Corticosteroid-dependent Asthma: Our Clinical Experience

Asma corticodependiente: nuestra experiencia clínica

To the Editor,

Corticosteroid-dependent asthma is defined as the need for daily administration of oral corticosteroids. This definition, however, is ambiguous, since it includes both patients who receive this treatment and experience little improvement, and those who benefit from it (with a varying degree of response). The GOAL study showed that only 7% of patients who were uncontrolled at maximum doses of fluticasone/salmeterol achieved control with an oral steroid regimen. Few studies have been conducted in this specific patient group, despite their clinical relevance. We report the case of a patient with corticosteroid-dependent asthma, and review the management and progress of all corticosteroid-dependent asthmatics seen in our specialist clinic (10 of a total of 475 patients).

A 69-year-old woman, non-smoker, with a diagnosis of late-onset, non-allergic asthma, IgE 770 kU/l, eosinophils 900/μm³, FENO 31 ppb. Asthma was initially poorly controlled with a combination of maximum doses of budesonide/formoterol, as indicated by asthma control test (ACT) 15, a severe exacerbation in the previous year, FEV₁ 64%, and positive bronchodilator challenge. Significant comorbidities included rhinosinusitis and obesity. Treatment with deflazacort 30 mg for 3 weeks increased ACT to 23 and FEV₁ to 67%, but when it was withdrawn, ACT returned to 16 and FEV₁ to 67%. Tiotropium (18 μg/day) was added to the combination of fluticasone/salmeterol (500/50 μg, but ACT remained unchanged, while FEV₁ rose to 70%. Treatment was subsequently switched to inhaled fluticasone (1000 μg/day), tiotropium (18 μg/day) and indacaterol (150 μg/day). The patient is currently free of exacerbations, her ACT is 24 and FEV₁ is 79%.

In our opinion, a patient who is uncontrolled and presents bronchial obstruction despite treatment with a combination of maximum dose inhaled long-acting corticosteroids (IC)-long-acting β₂ agonist (LABA) has corticosteroid-dependent asthma. In the case of our patient, her FEV₁ normalized (at least to >70%) and ACT rose to ≥20 after 3–4 weeks of treatment with deflazacort 30 mg. Subsequently, when the oral corticosteroid was discontinued, her clinical and functional status returned to the previous situation.

Clinical characteristics, treatment, and progress of patients with corticosteroid-dependent asthma

Ten of our patients (of 475 regularly seen in our consulting rooms) had corticosteroid-dependent asthma. They were typically middle-aged (49.2±15.1 years), with late onset of symptoms (7/10 cases), intense peripheral eosinophilia (eosinophils 565.0±286.8/μm³), elevated IgE (379.7±357.3 kU/l), FENO (31.7±13.2 ppb), and significant comorbidities (particularly obesity, rhinosinusitis, and polyposis). Despite the correct use of IC/LABA at maximum doses, these patients remained symptomatic with signs of bronchial obstruction, yet only 2 developed 2 or more severe exacerbations in a period of 1 year. It seems that in most cases, standard treatment can prevent exacerbations, while failing to provide full control of symptoms or normalization of lung function. This was achieved in all cases when an oral corticosteroid was added, although this treatment was unacceptable due to adverse events.

These 10 patients were managed by the same pulmonologist. For the 2 patients in whom severe exacerbations persisted, the treatment strategy consisted, firstly, of adding omalizumab to the regimen. The response of the patients who received omalizumab confirmed its efficacy in reducing exacerbations, but also its lack of effect on lung function. Persisting bronchial obstruction may explain why optimal control of symptoms is elusive in many patients.

The next step for all patients consisted of adding a long-acting muscarinic antagonist, a medication that has already demonstrated its efficacy in this clinical setting. This intervention helped improve patients’ lung function and symptoms, but to an insufficient degree in 7 cases. We decided to add indacaterol to these 7 patients’ regimens: this potent bronchodilator has demonstrated efficacy in chronic obstructive pulmonary disease, but little experience is available in asthma. This combined therapeutic strategy resulted in a significant improvement in lung function and symptoms (Table 1) among corticosteroid-dependent asthma patients, while avoiding the use of oral steroids.

Table 1
Clinical Progress and Treatment Modifications in the 10 Patients Diagnosed With Corticosteroid-dependent Asthma.

