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

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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 β2-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 β2-agonists.

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

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The authors report no financial or conflicts of interest.

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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 formoterol (of which 2 were not approved), 2 for terbutaline (of which 1 was not approved), and 1 for indacaterol. Twenty-one requests for formoterol (of which 3 were not approved) and 2 requests for salbutamol/terbutaline use.

**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. 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 hyperresponsiveness tests provide important complementary information that can aid asthma control. Also, the fact that a TUE is necessary for some IBAs while a DoU is sufficient for

<table>
<thead>
<tr>
<th>TABLE 1. Tests Performed in Athletes Whose Request to Use Asthma Medication Was Approved by the Portuguese Anti-doping Authority</th>
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<tbody>
<tr>
<td><strong>2009</strong></td>
</tr>
<tr>
<td>Spirometry</td>
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<tr>
<td>Bronchodilation test</td>
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<tr>
<td>Bronchoprovocation challenge</td>
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<tr>
<td>Methacholine</td>
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<tr>
<td>Mannitol</td>
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<tr>
<td>Exercise</td>
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<tr>
<td>Exhaled nitric oxide</td>
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<tr>
<td>SPT or sIgE</td>
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</tbody>
</table>

*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.
others has generated intense debate 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. 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.

**ACKNOWLEDGMENT**

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**REFERENCES**


### 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

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

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

Data are reported as positive/ performed (%).