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Environmental impact of inhaler devices on respiratory care: a narrative review

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ABSTRACT

Climate change is a huge and present threat to human health. This article aims to deepen the knowledge about the environmental impact of inhaler devices on their carbon footprint for patients and health professionals, providing information that allows a better choice of the type of device to be prescribed for the treatment of asthma and COPD. This narrative and nonsystematic review was carried out by searching databases (PubMed, Google Scholar, SciELO, and EMBASE) for articles published between 2017 and 2022, written in Portuguese or in English, using the search words "inhalation device" OR "environmental." The review showed that global warming cannot be addressed by focusing only on inhaler devices. However, the devices that we use to treat respiratory diseases such as asthma and COPD, which are diseases that are aggravated by climate change, are also causing that change. Therefore, health professionals, patient organizations, and industries should take a lead in health policies to offer affordable alternatives to inhalers containing hydrofluoroalkane.

Keywords: Asthma; Pulmonary disease, chronic obstructive; Environmental health; Nebulizers and vaporizers.

INTRODUCTION

Climate change is a huge and present threat to human health. It disproportionately affects the poorest and most vulnerable individuals, including those with pre-existing lung diseases. The emission of greenhouse gases (GHG) plays a significant role in the genesis of climate change. Actions to minimize it must be carried out to protect current and future generations from its worst effects.[1]

As a result of these actions, governments worldwide have committed to legislative changes to reduce GHG emissions.[2] Although the efficacy and safety of medical treatments are always a priority, the health sector has significantly contributed to the increase in GHG emissions. In recent years, the environmental impacts arising from all aspects of life have become an increasingly unavoidable condition, and inhalation therapies are no exception.[3]

Asthma and COPD are the most common chronic respiratory diseases and are among the leading causes of morbidity and mortality worldwide.[4] It is estimated that there are at least 300 million patients with asthma and 328 million patients with COPD.[5]

Inhalation is the preferred route for the treatment of asthma and COPD. For that, inhalers are used, which are devices that reduce the morbidity and mortality associated with both diseases and significantly improve the quality of life of patients.[6,7] Global initiatives advocate the gradual reduction of inhaler devices that use fluorinated gas as a propellant—pressurized metered-dose inhalers (pMDI)—since such devices are associated with significant environmental impacts.[8]

Three main classes of inhalation therapy devices are available for patients with asthma and COPD: pMDIs, dry powder inhalers (DPIs), and soft mist inhalers (SMIs).[9] The carbon footprint of these inhaler devices is distinct, being more intense with pMDIs in comparison with DPIs and SMIs. That means that new approaches must be considered to balance environmental goals with patient health and well-being, maintaining a diverse range of therapeutic options for patients and physicians.[10]

This article aims to deepen the knowledge about the environmental impact of inhaler devices on their carbon footprint for patients and health professionals, providing information that allows a better choice of the type of device to be prescribed in the treatment of asthma and COPD patients, aiming to reduce their environmental impact. It also aims to inform policymakers who wish to reduce the carbon footprint in health systems.

INHALER DEVICES

pMDIs

Until the early 1990s, pMDIs that contained chlorofluorocarbon (CFC) as propellants were the most common way to administer inhalation therapy to patients with asthma and/or COPD. In 1987, the Montreal Protocol,[11] which focused on substances capable of destroying the ozone layer, recommended the progressive elimination of CFCs because it not only

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destroys the ozone layer but also has the potential to contribute to the already extremely high global warming.[12] Since then, new forms of inhalation therapy have been developed for patients with asthma and/or COPD.[13,14] In Brazil, such as in all countries that complied with the Montreal Protocol, we only use hydrofluoroalkane (HFA) as a propeller for pMDIs.

The global warming potential (GWP) of gases indicates how much warming a gas causes over a given period (typically 100 years) in comparison with CO_2, which was defined as GWP = 1; therefore, all other gases have higher values.[15,16]

CFC used to be the propellant for pMDIs, and, more recently, HFA has been introduced. The GWP of HFA is significantly higher due to its composition: HFC-134a and HFC-227ea, whose GWP are 1,300 and 3,350, respectively.[6]

MDIs commonly prescribed for chronic respiratory diseases contain hydrofluorocarbons (HFCs), which are powerful greenhouse gases and a significant cause of climate change. HFCs in MDIs (HFC-134a and HFC-227ea) are 1,000-3,000 times more potent than CO_2 and persist in the atmosphere for 14 years, causing climatic feedbacks. Currently, HFC-152a is a developing propellant that has a lower GWP when compared with the existing ones. Its launch is scheduled for 2025. However, according to the Kigali Amendment to the Montreal Protocol,[11] HFC-134a, HFC-227ea, and HFC-152a are expected to be phased out between 2020 and 2050. However, countries are free to choose how to phase out these HFCs during that period.

