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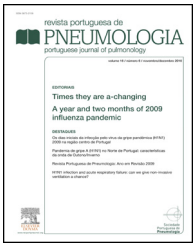

ORIGINAL ARTICLE

Exploratory study comparing dysautonomia between asthmatic and non-asthmatic elite swimmers

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Abstract
Background: Dysautonomia has been independently associated with training and exercise-induced bronchoconstriction. In addition, neurogenic airway inflammation was recently associated with swimmers-asthma. We aimed to assess the relation between autonomic nervous system and airway responsiveness of asthmatic elite swimmers.
Methods: Twenty-seven elite swimmers, 11 of whom had asthma, were enrolled in this exploratory cross-sectional study. All performed spirometry with bronchodilation, skin prick tests and methacholine challenge according to the guidelines. Pupillometry was performed using PLR-200™ Pupillometer. One pupil light response curve for each eye was recorded and the mean values of pupil's maximal and minimal diameters, percentage of constriction, average and maximum constriction velocities (parasympathetic parameters), dilation velocity, and total time to recover 75% of the initial size (sympathetic parameters) were used for analysis. Asthma was defined using IOC-MC criteria; subjects were divided into airway hyperesponsiveness (AHR) severity according to methacholine PD_{20} in: no AHR, borderline, mild, moderate and severe AHR. Differences for pupillary parameters between groups and after categorization by AHR severity were assessed using SPSS 20.0 ($p \leq 0.05$). In individuals with clinically relevant AHR, correlation between PD_{20} and pupillary parameters was investigated with Spearman's correlation test.
Results: No statistically significant differences were observed between asthmatic and non-asthmatic swimmers regarding parasympathetic parameters. When stratified by AHR, maximal and minimal diameters and percentage of constriction were significantly lower among those with severe AHR. Among swimmers with clinically relevant AHR ($n = 18$), PD_{20} correlated with *parasympathetic activity*: maximal ($r = 0.67$, $p = 0.002$) and minimal diameters ($r = 0.75$, $p < 0.001$), percentage of constriction ($r = -0.59$, $p = 0.011$) and latency ($r = 0.490$, $p = 0.039$).

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Conclusions: No significant differences were observed between asthmatic and non-asthmatic swimmers regarding parasympathetic parameters, but among those with relevant AHR an association was found. Although limited by the sample size, these findings support the relation between dysautonomia and AHR in asthmatic swimmers.

Introduction

An increased risk for asthma has been recognized in elite athletes who take part in endurance sports, such as swimming.[1] Classical postulated mechanisms behind exercise-induced asthma (EIA) include the osmotic, or airway-drying, hypothesis.[2] As water is evaporated from the airway surface liquid, it becomes hyperosmolar and provides an osmotic stimulus for water to move from any cell nearby, resulting in cell shrinkage and release of inflammatory mediators that cause airway smooth muscle contraction. In fact, the airways of athletes present increased inflammatory cells and levels of histamine, cysteinyl leukotrienes and chemokines; however these inflammatory changes are not consistently related to lung function or disease exacerbations and it has been thought that they represent physical injury secondary to rigorous hyperpnoea that will heal with rest.[3,4] Alternative hypotheses to explain EIA have been pursued.

Besides inflammatory mediators, the autonomic system also mediates the contraction and relaxation of bronchial smooth muscle. Cholinergic-parasympathetic nerves stimulate bronchoconstriction, whereas β2-adrenergic sympathetic and/or noncholinergic parasympathetic nerves cause bronchodilation.[3,4] Intensive training can have affect autonomic regulation by promoting the predominance of vagal activity, as a compensatory response to the sympathetic stimulation associated with frequent and intense training.[2] It has been hypothesized that repeated intensive training could provoke vagal hegemony, which induces not only the well-known resting bradycardia of athletes, but could also lead to a predisposition for increased bronchomotor tone and therefore susceptibility to bronchospasm.[2] This autonomic nervous system imbalance is known as *dysautonomia* and it has been previously shown, using pupillometry, that pupillary light reflex of endurance runners reveals an increased parasympathetic activity and reduced sympathetic activity.[5] But the relationship between these observations and asthma is not established.

Research into the hypothesis of dysautonomia in the pathogenesis of asthma in athletes is urgently needed because definite answers would allow for better targeted treatment of this specific asthmatic population. In the particular case of elite swimmers, in both asthmatic and healthy ones, an increase in bronchial responsiveness correlating with exercise intensity was demonstrated after 3000 m swimming in an indoor swimming pool.[6] Moreover, neurogenic airway inflammation was recently associated with swimmers-asthma.[7] Therefore, we aimed to assess the relationship between autonomic nervous system and airway responsiveness of elite swimmers with asthma. It was hypothesized that airway hyperesponsiveness in asthmatic swimmers is related to increased parasympathetic activity.

Methods

Participants

Swimmers of the FCPorto main swimming team were invited to participate. Athletes of over 14 years-old, who agreed to take part in the study, were enrolled. To be included, participants had to be elite swimmers, free from any respiratory infection in the 2 weeks before testing, not having drunk coffee or smoked in the 2 h prior to testing, not having taken exercise on the testing day, not using contact lenses and not having taken their asthma medication for 48 h (except for inhaled corticosteroids, which they had been asked to stop taking for at least 2 weeks prior to the study).

Subjects who met any of the following criteria would have been excluded from the study: under any systemic medication which could affect the central nervous system; any topical eye treatment; systemic conditions with known ocular involvement; orbit structure damage or surrounding soft tissue with open lesion or edema on the day of testing; a past history of ocular abnormalities or trauma.

None of the subjects was excluded based on the above mentioned criteria.

Study design

This is an exploratory cross-sectional study, developed in two visits. The first visit was in the morning (from 8 to 11 am) because of the circadian rhythm of the size of the pupil.[8] Medical history and potential medication were reviewed to determine eligibility. The eligible ones answered a structured questionnaire, and performed pupillometry, spirometry and skin prick testing. Subsequently, reversibility to salbutamol was evaluated. The second visit took place on a different day and a bronchial challenge with methacholine was performed to assess airway hyperresponsiveness (AHR). Asthma diagnosis was based on the typical clinical features in conjunction with objective documentation of airway dysfunction, either presenting reversibility or AHR, according to the criteria set by the International Olympic Committee to document asthma in athletes.[4,9]

The study was conducted according to the Declaration of Helsinki and approved by the Ethical Commission. All participants or their legal guardians/parents (in the case of participants under 18 years-old) signed an informed consent form.