Objective Evidence of Omalizumab Treatment Assessed by Forced Oscillation (FO)

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ABSTRACT

Rationale: Omalizumab is approved for treatment of moderate to severe asthmatic patients, dependent on systemic steroids or requiring high dose inhaled corticosteroids. Omalizumab results in subjective clinical improvement and decreased systemic steroids and high dose inhaled corticosteroids dose requirements, with marginal or no objective improvements in lung function as measured by traditional spirometry.

Methods: Twelve moderate to severe asthmatic patients were evaluated in an open-label safety study of omalizumab using Impulse Oscillometry Spirometry (IOS), a form of FO, in addition to spirometry. IOS delivers periodic air oscillations resulting in the measurement of reactance of the lungs, referred to as AX, and small airway resistance at 5 Hz, referred to as R5.

Results: IOS indices were significantly improved after 3 to 4 months of treatment, but were not paralleled by changes in spirometry (FEV1). Normal AX < 3.0 cm H2O/L. Mean AX was 26.9 cm H2O/L prior to, and 18.0 cm H2O/L after, 4 months of treatment with omalizumab. The difference after treatment was statistically significant (P<0.002). Mean R5 was 5.8 cm H2O/L prior to, and 4.8 cm H2O/L after, 4 months of treatment ($p < 0.003$). Mean FEV1 was 2.02 L before, and 1.98 L after, 4 months of treatment ($p = 0.66$).

Conclusions: We conclude that low frequency FO indices provide objective evidence of omalizumab efficacy, while such objective evidence is not available from spirometry. These data provide further support for the utility of FO in the clinical management of asthma. The objective measurement of airflow resistance and low-frequency reactance through IOS testing quantifies lung mechanical responses objectively, noninvasively, and unobtrusively, with increased patient comfort compared to spirometry.

BACKGROUND

- Moderate to severe asthma is associated with significant inflammatory changes in the lung tissue. If left uncontrolled, it can lead to airway remodeling and irreversible damage to lung function.
- Omalizumab has been approved for the treatment of moderate to severe asthma in patients who are not well controlled on steroids, whether systemic or high dose inhalation treatment.
- Even though the patients improved clinically and were able to be weaned off the steroids either partially or completely the lung function, as traditionally measured by spirometry with emphasis on forced expiration volume, improved only marginally, with a maximum of 10% in some of the patients.

METHODS

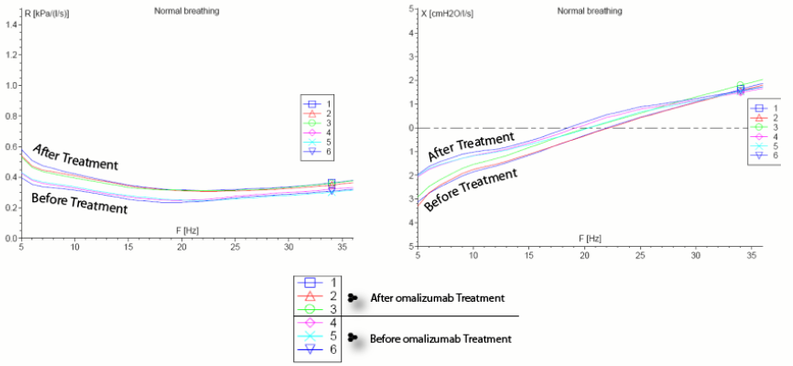
Figure 1: The IOS machine by Jaeger

Figure 2: The mouthpiece to measure IOS attached to the loudspeaker

RESULTS

	Act1	Act2	Act3	Act4	Act5	Act6
Date	01/28	01/28	01/28	06/27	06/27	06/27
Time	08:59	09:00	09:03	10:38	10:45	10:46
R5Hz	5.91	5.51	5.41	4.34	4.38	4.05
R15Hz	3.56	3.51	3.40	2.76	2.85	2.60
AX	23.7	23.2	18.8	13.8	14.5	12.2
Rin5	4.90	4.38	4.05	3.78	3.80	3.86
Rex5	6.22	6.38	6.89	4.87	4.89	4.18
AXi	12.89	12.97	10.65	11.26	11.87	11.42
AXe	32.82	34.36	28.52	16.27	16.81	12.80
COin5	0.6	0.6	0.7	0.8	0.8	0.8
COin10	0.9	0.9	0.9	0.9	1.0	1.0
COin15	1.0	0.9	1.0	1.0	1.0	1.0
COin20	1.0	0.9	1.0	1.0	1.0	1.0
COex5	0.6	0.6	0.5	0.8	0.8	0.8
COex10	0.8	0.9	0.8	0.9	0.9	1.0
COex15	0.9	0.9	0.9	1.0	1.0	1.0
COex20	0.9	0.9	0.9	1.0	1.0	1.0

A representative patient by data and graph before and after treatment with omalizuab



DISCUSSION

- Spirometry is effort-dependent and is a relative comparison to normal adults.
- Many of these patients who have chronic lung disease may not be able to show improvement in their lung function, either because of poor effort or persistent inflammatory changes.
- Forced oscillation through IOS provides a comfortable method to measure lung function without dependence on the patient's efforts.
- IOS can indirectly be a reflection of the inflammatory process in the lungs.
- IOS reflects a better diagnostic tool wherein the equipment measures both reactance and small airway resistance of the lungs.
- We have previously reported that AX and R5 may reflect improvement in lung function, even if the FEV1 measured through spirometry is unchanged or normal in patients with symptoms of asthma and allergic rhinitis.

CONCLUSION

- Low frequency FO indices provide objective evidence of omalizumab efficacy, while such objective evidence is not available from spirometry.
- These data provide further support for the utility of FO in the clinical management of asthma.
- FO is noninvasive and unobtrusive, with increased patient comfort compared to spirometry.