



The effect of mouth breathing on exercise induced fall in lung function in children with allergic asthma and rhinitis



Mirjana Turkalj^{a,b}, Jelena Živković^{a,*}, Marcel Lipej^a, Sandra Bulat Lokas^a, Damir Erceg^{a,b}, Srđan Ante Anžić^a, Robert Magdić^c, Davor Plavec^{a,b}

^a Reference Center for Clinical Pediatric Allergology of the Ministry of Health, Children's Hospital Srebrnjak, 10 000 Zagreb, Croatia

^b Faculty of Medicine, Josip Juraj Strossmayer University Osijek, Trg Svetog Trojstva 3, 31000 Osijek, Croatia

^c Faculty of Kinesiology, Horvačanski zavoj 15, 10 000 Zagreb, Croatia

ARTICLE INFO

Article history:

Received 24 December 2015

Received in revised form 13 April 2016

Accepted 14 April 2016

Available online 19 April 2016

Keywords:

Allergic rhinitis

Exercise-induced bronchospasm

Mouth breathing

Tachyphylaxis

Physical activity

ABSTRACT

Objectives: Exercise induced bronchospasm (EIB) represents a common feature of childhood asthma which is most commonly revealed during free running. On the other hand aerobic exercise shows significant beneficial effects in asthmatics especially on the reduction of the level of systemic inflammation and is recommended as part of its treatment. The aim of this study was to test how mandatory mouth breathing influences the exercise induced level of decrease in lung function according to the level of severity of allergic rhinitis (AR).

Methods: Free 6-minute running test preceded and followed by spirometry done with and without a nose clip a day apart was conducted in 55 children with moderate persistent asthma and AR. Children were divided into two groups according to the severity of nasal symptoms.

Results: There was a greater fall in forced expiratory volume in one second after exercise with a nose clip in children with less nasal symptoms than in children with more nasal symptoms (mean $\pm$ SD; -5.28 (7.91) vs. -0.08 (4.58), $p = 0.0228$) compared to testing without the nose clip (mean $\pm$ SD; LNS, $-1.31 \pm 3.89\%$, $p = 0.2408$; MNS, $-1.47 \pm 3.68\%$, $p = 0.2883$).

Conclusion: Our results show that regular mouth breathing due to nasal congestion may lessen the degree of EIB in patients with persistent AR and allergic asthma.

© 2016 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Allergic rhinitis (AR) is described as an allergic inflammation of the nasal mucosa or mucous membranes lining the nasal cavity [1,2]. This condition often coexists and shares common risk factors with asthma, including atopy, and might be the manifestation of the same disease [3,4]. Both environmental and genetic factors are involved in the development of AR but the underlying causes or risk factors still remain undefined [5]. Nowadays, AR is a common health problem affecting 10–25% of children worldwide [6,7], which may have a great impact on quality of life and can affect patients' sleep, work and school performance during the day [5,8].

AR often coexists with asthma but a significant number of physically active people suffer from AR without symptoms of asthma [2]. The main problem of this condition during exercise is nasal congestion. Athletes with AR encounter two major complications. The

first one occurs because allergens and other pollutants are not filtered by the nose, which increases concentrations deposited in the lower airways [9]. On the other hand, humidification, air warming and filtration are reduced which stimulates an increased presence of white blood cells and hypersensitivity of the lungs, decreasing their volume and capacity [9,10]. Furthermore, children often develop exercise-induced bronchospasm (EIB), which is described as an acute, transient narrowing of the airways that occurs during and mostly after exercise. Its clinical features are cough, wheezing, chest tightness and shortness of breath or excess mucus production [11]. There is especially high percentage of asthmatic children with EIB and it is considered to be one of the reasons for a low adherence to physical training. It is defined as a 15% decrease in peak expiratory flow rate (PEFR) or a 10% decrease in forced expiratory volume in 1 second (FEV₁) following exercise. Lung function measurements are done after physical activity at a level of submaximal effort, in comparison with pre-exercise baseline [12]. The exact mechanism is not fully understood but it is thought to involve cooling and drying of airways during physical activity, causing mast cells to release pro-inflammatory mediators [13]. This lasts for 15–20 minutes after starting or shortly after completed exercise. This is the reason why allergic children with nasal and/or bronchial hyperactivity can

* Corresponding author at: Reference Center for Clinical Pediatric Allergology of the Ministry of Health, Children's Hospital Srebrnjak, Srebrnjak 100, HR-10000 Zagreb, Croatia. Tel.: +385 1 6391 191; fax: +385 1 6391 188.

