New Modalities In Asthma Management

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ABSTRACT

Asthma is a chronic disease of airways with an underlying inflammatory component. Its prevalence has increased dramatically in recent years. Although inhaled steroids are the cornerstone in long term therapy of asthma, poor patient compliance and the systemic side effects especially when high doses are required in long term control of the disease are still a major concern.

So, as a result of the increased understanding of the pathophysiology of asthma, new classes of medications have been introduced during the last few years such as leukotriene antagonists and anti-IgE antibody. In this study we discussed a number of those new medications and their place in the treatment guidelines of asthma.

Key Words:

Asthma- New modalities in therapy

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List of Abbreviations

AA : Arachidonic Acid

APC: Antigen Presenting Cells

AHR: Airway Hyperresponsiveness

AIA: Acetylsalicylic acid Intolerant Asthma

AIU: Acetylsalicylic acid Intolerant Urticaria

ASA: Acetylsalicylic Acid

BAL: Bronchoalveolar fluid

b-FGF: basic Fibroblast Growth Factor

BHR: Bronchial Hyperresponsiveness

BK : Bradykinin

C5a: Complement 5a

cAMP: cyclic -3,5-adenosin monophosphate

CFC: Chlorofluorocarbon

CO : Carbon Monoxide

COPD: chronic obstructive pulmonary disease

COX1: cyclo-oxygenase 1 enzyme

Cys-LTs: Cysteinyl Leukotrienes

DNA: Deoxyribonucleic acid

DPI: Dry- Powder Inhaler

EAR: early allergic reaction

EIA: Exercise- Induced asthma

EIB: Exercise- Induced Bronchospasm

FCεRI: High- affinity receptor for IgE

FCεRII: Low- affinity receptor for IgE

FEV1: Frced Expiratory Volume in 1 second

FDA: US Food and drug administration

FVC: Forced Vital Capacity

GM- CSF: Granulocyte Macrophage Colony-stimulating factor

HDM: House Dust Mite

HFA: Hydrofluoroalkane

HPA: Hypothalamic- Pituitary- Adrenal axis

ICAM-1: Intercellular adhesion molecule-1

ICS: Inhaled Corticosteroids

IgE: Immunoglobulin E

ILs: Interleukines

ISAAC: International Study of Asthma and Allergies in Childhood

IT: Immunotherapy

LABA: Long Acting-B2 agonists

LAR: late allergic reaction

LBK: Lysylbradykinin

5-LO: 5- lipo-oxygenase enzyme

LTRAs: Leukotriene receptor antagonists

MDC: Macrophage-derived chemokine

MDI: metered dose inhaler

mIGE: membrane- bound IgE

MIP-1α: macrophage inflammatory protein- 1 α

mRNA: messenger ribonucleic acid

MTT: medical training therapy

NANC: nonadrenergic, noncholinergic inhibitory nervous system

NO: nitric oxide

NSAIDs: non-steroidal anti-inflammatory drugs

PDGF: platelet-derived growth factor

PEF: peak expiratory flow

PGD2: prostaglandin D2

PGE2: prostaglandin E2

PKA: protein kinase A

RANTES: regulated on activation normal T-cell expressed and secreted

RAST: radioallergosorbent tests

RCT: randomized controlled trials

RES: reticuloendothelial system

SCIT: subcutaneous immunotherapy

SIT: specific immunotherapy

SLAV: sublingual allergen vaccination

SLIT: sublingual immunotherapy

SPT: skin prick testing

RSV: respiratory syncytial virus

TFN-gamma: interferon gamma

TGF-beta: transforming growth factor- beta

TH: T-helper cells

TNF-α: tumor necrosis factor α

TXA2: thromboxan A2

WHO: world health organization

Introduction And Aim Of The Work

Asthma is a disease of air ways with an underlying inflammatory component **(Belvisi et al, 2004).**

Despite increase scientific knowledge about asthma and improved therapeutic options, the disease continues to cause significant morbidity and mortality **(Mintz, 2004).**

Although inhaled corticosteroids are the most effective long term therapy available for suppressing airway inflammation in persistent asthma, poor patients compliance is a major barrier to treatment **(O'Conell , 2005).**

There is a need for novel, safe treatment to tackle the underlying inflammation that characterized asthma pathology and to be developed as oral therapy in order to alleviate patient compliance issue especially in children **(Belvisi et al, 2004).**

New classes of medications have introduced during the last few years including leukotriene modifiers, long acting beta-adrenergic agonists, combination inhaled corticosteroids with long acting beta adrenergic agonists and anti-IgE antibodies **(Szefler, 2004).**

Anti-leukotriene agents are currently being studied as alternative first line agents to inhaled corticosteroids in mild to moderate chronic asthma **(Salvio and Hicks, 2004)**. Controlled clinical trials with the currently used leukotriene modifiers have established their efficacy in improving pulmonary function, reducing symptoms, decreasing night-time awakenings and decreasing the need for rescue medications **(Kemp, 2003).**

Anti-IgE, the newest therapeutic modality for asthma, a biologic agent to control allergic disorders, represents a fundamentally new concept in treatment **(Milgrom, 2004)**. It shows great promise as an adjunctive therapy in moderate to severe asthma patients (Lanier, 2003).

New guidelines suggest that immunotherapy can, in some cases, actually prevent the development of allergic asthma in children with allergic rhinitis **(Disease Management Advisor, 2003)**. It is the only treatment that can modify the natural history of asthma **(Jacobsen L., 2001).**

Pulmonary rehabilitation is a form of therapy for chronic lung diseases that becomes more and more important. It can improve endurance and quality of life **(Werner Karrer, 2005).**

Aim of The Work:

To provide insight into the new advances in management of bronchial asthma in children in comparison to the basic and currently used medications and show to what extent those new modalities may be used as alternative or combination treatment to the other medications.

DEFINITION

Asthma is a chronic inflammatory disease of airways that affects approximately 100 million people worldwide **(Kemp JP., 2003)**.

Asthma is a disease characterized by chronic airway inflammation and varying degrees of airflow limitation and airway hyperresponsi-veness, accompanied by recurrent episodes of coughing, wheezing, and dyspnea. Airflow limitation is at least partially reversible, either spon-taneously or with treatment. Many cells, including eosinophils, T cells, mast cells, airway epithelial cells and humoral factors contribute to airway inflammation. In patients with chronic disease, airflow limitation tends to become less reversible and it is common to see evidence of airway remodeling. Airway inflammation and airway remodeling are associated with airway hyperresponsiveness in sensitive patients **(Kager S. and Basel AG., 2005).**

Its causes and physiopathological mechanisms are various. The final result is a recurrent obstructive bronchial process, with sibilants and/or dyspnea, which causes an upset in functional respiratory tests, among which the maximum respiratory peak flowmeter diminished for age, sex and height of patient **(Hernando SV. et al, 2004)**.

In susceptible individuals, this inflammation causes symptoms which are usually associated with wide spread but variable airflow obstruction that is often reversible spontaneously or with treatment and causes an associated increase in responsiveness of airways to a variety of stimuli **(Visser et al, 2002)**.