

BRIEF COMMUNICATION

Usefulness of omalizumab in ten patients with severe occupational asthma

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Abstract

Background: The management of severe occupational asthma (OA) remains problematic and new alternative treatments providing better disease control are required, ideally enabling affected individuals to remain in their job.

Methods: Ten patients with severe uncontrolled OA were treated with the monoclonal anti-IgE antibody omalizumab. In six cases the causative agent was a high molecular weight (HMW) compound and in four cases it was a low molecular weight (LMW) chemical. All of the patients had well documented OA despite workplace adjustments.

Results: During treatment, nine patients exhibited a lower rate of asthma exacerbations and used less oral or inhaled corticosteroids. Seven patients were able to continue working at the same workplace as before treatment.

Conclusion: We have demonstrated that omalizumab is a potential treatment for severe uncontrolled OA and enabled seven of the ten patients in the study to remain in their job.

Patients with uncontrolled severe allergic asthma are a challenging and difficult-to-treat population in whom omalizumab might represent a new treatment option (1). Given the health consequences and socioeconomic impact of severe occupational asthma (OA) (2), it is important to establish whether omalizumab can enable patients with severe OA to keep their job.

We report the results of the first field study in a cohort of ten patients with OA treated with omalizumab and followed for a period of 6 months to 4 years. Questionnaires on the management of OA were sent to French pulmonologists specialized in severe asthma. Between 2009 and 2011, we received 13 reports of patients with OA receiving anti-IgE therapy, and of them, ten were selected for the study (Fig. 1). Three were excluded (insufficient follow-up period or unclear-cut history of OA).

Table 1 shows the patients' characteristics. In all cases, the diagnosis of OA was based on a well-documented clinical history. Asthma severity was clearly related to work conditions, the patients did not have work-aggravated asthma (3), and omalizumab had not been prescribed for preexisting severe atopic asthma.

In the six cases in which the causative agent was a high molecular weight (HMW) compound, skin prick tests were

positive and two patients also had a positive challenge test (wheat flour). The causative agents were wheat flour, cat, rabbit, storage mite and *Alternaria* (severe exacerbations strictly related to work facilities in a high concentration of spores).

In four cases, the causative agent was a low molecular weight (LMW) compound. The role of isocyanate was demonstrated by a challenge test in one patient (Genasic chamber), while another had significant levels of isocyanate-specific IgE (antitoluene diisocyanate: 0.13 units/ml, threshold >0.10 units/ml). In the acrylate case, the eviction/rechallenge tests were positive and skin prick tests remained negative to other occupational allergens. The role of tetrachloroethylene was supported by well-documented symptoms only in the workplace, while sensitization to mites and pollens was not relevant.

In all cases, workplace adjustments were made at the time of diagnosis of OA to maximize avoidance of the causative agent, although complete avoidance was not possible. During the follow-up, no change in occupational exposure and in habits or conditions of working were notified.

All patients had severe uncontrolled asthma and were receiving optimized asthma therapy: high-dose inhaled

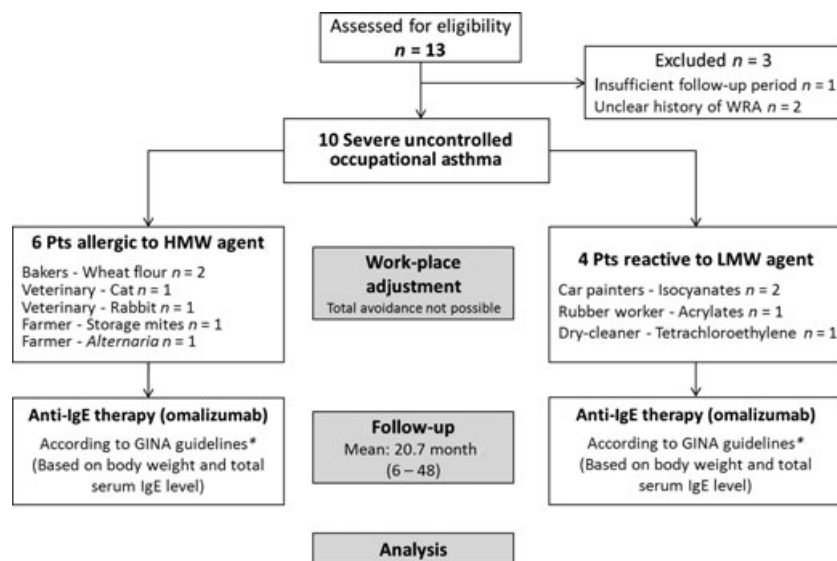


Figure 1 Study flow diagram. OA, occupational asthma; HMW, high molecular weight; LMW, low molecular weight. *Well-documented severe occupational asthma with persistent symptoms

despite therapy with both high-dose inhaled corticosteroids (ICS) and long-acting β_2 -agonists (LABAs).

