Allergol Immunopathol (Madr). 2014;42(5):493–499

Allergologia et immunopathologia

Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica

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REVIEW

Inhaled beclomethasone in pregnant asthmatic women – A systematic review

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Received 13 February 2013; accepted 25 March 2013
Available online 2 July 2013

KEYWORDS
Asthma;
Pregnancy;
Beclomethasone

Abstract The aim of this study was to systematically review the safety and efficacy of inhaled beclomethasone for asthma treatment in pregnant women. We performed a systematic review in Medline, LILACS and SciELO electronic databases in December 2012. A total of 3433 articles were found by using the keywords asthma, pregnancy and beclomethasone. Among these, 1666 were from Medline, via PubMed, and 1767 were from LILACS and SciELO. Nine of these articles were selected. Only one paper suggested an increased foetal risk for congenital malformations, and one other for offspring endocrine and metabolic disturbances. Data are mostly reassuring, supporting the use of glucocorticoid inhalants during pregnancy, and we found no evidence of inferiority in relation to efficacy and safety of beclomethasone compared to other drugs used in pregnant asthmatic women.

Introduction

Asthma is a chronic disease of lower airways, characterised by inflammation and increased responsiveness, which results in bronchial obstruction, partially or completely reversible and symptoms of dyspnoea, wheezing, cough and expectoration, which vary in intensity and frequency from patient to patient and in the same patient at different times.[1] Acute exacerbations can mainly occur with triggers by exposure and viral infections of airways.[1] It is the most common chronic disease among women in reproductive age[2] and can affect up to 8% of pregnant women.[3] When inadequately controlled, it is associated with increased risk for prematurity, low birth weight, congenital malformations, preeclampsia and caesarean section.[4]

Adverse outcomes of asthma can be avoided with proper control through educational, behavioural and pharmacological actions,[1,5] especially with the use of inhaled corticosteroids, whose efficacy and safety in pregnant asthmatic women have been extensively studied in recent years.[6,7]

One of the largest studies was the Swedish cohort published by Norjavaara and De Verdier (2003), which analysed the safety of budesonide in 2968 pregnant women.[8] Since then, this inhaled corticosteroid has been considered the most studied and safe for use in pregnant women and con-

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http://dx.doi.org/10.1016/j.aller.2013.03.009

sidered as class B by the American organ of Food and Drug Administration (FDA). There are no comparative studies about asthma treatment during pregnancy between beclomethasone and budesonide,[7] so, beclomethasone is being considered class C because of the limited available studies and not due to the presence of a known risk.

The knowledge of available evidence about the safety and efficacy of inhaled beclomethasone is important for clinical practice and the implementation of public health actions in the treatment of asthma because it is an accessible drug, with a low cost and, in Brazil, it is distributed for free by the public health service. The objective of this study is to present a systematic review about the efficacy and safety of beclomethasone used to treat pregnant asthmatic women.

Search strategy

The systematic literature review was performed through Medical Literature Analysis and Retrieval System Online (MEDLINE), Latin American and Caribbean Health Sciences (LILACS) and Scientific Electronic Library Online (SciELO) databases and the search data occurred in December 2012. A specific strategy was elaborated for each of them to the intersection of the descriptors (DECS) – keywords for retrieving subjects from scientific literature.

For Medline/PubMed, the search strategy was performed in two stages using the syntaxes (''Asthma''[Mesh]) AND ''Pregnancy''[Mesh] and (''Beclomethasone''[Mesh]) AND ''Pregnancy''[Mesh]. For LiLACS and SciELO, the keywords ''asthma'', ''beclomethasone'' and ''pregnancy'' were used.

Selection criteria

To be included in the analysis studies should be original articles (excluding editorials and review studies); have pregnant asthmatic women submitted to treatment with inhaled corticosteroids including beclomethasone, as research subjects; approach some of the following outcomes: congenital malformations risk, premature birth, caesarean delivery, intrauterine growth restriction, asthma exacerbations, pre-eclampsia, or childhood diseases; and be published in Portuguese, English or Spanish. Studies that did not define the number of patients using beclomethasone were excluded.

Data analysis

The articles selection consisted of three steps. The first one was based on reading the title of the articles. Those that clearly did not fit in any of the criteria for inclusion in this study were excluded. In the second step, the abstract of each selected article was read and, likewise, those that did not fit in any of the inclusion criteria were rejected. In the third step, the articles that were not excluded were fully read in the aim of selecting those which would be included in this review.

Crossing the keywords ''asthma'' and ''pregnancy'', and ''beclomethasone'' and ''pregnancy'' in the Medline database, via PubMed, 1666 articles were found. Among these, 1347 articles were eliminated due to the title, 292 were excluded by reading the abstracts and 12 after reading the full-text version. Nine non-repeated studies were selected for review. In the SciELO database, crossing the keywords ''asthma'' and ''pregnancy'', 13 articles were found and all of them were eliminated by the title. In the LILACS database, crossing the same keywords as for PubMed, 1717 articles were retrieved, 1430 were excluded by the title, 273 after abstract and 8 after full text reading. As a result, six studies were selected, all of them already selected, thus leaving the same nine articles retrieved through the PubMed search (flowchart shown in Fig. 1).

Results

The heterogeneity of articles did not allow to group them for a statistical analysis, so sufficient data was not found to conduct a meta-analysis. Because of this, the results of this study will be presented as a systematic review. According to the ''Cochrane Library'', if it is not possible to do a meta-analysis, the researcher should feel encouraged, by the line of research, on building a field for randomised clinical trials.[9]

It was decided to consider the following variables of the selected articles: author/year, study design, country, sample (total, using inhaled corticosteroids and using beclomethasone) and results, with the aim of doing a better presentation (Table 1).

Discussion

The first aspect to emphasise, after analysing the articles, is the lack of studies designed to specifically evaluate beclomethasone: only two out of nine articles.[12,18] Because of ethical reasons, the difficulty of proposing studies to evaluate drugs in pregnant women is understood. However, the subject deserves more attention because beclomethasone has been largely used in the past thirty years to treat pregnant asthmatic women. In fact, beclomethasone continues to be recommended as an alternative for budesonide during pregnancy by internationals protocols.[19] Most articles discuss about the efficacy and safety of inhaled corticosteroids in general, which is a recurrent subject of research in this area.[11,13–17]

The first publications from the 1980s sought to evaluate the drug efficacy and safety in a period in which it had never been used in pregnant women.[17,18] As a result, several case series studies emerged, which were important to suggest safety of using corticosteroids and to stimulate the emergence of new studies in the 1990s, at this time, more capable to evaluate risks and efficacy.[14–16] Cohort studies and clinical trials which were produced in the 1990s came to consolidate the idea of safety and efficacy of inhaled corticosteroids used in pregnant asthmatic women. In these studies, beclomethasone was the most used inhaled corticosteroid.

Publications about asthma treated in pregnancy with others drugs have become rare after the publication of a cohort study that evaluated budesonide in pregnant women in 2003.[8] Four articles[10–13] published after 2003 were found in this review. Among these, two prospective studies had their