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Review Article

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Health Risks and Benefits of International Travel for Adult Patients With Asthma

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Abstract

Asthma is a very prevalent condition. A significant proportion of patients with asthma will engage in travel for work or leisure purposes. Patients may be fearful of travel, especially during the current COVID-19 global pandemic. However, there are health benefits to be obtained, including leaving an area of high air pollution and travelling to an area of lower air pollution, travelling to high altitude, the beneficial effects of a low trigger environment and the psychological benefits associated with travel. Travel can be associated with improved diet and increased vitamin D exposure. Caution should be taken with alcohol consumption as it may worsen asthma. Whilst bariatric surgery has been shown to improve asthma symptoms and control, there are dangers associated with bariatric surgery tourism that the traveller should be made aware of. Travellers with asthma may experience jet lag and a worsening in their symptoms. Caution is required around exogenous melatonin use. Optimal asthma control pre-travel is essential. The destination should be carefully considered, in terms of air pollution, altitude and possible environmental triggers. Pre-travel, written asthma management plans should be reviewed and updated if necessary. Patients should carry more asthma medications than they think is necessary, including oral corticosteroids and a pressurised metered dose inhaler via spacer. Travellers with asthma should have a self-management plan in the event of exacerbations occurring during travel.

Keywords: Air Pollution, High Altitude, Stressors, Diet, Chronotherapy, Travel Advice

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Introduction

Asthma is a chronic heterogeneous respiratory condition. According to the Global Initiative for Asthma (GINA), asthma causes respiratory symptoms, limitation of activities of daily living, exacerbations that may require hospital admission, and ultimately may be fatal in cases of status asthmaticus.[1] Asthma is typically associated with airway hyper-responsiveness to direct or indirect stimuli, with variable expiratory airflow limitation. Over 339 million people worldwide are affected by asthma.[2] Trends in the incidence of asthma have varied. It continues to rise in low and middle-income countries but appears to have plateaued in some developed countries.[2] Risk factors for the development of asthma include genetic predisposition, tobacco smoke exposure, vitamin D deficiency, reduced exposure to microbiome diversity, and air pollution.[3] The goal of asthma management is to achieve good control of symptoms and to minimise future risk of exacerbations, persistent airflow limitation, side-effects of treatment and asthma-related mortality.[1] Since 2019, clinical recommendations specify that all adolescents and adults with asthma should receive inhaled corticosteroid (ICS)-containing controller treatment to reduce their risk of a major exacerbation.[4] The ICS can be delivered by regular daily ICS treatment or as needed ICS-LABA (long-acting beta-2 agonist). Short-acting beta-2 agonists alone are no longer recommended as first-line therapy.

A substantial proportion of patients with asthma will engage in international travel, for work or leisure purposes. Patients may be apprehensive about travelling for many reasons, including fear of asthma exacerbations requiring access to medical services in an unfamiliar environment. In this narrative review, the health benefits of travel in patients with asthma will be explored. Health benefits include leaving an area of high air pollution and travelling to an area of lower air pollution, travelling to high altitude, the beneficial effects of a low trigger environment, psychological benefits associated with travel, improved diet and lifestyle, and increased vitamin D exposure. Practical preventive advice for the clinician to

discuss with the patient at the pre-travel health consultation will also be outlined.

Air Pollution

Air pollution may cause exacerbations of pre-existing asthma but may also be responsible for new-onset asthma.[5] Urbanisation, particularly in the developing world, is an important contributor to asthma, largely due to increased outdoor air pollution.[5,6] Specific pollutants such as nitrogen dioxide, ozone and particular matter (PM) with a diameter less than 2.5 μm (PM2.5) in diameter can induce airway inflammation. This fine PM can deposit throughout the respiratory tract, particularly in the terminal bronchioles and alveoli. PM10 is particulate matter with a diameter less than 10μm (PM10) and includes dusts, pollens and moulds. Individuals with asthma who are exposed to ambient PM2.5 and high ozone levels, even for short periods, have more asthma symptoms and more frequent visits to the emergency department and hospitalisations due to their asthma.[7] A systematic review and meta-analysis of studies assessing the relationship of outdoor air pollution and peak expiratory flow (PEF) in adults with asthma demonstrated that acute exposure to air pollution (PM10 and PM2.5) were associated with decreases in PEF, particularly among non-smokers.[8]

