



International Study of Wheezing in Infants (EISL)

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The International Study of Wheezing in Infants (Estudio Internacional de Sibilancias en Lactantes [EISL]) is an international cross-sectional multi-centre study designed to assess the prevalence, severity and other factors related to infant wheezing during the first year of life in Latin America and the Iberian Peninsula. This study started in 2005 and currently there are participating centres in Latin America, Spain and Portugal.

The EISL study was developed to evaluate the prevalence and severity of recurrent wheezing during the first 12 months of life and the potential risk factors for wheezing and other respiratory diseases, such as pneumonia. The present study, like the ISAAC (International Study of Asthma and Allergies in Childhood), will use case-definitions and standardized methodology, thus improving the validity of comparisons and facilitating international collaboration.

The objectives of the EISL are:

1. To know the prevalence, severity and risk factors of recurrent wheezing during the first year of life of infants living in different parts of Latin America, Spain and Portugal, and to make comparisons within and between countries.
2. To evaluate at the individual level the hypotheses which have been suggested by the findings of past studies carried out in the first world.

3. To examine the relationship between recurrent wheezing and pneumonia in infants living in different areas of Latin America, Spain and Portugal, and to perform comparisons within and between countries.
4. To obtain reference measurements for evaluating future trends in the prevalence and severity of this disease.
5. To generate a network between the participating centres for future studies and to offer a framework for additional investigation on etiological and patho-physiological factors.

Basis and study design

The epidemiological and ecological aspects of this study –especially related to the first year of life- have been largely ignored and there are no international comparisons using the same methodology, which allow for comparisons. A crucial fact that supports the carrying out of the present study is the still high rate of mortality due to pneumonia in infants younger than one year of age in Latin America; a majority of those infants had prior episodes of wheezing (1,2). The present study defines recurrent wheezing as having had at least three episodes of wheezing during the first year of life. The population target is infants 12-15 months of age.

The methodology used in EISL is based on that of ISAAC (3-6). EISL participating centres are those which have successfully participated in ISAAC phase I or III and the main instrument is a core questionnaire on wheezing during the first year of life which incorporates epidemiological, therapeutic and ecological aspects. Furthermore, the study includes demographic and environmental information of each centre. As the main objective of EISL is to compare the data within and between countries, it has been estimated that each centre should recruit a random sample of 1000 to 3000 infants between 12 and 15 months of age. In those centres where the population of infants in that age range does not allow reaching the sample size, it should approximate the whole population of children of that age.

Parents attending the programmed health control at the 12th to 15th month of age in any centre in which those controls are carried out according to the national guidelines of each country, will be asked to complete the wheezing and risk factors questionnaire.

The definition of case and of its severity relies on questions about the key symptoms and about the diagnosis of the disease (i.e. asthma). The validity of the questionnaire has been tested and ratified in some of the participating centres. The Portuguese version of the questionnaire has been translated from Spanish into Portuguese and back-translated from Portuguese into Spanish.

Scientific background

Recurrent wheezing and acute lower respiratory infections play a very important role in the respiratory morbidity and mortality mainly in developing countries around the world. The reasons for the different prevalence and severity of recurrent wheezing in infants between developed (6-8) and developing (9,10) regions, are unknown. However it is possible that those differences are principally determined by a different exposure to environmental risk factors, especially those related to a low socio-economic condition (10). The early (from birth) and sustained exposure to aggressive inhalant agents seems to determine a wheezing phenotype usually related to viral lower respiratory infections, which starts during the three first months of life and evolves with more frequent and severe wheezing episodes, that are finally associated to complications, such as pneumonia (10). This wheezing condition which would be the predominant in Latin America is by no means benign as it is traditionally considered, and generates a very large number of consultations and consumption of health resources. Furthermore, it contributes enormously to the high morbidity and mortality from respiratory complications in infants of those regions, particularly those from deprived populations.

Recent evidence suggests that innate immunity could be altered by environmental exposures (including biological agents such as viruses) during the first three months of life, resulting in a larger number of wheezing episodes during the first year of life. Furthermore, in those patients, a larger environmental exposure would be related to more frequent and

perhaps more severe wheezing episodes (7,8,11). It is likely that environmental risk factors related to lower socio-economic conditions play a role in the prevalence and severity of wheezing (10,12,13). The different levels of economic development found in Latin America and in the Iberian Peninsula offer a great opportunity for verifying that and other hypotheses.

Importance of the proposed study

In spite of recurrent wheezing being an important health problem throughout the world, particularly in developing countries, the information on the prevalence of wheezing and of its characteristics and complications is scarce. This is a surprising fact, as it is possible that the events which will determine the asthmatic response later in childhood (immunological, clinical and functional) could be configured during the first months of life (7-11). There is no information as yet published coming from international multi-centre studies (using the same standardized methodology), on the true prevalence of recurrent wheezing during the first year of life among infants living in developing regions like Latin America and others. Neither are there comparative international studies on this issue which involve both developed and developing countries. A recent longitudinal study (birth cohort) from Latin America suggests that recurrent wheezing would be much more frequent and severe in developing countries as compared to developed ones (10).

It is likely that, as occurred with asthma studies (5,14), there are true differences in prevalence and wheezing phenotypes between centres and countries. The present study will allow to evaluate different aspects of recurrent wheezing during the first year of life in countries sharing the same language and similar customs, but differing significantly in the level of economic development.

The present study will obtain, for the first time, information for testing several current hypotheses on infant wheezing, coming from studies performed in developed countries, mainly in English-speaking countries.

The EISL offers a unique opportunity for the scientific integration and for the networking of the participating centres. There is no doubt that the comparisons between

the results obtained in Latin America and those coming from the original countries, Spain or Portugal, will provide very valuable epidemiological and ecological international information on recurrent wheezing during the first year of life, which is currently lacking in the world medical literature.

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