It is assumed that resulting from the high GWP values of HFC-134a and HFC-227ea, the use of HFCs in pMDIs accounted for direct emissions of approximately 18,000 ktCO_2eq in 2018, representing approximately 0.03% of total global GHG emissions in that year.[17] In terms of CO_2eq emissions, a single dose of two jets of an HFC-134a pMDI is comparable to day-to-day activities emissions, such as traveling two kilometers on a Seat Ibiza Ecomotive car.[18,19]

DPIs

DPIs are devices that provide powdered medication (active ingredient mixed with excipients) without the need for a propellant gas. They are safe and effective for most patients, do not contain GHG, and are activated by forced patient inspiration. Thus, their life cycle assessments are substantially lower than those for pMDIs.[16,20]

Real-world evidence shows that the combined administration of inhaled corticosteroids and long-acting β_2 agonists in a single daily dose using a DPI can improve asthma control and adherence to treatment and can reduce the carbon footprint resulting from medical care. In addition to simplifying therapy, it improves asthma control and reduces GHG emissions. If we focus on patients with partially controlled or uncontrolled asthma, who might use large amounts of short-acting β_2 agonists (SABA) via a pMDI, instead of prioritizing inhaled corticosteroids via DPIs, there will be golden opportunities to make asthma treatment more effective, safe, and environmentally friendly.[21]

Patients who switched from pMDI-based maintenance therapy to DPI-based maintenance therapy more than halved their inhaler carbon footprint with no loss of asthma control. The inhaler's remaining carbon footprint can be reduced by switching from pMDI to DPI rescue medications or alternative lower carbon footprint rescue inhalers, if available.[22]

GHG emissions from asthma exacerbation management were highest for severe/life-threatening events, followed by moderate exacerbations. Treatment to reduce the severity and occurrence of exacerbations, such as effective, long-term control therapy using low emitting DPIs can help mitigate asthma care emissions. For mild exacerbations, the use of DPIs can eliminate associated emissions.[23]

In addition to a lower global warming potential, DPIs have additional benefits over pMDIs in other domains and should be considered as first-line therapy when clinically appropriate.[24]

SMIs

SMIs are small portable devices that produce aerosols of breathable diameter from aqueous formulations. These new-generation devices produce an aerosol by mechanisms other than those described for nebulizers. They consist of the collision of two jets of liquid to produce an aerosol, force the liquid through tiny holes with micron diameters, or use a mesh/vibrating plate or other new mechanisms (e.g., electrohydrodynamic effects). The improved efficiency and smaller aerosol particle size provided by these devices ensure that the aerosol generated is deposited deep into the lungs. SMIs are currently more expensive than standard pMDIs and DPIs.[3]

Nebulizers can also be used—although this typically occurs in an emergency setting or in cases when patients cannot use pMDIs or DPIs because they have physical or cognitive impairments or in patients who are at risk of having severe symptoms/exacerbations.[6]

It is difficult to make accurate comparisons among studies on the relative carbon footprint of inhalers due to the different methodologies employed. However, in general, all DPIs and SMIs have a substantially smaller carbon footprint than do pMDIs. Other environmental benefits may come from reusable inhalers and longer treatment packages (e.g., 90-day options instead of 30-day inhalers).