Traffic-related air pollution (TRAP) is a complex mixture of particulate matter, derived from a number of sources including combustion (e.g. carbon), non-combustion (tyre and brake ware) and primary gaseous emissions.[5] A number of factors contribute to the type and quantity of particulate matter emitted, including vehicle type, age, condition, fuel type and road type.[9] The concentration of TRAP constituent pollutants lessens with increasing distance from roadways. It is estimated that thirteen percent of global asthma incidence in children may be attributable to TRAP.[10] Travellers with asthma should be aware that they may be travelling to cities with higher levels of TRAP compared to that in their countries of origin. The high levels of TRAP in many developing countries and the high levels of ambient cigarette smoke in countries without smoking bans in public places may challenge the asthmatic traveller, particularly if compliance with their ICS inhaler is poor.[11] In contrast, travelling to cities and areas with lower levels of TRAP can lead to improved air quality and reduced rates of asthma exacerbation. Travellers should monitor the local air quality index using reliable data sources (Table 1). These helpful indicators provide local information on air quality, classifying it on a scale from good to very poor. Travellers with asthma are a particularly vulnerable group due to increased airway inflammation provoked by exposure to pollutant antigens.[12] When air quality is classified as moderate, they should consider reducing strenuous physical outdoor activity. Their reliever inhaler should always be carried with them. When driving, their windows should be closed, especially when in traffic. When exercising, efforts should be made to avoid busy main roads where possible.

Table 1. Useful Web-Based Resources for Asthma Patients and Their Healthcare Providers

Organisation	Website Address
United States Environmental Protection Agency	https://www.epa.gov/outdoor-air-quality-data
UK-AIR on behalf of UK Department for Environment, Food and Rural Affairs	https://uk-air.defra.gov.uk/
National Travel Health Network and Centre, UK	https://travelhealthpro.org.uk/factsheet/94/respiratory-diseases
Asthma and Allergy Foundation of America	https://www.aafa.org/traveling-with-asthma-allergies/
Asthma UK and British Lung Foundation Partnership	https://www.asthma.org.uk/advice/living-with-asthma/travel/

High Altitude

High altitude climate therapy (also known as 'alpine' therapy) has been recognised as a treatment option for those with severe asthma. The success of high altitude was largely thought to be due to the absence of the house dust mite allergen at altitudes greater than 1600 metres.[13] At altitudes up to 2000 metres, asthmatic travellers receive the benefits of decreased allergens and reduced airflow resistance. However, at altitudes above 2500 metres, the cold dry air may induce an asthma exacerbation.[14] Rijssenbeek-Nouwens et al examined the effects of 12 weeks residence at high altitude in adults with severe refractory asthma, with and without allergic sensitisation to the house dust mite.[15] Asthma symptoms, asthma-related quality of life, sino-nasal symptoms, post-bronchodilator forced expiratory volume in one second (FEV1) and exercise tolerance improved similarly in both groups, irrespective of prior sensitisation status. Daily oral corticosteroid requirements also decreased. A number of beneficial effects at high altitude were proposed. These included reduced pollution levels; decreased air density causing reduced respiratory resistance; and removal of psychological stressors. These patients also benefited from a multidisciplinary comprehensive treatment approach, including a personalised treatment plan and daily supervised exercise.