<table>
<thead>
<tr>
<th></th>
<th>Initial</th>
<th>Final</th>
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<tbody>
<tr>
<td>ACT</td>
<td>16.9±3.8</td>
<td>22.5±2.7</td>
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<tr>
<td>Exacerbations/patient/year</td>
<td>0.32</td>
<td>0</td>
</tr>
<tr>
<td>FEV₁%</td>
<td>53.5±14.2</td>
<td>76.4±13.3</td>
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<tr>
<td>Oral corticosteroids</td>
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<tr>
<td>Omalizumab</td>
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<td>2</td>
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<tr>
<td>LAMA</td>
<td>0</td>
<td>10</td>
</tr>
<tr>
<td>Indacaterol</td>
<td>0</td>
<td>7</td>
</tr>
</tbody>
</table>

ACT: asthma control tests; FEV₁%: forced expiratory volume in 1 second; LAMA: long-acting anticholinergics.

Authorship

Study concept and design, data collection, analysis of results, interpretation of findings, and drafting the manuscript: Pérez de Llano.

Study design and data collection: García Rivero and Pallares.

Data collection: Mengual.

Data analysis and interpretation of results: Golpe.

Conflict of Interests

Dr Pérez de Llano has received payment from Novartis, Boehringer, Chiesi, Almirall, Esteve and Ferrer, for presentations at medical congresses, consultancy, and coordination or participation...
in clinical research projects. He has also been invited to attend national or international congresses by some of these companies.

References


Luis Alejandro Pérez de Llano,ᵃᵇ Juan Luis García Rivero,ᵇ Abel Pallarés,ᶜ Noemí Mengual,ᵃ Rafael Golpeᵃ

ᵃ Servicio de Neumología, Hospital Universitario Lucus Augusti, Lugo, Spain
ᵇ Unidad de Neumología, Hospital Comarcal de Laredo, Laredo, Cantabria, Spain
ᶜ Servicio de Neumología, Complejo Hospitalario de Pontevedra, Pontevedra, Spain

*Corresponding author.
E-mail address: eremos26@hotmail.com (L.A. Pérez de Llano).

Double or Dual Bronchodilation: Defining the Correct Term

Broncodilatación doble o dual: definiendo el término correcto

To the Editor,

For some time, pharmacological treatment of chronic obstructive pulmonary disease (COPD) has been based on bronchodilation. Current guidelines recommend the use of a long-acting bronchodilator (LABD) as initial therapy for this disease.¹ The guidelines also recommend adding a second LABD of a different class in specific cases to boost the clinical effect of improved bronchodilation.¹ In recent years, ample scientific evidence and clinical experience has led to the acceptance of the novel approach of combining 2 LABDs in a single device.²

As in all new ideas, the concepts under consideration must be well defined to avoid confusion. This new treatment modality is currently known as dual bronchodilation.³ Yet the term “dual” implies a single substance with 2 different features or properties,² while “double” describes a combination of 1 compound with another similar compound, that work together with the same aim.⁴ While a first reading might suggest that both terms have a similar meaning, there is a nuance that must be understood when discussing bronchodilators.

When 2 LABDs are administered together, we are in fact giving 2 different molecules. They are similar, in that they are both bronchodilators, but each one has its own characteristic pharmacology that works with the other to achieve the same objective: dilate the bronchi. Thus, the most accurate term for this treatment modality would be “double”. Indeed, according to the above-mentioned definition, a dual bronchodilator would be one that was capable of doing the work of two. These bronchodilators include the so-called muscarinic antagonist and β₂ agonists (MABA). MBAs are a new family of molecules that really do have dual activity: they block muscarinic receptors, while simultaneously inhibiting β₂ adrenergic receptors.³ Curiously, this new family of molecules has also been described in the literature as a dual bronchodilator,³ thus adding to the confusion. However, the mechanism of action of MBAs is completely different to bronchodilation achieved by the concomitant administration of 2 different LABDs, and, according to the above-mentioned definition, they may be authentically considered dual bronchodilation. We propose, then, using the term “double” to refer to the combined administration of 2 LABDs, and reserving the term “dual” for MBAs.

References


José Luis López-Campos,a,b,c María Abad-Abrazza,a Carmen Calero-Acuña,a,b

ᵃ Unidad Médico-Quirúrgica de Enfermedades Respiratorias, Instituto de Biomedicina de Sevilla (IBIS), Hospital Universitario Virgen del Rocío/Universidad de Sevilla, Sevilla, Spain
ᵇ CIBER de Enfermedades Respiratorias (CIBERES), Instituto de Salud Carlos III, Madrid, Spain
ᶜ Corresponding author.
E-mail address: lcampos@separ.es (J.L. López-Campos).

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