E-mail address: zivkovic@bolnica-srebrnjak.hr (J. Živković).

experience more intense symptoms with training and performance [14]. Although there is high percentage of asthmatics with EIB in children, physical activity is commonly prescribed as a rehabilitation treatment for asthma in children and recent studies show beneficial effects of aerobic training on allergic inflammation [15]. This is why focus of most studies has been to determine whether the improved exercise performance can result in improved quality of life with fewer symptoms and complications. As many children with AR breathe through their mouth during exercise, we wanted to assess if mandatory mouth breathing has an effect on their physical performance or on a decrease in lung function after exercise/development of EIB. The aim of this study was to test how mandatory mouth breathing influences the exercise induced decrease in lung function according to the level of severity of the AR.

2. Material and methods

2.1. Experimental design

This case–control repeated measurement study was done during children's Asthma Camp, at island Lošinj in the Adriatic Sea. This destination for the Asthma Camp was chosen because of its geographical position in the middle of the northern Adriatic with clear air and mild Mediterranean climate, which gives children with asthma the opportunity for a climate therapy. The Camp is organized at the end of the summer school term, in the second half of June. Children have the opportunity to socialize with peers sharing the same problems, learn more about their disease and how they can manage it more easily through play, entertainment, sports and various workshops. Children are supervised by a team of highly specialized professionals, including pediatricians, psychologists, kinesiologist, pedagogues, registered nurses, physiotherapists and occupational therapist. The experiment was designed as a comparison between two comparable groups of children with a distinctly different level of nasal symptoms. Data about allergy and IgE were gathered from the Hospital digital medical records. Fraction of exhaled nitric oxide ($F_{E}NO$) was measured on site at Asthma Camp using a portable $F_{E}NO$ device (NIOX MINO, Aerocrine AB, Sweden) according to the ATS/ERS guidelines [16]. Spirometry was measured using MasterScreen spirometer (CareFusion, Germany) according to the ATS/ERS standards [17]. Both groups were tested on two occasions divided by one day apart. Prior to exercise testing, an appropriate washout period for short acting and long acting beta

agonist medication and leukotriene modifiers was done in all subjects (6, 12 and 24 hours respectively). The exercise test followed by lung function measurement was done as a 6-minute free running test (6-MRT) in all children with (mandatory mouth breathing) and without nose clip on different occasions. Before and after 6-MRT, heart rate and saturation of blood with oxygen (SO_2) were measured on an index finger using a pulse oximeter (Fingertip oximeter, PRINCE-100C, Heal Force, Shanghai, China). The spirometry was performed before, 5 minutes and 20 minutes after these 2 exercises. During this study there were no financial and personal relationships with any organizations that could influence (bias) their work.

2.2. Participants

Among the patients treated in our hospital, 55 children (24 girls, mean age 12.6 years) with moderate persistent asthma and comorbid AR were chosen for this study. The subjects were enrolled in the study after their legal guardians have read, agreed to, and signed the informed consent form approved by the Institutional Ethics Committee (IEC). The subjects were assessed for inclusion and exclusion criteria at screening visit after signing the informed consent. They were included if they had a diagnosed asthma for at least a year before the study, with regular control visits at our outpatient clinic at which point regular asthma control and adherence assessment was done together with lung function and $F_{E}NO$ measurements. All patients were tested for allergy (skin prick test to standard series of aeroallergens and specific IgE as indicated) at least at the time of diagnosis. Exclusion criteria consisted of any other diseases (none of the included patients had a problem with cardiovascular and musculoskeletal systems and had no other pulmonary disease) or use of any medication that might influence test results. Also, none of the children had adenoid enlargement. Their asthma was well controlled under their regular treatment and they were participating daily in an aerobic fitness program. Allergic rhinitis was diagnosed after examination by pediatric otolaryngologist and assessed by total nasal symptom score (TNSS, sum of individual nasal symptoms of congestion, itching, rhinorrhea, and sneezing) according to a previous study [18] and as recommended by the US Food and Drug Administration (FDA) and the European Medicines Agency (EMA) [19,20]. Patients were then divided into two subgroups according to the group median value of TNSS: (1) less nasal symptoms (LNS); (2) more nasal symptoms (MNS). The groups were balanced ($p > 0.05$; Table 1) according to their baseline characteristics

