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EDITORIAL

About the Role of Indacaterol in Obstructive Airways Disorder: CON☆

A propósito do papel do Indacaterol na Patologia Obstrutiva das vias aéreas: CONTRA

Chronic obstructive pulmonary disease (COPD), a condition characterized by not fully reversible, inexorably progressive airway obstruction, has benefited in the last decade of relevant therapeutic progress. A prominent step forward was the settlement of effective and secure results in maintenance therapy. However, one should bear in mind that this disease is heterogeneous. In several clinical settings with different prognosis, a similar severity grade of airway obstruction may be found.^{1,2}

This evidence has been recently reinforced, and seriously questions many conclusions in COPD studies on maintenance therapy. In the case of a poor randomisation of populations, different groups may be under scrutiny, despite a comparable severity of obstruction.

Indacaterol arises in this therapeutic setting pretending to represent a real advance, capable of protagonizing the choice of the practitioner.^{3,4,5}

The excellent results obtained in several therapeutic trials should not pass beyond an accurate appraisal, which brings up some limitations to its wider range application.

Some definite limitations to the isolated use of long acting β -agonists in asthma are well known,⁶ due to safety limitations on these patients. So far these limitations do not apply to COPD, but there is not enough published evidence on this subject about indacaterol, due to insufficient duration of their double-blind controlled studies. Moreover, these studies have been restricted to severe and moderate severity COPD cases, excluding till now respiratory and/or cardiac insufficiency, the very severe COPD cases. Admitting the need of a substantial portfolio of experimental evidence in novel medications, paving the bridge for a real world of clinical practice, it is even more important to fully grant

its safety, through a wide multicenter basis of information, building a satisfactory confidence ballast. Indacaterol still yields a scarce background of data, in my opinion. To support a COPD maintenance therapy instrument, long standing evidence, at least two-year non-stop controlled parallel double-blind design, is needed. These conditions will better approach daily practice and this type of studies is indispensable and still missing, even for indacaterol.

Indacaterol widely claimed a faster activity onset, recently proved in relation to other COPD maintenance therapy agents and similar to salbutamol. This characteristic should represent a grant in therapeutic compliance, in the long run.⁷ However, this faster onset of action is only statistically significant on the first day of therapy, in comparative studies to tiotropium.^{8,9}

On the other side, patients are frequently misleading their inhalatory therapeutic schedule. The acknowledged data for indacaterol still do not prove a fair safety in this hypercompliant patients on fast relief of indacaterol, specially in exacerbation outbursts, abusively accumulating inhalation doses. Should dosage limits be important so far, the safety can be compromised, in a way that has not been fully clarified.

On the 5 main clinical studies which derivate indacaterol data, the main adverse effect is COPD evolution worsening,¹⁰ and the commoner is irritative cough following the administration of the drug, which deserves further explanation on novel longer range data.

For COPD maintenance approach it is not enough to grant stable bronchodilation and dyspnea or quality of life improvements.¹¹ Support to muscle rehabilitation and the prevention of acute severe exacerbations should be demonstrated, as long as the effect on respiratory function decline and on all-cause mortality.¹² More data on these fields are needed for indacaterol, comparatively to other pharmacological options to long term COPD maintenance therapy.

Another objection to a first choice of therapy in COPD with β -agonist drugs is the recently reinforced finding that

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cholinergic receptors have a more prominent role in COPD pathogenesis than adrenergic receptors, linked to COPD inflammatory outburst mechanisms.¹³

Some published data have recently favoured the combination of indacaterol and long-acting anticholinergics in patients not satisfactorily controlled with a single long-acting bronchodilator agent, as a more efficacious and safe option for the long-term moderate-to-severe COPD maintenance therapy,¹⁴ reinforcing a previously favoured strategy of maximal bronchodilation, as a primary outcome of pharmacological intervention on these COPD severity stages.

In conclusion, longer studies of proved scientific quality are needed to enable indacaterol as a valuable therapeutic instrument for the maintenance approach of COPD, either isolated or in combination.

Conflict of interests

Dr. José M. Reis Ferreira is a respiratory practitioner in Air Force Hospital, Lisbon, and has not declared interests on this field. He has received fees for respiratory external consulting activities and Advisory Board participations (Spiriva-tiotropium) or in workshops from Boehringer Ingelheim, Lda and Portuguese OM Pharma, training activities in COPD from Pharmacy National Association and GSK, and has received financial support for travelling, accommodation and/or inscription fees in scientific events or courses from BIAL Pharma, Astra Portuguesa, Laboratórios Vitória, Boehringer Ingelheim, Tecnifar, Carefusion (Viasys), Pulmocer – Equipamentos Médicos, Lda, Portuguese Radiometer, Vitalair, Gasin and Merck Sharp & Dohme/Schering Portuguesa.

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