IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

Human Journals
Review Article
May 2020 Vol.:18, Issue:2

Biomarkers of Asthma

IJPPR
INTERNATIONAL JOURNAL OF PHARMACY & PHARMACEUTICAL RESEARCH
An official Publication of Human Journals
ISSN 2349-7203
HUMAN

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Submission: 23 April 2020
Accepted: 01 May 2020
Published: 30 May 2020

Keywords: Biomarkers, Difficult asthma, Inflammation, Phenotype, Severe

ABSTRACT

It is defined as a chronic and heterogeneous disabling respiratory disease which is characterized by different mechanism. The purpose of this review is to highlight the current and seminal literature that informs the understanding of the clinical and investigative utility of biomarkers in asthma. This review deals with the procedure of how to be precise about selecting the best biomarker in asthmatic patient which regulate disease in individual and to use the best validated treatment underlying the disease**.** The use of advanced biostatistical technique and combinatorial analysis has led to additional advances in utility of biomarkers.

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INTRODUCTION

It is generally regarded as a heterogeneous disease that group different disease in a single frame because the treatment and diagnosis is based on individual symptoms like cough, chest tightness, SOB, wheezing. The practice of personalized medicine in asthma is very limited. Keeping the International global Initiative for asthma (GINA) guidelines in mind the pharmacological treatment is based on the severity of the disease. Despite a whole ongoing research in last year which is based on the identification of biomarkers for asthma only a few biomarkers indicative of T2 high asthma have been described. (e.g.:-IgE, eosinophils in blood/sputum, FeNO, periostin) and their utility in diagnosis prognosis and therapy is still controversial. This review will summaries the recent knowledge about the biomarkers identified of asthma with special focus on those with higher chances.

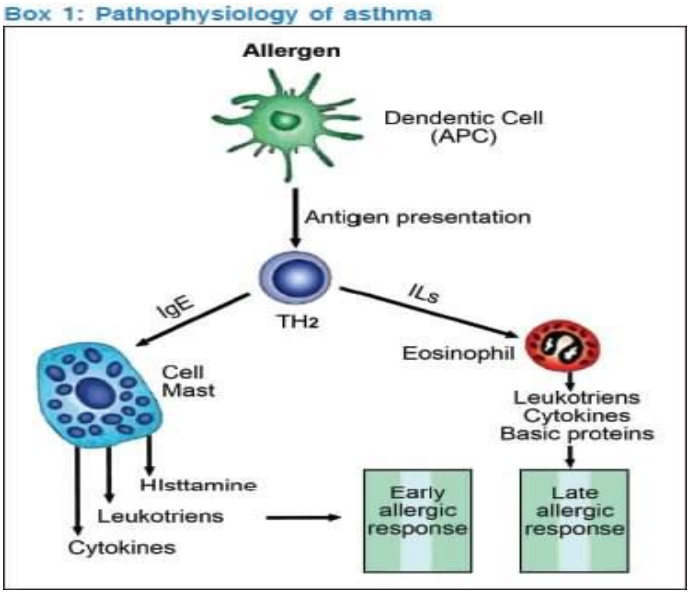

Fig:-1

BIOMARKERS

BLOOD CELLS AND SERUM BIOMARKERS:

It is a micro invasive procedure and a prognostic biomarker in asthmatic patient with type 2 inflammation. In a recent study it shows that blood eosinophil count>400 cells/ml is more severe and shows acute respiratory event whereas blood eosinophil count <400 cells/ml is less severe. There is a relationship associating between eosinophil in blood and in sputum, the use of blood eosinophil is to identify sputum eosinophil is still debated because of the

relatively false negative and false positive rate. Evidence of this biomarker can help to select targeted treatment for severe asthmatic patient particularly those related to the main stimulant of eosinophil recruitment and differentiation of IL-5.

PERIOSTIN

It is measured in the serum and is an extracellular matrix protein secreted by the epithelial cells in response to IL-13. It is associated with T2 high eosinophilic asthma. It causes greater lung function decline and severe airflow obstruction. It requires sensitive ELISA kits which are yet not widely distributed. It is found to be associated with a better response to anti IL-13 therapy.