Table 1
Subjects' baseline characteristics according to the severity of nasal symptoms (LNS vs. MNS).

Characteristic	LNS (n = 26)	MNS (n = 29)	Statistics
Sex, girls (%)	14 (53.8)	10 (34.5)	$\chi^2 = 1.377$, $P = 0.2413$
Age, mean (SD), years	12.7 (1.9)	12.4 (2.1)	$t = 0.519$, $P = 0.6055$
Sensitized to:			
Mites (%)	17 (65.4)	18 (62.1)	$\chi^2 = 0.029$, $P = 0.8655$
Pollen (%)	16 (61.5)	18 (62.1)	$\chi^2 = 0.019$, $P = 0.8918$
Food (%)	11 (42.3)	15 (51.7)	$\chi^2 = 0.086$, $P = 0.7693$
High total IgE (%)	12 (46.2)	6 (20.7)	$\chi^2 = 2.964$, $P = 0.0852$
FEV1, mean (SD), % predicted	110.6 (23.5)	105.3 (14.6)	$t = 1.018$, $P = 0.3133$
FVC, mean (SD), % predicted	103.6 (19.8)	101.7 (14.5)	$t = 0.414$, $P = 0.6805$
PEF, mean (SD), % predicted	109.7 (27.7)	94.9 (16.5)	$t = 2.436$, $P = 0.0183$
MEF50, mean (SD), % predicted	102.5 (35.9)	87.7 (31.8)	$t = 1.622$, $P = 0.1108$
FENO, mean (SD), ppb	40.7 (30.4)	41.2 (34.0)	$t = 0.051$, $P = 0.9599$
Heart rate at rest, mean (SD), min^{-1}	87 (9)	82 (16)	$t = 1.434$, $P = 0.1576$
SO_2 at rest, mean (SD), %	97.6 (1.1)	98.3 (0.5)	$t = 1.499$, $P = 0.4291$
6-MRT, mean (SD), min	1138 (124)	1066 (156)	$t = 1.744$, $P = 0.0880$
Max heart rate after 6-MRT, mean (SD), min^{-1}	196 (9)	190 (11)	$t = 1.583$, $P = 0.1205$
SO_2 after 6-MRT, mean (SD), %	97.4 (1.2)	97.1 (1.4)	$t = 0.815$, $P = 0.4191$

Values in boldface are statistically significant.

FEV1, forced expiratory volume in one second; FVC, forced vital capacity; PEF, peak expiratory flow; MEF50, maximal expiratory flow at 50%; FENO, fractional exhaled nitric oxide; 6-MRT, 6-minute free running test; LNS, less nasal symptoms; MNS, more nasal symptoms; SO_2 , saturation of blood with oxygen.

Table 2

Results of two 6-minute running tests (6-MRT) according to the severity of nasal symptoms (LNS vs. MNS).