RECYCLING

Currently, less than 1% of inhaler devices are recycled every year. Their recycling has the potential to eliminate all emissions associated with their disposal; however, it is mandatory to recycle between 81% and 87% of the inhaler devices currently in use.[16] In clinical practice, such end-of-life recycling rates

can be very difficult to achieve and require significant investment and behavioral changes; nevertheless, if recycling schemes were launched now, they would achieve reductions in the short term.[9]

Recycling inhalers at specific locations such as pharmacies, as opposed to landfill disposal, should enable the reuse of plastic or aluminum components and reduce CO_2 emission.[21]

Improper disposal of pMDI devices with unused doses is especially worrying, because it not only increases the prescription load, but disused devices continue to release GHG, which persist in the atmosphere for up to 50 years.[9,17]

In a position statement on environment and lung health,[21] the British Thoracic Society has highlighted the importance of informing patients about how to avoid disposing of inhalers in landfills with the following recommendations:

- Expansion of recycling and disposal schemes to prevent remaining propellant gases from being released into the atmosphere and avoid waste of plastic packaging, and
- Information on where recycling and disposal schemes are available, including which major local pharmacy chains would offer the service.

MEDICAL CARE

The health sector needs to reduce GHG emissions to help mitigate climate change.[25] For that, proven and medically safe ecological alternatives are needed.[26] Indeed, the medication chosen must be appropriate for each patient. The final choice of the inhaler device must comply with different factors, such as the real efficacy of the molecules, factors related to patient use, cost, patient preference, "custom and practice" of the physician, clinical evaluation, appropriate education, and evaluation programs to ensure the correct technique for inhaler use.[21] Patient choice can also be improved by increasing the diffusion of publicly available information on the environmental impact of different inhalation products.[2,14,27,28]

Pepper et al.[29] warned that there is evidence that the short-term exposure to ozone may cause morbidity in individuals with asthma and suggested that exposures to levels below the currently allowed standard[30] may be associated with an increased use of SABA.

In an interview with inhaler prescribers, Walpole et al.[31] reported that only 9% discuss the environmental impact of inhalers with patients, and only 13% discuss the disposal of inhalers. However, 46% of the respondents said they would educate patients about the environmental impacts of inhalers.

Although some practical (dis)advantages of pMDIs and DPIs are known, it should be noted that[20]:

- The global warming effect of pMDIs is mainly caused by their use (95-98%), not by the manufacture of this class of inhaler devices.
- Unknown amounts of propellant gases may remain in the canister after use and, in variable time, will be released into the atmosphere.
- Most pMDIs do not have dose counters.
- Without a dose counter, it can be difficult to know how many doses are left in the device.
- Inadvertent use of empty pMDIs can lead to preventable exacerbations or even avoidable hospital admissions.
- Inadvertent replacement of a pMDI that still contains medications would incur unnecessary costs.
- Adherence to inhalation instructions can be problematic when changing devices, because not every patient uses a pMDI with the recommended spacer.
- Switching to a DPI can improve adherence to guidelines because spacer use is not required.
- Changes without sufficient education can result in lack of control of the disease, exacerbations, and increased use of health services.

CURRENT SITUATION

SABA via pMDIs accounts for a considerable share of the total inhaler market. They are cheaper than DPIs, and their overuse is common in many countries. Recent studies have shown that most of all SABA inhalers for asthma were prescribed to patients who were likely to use them excessively (≥ 3 inhalers prescribed per year).[32,33]

In Brazil, the real situation regarding the use of inhaler devices is not completely known. Table 1 shows the numbers of devices marketed from 2017 to 2021 according to therapeutic agents and devices. As we can see, there was an increase in sales during the period. It is worth highlighting the decrease in SABA sales during 2021,[34] a year that coincided with the

Table 1. Medications and inhaler devices (in units) used in the treatment of asthma and marketed in Brazil.

Medication/ID	Year[a]				
	2017	2018	2019	2020	2021
SABA/pMDI	6,659,604	8,734,188	8,913,888	9,071,179	7,767,193
LAMA/SMI	956,267	1,078,453	1,252,303	1,507,886	1,539,340
IC+LABA/pMDI (HFA propellant)	995,709	1,086,145	1,164,031	1,337,000	1,564,198
IC+LABA/DPI	7,765,098	7,764,689	8,627,569	9,561,575	10,004,885

Based on Walpole et al.[31] ID: inhaler device; SABA: short-acting β_2 agonists; pMDI: pressurized metered-dose inhaler; LAMA: long-acting muscarinic antagonists; SMI: soft mist inhaler; IC: inhaled corticosteroids; LABA: long-acting β_2 agonists; HFA: hydrofluoroalkane; and DPI: dry powder inhaler. [a]The period between July 1 and June 30 of the following year.

peak of the COVID-19 pandemic, when social isolation was more effective.[35]

A recently published alert has indicated how much CO_2 equivalent is released (carbon footprint) by activating inhaler devices per pharmacological agent[36] (Table 2).

