

Impact of Changes in Anti-doping Regulations (WADA Guidelines) on Asthma Care in Athletes

Mariana Couto, MD,*† Luís Horta, MD, PhD,‡ Luís Delgado, MD, PhD,*†
Miguel Capão-Filipe, MD,*§ and André Moreira, MD, PhD*†

Objective: To investigate how changes to the World Anti-Doping Agency (WADA) guidelines on asthma medication requests have impacted the management of asthmatic athletes in Portugal.

Design: Retrospective analysis of asthma medication requests submitted in 2008 to 2010.

Setting: Portuguese Anti-Doping Authority database.

Participants: Athletes requesting the use of inhaled corticosteroids and/or β_2 -agonists.

Independent Variables: Demographic, therapeutic, and diagnostic test data.

Main Outcome Measures: Yearly changes in number of asthma medication requests and diagnostic procedures.

Results: We analyzed 326 requests: 173 abbreviated Therapeutic Use Exemptions (TUEs) in 2008 (objective tests not required), 9 Declaration of Use (DoU) and 76 TUEs in 2009, and 39 DoU and 29 TUEs in 2010. Spirometry was performed in 87% and 37% of athletes in 2009 and 2010, respectively; the corresponding figures for bronchoprovocation were 59% and 16%, almost all positive in both years.

Conclusions: Applications for inhaler use have decreased by approximately half since objective asthma testing became mandatory. Our findings show that WADA guidelines have an impact on asthmatic athletes care: In 2009 a more rigorous screening was possible, leading to withdrawal of unnecessary medication. Constant changes, however, jeopardize this achievement and nowadays introduce safety issues stemming from the unsupervised use of inhaled β_2 -agonists.

Key Words: asthma, airway hyperresponsiveness, anti-doping, bronchoconstriction, exercise, inhaled beta-2 agonists, sports, WADA

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From the *Allergy, Asthma & Sports Unit, Immunoallergology Department, Centro Hospitalar São João E.P.E., Porto, Portugal; †Immunology Laboratory, Faculty of Medicine, University of Porto, Porto, Portugal; ‡Anti-Doping Authority of Portugal, Lisbon, Portugal; and §Internal Medicine Department, Baixo-Vouga Hospital Center, Aveiro, Portugal.

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Correspondence Author: Mariana Couto, MD, Serviço de Imunoalergologia, Centro Hospitalar São João, EPE, Alameda Prof. Hernâni Monteiro 4200-319 Porto, Portugal (marianafercouth@gmail.com).

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INTRODUCTION

Diagnosing asthma in athletes is challenging. Multiple phenotypes of asthma exist, and different underlying mechanisms contribute to etiopathogenesis.^{1,2} Also, alternative diagnoses must be considered,³ and in athletes, symptoms are poor predictors of this condition.⁴ Objective evidence (eg, positive bronchodilator or bronchoprovocation test), thus, is needed to confirm a diagnosis in this setting.⁵