Characteristic	LNS (n = 26)	MNS (n = 29)	Statistics
6-MRTwnc, mean (SD), m	1081 (106)	1036 (179)	t = 1.046, P = 0.3009
Max. heart rate after 6-MRTwnc, mean (SD), min ⁻¹	195 (9)	190 (16)	t = 1.564, P = 0.1237
SaO ₂ after 6-MRTwnc, mean (SD), %	96.3 (3.0)	97.3 (1.0)	t = 1.594, P = 0.1179
FEV ₁ wnc change from baseline after 5 minutes, mean (SD), %	-5.28 (7.91)	-0.08 (4.58)	P = 0.0228*
FEV ₁ wnc change from baseline after 20 minutes, mean (SD), %	-3.88 (8.59)	-1.25 (4.22)	P = 1.0000*
6-MRTw/nc, mean (SD), m	1138 (124)	1066 (156)	t = 1.744, P = 0.0880
Max. heart rate after 6-MRTw/nc, mean (SD), min ⁻¹	196 (9)	190 (11)	t = 1.583, P = 0.1205
SaO ₂ after 6-MRTw/nc, mean (SD), %	97.4 (1.2)	97.1 (1.4)	t = 0.815, P = 0.4191
FEV ₁ w/nc change from baseline after 5 minutes, mean (SD), %	-1.31 (3.89)	-1.47 (3.68)	P = 1.0000*
FEV ₁ w/nc change from baseline after 20 minutes, mean (SD), %	0.19 (3.59)	-0.40 (3.54)	P = 1.0000*
6-MRTwnc vs. 6-MRTw/nc	t = 0.896, P = 0.3753	t = 0.685, P = 0.4967	NA
FEV ₁ wnc vs. FEV ₁ w/nc 5 minutes after 6-MRT	P = 0.2408*	P = 1.0000*	NA
FEV ₁ wnc vs. FEV ₁ w/nc 20 minutes after 6-MRT	P = 0.2002*	P = 1.0000*	NA

Values in boldface are statistically significant.

FEV₁, forced expiratory volume in one second; 6-MRT, 6-minute free running test; LNS, less nasal symptoms; MNS, more nasal symptoms; SaO₂, saturation of blood with oxygen; wnc, with the nose clip; w/nc, without the nose clip; SD, standard deviation.

* P for post hoc analysis with Bonferroni correction.

(sex, age, sensitization, total IgE level, baseline lung function, F_ENO, baseline heart rate and SaO₂) except for peak expiratory flow (PEF) that was significantly lower in the MNS group (94.9% vs. 109.7% expected, p = 0.0183) representing the congestion in the upper airways.

2.3. Statistical analysis

Continuous variables were presented as mean and standard deviation (SD) and categorical as absolute and relative frequencies (%). Comparison of continuous variables between groups was made using Student's t-test and for categorical variables using chi-squared test. Differences in the fall in lung function (FEV₁) between the groups and between two 6-MRTs were done using repeated measurements ANOVA with post hoc analysis using Bonferroni correction. P < 0.05 was considered statistically significant for all tests performed. The analyses were performed using STATISTICA, version 10 (StatSoft, Inc., Tulsa, OK, USA).

3. Results

Two groups (LNS and MNS) were not significantly different according to their physical fitness (track run during 6-MRT and heart rate and SaO₂ after the test; P > 0.05 for all; Table 1) but there was a significantly different pattern of the fall of FEV₁ after two different 6-MRT (with and without nose clip during exercise) in these two groups (F = 5.121, P = 0.0258 for the interaction of severity of nasal symptoms and nasal breathing during 6-MRT; repeated measures ANOVA; Table 2 and Fig. 1).

There was a significantly greater fall in FEV₁ 5 minutes after 6-MRT with a nose clip in a LNS subgroup (mean ± SD; -5.28 ± 7.91%) than in MNS subgroup (mean ± SD; -0.08 ± 4.58%, p = 0.0228). The difference was also evident when compared to the 6-MRT without the nose clip (mean ± SD; LNS, -1.31 ± 3.89%, p = 0.2408; MNS, -1.47 ± 3.68%, p = 0.2883; Table 2), although it did not reach statistical significance after Bonferroni correction. Contrary to the testing with the nose clip, there were no significant differences in a FEV₁ fall 5 minutes after 6-MRT when the same patients were tested (6-MRT) without the nose clip (p > 0.05 for all comparisons; Table 2).

4. Discussion

AR affects nasal function depending on the type and severity, and the interaction with environment and exposure to allergens. Symptoms that can range from only annoying to life-threatening [21] and are often triggered during exercise, which leads to decreased physical activity. Most common symptoms of AR occurring during exercise are runny nose and nasal blockage, leading to nasal

congestion and mouth breathing. This can influence performance and was the reason why we compared groups of children with different levels of nasal symptoms assessing possible complications that can interfere with their ability to participate in daily fitness program with a specific focus on exercise induced airway narrowing. EIB is the most common complication that is present during exercise and recent studies show that it has a broad impact on the lives of patients suffering from allergies [11,12]. It is highlighted that exercise is one of the triggers for asthma attacks and nearly half of the respondents (46%) reported that their condition had an effect on their exercise performance [12,22].