Table 1 Demographic, occupational, and follow-up data

Patient	Sex	Age	Smoker	Occupation	Agent	Duration OA	Atopy	Total IgE level	Follow-up
1	M	31	—	Baker	Wheat flour	6	+	106	6
2	F	34	—	Veterinary	Cat	7	+	39	18
3	M	45	+	Farmer	Storage mites	3	+	1376	48
4	M	40	—	Veterinary	Rabbit	2	+	76	42
5	M	20	—	Farmer	Alternaria	0.5	+	53	8
6	F	57	—	Baker	Wheat Flour	8	+	833	28
7	M	56	+	Car painter	Isocyanate	5	+	1029	19
8	M	47	—	Dry-cleaner	Tetrachloroethylene	2	+	257	12
9	M	24	—	Car painter	Isocyanate	1	+	1307	30
10	M	20	—	Rubber worker	Acrylate	4	—	57	6
Mean		37.4				3.85		513	21.7

OA, occupational asthma. The duration of OA is given in years since diagnosis, and the follow-up during anti-IgE treatment is given in months. Total IgE level is given in units/ml.

corticosteroids (mean daily beclomethasone-equivalent dose: 3200 μg) combined always with long-acting beta-agonists; inhaled rescue medication was used at least 1 day per week. They all had experienced severe exacerbations requiring an emergency consultation and prescription of oral corticosteroids (2–8 exacerbations during the past year; mean 5.2), sleep disturbances, impaired quality of life or missed work days due to asthma. Five patients received daily oral corticosteroids (mean daily prednisone-equivalent dose: 19 mg; range: 10–30 mg). Before omalizumab treatment, six patients had a $\text{FEV}_1 \leq 80\%$ of the predicted value (Table 2).

Omalizumab therapy was introduced according to GINA guidelines (4) and was initiated 0.5–8 years after diagnosis (mean: 3.85 years) (Table 1). The dose of anti-IgE therapy was based on body weight and total serum IgE level, with a maximum dose of 600 mg every 2 weeks if IgE level was more than 700 units/ml. Mean total serum IgE was 513 units/ml (range: 39–1376).

The patients were followed for at least 6 months during omalizumab therapy (mean: 21.7 months; maximum: 48 months), and asthma control was assessed for the first time 4 months after the start of treatment. Omalizumab was well tolerated by all the patients studied.

Asthma control improved in 9 of 10 patients, determined by the number of severe exacerbations per year (mean before omalizumab: 5.2; mean after evaluation of omalizumab therapy: 0.5, range: 0–2), and five experienced no exacerbation (Table 2). Optimal control was achieved in four patients and five were partly controlled according to the GINA classification (4).

Omalizumab therapy enabled 3 of 5 patients to discontinue oral corticosteroids. The mean dose of oral corticosteroids decreased from 19 to 3 mg/day at the end of the study (a decrease by 84%). Four patients reduced inhaled corticosteroids from a mean beclomethasone-equivalent dose from 3200

Table 2 Asthma parameters before and after anti-IgE therapy

Patient	FEV ₁ pre %	FEV ₁ post %	Asthma control post	ICS pre (µg/day)	ICS post (µg/day)	Nb exacerb pre	Nb exacerb post	OC pre (mg/day)	OC post (mg/day)	Continued exposure to OAg	Continued occup
1	80	91	Partly control	4000	2000	4	0*	0	0	Yes	Yes
2	76	75	Optimal control	4000	2000	6	1	0	0	Yes	Yes
3	80	80	Partly control	2000	2000	4	2	20	0	Yes	Yes
4	107	125	Optimal control	4000	4000	6	1	15	0	Yes	Yes
5	118	115	Optimal control	4000	4000	2	0	0	0	Yes	Yes
6	93	93	Optimal control	4000	4000	6	0	30	0	Yes	No
7	70	87	Partly control	4000	2000	4	1	0	0	Yes	No
8	87	104	Partly control	1000	500	4	0	0	0	Yes	Yes
9	69	98	Partly control	2000	2000	8	0	20	5	Yes	Yes
10	36	36	Uncontrol	3000	3000	8	4*	10	10	Yes	No
Mean	81.6	90.4		3200	2550	5.2	0.5	19	3		

Pre, prior to anti-IgE therapy; post: during anti-IgE therapy; FEV₁: forced expiratory volume in 1 s, expressed as percentage of the predicted value; asthma control using GINA guidelines; ICS, inhaled corticosteroids, expressed in µg/day of beclometasone-equivalent; Nb exacerb: number of severe asthma exacerbations per year; OC, oral corticosteroids, expressed in mg/day of prednisone-equivalent; OAg, occupational agent; occup, occupation.