EXHALED NITRIC OXIDE

It is produced by the synthases of NO some of which can be induced by cytokines including Interferon gamma, IL -1 beta, Tumour necrosis factor alpha, IL -4 and IL -13. It is seen in increased level in type 2 asthma. It is a predictive and dynamic biomarker to determine therapeutic benefit from corticosteroid level of less than 25 ppb is normal in adult and a level greater than 50 ppb is elevated. It has the limited utility to predict sputum eosinophilia. ICS typically suppresses FeNO levels and is useful as a marker of complications among asthmatic patients.

URINE METABOLITES

It is a potential biomarker which is due to post transitional modification of tyrosine protein residue by hypobromous acid produced by activated eosinophils bromotyrosine is formed. Its concentration is higher in patient with allergic asthma. Its concordance is not that high so in the clinical setting it would be best when assessed as a part of larger panel of inflammatory biomarkers.

Leukotriene E4 is a stable product of cysteinyl leukotriene metabolism. Its concentration is high in children with allergic asthma and adults with aspirin exacerbated respiratory disorder. A recent Meta analysis shows that ULTE4 is a high predictive biomarker for the aspirin exacerbated respiratory disease. Increased in ULTE4 is due to tobacco smoke.

CELLULAR BRONCHIAL SAMPLES AND BRONCHIAL BIOPSY:

The most invasive method is to study airway changes in the fiberoptic bronchoscopy with endobronchial biopsy. CD4+ cells expressing both IL-4, IL-17 predicted greater risk of severity of asthma.Thermoplasty is the first treatment which specifically targets airway remodeling and helps in the reduction of airway smooth muscle thereby reducing the airway problem.

SPUTUM CELLS AND MEDIATORS:

It is a non invasive method and to obtain samples for this the patient need to nebulise with 3% saline for 20 mins.The sputum is centrifuged and stained and different types of cell types are recognized. Sputum quantitative cell count is the reference standard and this method is feasible even on frozen samples.

Four Inflammatory phenotypes have been found in the Severe Asthma Research Program(SARP) cohort -Eosinophilic(>=2% eosinophils in induced sputum) Neutrophilic (>=40% neutrophils) mixed granulocytic and paucigranulocytic. It analysis identifies 3 transcriptome associated clusters (gene cluster) corresponding to eosinophilic, neutrophilic and paucigranulocytic phenotypes.

The high level of group 2 ILC in the sputum is related with severe asthma whose airway eosinophilic is greater than 3% despite normal blood eosinophil which is <300ml suggesting that these cells could be a potent novel biomarker inspite of having its own limitations.

DISCUSSION

During the years of research many biomarkers have been developed but only a few of them is generally used in clinical practice so far. All the biomarkers which shows a good predictive diagnostic efficiency also has its limit. A good biomarker should identify the prognosis easily with minimum discomfort or risk of the patient. Unfortunately, an ideal biomarker does not exist and the overlap between the biomarker is a reality. Biomarkers although having an advantage of determining the phenotype and endotype may also have a predictive value for the response to biologic treatment. In recent years we will have a more scientific way to identify the right biological therapy for each patient in a more personalized and precise medicine approach to the disease treatment.

CONCLUSION

The type of medicines and treatment to be implemented to asthmatic patient requires a proper detection of valid biomarkers. Various biomarkers are used clinically to predict the response to different therapies like steroid or biological therapies. These biomarkers are limited in number. If a patient with severe allergic asthma (high level of serum total IgE, high FeNO) despite a step 4 or 5 treatment of GINA guideline if it fails it is treated with another biological therapy (if blood eosinophilia is>=300 cells/ml)based on the condition and severity of the patient.

Furthermore research is needed for the validation of biomarkers particularly in non T2 pathways.

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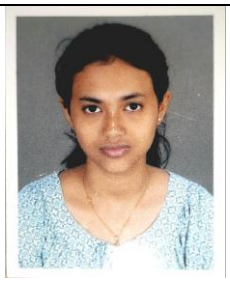

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