Association Between Interleukin-8 Levels in Bronchoalveolar Lavage Fluid and its Correlation with Severity in Children With Bronchiectasis

Thesis

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Contents

List of Abbreviations

ACTs	: Airway Clearance Techniques
AIDS	: Acquired immune deficiency syndrome
BAL	: Bronchoalveolar lavage
BE	: Bronchiectasis
CF	: Cystic fibrosis
CFTR	: CF transmembrane conductance regulator
cHRCT	: Chest High-Resolution Computed Tomography
CRP	: C-reactive protein
CSLD	: Chronic suppurative lung disease
CXCR2	: Chemokine Receptor 2
DPB	: Diffuse panbronchiolitis
FAE	: Flexible airway endoscopy
HRCT	: High-resolution computed tomography
HVMA	: High-speed video microscopy analysis
ICS	: Inhaled corticosteroids
LABA	: Long-acting beta2- agonist
MMP	: Matrix metalloproteinase
MRI	: Magnetic resonance imaging
MVCC	: Mutation Varying clinical consequence
NBS	: Newborn screening
NCFB	: Non-cystic fibrosis bronchiectasis
NE	: Neutrophil elastase
NTHi	: Non-typeable H. influenza

NTM	: Nontuberculous mycobacteria
Pa	: Pseudomonas aeruginosa
PBB	: Protracted bacterial bronchitis
PCD	: Primary ciliary dyskinesia
PIDs	: Primary immunodeficiency disorders
rhDNase	: Recombinant human deoxyribonuclease
SAA	: Serum amyloid A
sTREM-1	: Soluble triggering receptor expressed on myeloid cells-1
TEM	: Transmission electron microscopy
TIMPs	: Tissue inhibitors of metalloproteinases
TNF-alpha	: Tumor necrosis factor-alpha

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Introduction

Bronchiectasis is a complex chronic respiratory condition resulted from a vicious cycle of chronic infection and airway inflammation leading to permanent dilatation of the bronchial lumen with permanent lung tissue damage and progressive decline in lung function and is associated with significant morbidity in children that extend beyond the respiratory system and include cardiac and psychological effects **(Pizzutto et al., 2017).**

Clinical and functional features of bronchiectasis are chronic wet cough which is usually the commonest finding, exertional dyspnea, hemoptysis, digital clubbing, and chest wall deformities. Recurrent wheezing and growth failure are additional symptoms that may be found. Repeated episodes of pulmonary exacerbations are associated with progressive decline in lung function and reduced quality of life **(Gallucci et al., 2017).**

Chronic neutrophil-dominant airway inflammation is a key feature of bronchiectasis and activated neutrophils represent a key component of the "vicious cycle" of lung damage through the release of their harmful cellular contents, particularly, cell-derived proteases and reactive oxygen species **(Chalmers et al., 2015).**

In addition, airway secretions in patients with BE is rich in potent neutrophilic chemoattractant cytokines, including IL-1b, tumor necrosis factor-a, IL-8, and leukotriene B4 produced by the stimulatory effects of hyperactive alveolar macrophages. This persistent cytokine milieu results in chronic neutrophilic recruitment to the alveoli and progressive tissue damage **(Derek et al., 2016).**

Bronchoscopy is indicated in cases of bronchiectasis as recommended by The British Thoracic Society in 2010, it is useful for sampling of lower respiratory tract secretions and obtaining microbiological results in patients and for obtaining endobronchial biopsy of airway cilia to investigate causes of bronchiectasis **(Pasteur, 2010).**

The evaluation of cellularity is one of the principal indications for BAL, from the alveolar environment. The analysis of cytokines, as well as of pro- and anti-inflammatory molecules, in the BAL fluid is also the focus of increasing interest, both in clinical practice and research.

Aim of the Work

The aim of this study is to evaluate the degree of bronchial inflammation in patients with bronchiectasis by measuring the levels of airway interleukin-8 as an inflammatory biomarker and assessment of bronchoalveolar lavage fluid neutrophilic count to correlate their values with disease severity.

Chapter (1)

Bronchiectasis

Bronchiectasis (BE) is a heterogeneous disease associated with significant morbidity in children that extend beyond the respiratory system and include cardiac and psychological effects and is defined as a complex chronic respiratory condition in which an area of the bronchial lumen is permanently and abnormally widened, with accompanying chronic infection, airway inflammation, and progressive decline in lung function **(Pizzutto et al., 2017).**

Bronchiectasis is found in a variety of pulmonary diseases and is caused by long-term excessive inflammatory damage to the airways, which results in tissue breakdown, structural modification in the bronchial wall and remodeling resulting in permanent irreversible dilation of the bronchial lumen, and the key clinical symptoms of chronic productive cough and shortness of breath **(Martínez-García et al 2017), (Schäfer et al., 2018).**

Incidence and prevalence:

The introduction of high-resolution computed tomography (HRCT) and the advances in diagnostic techniques resulted in diagnosing bronchiectasis earlier and at earlier stages leading to an apparent increase in the prevalence of bronchiectasis worldwide with some countries reporting childhood fatalities, and a growing appreciation of economic cost **(Gallucci et al., 2017).**

The prevalence of bronchiectasis in the United States and worldwide is unknown and the true disease burden from the disease in children is difficult to ascertain as the diagnosis is often delayed and depends upon the populations studied, physician awareness, and availability of cHRCT scans **(Marcella Gallucci., et al. 2016).**

The incidence among European populations is estimated to be around 0.2 / 100,000 in UK and 2,3/100,000 in Ireland but globally, the prevalence of chronic suppurative lung disease (CSLD) in high-income countries over the last 50 years has declined with the introduction of antibiotics, immunizations, improved hygiene, nutrition, and access to medical care **(McCallum and Binks, 2017).**

However, a substantial burden of CSLD still persists among socially disadvantaged populations of high-income