



Severe asthma in Brazil: from diagnosis to treatment

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Improved access to inhaled corticosteroids has contributed to an important reduction in asthma-related morbidity and mortality in Brazil and worldwide.^(1,2) However, some individuals with asthma remain symptomatic despite having been prescribed adequate doses of inhaled maintenance therapy. For these patients, it is crucial to confirm that the asthma diagnosis is correct, as well as to identify and mitigate modifiable aggravating factors that contribute to the lack of asthma control, such as improper use of inhalers, poor treatment adherence, exposure to environmental stimuli, and uncontrolled comorbidities. After that, if asthma remains uncontrolled, a diagnosis of severe asthma can be established.⁽³⁾

Approximately 3.7% of asthma patients have severe disease.⁽⁴⁾ Despite this relatively low prevalence, patients with severe asthma are particularly susceptible to loss of quality of life and lung function, as well as to exacerbations requiring hospitalization.^(5,6) In addition to the unfavorable outcomes directly related to asthma, the use of high doses of inhaled medications and the frequent use of systemic corticosteroids in these patients, despite minimizing morbidity and mortality from respiratory events, add morbidity related to the systemic effects of these drugs.⁽⁷⁾ Among the most relevant systemic effects are loss of bone mineral density, increased blood glucose, weight gain, immunosuppression, etc.

This worrisome scenario has given rise to research aimed at better understanding the determinants of severe asthma. Advances in knowledge of immunopathology and pathophysiology have allowed the development of new treatments,⁽⁸⁾ and clinical trials have shown that drugs previously used for other respiratory diseases, such as long-acting antimuscarinic bronchodilators, are also effective for the treatment of severe asthma.⁽⁹⁾ Inhaled corticosteroids associated with long-acting β_2 agonist bronchodilators are usually the main therapeutic regimen for patients with severe asthma, whereas the addition of other drugs or non-pharmacological therapies should be guided by the phenotypic characteristics of each patient.⁽¹⁰⁾ As an example, some biologic drugs are indicated for severe eosinophilic asthma, whereas the anti-IgE antibody is indicated for atopic individuals with high IgE; azithromycin, despite less robust evidence, has been indicated to prevent asthma exacerbations; and bronchial thermoplasty is the last resort for patients who do not respond to or do not meet criteria for biologic drugs.

If, on the one hand, the diversity of therapeutic options and the concept of precision therapy contribute to improving the prognosis of severe asthma, on the

other hand, they make the management of this disease a little more complex. Therefore, severe asthma should be managed by specialists. However, it is not feasible that all patients with this condition are referred to centers of excellence that are usually affiliated with medical schools or with tertiary care centers in medium-sized and large urban areas. It is necessary that health care professionals who treat respiratory diseases in the secondary care setting are also trained and have the necessary resources to identify and treat severe asthma. It is in this context that the *Sociedade Brasileira de Pneumologia e Tisiologia* (SBPT, Brazilian Thoracic Association) has published the "2021 Brazilian Thoracic Association recommendations for the management of severe asthma".⁽¹¹⁾ This document was compiled by a panel of 17 pulmonologists with clinical and research experience in severe asthma. The text objectively and didactically addresses the most relevant and up-to-date topics on this subject, such as the criteria for diagnosing severe asthma; useful biomarkers for phenotyping; important aspects of the immunopathology of severe asthma, the understanding of which is necessary to comprehend the rationale for using phenotype-guided management strategies; and the therapeutic options available in Brazil. When discussing the available therapies, the SBPT document⁽¹¹⁾ not only presents efficacy and safety results from the most recent clinical trials, but also provides evidence from real-world pragmatic studies that are adequate to the Brazilian reality.

This document⁽¹¹⁾ has the great merit of facilitating the dissemination of the most up-to-date knowledge on the subject, but disseminating this knowledge is just one of the necessary steps for widespread diagnosis and treatment of severe asthma. Currently, there are structural limitations outside referral centers that can make it difficult to comply with the SBPT recommendations in the context of the Brazilian *Sistema Único de Saúde* (SUS, Unified Health Care System). For example, the large number of patients relative to the number of health care professionals who treat respiratory diseases limits the amount of time available for each patient's consultation, which can compromise the quality of assessment; patients treated in public health care services often have financial limitations to solve household environmental problems; simple ancillary tests, such as spirometry, are not always available in less-populated urban areas; and complex ancillary tests required for the diagnosis of severe asthma, despite having progressively become more accessible, are not yet widely available.⁽¹²⁾ In addition, access to biologic drugs and bronchial thermoplasty, which are not

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effectively available via SUS, is difficult. Fortunately, the latest update of the Brazilian National Ministry of Health's clinical protocols and therapeutic guidelines for asthma⁽¹³⁾ incorporates two biologic agents, namely omalizumab and mepolizumab, into the treatment regimen for severe asthma proposed by SUS, opening up the possibility that these drugs will be available in the not too distant future.