The pathogenesis of EIB is defined by more than one factor and therefore is not completely understood. It is believed that the air that is exchanged during the exercise is often colder than body temperature and thus less saturated with water. Large minute ventilation often disables the upper airways to warm and humidify inhaled air effectively so cool and dry air reaches distal airways. Cold air causes narrowing due to reactive hyperemia of the bronchial vasculature. [11,23].

Based on F_ENO level, which is a quantitative, noninvasive and safe method of measuring eosinophilic airway inflammation, children with asthma can be prescreened into a group with high F_ENO, indicating the need for EIB testing or into a group with near normal F_ENO for whom EIB is unlikely. Kanazawa et al. showed that

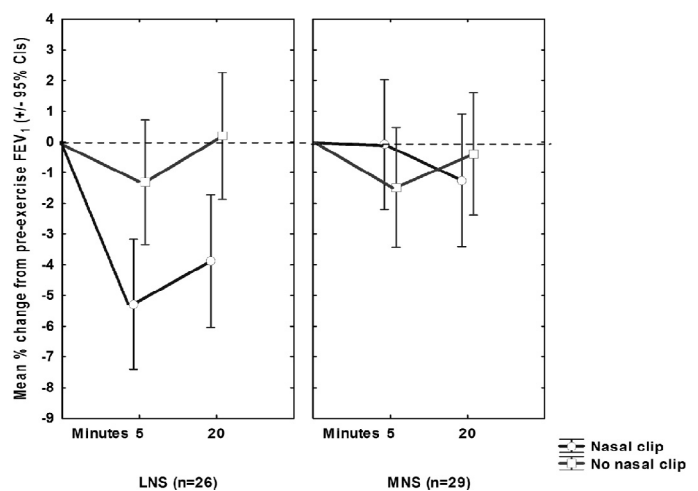


Fig. 1. Mean change in FEV₁ from baseline (%) for both 6-minute running tests (6-MRT) according to the severity of nasal symptoms; P = 0.0258 for the interaction of severity of nasal symptoms and mouth breathing.

excessive production of NO in the airways correlates with the severity of EIB in asthmatic patients so assessment of $F_E\text{NO}$ values could lead to an increased understanding of individual features of asthma (phenotype) and the need for prevention and treatment of EIB [24]. Children in our study had in both groups comparative $F_E\text{NO}$ values higher than normal (mean > 40 ppb), thus indicating the need for EIB testing in most of them.

Usually during exercise children breathe faster and at a submaximal effort inhale mostly through their mouth so the air is not filtered as it is with breathing through the nose, causing the air to be cooler and dryer, increasing the load to lower airways. Also, data found in studies of EIB demonstrate that the environment in which training is held may contain allergens and/or pollutants that can be associated with oxidative stress, which may enhance the development of EIB [25]. The occurrence of EIB depends on the humidity and temperature of the inspired air [26] which could possibly be a contributing factor to our results, considering that our study was held in the middle of the northern Adriatic with clear air and mild Mediterranean climate at air temperatures of 22–24 °C.

The other possible mechanism behind our results is that the children with chronically blocked nose and day-to-day mouth breathing do adapt in time and consider this a “normal” condition. The importance of nasal reflexes is undoubted and is mediated via trigeminal nerves [26]. The main reason for our results could be adaptation of reflex activity which occurs when nerves are repetitively stimulated in one way, leading to a state known as tachyphylaxis where sensory stimuli induce a lowering of the frequency of impulses [27]. This adaption to mouth breathing is probably why there were no significant differences in a FEV_1 fall 5 minutes after 6-MRT in testing without the nose clip. Contrary to this, testing with the nose clip showed that children who usually have less nasal symptoms had more problems and could forcefully exhale smaller amount of air, which we can again connect to the fact that children in this group are not used to breathing only through their mouth and consequently have more difficulties. In addition, as both groups had increased and comparable $F_E\text{NO}$ values, it appears that the level of airways eosinophilic inflammation had no effect on the results. Different studies have used 6-minute free running or walking test with a nose clip like we did, but they mostly used it to study whether an exercise challenge protocol is suitable for measuring EIB and to check the occurrence of EIB [26,28,29]. To our knowledge, none of them studied children with both asthma and allergic rhinitis or used these tests to see how a mandatory mouth breathing influences the exercise induced level of decrease in lung function.

