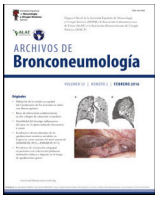
Archivos de Bronconeumología 57 (2021) 621–622

Sociedad Española de Neumología y Cirugía Torácica SEPAR

ARCHIVOS DE Bronconeumología

www.archbronconeumol.org



Editorial

Tapering of Oral Corticosteroids for the Treatment of Asthma

Disminución gradual de los corticosteroides orales en el tratamiento del asma

The use of oral corticosteroids (OCS) as a long-term therapy for asthma management is restricted to Global Initiative for Asthma (GINA) 'step-5' patients (i.e. the most severe level of disease), whose level of asthma control is unsatisfactory despite the use of high doses of maintenance inhalers or appropriate biologicals.[1] In the latter scenario, the daily OCS dose cited in GINA is not expected to exceed 7.5 mg/d,[1,2] and current opinion restricts OCS use to those patients who are ineligible for biologicals. Avoiding OCS is an old issue, and OCS sparing has been used as a pertinent outcome by which to judge alternative therapies at least since the 1990s.[3–5] Nevertheless, recent studies indicate that real-world OCS usage appears to spill over the 'step-5' boundary, with OCS remaining overused for asthma management.[6–8] The side effects of OCS usage can appear with seemingly small cumulative doses (starting as just >500 mg/year[9]), and can include obesity, diabetes, adrenal insufficiency, osteoporosis/fractures, cataracts or glaucoma.

In this context, it is important to remind the asthma care community that the use of OCS for long-term asthma management should be a last resort and cumulative doses >500 mg/year a red flag for referral to a specialist, especially if comorbidities are present. We further propose that OCS usage be envisioned more as a cycle of multi-level evaluation with a constant potential for dose reduction, than as a "steady maintenance" therapy per se. Following evaluation of OCS response, achieved stability in asthma control, and unwanted OCS side effects, a decision as to whether or not to attempt OCS tapering should be systematically encouraged. This point of view is supported by a recent Delphi study summarizing the views of 131 asthma and/or OCS tapering experts from around the world.[10] One of the most important consensuses drawn from the latter study was that the circumstances under which OCS tapering was not appropriate were restricted to EGPA/ABPA that relapses during tapering. Side effects such as adrenal insufficiency or withdrawal symptoms were not considered good reasons to preclude attempts at tapering. An initial failure in tapering should result in choosing a next, slower tapering speed after disease control is re-established. In general, a respiratory disease specialist who prescribes OCS for asthma management should also de facto be (or become) experienced in OCS tapering.

OCS tapering is not, however, without its challenges. First, it must often be individualized to each patient's circumstances. A physician may decide that a patient with certain risk factors for tapering failure should start at a slow rhythm, while another who lacks such factors or who is taking particularly high doses of OCS may be able to taper at a faster pace. Head-way into providing adaptable tapering algorithms has been made, with the OCS Tapering Delphi Consensus[10] providing a general algorithm structure, and the ongoing PONENTE study providing an example of a specific and reproducible tapering plan in the context of biologicals.[11]

An additional challenge is how to detect and manage adrenal insufficiency (AI) when it arises during OCS tapering. An important result demonstrated by the OCS Tapering Delphi consensus is just how little experts agree on many issues surrounding AI. Starting with the extent or the variability with which OCS can affect the hypothalamic-pituitary-adrenal axis, moving through the need for replacement therapy or its circadian rhythms, or any notion of switching to hydrocortisone or not, the vast majority of statements proposed by and then evaluated by the expert panel concerning AI failed to reach consensus (despite the presence of expert endocrinologists). The experts nevertheless agreed that AI is insufficiently assessed or under-recognised in OCS-treated asthma, and that it should be assessed using fasting morning cortisol, and in case of intermediate results, follow up with a (short) tetracosactide/cosyntropin test.[10] Beyond performing assessments when symptoms or OCS tapering failure are encountered, a formal rhythm for regular AI testing was not specified. Aside from the consensus, we suggest that future research should consider the slopes/trends generated by regular AI assessments as predictive of future insufficiency.

In contrast with AI, the OCS tapering expert panel quickly reached consensus on a large majority of statements concerning patient–physician shared decision-making, underlining that the latter should be systematically implemented in as much as possible. The perceived benefits were multiple and included improving patient knowledge and empowerment over their condition. In particular, the asthma care community should take note of the following pieces of advice for OCS self-managers that achieved positive consensus: (i) if possible, do not opt for regular OCS use; (ii) the lowest active dose of OCS for the shortest duration is preferable; (iii) closely monitor symptoms while tapering, including those of AI; (iv) help the process of OCS tapering by overcoming minor discomfort related to it.[10] The experts also agreed that certain patients are wary of OCS tapering because they associate OCS with their safety; appropriate educational opportunities during the shared decision-making process may help empower tapering.