A systematic review and meta-analysis published in 2016 acknowledged the varying quality of publications in this area, largely due to study heterogeneity and small sample size.[16] Despite this, meta-analysis of FEV1 demonstrated significant improvement after high altitude climate therapy. However, the potential long-term benefit of high altitude therapy after the patient returns to lower altitude or in combination with other treatments is unknown. As travellers ascend to high altitudes (typically over 2500 m), the risk of acute mountain sickness and high-altitude pulmonary oedema (HAPE) increases. HAPE can manifest as a dry cough, shortness of breath and reduced exercise tolerance. It is important for travellers not to dismiss these symptoms and attribute them in error to their underlying asthma. Equally, other differential diagnoses should be considered, such as the widely recognised 'Khumbu cough/high altitude hack', pulmonary embolism, pneumonia and atypical respiratory infections such as pertussis.[17]

Psychological Effects of Travel

Travel can have a number of psychological benefits for patients with asthma. Psychological stress has long been recognised as a potential immunomodulator. Psychological stress occurs when a person feels unable to cope with their environmental

demands and it has been associated with 10%–15% of asthma exacerbations.[18] Patients with asthma report higher levels of negative emotion and exacerbations of asthma have been linked to time periods of increased emotion.[19] A number of mechanisms have been postulated for the relationship between asthma and emotion, including vagal and alpha-sympathetic hyperreactivity, obstruction in the larger airways, individual response stereotypy, facial muscle tension, heightened respiratory drive and hyperventilation.[19] Both active and passive stressors are associated with increased activation of the sympathetic nervous system in adults and children.[20] The treatment of asthma requires the clinician to pay attention to both the physiological as well as the psychological factors.[21] Patients with asthma who experience chronic stressors may benefit from an opportunity to travel overseas. It is important that they plan their trip well in advance of departure and are aware of potential travel-related environmental stressors such as noise, sleep deprivation and navigational challenges.

Dietary Effects of Travel

Travel may be associated with a number of enhanced lifestyle measures. The classical 'Western' diet, with a high intake of sugar, processed meats and high-fat dairy products, has been associated with an increase in adult asthma morbidity, possibly due to its pro-inflammatory properties.[22] The Mediterranean diet, traditionally high in fruit, vegetables, dietary fibre and omega-3 fatty acids, has anti-inflammatory properties and is associated with improved asthma control.[23,24] Travellers should be mindful of the predominant diet that they will encounter whilst travelling and make an effort to eat as healthily as possible.

Vitamin D and Asthma

Travel to sunnier destinations is associated with increased vitamin D exposure. Vitamin D is a pre-prohormone obtained from skin exposure to ultraviolet B light and dietary intake from sources including fish oils, fish, egg yolk and dietary supplementation.[25] Vitamin D deficiency is common in patients with asthma and has been associated with an increased risk of asthma exacerbations, higher levels of airway inflammation and reduced lung function.[26] However, clinical trials of vitamin D supplementation are conflicting, with minimal effect on asthma symptoms, and do not unequivocally support the beneficial role of vitamin D in asthma.[26] It has been demonstrated that annual hospitalisation rates for children with asthma are inversely associated with total hours of sunshine in English regions.[27] Further studies into the role of vitamin D obtained from sunshine whilst travelling and its effect on asthma exacerbations in adults are required.

Alcohol and Asthma

Travellers engaging in travel for leisure may frequently drink more alcoholic beverages than usual. Alcoholic drinks, particularly wine, have been demonstrated to worsen symptoms of asthma.[28] The exact mechanisms of these reactions are not fully known, however it may be due to the histamine-releasing effect of acetaldehyde.[29] Travellers should be advised about the dangers of excessive alcohol consumption whilst travelling.

Meditation and Yoga Tourism

Meditation and yoga are pursuits that patients may engage in whilst travelling. These are also associated with improved asthma outcomes.[23] Yoga is associated with breathing retraining exercises. Other breathing exercises include the Buteyko breathing technique and deep diaphragmatic breathing. These techniques manipulate the breathing pattern and encourage relaxation, nasal breathing, breath holding and abdominal breathing. A Cochrane review and meta-analysis of the effect of breathing exercises on asthma demonstrated that breathing exercises may have positive effects on quality of life, hyperventilation symptoms and lung function.[30] Thus, participation in yoga retreats and wellness tourism should be encouraged among patients living with asthma.