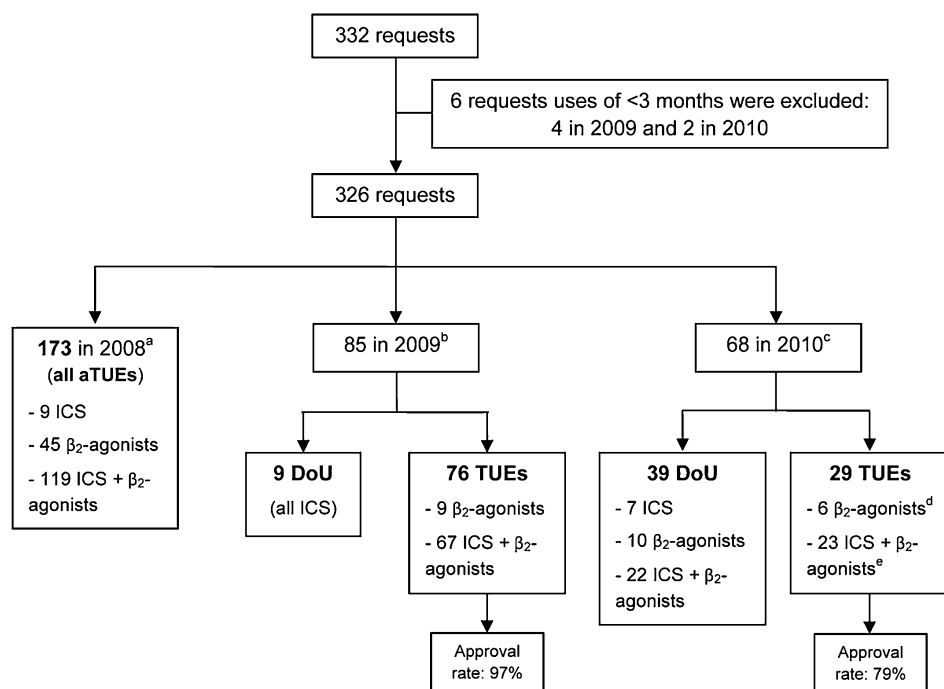
The recommendation of the International Olympic Committee Medical Commission (IOC-MC) for Olympic athletes to present objective evidence of asthma before allowing the use of inhaled β_2 -agonists (IBAs), in place since 2002, has facilitated the study of how asthma impacts different sports and has benefited athletes by ensuring better care. In 2009, the World Anti-Doping Agency (WADA) followed the IOC approach, extending it to all other athletes.⁶ The WADA guidelines on asthma, however, have changed in recent years. Before 2009, an abbreviated Therapeutic Use Exemption (aTUE), which did not require objective evidence of asthma, accompanied by a physician's report of asthma, was sufficient for requesting permission to use inhaled corticosteroids (ICS) and inhaled formoterol, salbutamol, salmeterol, and terbutaline. In 2009, however, aTUEs were withdrawn and replaced by a Declaration of Use (DoU) for ICS and a full Therapeutic Use Exemption (TUE) requiring objective evidence for the same 4 IBAs. In 2010, the DoU was extended to salbutamol and salmeterol, but the other IBAs still required a TUE.

The aim of this study was to assess the impact of WADA guideline changes on asthma medication requests by Portuguese athletes.

METHODS

We retrospectively analyzed asthma medication requests submitted to the Portuguese Anti-Doping Authority between 2008 and 2010. Athletes older than 16 years who requested permission to use ICS and/or IBAs for more than 3 months were included. Data on respiratory symptoms, medication requested, spirometry, and atopy (at least 1 positive skin prick test or positive specific IgE) were collected. A diagnosis of asthma was based on a positive bronchodilator test or bronchoprovocation test.⁵ Exhaled nitric oxide results were converted to personal predicted values using the FeNO Interpretation Aid tool (<http://www.enovis.org>) and considered increased if above 150% of predicted. Data were expressed as median and range, and categorical variables were compared using the χ^2 or Fisher

FIGURE 1. Flow chart showing requests for asthma medication submitted by athletes to the Anti-Doping Authority of Portugal between 2008 and 2010. Notes: ^aIn 2008, only an abbreviated TUE was required for ICS and IBAs salbutamol, salmeterol, formoterol, and terbutaline (ie, no objective testing or approval was required). ^bIn 2009, salbutamol, salmeterol, terbutaline, and formoterol required a full TUE and ICS required a DoU. ^cIn 2010, salbutamol, salmeterol, and ICS required a DoU while terbutaline and formoterol required a full TUE. ^dThree requests for formoterol (of which 2 were not approved), 2 for terbutaline (of which 1 was not approved), and 1 for indacaterol. ^eTwenty-one requests for formoterol (of which 3 were not approved) and 2 requests for salbutamol/terbutaline use.



exact test (statistical significance, $P < 0.05$). Analyses were performed using SPSS version 18.0 (SPSS Inc, Chicago, Illinois).

RESULTS

We analyzed requests from 326 athletes [254 males; median age, 24 years (range, 16-62 years)] (Figure 1). The requests were as follows: in 2008, 173 aTUEs were submitted; in 2009 and 2010, 9 and 39 DoU were submitted, respectively; regarding TUEs, the approval rate was 97% (74 of 76) in 2009 and 79% (23/29) in 2010 ($P = 0.005$). Requests for ICS combined with IBAs were the most frequent. Requests for isolated IBAs increased significantly from 2009 to 2010 (from 9 to 16, $P = 0.03$). The clinical and diagnostic tests performed are shown in Table 1 and the corresponding results in Table 2. No tests were reported in 2008 because all the requests submitted in that year were aTUEs.