The first step in solving a problem is getting to know it. We will work so that the "2021 Brazilian Thoracic Association recommendations for the management of severe asthma"⁽¹¹⁾ will be widely disseminated to physicians in our specialty and to those in related specialties and that pertinent information will be available to primary health care professionals, their patients, and health care administrators.

REFERENCES

1. Suissa S, Ernst P, Benayoun S, Baltzan M, Cai B. Low-dose inhaled corticosteroids and the prevention of death from asthma. *N Engl J Med.* 2000;343(5):332-336. <https://doi.org/10.1056/NEJM200008033430504>
2. Bezerra de Menezes M, Ponte EV, Bertagni Mingotti CF, Carvalho Pinto RM, Bagatin E, Bião Lima V, et al. Provision of inhaled corticosteroids is associated with decrease in hospital admissions in Brazil: A longitudinal nationwide study. *Respir Med.* 2020;166:105950. <https://doi.org/10.1016/j.rmed.2020.105950>
3. Lago VCD, Vale SAD, Godoy I. Yes, there really are individuals with severe asthma: the importance and limitations of data obtained from specialized centers. *J Bras Pneumol.* 2020;46(3):e20200191. <https://doi.org/10.36416/1806-3756/e20200191>
4. Hekking PW, Wener RR, Amelink M, Zwinderman AH, Bouvy ML, Bel EH. The prevalence of severe refractory asthma. *J Allergy Clin Immunol.* 2015;135(4):896-902. <https://doi.org/10.1016/j.jaci.2014.08.042>
5. Silva JN, Rocha A, de Souza IA, Athanazio R, Ponte EV. Does peripheral blood eosinophil count predict lung function improvement in adult subjects with asthma?. *Ann Allergy Asthma Immunol.* 2021;127(3):388-389. <https://doi.org/10.1016/j.ana.2021.05.024>
6. Ponte EV, Mingotti CFB, Mamoni RL, Marchi E, Martinelli JE, de Menezes MB, et al. Hospital admission rate in children and adolescents with mild persistent asthma. *Pediatr Pulmonol.* 2021;56(7):1889-1895. <https://doi.org/10.1002/ppul.25363>
7. Ponte EV, Mingotti CB, Souza-Machado C, Silva JN, Chequi L, Arbex FF, et al. Comparing hospital admissions, comorbidities, and biomarkers between severe asthma and Gold III-IV chronic obstructive pulmonary disease. *Clin Respir J.* 2021;10.1111/crj.13435. <https://doi.org/10.1111/crj.13435>
8. Marques Mello L, Viana KP, Moraes Dos Santos F, Saturnino LTM, Kormann ML, Lazaridis E, et al. Severe asthma and eligibility for biologics in a Brazilian cohort. *J Asthma.* 2021;58(7):958-966. <https://doi.org/10.1080/02770903.2020.1748049>
9. Kim LHY, Saleh C, Whalen-Browne A, O'Byrne PM, Chu DK. Triple vs Dual Inhaler Therapy and Asthma Outcomes in Moderate to Severe Asthma: A Systematic Review and Meta-analysis. *JAMA.* 2021;325(24):2466-2479. <https://doi.org/10.1001/jama.2021.7872>
10. Alves AM, Mello LM, Matos ASL, Cruz AA. Clinical features and associated factors with severe asthma in Salvador, Brazil. *J Bras Pneumol.* 2020;46(3):e20180341. <https://doi.org/10.36416/1806-3756/e20180341>
11. Carvalho-Pinto RM, Cançado JED, Pizzichini MMM, Fiterman J, Rubin AS, Cerci-Neto A, et al. 2021 Brazilian Thoracic Association recommendations for the management of severe asthma. *J Bras Pneumol.* 2021;47(6):e20210173.
12. Ponte EV, Fanelli MF, Ferreira RTR, Pereira JF, Alcadipane MSES, de Lima VB, et al. Lung Cancer Mortality and the Availability of Chest Computerized Tomography: A Longitudinal Nationwide Study. *Cancer Invest.* 2020;38(5):270-276. <https://doi.org/10.1080/07357907.2020.1768400>
13. Brasil. Ministério da Saúde [homepage on the Internet]. Brasília: Ministério da Saúde; c2021 [updated 2021 Aug 24; cited 2021 Sep 20]. Portaria Conjunta Nº 14, de 24 de Agosto de 2021. Aprova o Protocolo Clínico e Diretrizes Terapêuticas da Asma. [Adobe Acrobat document, 105p.]. Available from: <https://www.gov.br/saude/pt-br/assuntos/protocolos-clinicos-e-diretrizes-terapeuticas-pcdt>