Patients With Asthma and Bariatric Surgery Tourism

A major risk factor and disease modifier of asthma is obesity, whereby obesity or increased adiposity may often precede the development of asthma.[31] Obese adults have more severe asthma, more symptoms, reduced response to asthma medications, more frequent and severe exacerbations and an increased risk of hospitalisations.[31,32] Bariatric surgery leads to significant and sustained weight loss in morbidly obese patients.[33] A number of studies have demonstrated positive asthma outcomes post bariatric surgery. Dixon et al demonstrated a significant improvement in asthma control and asthma-related quality of life post bariatric surgery.[34] Boulet et al reported improved symptoms, reduced requirement for asthma medications, improved pulmonary function parameters and improved airway hyper-responsiveness in patients with asthma post bariatric surgery.[35] Bariatric surgery has also been shown to reduce the risk of asthma exacerbations requiring attendance at the emergency department or hospitalisation by half.[36]

Because of long waiting times or unavailability of bariatric services in their home country, patients with asthma and morbid obesity may engage in international travel to avail of services.[37] Whilst ultimately, bariatric surgery improves outcomes for morbidly obese patients with asthma, the traveller crossing international borders should be made aware of the potential risks of bariatric surgery tourism. These include the lack of continuity of care after the procedure, insufficient communication to the patient's regular healthcare providers in their home country, uncertainty about the professional licensure of bariatric surgeons in some jurisdictions and higher complication rates, including infections with multi-drug resistant micro-organisms.[37,38] The higher complication rates can lead to a substantial financial burden on the patients native healthcare system.[39,40]

Jet Lag and Asthma

Circadian rhythms are daily oscillations in physiological parameters and behaviours that follow a 24-hour cycle. The generation of circadian rhythms is entrained to environmental

cues (Zeitgebers), the most important of which is light.[41] Mammalian circadian rhythms are controlled by a master clock located in the suprachiasmatic nucleus in the hypothalamus. Asthma symptoms demonstrate a circadian variation, with symptoms classically worse at night, particularly in the early hours of the morning. Nocturnal symptoms are an important parameter in assessing asthma control and if present, require escalation of asthma treatment.[1] Nocturnal symptoms are associated with increased asthma mortality. The majority of respiratory arrests and sudden deaths in patients with asthma occur between midnight and 8am.[42] FEV1 and PEF have a circadian variation in the general population, with the nadir occurring at approximately 4am.[43] However, in patients with asthma, the amplitude of the circadian rhythm of both FEV1 and PEF is magnified greatly.[44] A potential role for the clock gene BMAL1 in modulating viral exacerbations in asthma was found, when BMAL1 deficient mice developed extensive asthma-like airway changes post viral infection, including mucous production and increased airway resistance.[45]

Chronotherapy refers to the timing of drug administration at different times in the circadian cycle to allow for maximal therapeutic effects and minimisation of side effects. It has been shown that the best time of the day to take systemic and inhaled corticosteroids is in the afternoon or early evening, with a significant increase in FEV1 and decreased airway inflammatory cells.[43,46] Melatonin is produced by the pineal gland and is an endogenous neurohormonal controller of circadian rhythms. Exogenous melatonin is a standard treatment for circadian rhythm sleep disorders. It has been shown to have pro-inflammatory effects in patients with asthma[47] and elevated serum melatonin is associated with nocturnal worsening of asthma.[48] When patients with asthma travel long distances and cross numerous time zones, they will experience jet lag. Melatonin should not be used routinely in this patient cohort. Their asthma symptoms may also worsen with jet lag. Careful timing of their asthma medications is, therefore, advised.