DISCUSSION

The introduction of mandatory objective criteria for inhaler use (2009) decreased the requests submitted to the Portuguese Anti-Doping Authority by approximately half, suggesting that a large number of athletes were receiving medication based on symptoms only. The relative similarity between the proportion of positive tests in 2009 and 2010 suggests that the more rigorous testing criteria strategy is reliable. We also saw that changes to the WADA guidelines on IBAs in 2010 led to a dramatic decrease in the number of tests performed in Portuguese athletes with asthma.

Our findings clearly show that WADA guidelines have an impact on the care of athletes with documented asthma and influence how respiratory symptoms are managed and treated in these patients. A study that evaluated the impact of IOC-MC rules found that 21% of British Olympic athletes

were receiving asthma medication for which there was no clinical indication.⁷ In Portugal, changes to the WADA 2009 Prohibited List permitted more rigorous screening of asthmatic athletes, thanks to the implementation of objective criteria for inhaler use. The new requirements also led to the withdrawal of unnecessary medication. It improved athlete's care by investigation of alternative diagnoses.

Constant changes to WADA guidelines, however, jeopardize the achievements made to date and adversely affect the health of asthmatic athletes. Diagnosis of asthma is complex, and lung function, airway inflammation, and hyper-responsiveness tests provide important complementary information that can aid asthma control.⁸ Also, the fact that a TUE is necessary for some IBAs while a DoU is sufficient for

TABLE 1. Tests Performed in Athletes Whose Request to Use Asthma Medication Was Approved by the Portuguese Anti-doping Authority

	2009 (n = 83)	2010 (n = 62)	P
Spirometry	72 (87)	23 (37)	<0.001*
Bronchodilation test	37 (45)	15 (24)	0.011*
Bronchoprovocation challenge	49 (59)	10 (16)	<0.001*
Methacholine	46 (55)	9 (15)	—
Mannitol	0	1 (2)	—
Exercise	3 (4)	0	—
Exhaled nitric oxide	15 (18)	6 (10)	0.155
SPT or sIgE	56 (67)	18 (29)	<0.001*

No tests were reported in 2008 because it was not necessary to provide objective evidence of asthma at this time. Data are reported as n (%).

*Statistically significant.

SPT, skin prick tests; sIgE, specific immunoglobulin E.

TABLE 2. Reported Symptoms and Positive Test Results in Athletes With Asthma Who Submitted a Therapeutic Use Exemption Application to the Anti-doping Authority of Portugal

	2009 (n = 83)	2010 (n = 62)
Respiratory symptoms	81 (98)	62 (100)
Airflow limitation on spirometry	12/72 (17)	4/23 (17)
Positive bronchodilation	20/37 (54)	8/15 (53)
Positive bronchoprovocation	46/49 (94)	10/10 (100)
Airway allergic inflammation*	10/15 (67)	2/6 (33)
Atopy	50/56 (89)	15/18 (83)

Data are reported as positive/performed (%).

*Defined as exhaled nitric oxide >150% of predicted value for age and height, calculated using the FeNO Interpretation Aid tool (<http://www.enovis.org>).

others has generated intense debate⁹ and led to different management strategies being used in this setting, as evidenced by our study. In 2010, for example, athletes could avoid objective testing by simply applying to use an IBA that required a DoU.

Our findings are limited by the retrospective nature of the study and the fact that the data we collected were anonymous. However, we are certain that the decrease in requests observed in 2009 is not due to the fact that athletes were already covered by a previous submission as renewal was yearly at that time. TUEs now last for 4 years and we can therefore be sure that no repetitions occurred in 2010.

Our study contributes to overcoming the paucity of data regarding asthma in Portuguese athletes. Moreover, we have evaluated how changes in WADA guidelines have impacted the clinical management of asthma in this setting. In the 2012 WADA guidelines, unrestricted use of inhaled salbutamol, salmeterol, or formoterol is permitted as long as specified doses are not exceeded. Such a change, however, might lead to an increased use of long-acting IBAs, without ICS. This is a matter of concern as IBAs may mask worsening of airway inflammation; furthermore, airway inflammation might contribute to the downregulation of IBA receptors.¹⁰ Therefore, although the 2012

guidelines may seem fairer and improve access to treatment among asthmatic athletes, they introduce safety issues stemming from the unsupervised use of IBAs. As shown by our study, in the absence of mandatory objective testing for certain asthma medications, athletes may choose not to undergo lung function tests. The risks associated with such a decision should be investigated in new prospective studies.

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