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EDITORIAL ARTICLE

CLINICAL PHENOTYPE-DRIVEN TREATMENT IN ASTHMATIC PATIENTS: AN EVIDENCE

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Asthma is a complex inflammatory disease and current therapy remains inadequate in many patients. There is phenotypic heterogeneity in its clinical expression as a consequence of gene-environment interactions and heterogeneity in response to therapy. There is an increasing recognition that asthma encompasses several underlying pathological processes that develop as a consequence of a variety of gene–environmental interactions that give rise to a different clinical asthma phenotypes. The concept that 'one size does not fit all' is also exemplified by the heterogeneity in asthma treatment response.(1)

The clinical and molecular asthma phenotyping approaches are a significant advance in our understanding of the pathophysiology of asthma, revealing several distinct subclinical phenotypes, driven by different pathophysiological mechanisms. Clustering methodology to describe phenotypes is becoming increasingly popular both clinically and at a molecular level. The challenge is targeting asthma subphenotypes with appropriate existing and novel therapies. It is no longer helpful to think of asthma as a single disease entity for which one treatment will treat all patients.(2)

In our previous study.(3) it was hypothesized that asthmatic children are variable in their response to controller medications based on the clinical phenotype of asthma and whether clinical asthma phenotype will affect the response to therapy. The variability of response to inhaled corticosteroids (ICS) and leukotriene receptor antagonist (LTRA) was evaluated in asthmatic children according to the patient clinical phenotypes (wheezy and shortness of the breath group). Asthmatic children presented with wheeze showed significant improvement of FEV_1 at 4 weeks in both montelukast-treated group (65.9% at baseline to 79.7%, $P < 0.05$) and fluticasone - treated group (65.8% at baseline to 82.3% at 4 weeks, P< 005.) comparing the differential response between the two medications was found to be insignificant. In the same group of children, eosinophilic percentage showed significant decrease from baseline at 4 weeks of therapy in both montelukast-treated group (7.8% to 5.6%, $P<0.05$) and fluticasone-treated group (8.8%–6.7%, $P<0.05$). The differential response between both medications was found to be insignificant(3) Table 1.

On the other aspect asthmatic children presented with shortness of breath showed significant improvement in FEV1 only in fluticasone treated group (66.7%–86.2%, $P < 0.05$), while it was insignificant in montelukast-treated group (61.7%–75%). The same group of children showed significant decrease of eosinophilic percentage by 9% ($P < 0.05$) in the fluticasone treated group, while insignificant decrease by 1.4 % was noted in the montelukast-treated group(3) Table 2.

Collectively, these data hypothesize that response to montelukast and fluticasone vary considerably according to the clinical phenotypes of asthmatic patient. Response to montelukast was found to be significantly effective in asthmatic children presented with wheeze in comparison to those presented with shortness of breath. Whereas ICS provide favorable and significant clinical benefit in both asthmatic phenotypes.(3)

Thus our finding would highlight the need for easier criteria with simple investigations to tailor asthma medicines to be cost effective with less side effects.

Table 1. Effect of Montelukast Versus Fluticasone on the Immunological Profiles and Pulmonary Function of Patients Presenting with Cough and Wheezes.

	Group A			Group C			P
	Before treatment	After treatment	Percentage treatment	Before treatment	After treatment	Percentage treatment	
sICAM-1	702.2 (45.7)	679.6 (68.2)	-10.6	731.5 (67.2)	622.4 (47.3*)	-7.4	0.22
sVICAM-1	931 (264.3)	853.1 (239.7)	1.3	817.6 (221)	728.4 (245)	-9.39	1.1
sIL-2R	3,976 (523.9)	3,961.4 (498.6)	0.56	3,531.6 (564.2)	3,465.6 (515.7)	-3.58	0.2
IgE level	187.2 (29.7)	182.6 (18.2)	-1.1	180.8 (57.3)	192.4 (40.2)	-3.58	0.8
Eosinophilic percentage	7.8 (1.7)	5.6 (3.5*)	-39.36	8.8 (2.5)	6.7 (2.6*)	-23.67	0.9
FEV_1	65.9 (3.3)	79.7 (11.3*)	29.22	65.8 (8.1)	82.3 (11.8*)	27.5	0.9

Data are expressed as mean (SD).
*P <0.05 is significant (for each group before and after treatment).
Mann-Whitney U-test used to compare both group.
Group A: Patient presented with cough and wheeze and treated with montelukast.
Group C: Patient presented with cough and wheeze and treated with Fluticasone.

Table 2. Effect of Montelukast Versus Fluticasone on the Immunological Profiles and Pulmonary Function of Patients Presenting with Cough and Shortness of Breath.

	Group B			Group D			P
	Before treatment	After treatment	Percentage treatment	Before treatment	After treatment	Percentage treatment	
sICAM-1	701.2 (67.6)	689.6 (64.6)	-14.7	732.3 (86.3)	618.6 (81.1*)	-11.4	0.54
sVICAM-1	943 (327.5)	841.7 (253.3)	11.4	800.8 (211.5)	738 (189.4)	6.4	0.6
sIL-2R	3,673.3 (196.7)	3,470.5 (20.1)	3.8	4,003 (552.4)	3,577.4 (604.7)	1.98	0.53
IgL level	171.8 (36.4)	162.1 (31.1)	-7.1	207.7 (35.5)	145.6 (52.1)	-6.5	0.8
Eosinophilic percentage	6.1 (2.6)	5.6 (3.5)	-1.4	8.7 (1.9)	5.6 (3*)	-9	0.74
FEV_1	61.7 (9.3)	75 (13.3)	32.2	66.7 (9.2)	86.2 (12*)	32.8	0.88

Data are expressed as mean (SD).
*P <0.05 is significant (for each group before and after treatment).
Mann-Whitney U-test used to compare both group.
Group B: Patient presented with cough and shortness of breath and treated with montelukast.
Group D: Patient presented with cough and shortness of breath and treated with Fluticasone.

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