

Long-term EAACI Research Fellowship

Research Fellow: Justyna Czeladzka, MD

Host supervisor: Prof. Zsolt Szépfalusi

Location: Medical University of Vienna, Department of Pediatrics and Adolescent Medicine, Vienna, Austria

Research title: "The mechanisms and biomarkers of exercise-induced bronchoconstriction in athletes. A bicentric clinical study."

Fellowship period: 01.03.2018 – 30.09.2019

Type of project: clinical study

Background:

The prevalence of bronchospasm among athletes is higher than in general population and it is constantly increasing. This phenomenon is not well researched. It remains unclear whether the physical effort itself produces bronchoconstriction or it just triggers the bronchospasm in susceptible asthmatic individuals. The *exercise-induced asthma* (EIA) and *exercise-induced bronchospasm* (EIB) have been recently described as separated terms and different treatment strategies have been suggested. However, the pathophysiology of EIB without asthma is poorly understood. The postulated mechanisms include osmotic and thermal hypotheses as well as recently proposed epithelial injury and inflammation hypotheses.

Aim of the study:

The aim of the study was to describe the mechanisms of exercise-induced bronchospasm and to verify its association with IgE-mediated hypersensitivity reaction as well as to look for the biomarkers and risk factors of non-IgE-mediated exercise-induced bronchospasm. Additionally the prevalence of exercise-induced bronchospasm among athletes will be estimated, the application of field exercise challenge test in screening of athletes will be evaluated and athlete-specific asthma questionnaire will be validated.

Materials and methods:

The study was a clinical study, a part of a bicentric clinical study. The other part was carried out in Poland and was supported by Wroclaw Medical University.

The study was carried out on the group of athletes performing different types of sports with high intensity and regularly since at least 4 years and minimum 7 hours per week.

Initially, the author's athlete-specific questionnaire for exercise-induced bronchoconstriction was carried out to estimate the subjective symptoms of bronchoconstriction during physical effort.

Afterwards, the sport-specific field exercise challenge test was performed. The conditions such as temperature and humidity as well as lactate measurements were noted for further analysis. The athletes who scored positive in questionnaire and presented decline in FEV1 after exercise were further investigated. Detailed medical interview and medical examination was performed. The allergy work out was done, including SPT and allergen specific IgE-antibodies. In consequence the study group was divided into IgE-sensitized and non-IgE-sensitized individuals. The blood sample was taken from each subject in addition to describe immunological profiles (including profiles of lymphocytes, inflammatory cytokines, basophile activation test and CCL16 levels). The second part of the study was intended for laboratory exercise challenge test, accompanied by blood sample being taken before and just after the challenge. The samples should be laboratory tested in search of the mechanisms of exercise-induced bronchospasm, especially the differences between IgE-mediated and non-IgE-mediated mechanisms.

Changes and challenges:

Planning and conducting the clinical trial in the foreign country was a huge challenge. We experienced some regulatory difficulties which led to delay in the recruitment process. The recruitment process, data collecting and analyzing still continue.

Observing the FEV1 decrement in the elite athlete requires adequate exercise and environmental stress which is not easy to ensure.

Performing such a complex clinical study required more time than expected and it needed to be prolonged.

Tasks personally performed by the JM:

Planning and conducting the clinical study was performed by myself, including obtaining the informed consent forms, evaluating inclusion criteria, preparing and carrying out the author's athlete-specific questionnaire for exercise-induced bronchoconstriction, performing the sport-specific field exercise challenge test, performing detailed medical interview and examination, performing allergy work out, analyzing the data and dividing the subjects into two study groups (IgE-dependent and IgE-independent), collecting the blood for further analysis and preparing them to be stored.

Results:

We tested 150 athletes, of which 45 met the criteria for further analysis. The recruitment process and data analyzing continue still.

At this point the prevalence of allergic diseases in the study group is higher than in the general population and correlated with training load. The IgE-sensitization is presented in majority of the subject who showed bronchoconstriction. The athlete-specific asthma questionnaire seems to be an useful tool in initial screening of athletes and will be validated in relation to objective medical findings. Specific field exercise challenge test allows to screen the athletes in their usual training condition and seemed to be more adequate for that group. Nevertheless, standardization of the test is challenging. The inadequate exercise and environmental stress lead to false negative results. Lactate-measurements might be a good predictor for exercise load during the challenge.

Impacts and benefits of this study:

The greatest benefit of the study might be unraveling the mechanisms of exercised induced bronchospasm (EIB), which is independent of IgE-mechanisms. Describing the biomarkers and the risk factors for its development seemed to be significant as well. Furthermore, the elaboration of the new standards in asthma/bronchospasm management might have an impact on medical care of athletes.

Personal reflection and acknowledgments:

Firstly, I would like to express my gratitude towards the EAACI for choosing me to be the winner of long-term research fellowship award 2018.

The fellowship provided me with fantastic learning opportunities concerning managing a clinical trial but also learning new methodologies as well as cooperating in the laboratory with fellow scientists.

I would like to express my gratefulness to my host supervisor, Professor Szepfalusi for giving me the opportunity to pursue this project in his center, for mentoring and research support throughout the year. Fortunately, Professor Szepfalusi has given me the best opportunity to prolong my stay for the following year in order to finish my research project and produce the good quality research publications.

My sincere thanks go to Professor Jutel for his encouraging research support, research guidance, and insightful comments which incited me to widen my research from various perspectives.

Finally, I strongly encourage any young scientists with an interest in the field of clinical immunology and allergy to participate in the EAACI fellowship awards.