

Exercise-Induced Wheezing among Japanese Pre-School Children and Pupils

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ABSTRACT

Background: Exercise-induced wheezing (EIW) may be a symptom of asthma and is a predictor of exercise-induced bronchoconstriction, transient narrowing of the lower airway following exercise in the presence or absence of diagnosed asthma. Population-based studies with a large sample of EIW in relation to age, sex, current asthma severity and medication usage have been sparse.

Methods: International Study of Asthma and Allergies in Childhood questionnaires were distributed at 885 nurseries, 535 primary schools, 321 junior high schools and 190 high schools, respectively, across Japan, and the corresponding data on 46,597, 41,216, 45,960 and 51,104 children were analyzed.

Results: Prevalence of EIW was 4.8, 4.7, 17.9 and 15.4% for each of the four educational facility types, respectively. Among 24,103 current asthmatics, 20.9, 28.7, 76.1 and 73.6% of subjects for the 4 educational facility groups reported to have experienced EIW, respectively. Severity of current asthma was associated with the risk of EIW; odds ratio (95% confidence interval) of children with asthma attack every day for having EIW once a week or more, using intermittent asthmatics as reference group, were 24.48 (19.33 to 31.01) adjusted for other covariates. Among current asthmatic kindergartners, increase in risk for EIW due to ascending severity of current asthma was mitigated by daily use of leukotriene receptor antagonist (p for interaction = 0.071).

Conclusions: EIW was not rare among current asthmatic children. An increased risk for EIW was in accordance with increasing severity of current asthma and this relation was mitigated with leukotriene receptor antagonist daily use among kindergartners.

KEY WORDS

bronchial asthma, childhood asthma, inhaled steroid, leukotriene receptor antagonist, wheeze

ABBREVIATIONS

EIW, Exercise-induced wheezing; EIB, Exercise-induced bronchoconstriction; ISAAC, International Study of Asthma and Allergies in Childhood.

INTRODUCTION

Exercise is a trigger of bronchial asthma attack¹ in some cases and exercise-induced asthma might be defined as one of early childhood onset phenotypes.² Meanwhile, diagnosis of asthma can be initiated with a report of wheezing during and/or after exercise, exercise-induced wheezing (EIW); and asthma attack

triggered by exercise may have a rapid exacerbation and possibly contribute to urgent medical visit.³ Report of EIW is a clinical expression of diseases other than bronchial asthma in some cases and it has been stated self-reported EIW alone should not be used to define exercise-induced bronchoconstriction (EIB) exactly in the absence of indirect and/or direct challenge tests.⁴ An aim of the present study was to de-

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lineate a prevalence of EIW among more than 180,000 children aged 3 to 18 in relation to age, sex, severity of asthma and medication usage in a nationwide cross-sectional survey conducted in 2008⁵⁻⁷ in order to provide an insight for clinician and public health physician seeing asthmatic patients and those patient populations. Although a study with the concomitant use of provocation challenge test is ideal to correlate EIW with bronchial asthma rigorously, large-sized population-based studies with challenge tests are unlikely to execute and such tests are likely unfeasible for small children. Ponsonby and colleagues found the exercise challenge had sensitivity and specificity estimates for exercise-induced wheeze based on the ISSAC question of 0.60 and 0.77 for 7-year old or older children, respectively, using a 12% or greater fall in FEV1 post-exercise as a positive test response.⁸ Although an Italian group reported the prevalence of wheeze with exercise based on the International Study of Asthma and Allergies in Childhood (ISAAC) questionnaire were 2.2 and 1.2% for 9,674 boys and 9,062 girls aged 6 to 7, respectively,⁹ findings on EIW based on large samples from general populations are sparse.

METHODS

STUDY SUBJECTS

The present analysis was based on the nation-wide cross-sectional survey of asthma and other allergic diseases in Japan a part of which survey was mentioned elsewhere⁵⁻⁷ and relevant details were briefly described here. The study subjects were recruited as follows. Firstly 1,109 nurseries, 672 primary schools, 396 junior high schools and 219 high schools were selected and asked for participation in this survey by each of the 47 prefectural boards of education in response to our request to secure 1,000 or more participants in each prefecture without any other intention. Among those nurseries and schools 885 (79.8%), 535 (79.6), 321 (81.1) and 190 (86.8) agreed to the requests by prefectural boards of education, respectively. Secondly a Japanese version of the ISAAC questionnaire¹⁰ was distributed from April to July 2008 to parents of 47,915 pupils aged 6 - 8 in the first and second grades of the primary schools, 63,359 pupils aged 13 - 15 in the first and second grades of the junior high schools and 67,944 aged 16 - 18 in the first and second grades of the high schools located in all 47 prefectures of Japan. A questionnaire based on the ISAAC one with additional enquiries regarding diagnosis for ever having asthma in kindergartners was also sent to parents of 50,959 kindergartners aged 3 - 6 years. Forty-seven thousand, two hundred and ninety-one parents of the kindergartens responded to our survey (response rate = 92.8%) while 92.1% of parents of the pupils attending primary schools, 78.8 and 81.6% of the pupils at junior high school and high school answered, respectively. A response was de-

defined as invalid 1) if the child's age was not in agreement with the grade of nursery or schools, or 2) a) the responder did not answer to a question, "Have you (or your child) ever had wheezing or whistling in the chest at any time in the past?", or b) the responder answered "yes" to the above question but did not answer to another question, "Have you (or your child) had wheezing or whistling in the chest in the past 12 months?" The invalid response numbered 279, 327, 1,452 and 1,498 for kindergartners, primary school pupils, junior high school and high school pupils, respectively; and those with the invalid response were excluded from the study subjects. We further excluded 423 subjects with unknown sex; and then 8,323 undetermined for presence of EIW as defined in the following section were omitted. Thus, 46,597 kindergartners, 41,216 pupils, 45,960 junior high school pupils and 51,104 high school pupils were used for the present study.

DEFINITION OF ASTHMA, EIW AND MEDICATION USAGE

We defined having current asthma if a child or a parent answered "Yes" to both of two questions, "Have you (or your child) ever had wheezing or whistling in the chest at any time in the past?" and "Have you (or your child) had wheezing or whistling in the chest in the past 12 months?" Severity of asthma (intermittent, mild, moderate, or severe) was assigned for current asthmatic children according to reported frequency of wheezing in the past 4 weeks: none, monthly or more but not weekly, weekly or more but not every day and every day. Having EIW was defined if a child or a parent answered "Yes" to a question, "In the past 12 months, has your (or your child's) chest sounded wheezy during or after exercise?" regardless of the answer to the question in regards to having current asthma as mentioned above. Severe EIW was defined if reported frequency of wheezing during or after exercise was weekly or more in the past 4 weeks. Among kindergartners whose parents answered "No" to the above question regarding EIW in the past 12 month, 231 kindergartners were reported to have such wheezing once or more during or after exercise in the past 4 weeks. Similarly 1,475 pupils reported by themselves or by parents (for primary school pupils) to have wheezing with the same frequency as that for kindergarten in spite of the fact that they reported no wheezy episodes during or after exercise in the past 12 months. Those 1,706 children were re-classified as having EIW in the present analysis.

Age and sex were specified as they were answered in the completed questionnaires. Inhaled medication daily use was defined if the subject or subject's guardian answered Flutide[®] (fluticasone propionate), Qvar[®] (beclometasone dipropionate), Pulmicort[®] (budesonide), or other inhaled medication was used

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