Practical Travel Advice for Patients With Asthma

Practical travel advice should be provided at the pre-travel consultation. Patients should ensure their daily asthma management is under control prior to travel. Their written asthma management plan should be reviewed and updated if necessary. A letter may be provided by the doctor, describing the asthma diagnosis and current medications. The travel insurance policy should be reviewed to ensure it specifically includes asthma and that it offers the cover the patient requires. Patients should consider ordering and wearing a medical identification bracelet, especially if they have severe allergies. Influenza and hepatitis B vaccinations are recommended. Patients should carry more asthma medications than they think is necessary for their trip. If a patient wishes to travel with a nebuliser, portable models are available. According to a recent study, use of an incorrect mains voltage with jet nebulisers results in marked reduction in their output. Patients with chronic respiratory conditions such as asthma, who take nebulised drugs, should check that they are using the correct voltage with their nebuliser compressor to avoid the risk of sub-optimal dosing of their nebulised medications.[49]

In addition to all regular asthma medications, carriage of an emergency supply of prednisolone in the hand luggage is strongly recommended.[50] Asthmatic travellers may be concerned that the synthetic pyrethroid insecticides, used for aircraft disinsection to prevent the international spread of vectors and vector-borne diseases, may exacerbate their symptoms. However, no cases of asthmatic reactions due to the application of synthetic pyrethroids have been reported in the aircraft setting.[51] The normal aircraft cabin environment should not cause any specific problems for a passenger with well-controlled asthma. All aircraft emergency kits are required to contain a bronchodilator inhaler but not a nebuliser. However, a bronchodilator taken via a volumatic spacer is just as effective as a nebuliser.[52] If an air passenger experiences an acute exacerbation of asthma on board, the patient's own bronchodilator should be administered via a spacer and repeated until symptomatic relief is obtained.[50] During the current COVID-19 pandemic, patients with asthma may have reduced opportunities to travel and may be fearful of travelling for essential purposes.[53] GINA advise that asthma patients with COVID-19 should continue to take their prescribed medications, particularly their ICS, or oral corticosteroids if required.[1] Nebulisers should be avoided where possible, due to increased risk of dissemination of COVID-19 to others. The preferred treatment during an exacerbation is a pressurised metered dose inhaler via a spacer. Risk of hospitalisation due to COVID-19 in patients with asthma is associated with increasing age and associated co-morbidities.[54]

Study Limitations

This is the first narrative review that we are aware of that focuses on the health benefits and risks of international travel in patients with asthma. It is a neglected field of research, and as such, publications in this field are limited. The articles that are available often do not focus on the health benefits of travel *per se* for the asthmatic traveller. As such, the benefits had to be inferred by the authors for the purposes of this study. Another limitation was the restriction of the literature search to articles published in the English language only.

Conclusion

In summary, asthma is an extremely prevalent medical condition. Whilst patients may be fearful of travel, especially during the current global pandemic, there are a number of health benefits to be obtained. It is imperative that patients have optimal control of their asthma pre-travel. The destination should be carefully considered, in terms of air pollution, altitude and possible environmental triggers. Travellers with asthma should rehearse a self-management plan in the event of exacerbations occurring during travel.

Recommendations for Further Research

With the increasing use of mobile technology, travellers with asthma have the opportunity to gather an enormous amount

Review Highlights

What Is Already Known?

Asthma is a chronic heterogeneous lung condition associated with airway hyperresponsiveness and airflow limitation. Patients with asthma may be fearful of travel for numerous reasons.

What Does This Study Add?

This study provides a comprehensive review of the literature. It is the first review to look specifically and thoroughly at the many health benefits associated with international travel, including travelling to areas of lower air pollution, higher altitude, a low-trigger environment, and improved diet and lifestyle. It provides practical advice for patients with asthma at the pre-travel consultation.

of geo-located health data whilst engaging in travel, ranging from tracking of physical activity, health symptoms, sleep quality and weather conditions. This will be illuminated by further research in this area in the future. Qualitative studies, which describe the travel health and illness experiences of travellers with asthma, would also provide valuable insights thereby enhancing the utility of the pre-travel consultation.

Authors' Contributions

GTF conceived the idea for the manuscript. SMW and GTF researched the material. SMW prepared the first draft of the manuscript, which was edited for significant intellectual content by GTF. Both authors approved the final version of the manuscript.

Conflict of Interest Disclosures

The authors declare that they have no conflicts of interest.

Ethical Approval

Not applicable.

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