5. Conclusion

According to different studies EIB is usually triggered because children tend to breathe through their mouth during exercise, increasing the load to lower airways [22,25]. However, adaptation of the children with AR to a day-to-day mouth breathing, due to nasal congestion, leads to tachyphylaxis, which is why they consider this a “normal” condition. Results of our research imply that regular mouth breathing in children with persistent AR and allergic asthma may reduce the degree of EIB. Also, many studies suggest that growth in exercise capacity reduces EIB and use of corticosteroids [15,21], which is why asthma and rhinitis should not be seen as a limitation for physical activity or sports.

References

- [1] E. Angiera, J. Willington, Management of allergic and non-allergic rhinitis: a primary care summary of the BSACI guideline, *Prim. Care Respir. J.* 19 (3) (2010) 217–222.
- [2] D.M. Quillen, D.B. Feller, Diagnosing rhinitis: allergic vs. nonallergic, *Am. Fam. Physician* 73 (9) (2006) 1583–1590.
- [3] A. Navarro, A. Valero, B. Juliá, S. Quirce, Coexistence of asthma and allergic rhinitis in adult patients attending allergy clinics: ONEAIR study, *J. Investig. Allergol. Clin. Immunol.* 18 (4) (2008) 233–238.
- [4] R. Shaaban, M. Zureik, D. Soussan, C. Neukirch, J. Heinrich, J. Sunyer, et al., Rhinitis and onset of asthma: a longitudinal population-based study, *Lancet* 20 (2008) 1049–1057.
- [5] I. Dávila, J. Mullol, M. Ferrer, J. Bartra, A. del Cuvillo, J. Montoro, et al., Genetic aspects of allergic rhinitis, *J. Investig. Allergol. Clin. Immunol.* 19 (1) (2009) 25–31.
- [6] T. Sanford, Allergic rhinitis in children, *Mo Med.* 105 (3) (2008) 230–234.
- [7] P.J. Turner, A.S. Kemp, Allergic rhinitis in children, *J. Paediatr. Child Health* 48 (2012) 302–310.
- [8] W. Storms, Allergic rhinitis-induced nasal congestion: its impact on sleep quality, *Prim. Care Respir. J.* 17 (1) (2008) 7–18.
- [9] E.W. Derman, D. Hawarden, M.P. Schwellnus, Allergic rhinoconjunctivitis in athletes – mechanisms of impaired performance and implications for management, *Curr. Allergy Clin. Immunol.* 23 (2) (2010) 59–62.
- [10] E.C. Correa, F. Berzin, Mouth breathing syndrome: cervical muscles recruitment during nasal inspiration before and after respiratory and postural exercises on Swiss Ball, *Int. J. Pediatr. Otorhinolaryngol.* 72 (2008) 1335–1343.
- [11] J.P. Parsons, J.G. Mastronarde, Exercise-induced bronchoconstriction in athletes, *Chest* 128 (2005) 3966–3978.
- [12] S.W. Stoloff, G.L. Colice, M.L. Hayden, T.J. Craig, N.K. Ostrom, N.S. Eid, et al., Exercise-induced bronchospasm: implications for patients with or without asthma in primary care practice, *Int. J. Gen. Med.* 4 (2011) 779–782.
- [13] S. Bonini, M. Bonini, J. Bousquet, V. Brusasco, G.W. Canonica, K.H. Carlsen, et al., Rhinitis and asthma in athletes: an ARIA document in collaboration with GA2LEN, *Allergy* 61 (2006) 681–692.
- [14] N. Koles, Treating allergic rhinitis in the athlete, *Rhinology* 40 (2002) 211–214.
- [15] A. Fanelli, A.L. Cabral, J.A. Neder, M.A. Martins, C.R. Carvalho, Exercise training on disease control and quality of life in asthmatic children, *Med. Sci. Sports Exerc.* 39 (2007) 1474–1480.