An important stimulus behind the current interest in OCS tapering is the advent and success of biological therapies. Several

1579-2129/© 2021 SEPAR. Published by Elsevier España, S.L.U. All rights reserved.

physiological pathways that can result in a steroid-responsive high-T2 asthma phenotype are now successfully targeted by different biologicals. The reader should note that the success of a biological is not only judged according to improvement in asthma control and successful prevention of exacerbations, but also by the success of OCS tapering. Again referring to the OCS Tapering Delphi study, rapid, positive consensus was achieved for the notion that OCS tapering should be re-attempted every time a new biological treatment for eosinophilic asthma patients becomes available, and that not achieving a >50% reduction in OCS dose is a failure for a given biological therapy that may mandate switching treatment strategies. Failure to achieve OCS weaning within the 12 months following the initiation of a biological was also considered a good reason for switching.[10] In conclusion, the asthma care community should be encountering increasingly frequent opportunities for OCS tapering, and is behoved to do so.

Funding

No funding was obtained in the context of this invited editorial.

Conflicts of Interest

CS reports a previous grant from Astra Zeneca; AB reports grants, personal fees, non-financial support and other from Astra Zeneca, grants, personal fees and other from GSK, grants, personal fees, non-financial support and other from Boeringher Ingelheim, personal fees, non-financial support and other from Novartis, personal fees and other from Teva, personal fees and other from Regeneron, personal fees, non-financial support and other from Chiesi Farmaceuticals, personal fees, non-financial support and other from Actelion, other from Gilead, personal fees and non-financial support from Roche, outside the submitted work.

References

1. Global Initiative for Asthma. Global strategy for asthma management and prevention; 2020.
2. Boulet L-P, Godbout K. Oral corticosteroids tapering in severe asthma. Am J Respir Crit Care Med. 2020.
3. Lacronique J, Renon D, Georges D, Henry-Amar M, Marsac J. High-dose beclomethasone: oral steroid-sparing effect in severe asthmatic patients. Eur Respir J. 1991;4:807–12.
4. Mullarkey MF, Lammert JK, Blumenstein BA. Long-term methotrexate treatment in corticosteroid-dependent asthma. Ann Intern Med. 1990;112:577–81.
5. Nelson HS, Busse WW, deBoisblanc BP, Berger WE, Noonan MJ, Webb DR, et al. Fluticasone propionate powder: oral corticosteroid-sparing effect and improved lung function and quality of life in patients with severe chronic asthma. J Allergy Clin Immunol. 1999;103:267–75.
6. Bleecker ER, Menzies-Gow AN, Price DB, Bourdin A, Sweet S, Martin AL, et al. Systematic literature review of systemic corticosteroid use for asthma management. Am J Respir Crit Care Med. 2020;201:276–93.
7. Bourdin A, Fabry-Vendrand C, Ostinelli J, Ait-Yahia M, Darnal E, Bouee S, et al. The burden of severe asthma in france: a case-control study using a medical claims database. J Allergy Clin Immunol Pract. 2019;7:1477–87.
8. Tran TN, King E, Sarkar R, Nan C, Rubino A, O'Leary C, et al. Oral corticosteroid prescription patterns for asthma in France, Germany, Italy and the UK. Eur Respir J. 2020:55.
9. Price DB, Trudo F, Voorham J, Xu X, Kerkhof M, Ling Zhi Jie J, et al. Adverse outcomes from initiation of systemic corticosteroids for asthma: long-term observational study. J Asthma Allergy. 2018;11:193–204.
10. Suehs CM, Menzies-Gow A, Price D, Bleecker ER, Canonica GW, Gurnell M, et al. Expert consensus on the tapering of oral corticosteroids for the treatment of asthma: a delphi study. Am J Respir Crit Care Med. 2020.
11. Menzies-Gow A, Corren J, Bel EH, Maspero J, Heaney LG, Gurnell M, et al. Corticosteroid tapering with benralizumab treatment for eosinophilic asthma: PONENTE Trial. ERJ Open Res. 2019:5.

Carey M. Suehs [a,b,*], Arnaud Bourdin [a,c]
[a] *Department of Respiratory Diseases, Univ Montpellier, CHU Montpellier, Montpellier, France*
[b] *Department of Medical Information, Univ Montpellier, CHU Montpellier, Montpellier, France*
[c] *PhyMedExp, CNRS, INSERM, Univ Montpellier, CHU Montpellier, Montpellier, France*

[*] Corresponding author.
E-mail address: c-suehs@chu-montpellier.fr (C.M. Suehs).