play in the hyporesponsiveness of ventilatory drive in COPD patients.

MATERIALS AND METHODS

Subjects

Fifteen Thai COPD patients (12 males and 3 females), aged 55-83 years, who had smoked more than 40 packs of cigarettes per year for a minimum of 15 years and exhibited partial or irreversible airways obstruction ($FEV_1/FVC < 75\%$, which gave $< 15\%$ response to a $beta_2$ selective sympathomimetic) were studied. Patients with bronchial asthma or pulmonary tuberculosis were excluded. The subjects were divided according to an index of ventilatory drive to carbon dioxide ($\triangle P/\triangle Pco_2$) during rebreathing (obtained by a modified method used by Read[3,7]) into two groups: (a) seven patients (5 males and 2 females) with normal ventilatory drive (for normal Thais $\geqslant 0.963$ $cmH_2O.mmHg^{-1}$) and (b) eight patients (7 males and 1 female) with low ventilatory drive (< 0.963 $cmH_2O.mmHg^{-1}$). They were also divided into two other groups according to an index of unstimulated mouth occlusive pressure as resting ventilatory drive (Pu): (a) three patients (2 males and 1 female) with low resting ventilatory drive ($Pu < 3.8$ cmH_2O and (b) 12 patients (10 males and 2 females) with normal resting ventilatory drive ($Pu \geqslant 3.8$ cmH_2O).

Methods

For determination of HLA antigen, peripheral blood lymphocytes were separated by centrifugation over Ficoll-Hypaque. HLA-A, -B typing was performed by using standard complement-dependent microlym-

From *Department of Medicine and **Department of Transfusion Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.

Correspondence : Dr. N. Maranetra

Table 1. HLA antigen distribution in two groups of COPD patients according to ventilatory drive to hypercapnia

	Phenotype frequency (%)		Fisher's Exact Test p value (2–tailed)
	Low $\Delta P / \Delta Pco_2$	Normal $\Delta P / \Delta Pco_2$	
HLA–A			
A1	12.5	0	0.533
A2	50	14.3	0.1818
A3	–	–	–
A24	37.5	14.3	0.3385
A26	0	14.3	0.466
A28	0	14.3	0.466
A11	25	42.9	0.426
$A11^{SH}$	25	28.6	0.6615
A31	–	–	
Aw33	37.5	42.9	0.622
A–blank	12.5	28.6	0.446
HLA–B			
B51	–	–	–
B7	15.2	0	0.533
B44	12.5	14.3	0.733
B13	12.5	14.3	0.733
B15	–	–	
Bw62	12.5	28.6	0.446
Bw75	25	–	0.266
B16	–	–	
B38	12.5	–	0.533
B39	–	14.3	0.466
B17	25	14.3	0.553
Bw57	–	–	–
Bw58	–	–	–
B18	–	–	–
Bw22	0	14.3	0.466
B27	25	14.3	0.553
B35	–	–	–
B40	12.5	14.3	0.733
Bw60	–	28.6	0.2
Bw61	–	–	–
Bw46	12.5	14.3	0.733
B–blank	37.5	28.6	0.573
HLA–DR			
DR1	–	–	–
DR2	37.5	28.6	0.573
DR3	12.5	14.3	0.733
DR4	12.5	42.9	0.230
DR5	–	–	–
DRw11	12.5	14.3	0.733
DRw12	25	28.6	0.6615
DRw6	25	28.6	0.6615
DR7	12.5	14.3	0.733
DRw8	37.5	–	0.123
DR9	12.5	14.3	0.733
DRw10	–	–	–
DR–blank	–	14.3	0.466

Table 2. HLA antigen distribution in two groups of COPD patients according to resting ventilatory dirve

	Phenotype frequency (%)		Fisher's Exact Test p value (2–taited)
	Low resting ventilatory drive	Normal resting ventilatory drive	
HLA–A			
A1	0	8.3	0.8
A2	33.3	33.3	0.758
A3	–	–	
A24	0	33.3	0.3626
A26	33.3	0	0.20
A28	0	8.3	0.8
A11	33.3	33.3	0.758
$A11^{SH}$	0	33.3	0.3626
A31	–	–	–
Aw33	66.7	33.3	0.341
A–blank	33.3	16.7	0.516
HLA–B			
B51	–	–	=
B7	33.3	0	0.2
B44	0	16.7	0.628
B13	0	16.7	0.628
B15	–	–	
Bw62	0	25	0.483
Bw75	0	16.7	0.628
B16	–	–	
B38	0	8.3	0.8
B39	0	8.3	0.8
B17	33.3	16.7	0.516
Bw57	–	–	–
Bw58	–	–	–
B18	–	–	–
Bw22	0	8.3	0.8
B27	0	25	0.483
B35	–	–	–
B40	0	16.7	0.628
Bw60	66.7	0	0.02857* (OR=42)
Bw61	–	–	
Bw46	35.3	8.3	0.371
B–blank	33.3	33.3	0.758
HLA–DR			
DR1	–	–	
DR2	0	41.7	0.2637
DR3	33.3	8.3	0.3714
DR4	33.3	25	0.637
DR5	–	–	
DRw11	33.3	8.3	0.3714
DRw12	33.3	25	0.637
DRw6	–	33.3	0.3626
DR7	0	16.7	0.628
DRw8	33.3	16.7	0.516
DR9	33.3	8.3	0.3714
DRw10	–	–	
DR–blank	0	8.3	0.8

phocytotoxicity assay;[8] HLA-DR typing was performed by a modified complement-dependent microlymphocytotoxicity assay.[9] A set of well-defined sera comprising 10 specificities for the A-locus and 21 specificities for the B-locus and 12 specificities for the DR locus was used; for each specificity, at least 2-3 or more sera well characterised for their specificities were used.

For statistical analysis, Chi-square (Yates' correction) and Fisher's exact test were used. The Odds ratio (OR) was also calculated.

RESULTS

The findings are presented in Tables 1 and 2. There was a significant increase in HLA-Bw60 frequency in the group of COPD patients with low ventilatory drive (using unstimulated pressure) (OR = 42, P = 0.0285), but not in the group of low ventilatory drive index using $\triangle P/\triangle Pco_2$.

DISCUSSION

While it has been reported that HLA-DR7 may have an immunogenetic role in conferring on the Thai population resistance against COPD,[6] the finding in the present study of a high HLA-Bw60 prevalence among patients with low ventilatory drive raises the possibility that HLA-Bw60 acts as a genetic determinant of ventilatory drive in these special groups of COPD patients.

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