- [16] A.R. Dweik, P.B. Boggs, S.C. Erzurum, C.G. Irvin, M.W. Leigh, J.O. Lundberg, et al., An official ATS clinical practice guideline: interpretation of exhaled nitric oxide levels (FENO) for clinical applications, *Am. J. Respir. Crit. Care Med.* 184 (2011) 602–615.
- [17] M.R. Miller, J. Hankinson, V. Brusasco, F. Burgos, R. Casaburi, A. Coates, et al., Standardisation of spirometry, *Eur. Respir. J.* 28 (2005) 319–338.
- [18] E.O. Meltzer, C. LaForce, P. Ratner, D. Price, D. Ginsberg, W. Carr, MP29-02 (a novel intranasal formulation of azelastine hydrochloride and fluticasone propionate) in the treatment of seasonal allergic rhinitis: a randomized, double-blind, placebo controlled trial of efficacy and safety, *Allergy Asthma Proc.* 33 (2012) 324–332.
- [19] DA Guideline, Guidance for Industry, Allergic rhinitis: clinical development programs for drug programs, US Department of Health and Human Services, FDA Center for Drug Evaluation and Research, 2000, <http://www.fda.gov/downloads/Drugs/ GuidanceComplianceRegulatoryInformation/Guidances/ucm071293.pdf> (accessed 17.02.14).
- [20] EMA Guideline, Guideline on the clinical development of medicinal products for the treatment of allergic rhinoconjunctivitis, CHMP/EWP/2455/02, 2004, http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003554.pdf (accessed 17.02.14).
- [21] J. Neder, L. Nery, A. Silva, A. Cabral, A. Fernandes, Short term effects of aerobic training in the clinical management of moderate to severe asthma in children, *Thorax* 54 (1995) 202–206.
- [22] T. Sinha, A.K. David, Recognition and management of exercise-induced bronchospasm, *Am. Fam. Physician* 67 (2003) 769–774.
- [23] U.S. National Library of Medicine, Medical Encyclopedia, Allergic rhinitis, A service of the U.S. National Library of Medicine National Institutes of Health, 2014, <http://www.nlm.nih.gov/medlineplus/ency/article/000813.htm> (accessed 03.03.14).
- [24] H. Kanazawa, K. Asai, K. Hirata, J. Yoshikawa, Vascular involvement in exercise-induced airway narrowing in patients with bronchial asthma, *Chest* 122 (2002) 166–170.
- [25] J.M. Weiler, S.D. Anderson, C. Randolph, S. Bonini, T.J. Craig, D.S. Pearlman, et al., Pathogenesis, prevalence, diagnosis, and management of exercise-induced bronchoconstriction: a practice parameter, *Ann. Allergy Asthma Immunol.* 105 (2010) S1–S47.
- [26] P.R. Basso, M. Jamami, B.V. Pessoa, I.G. Labadessa, E.M.G. Regueiro, V.A.P. Di Lorenzo, Assessment of exercise capacity among asthmatic and healthy adolescents, *Rev. Bras. Fisioter.* 14 (3) (2010) 252–258.
- [27] J.G. Widdicombe, Pulmonary and respiratory tract receptors, *J. Exp. Biol.* 100 (1982) 41–57.
- [28] S. Berntsen, T. Stensrud, F. Ingjer, A. Vilberg, K.H. Carlsen, Asthma in medium altitude – exercise-induced bronchoconstriction in hypobaric environment in subjects with asthma, *Allergy* 60 (2005) 1308–1311.
- [29] H. Johansson, K. Norlander, L. Berglund, C. Janson, A. Malinowski, L. Nordvall, et al., Prevalence of exercise-induced bronchoconstriction and exercise-induced laryngeal obstruction in a general adolescent population, *Thorax* 70 (2015) 57–63.