*Follow-up of only 6 months.

to 2550 µg/day, a decrease by 20% (Table 2). An improvement in FEV₁ was reported for five patients.

Seven patients were able to continue working at the same workplace as before treatment. Three patients had to stop job. Patient 10 (acrylates), the most severe, kept frequent uncontrolled symptoms and a very low FEV₁. The patient 7 (isocyanates) was responder but underwent an early retirement at the age of 58. The patient 6 had soon stopped working 4 months before treatment, but remained symptomatic to flour for an indirect exposure. Despite a control of asthma, she did not return to work.

Our study demonstrated the efficacy of omalizumab in the atopic patients, regardless of whether the causative agent was HMW or LMW.

Our results confirm previous publications that have demonstrated a clinical benefit from omalizumab therapy in OA caused by HMW agents in healthcare workers with latex allergy (5) and in baker's asthma (6, 7).

However, in our study, 3 of 9 atopic patients had OA induced by a LMW chemical.

Two types of OA are distinguished in the international classification: immunologic OA and nonimmunologic (irritant-

induced) OA (8). Consequently, the efficacy of anti-IgE therapy in our three patients with OA induced by a LMW agent suggests that an immunologic mechanism was involved.

It must be stressed that 7 of 10 patients were able to remain in their job, as has previously been reported with omalizumab (6, 7). This is important, because the financial consequences and loss of income are significantly higher in subjects with OA who leave their job than in those who retain their position (9).

We have demonstrated that omalizumab is a potential treatment for OA induced by LMW and HMW agents in atopic patients. Omalizumab could help patients who are unable to avoid allergen exposure in their workplace and may have a role in preventing the socioeconomic and financial consequences related to the loss of employment.

Conflict of interest

François Lavaud, Philippe Bonniaud, Jean Charles Dalphin, Christophe Leroyer, Dominique Muller, Rafik Tannous, Gilles Mangiapan and Frédéric De Blay are consultants for Novartis-France.

References

- Humbert M, Beasley R, Ayres J, Slavin R, Herbert J, Bousquet J et al. Benefits of omalizumab as add-on therapy in patients with severe persistent asthma who are inadequately controlled despite best available therapy (GINA 2002 step 4 treatment): INNOVATE. *Allergy* 2005;**60**:309–316.
- Vandenplas O, Toren K, Blanc PD. Health and socioeconomic impact of work-related asthma. *Eur Respir J* 2003;**22**:689–697.
- Moscato G, Pala G, Barnig C, De Blay F, Del Giacco SR, Foletti I et al. EAACI consensus statement for investigation of work-related asthma in non-specialized centres. *Allergy* 2012;**67**:491–501.
- Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention: NIH Publication 02-3659 issued January 1995 (updated 2002, 2003; accessed 15 October 2011). At: <http://www.ginasthma.com>.
- Leynadier F, Doudou O, Gaouar H, Le Gros V, Bourdeix I, Guyomarch-Cocco L et al. Effect of omalizumab in health care workers with occupational latex allergy. *J Allergy Clin Immunol* 2004;**113**:360–361.
- Olivieri M, Biscardo CA, Turri S, Perbellini L. Omalizumab in persistent severe bakers' asthma. *Allergy* 2008;**63**:790–791.
- Perez Pimiento A, Bueso Fernandez A, Garcia Loria J, Rodriguez Cabrerios MI, Mosquera MR, Garcia Cubero A. Effect of omalizumab treatment in a baker with occupational asthma. *J Investig Allergol Clin Immunol* 2008;**18**:490–491.
- Maestrelli P, Boschetto P, Fabbri LM, Mapp CE. Mechanisms of occupational asthma. *J Allergy Clin Immunol* 2009;**123**:531–542.
- Ameille J, Pairon JC, Bayeux MC, Brochard P, Choudat D, Conso F et al. Consequences of occupational asthma on employment and financial status: a follow-up study. *Eur Respir J* 1997;**10**:55–58.