COMPARISON TABLES OF CARBON FOOTPRINT

Data on the actual carbon footprint of individual inhalers are very limited; therefore, the following tables provide indicative rather than actual values. The carbon footprint for comparisons estimated that a typical car's average trip (9 land miles) produces 2,610 gCO_2eq (or 290 gCO_2eq per mile). The numbers are based on the mean CO_2eq values per inhaler as estimated by PrescQIPP.[37] The U.S. Environmental Protection Agency estimated that, in 2020, the discharge and leakage of HFA-containing pMDIs were responsible for generating 2.5 million metric tons of CO_2eq, the approximate equivalent to the emissions of 550,000 passenger vehicles driven for a year.[38] More objectively, the city of Uruguaiana, at the border between Brazil and Uruguay in the southern region of the country, has a public health care program for patients with asthma that quantitatively calculated the dispensation of SABA via pMDIs in one year (Table 3); therefore, we can have a picture of such a reality.

FINAL CONSIDERATIONS

The latest International Panel on Climate Change report[38] called for "urgent action to keep the global average temperature rise below 1.5°C," halting the destruction of nature. However, there remains an uncomfortable recognition that the provision of health services has contributed to global warming.[39]

Global warming cannot be addressed by focusing only on inhaler devices. However, the drugs that we use to treat respiratory diseases such as asthma and COPD, which are diseases that are aggravated by climate change, are also causing climate change.[27]

From the point of view of the industry and government, several pharmaceutical companies and national health organizations have developed 'Net Zero' commitments to achieving zero carbon emissions in their operations.[37] For companies that manufacture current HFC-containing pMDIs, they may represent a substantial proportion of the entire carbon footprint of the company.[3,40-44] More recently, published figures indicate that the use of pMDIs accounts for 13% and 36%, respectively, of AstraZeneca's and GSK's total carbon emissions.[45,46] Pharmaceutical companies should consider these issues in their strategic planning for new developments in inhalation therapy, such as reusable inhalers or longer treatment packages (e.g., 90-day rather than 30-day options),[47] so that they could reduce their carbon footprint.[3]

In conclusion, as long as we can offer safe and effective treatment to our patients, we cannot simply ignore the environmental aggression that other treatments can cause. Professional and patient organizations should take the lead in health policies to offer affordable alternatives to inhalers containing HFA. Following efficacy and safety considerations, comprehensive data on the carbon footprint of inhalation therapies will enable patients and their caregivers to make informed decisions about inhalation treatment. Pharmaceutical companies should consider these issues in their strategic planning for new developments in inhalation therapy. Hospital and health plan forms should also consider the environmental risks of inhaler propellants and prioritize options not containing HFA.

Responding to the threat of climate change will require innovation, leadership, and a broad perspective, but action is crucial if we are to protect the health of our patients.

AUTHOR CONTRIBUTIONS

All authors participated in the drafting and revision of the manuscript, as well as in the approval of the final version.

CONFLICTS OF INTEREST

None declared.

Table 2. Amount of CO_2 equivalent released per puff [CO_2eq/puff (g)] according to the pharmacological agent and device.

Product	CO_2eq/puff (g)
SABA (albuterol)[a]	60.4
LAMA DPI	18.75
LAMA SMI	13.0
IC+LABA DPI	18.75
IC+LABA pMDI	163.5

Based on Cabrera et al.[33] and IQVIA Brasil.[34] SABA: short-acting β_2 agonists; LAMA: long-acting muscarinic antagonists; DPI: dry powder inhaler; SMI: soft mist inhaler; IC: inhaled corticosteroids; and pMDI: pressurized metered-dose inhaler. [a]Hydrofluoroalkane propellant.

Table 3. Dispensation of short-acting β_2 agonists via pressurized metered-dose inhaler in the city of Uruguaiana, Brazil.

Year[a]	Assisted patients	pMDI, n	Puffs, n	CO_2eq (kg)
2018	848	1,446	289,200	1,746.8
2019	1,313	2,459	491,800	2,970.5
2020	933	2,231	446,200	2,695.0
2021	1,276	2,761	552,200	3,335.3

[a]From January 1 to December 31.

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