

Systematic Review to Assess Use of Anti-inflammatory Therapy in Treatment of Asthmatic Children

Thesis

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مراجعة منهجية لتقييم استخدام الأدوية المضادة للالتهابات في علاج الربو الشعبي عند الأطفال

رسالة

توطئة للحصول على درجة الماجستير في طب الأطفال

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Summary and Conclusion

A systematic review is a literature review focused on a research question that tries to identify, appraise, select and synthesize all high quality research evidence relevant to that question. Systematic reviews of high-quality randomized controlled trials are crucial to evidence-based medicine.

Asthma is an important chronic airway disease worldwide, and its prevalence is increasing in all regions. The goal of asthma management is to achieve optimum disease control, so different measures such as clinical assessment (symptoms and quality of life), functional parameters (spirometry), and biomarker of inflammation are used to evaluate asthma control.

The recognition that asthma is a chronic inflammatory disorder of the airways has resulted in an increased emphasis on the use of anti-inflammatory drugs. Anti-inflammatory drugs reduce inflammation and prevent permanent injury in the lungs and also help prevent asthma attacks from occurring, so anti-inflammatory drugs are the corner stone of asthma treatment.

The aim of the present study was to assess when to begin and when to stop anti inflammatory therapy in asthmatic children.

We started by searching of published studies was performed in the electronic database in the last 20 years available through MEDLINE pubmed, MEDLINE Ovid and Cochrane controlled trials register.

Searching the electronic data base for literature review identified 65 Published studies, 55 articles of them were excluded (15 of them excluded by title and abstract and 40 of



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List of Abbreviations

	Abbrev.
Alpha-1-antitrypsin	AAT
Airway hyper responsiveness	AHR
Apical Presenting cells	APCs
Beclomethasone Dipropionate	BDP
Bronchial Hyper responsiveness	BHR
Bronchitis obliterans-organizing pneumonia	BOOP
Broncho-pulmonary dysplasia	BPD
Critically Appraised Topics	CATs
Chemokines 3	CC3
Complement 14	CD14
Cystic fibrosis	CF
Congestive heart failure	CHF
Chronic obstructive pulmonary disease	COPD
cysteinyl leukotrienes	CysLTs
Dry powder inhaler.	DPI
Evidence based medicine	EBM
Electrocardiogram	ECG
Exercise-induced Asthma	EIA
Expert Panels Report	EPR
Environmental tobacco smoke	ETS
Food and Drug Administration	FDA
Forced expiratory volume in first second	FEV1
Gastro-esophageal reflux disease	GERD
Global Initiative For Asthma	GINA
G-protein-coupled receptor 35	GPR35
House dust mites	HDM
Inhaled Corticosteroids	ICS
Immunoglobulin E	IgE
Interleukin	IL
Intention-to-treat	ITT
Long Acting B2 Agonist	LABA
Leukotriene receptor antagonists	LTRA

	Abbrev.
5-lipoxygenase	LOX5
Meter-dose inhaler	MDI
Messenger RNA	mRNA
National Asthma Education and Prevention Program	NAEPP
National Heart, Lung, and Blood Institute	NHLBI
Nitrous oxide	NO
Ozone	O3
Pressure of carbon dioxide	Pco2
Phosphodiesterase Inhibitors 4	PDE4
Peak Expiratory Flow Rate	PEFR
Pulmonary function tests	PFTs
Randomized controlled trials	RCT
Respiratory syncytial virus	RSV
Short Acting B2 Agonist	SABA
Sodium cromoglycate	SCG
Sublingual Immunotherapy	SLIT
Sulphur dioxide	SO2
Systematic Review	SR
T helper	Th
T-cell immunoglobulin mucin	TIM
Vital capacity	VC
Vocal cord dysfunction	VCD
World Health Organization	WHO

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Introduction

A Systematic review is a "study of the studies" all relevant research is analyzed in an effort to determine the overall evidence for an intervention. A systematic review is a literature review focused on a single clear question, which tries to identify, select and appraise all high quality research evidence relevant to that question then makes assessment of the included studies and synthesis of findings and interpretation. Systematic review are generated to answer specific, often narrow, clinical question in depth (**Garg et al., 2008**)

Bronchial Asthma is the commonest chronic inflammatory disorder of the airways. That is often reversible either spontaneously or with treatment (**GINA, 2011**).

The recognition that asthma is a chronic inflammatory disorder of the airways has resulted in an increased emphasis on the use of anti-inflammatory drugs. Anti-inflammatory drugs reduce inflammation and prevent permanent injury in the lungs and also help prevent asthma attacks from occurring (**GINA, 2010**).

The principal anti-inflammatory drugs are corticosteroids and to a lesser extent sodium cromoglycate, nedocromil sodium and leukotriene receptor antagonist. Several other drugs and therapies may also have anti-inflammatory effects in asthma. The early use of prophylactic anti-inflammatory agents is advocated in the treatment of chronic asthma. It is hoped that this treatment scheme will result in a reduction in the morbidity and mortality from this common chronic condition (**Guilbert et al., 2006**).

There are some controversies about different guidelines in treatment of asthmatic children as the latest GINA report now emphasizes asthma control (controlled, partly controlled,

uncontrolled) rather than asthma severity for indication of anti-inflammatory therapy. This therapy is initiated and adjusted in a continuous cycle (assessing asthma control, treating to achieve control, and monitoring to maintain control) If asthma is not controlled on the current treatment regimen, treatment should be stepped up until control is achieved. When control is maintained for at least three months, treatment can be stepped down (**GINA, 2011**).

The PRACTALL report recommends that identification of the asthma phenotype is important in the subsequent asthma management (**Bacharier et al., 2008**). In general, inhaled corticosteroids are the first choice preventer medications. Leukotriene receptor antagonists (LTRA) can be used as monotherapy instead of inhaled corticosteroids if symptoms are intermittent or mild. LTRA can also be suggested as first line preventer treatment for viral-induced wheeze to reduce the frequency of exacerbations in young children aged 2–5 years (**Bisgaard, 2005**).

Despite a wealth of literature on anti-inflammatory drugs and asthma, controversy remains as to its indication, effects, when to start, and end of therapy. Differences in populations studied, methods used, definitions of outcomes, and criteria for therapy may all be responsible for the variations in reported results, necessitating systemic review to be carried out and reach definite resolution of all such topics.

Aim of the Work

This is a systematic review to assess the following question: when to begin and when to stop anti inflammatory therapy in asthmatic children?

Chapter 1

Evidence Based Medicine (EBM) and Systematic Review

Definition of EBM:

Evidence based medicine (EBM) is a problem solving approach in which solution are sought for questions that arise during clinical practice. It is defined as the integration of best research with clinical expertise and patient value **(Guyatt et al., 2008)**.

EBM involves two fundamental principles in clinical decision-making. First, the evidence is always interpreted together with the patient's values and preferences by weighing the benefits and risks, and the costs associated to the treatment compared to the alternatives. Second, the strength of available evidence may be variable, constituting a hierarchy of evidence on the basis of the ability of the study to avoid systematic bias **(Anttila, 2008)**.

EBM is the integration of clinical expertise, patient values, and the best evidence into the decision making process for patient care. Clinical expertise refers to clinician's cumulated experience, education and clinical skills. The patient brings to the encounter his or her own personal and unique concern, expectations, and values. The best evidence is usually found in clinically relevant research that has been conducted using sound methodology **(Sestini and Irving, 2009)**.