Methotrexate Induced Lung Diseases in Rheumatoid Arthritis Patients

Thesis

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List of Abbreviations

Abb.	Full term
ACPA	*Anti citrullinated peptide antibodies*
ATS	*American Thoracic Society*
BALT	*Bronchus-associated lymphoid tissue*
C.B.C	*Complete blood counts*
CCP	*Anti-cyclic citrullinated peptide*
COPD	*Chronic obstructive pulmonary disease*
CPFE	*Combined pulmonary fibrosis and emphysema*
CRP	*C-reactive protein*
CTD	*Connective tissue disease*
DAD	*Diffuse alveolar damage*
DIP	*Desquamative interstitial pneumonia*
E.S.R	*Erythrocyte sedimentation rate*
ECM	*Extracellular matrix*
ERV	*Expiratory reserve volume*
EULAR	*European league against rheumatism*
EV	*Extrapolated volume*
FET	*Forced expiratory time*
FRC	*Functional reserve capacity*
FRC	*Functional reserve capacity*
FVC	*Forced vital capacity*
GOLD	*Global Initiative for Obstructive Lung Disease*
HAQ	*Health Assessment Questionnaire*
HLA	*Human leukocyte antigen*
HRCT	*High-resolution computed tomography*
IC	*Inspiratory capacity*
IL	*Interleukins*
ILD	*Interstitial lung disease*

IPF .....Idiopathic pulmonary fibrosis
IPF .....Idiopathic pulmonary fibrosis

List of Abbreviations *(Cont...)*

Abb.	Full term

LIP .....Lymphocytic interstitial pneumonia
LPD .....Lymphoproliferative disorder
MMP .....Matrix metalloproteinases
NSIP .....Nonspecific interstitial pneumonia
PDGF .....Platelet derived growth factor
RA .....Rheumatoid arthritis
RA-ILD .....Rheumatoid arthritis associated-ILD
RF .....Rheumatoid factor
RV .....Residual volume
SNPs .....Single Nucleotide Polymorphisms
TLC ..... Total lung capacity
TNF ..... Tumor necrosis factor
UIP ..... Usual interstitial pneumonia
VAS ..... Visual Analog Scale
VC ..... Vital capacity
VEGF ..... Vascular endothelial growth factor

INTRODUCTION

Rheumatoid arthritis (RA) is a progressive, systemic autoimmune disorder characterized by articular and extra-articular manifestations. The lung is commonly a site of extra-articular disease. Within the lung, manifestations of RA vary and may include airways, parenchymal, vascular, and pleural disease. Manifestations of lung disease in RA typically follow the development of articular disease, but in some instances lung involvement is the first manifestation of RA and is the most aggressive feature of the disease ***(Lee et al., 2007).*** Clinicians should therefore remain alert to the possibility of lung disease in all patients with RA.

RA is the most common connective tissue disease (CTD), with a prevalence of 0.5% to 2% in the general population ***(Gabriel et al., 2003).*** The disease occurs more frequently in women than in men with a ratio of 3:1. Extra-articular disease occurs in approximately 50% of patients, with the lung being a common site of involvement ***(Turesson et al., 2002).*** Lung involvement may occur in as many as 67% of patients, although some reports indicate a lower incidence (around 10%–20%) ***(Bilgici et al., 2005).*** This wide variation reflects differences in study design, study populations, and the way that lung disease in RA is defined. Many patients with RA have no clinical symptoms of respiratory disease despite radiographic or physiologic evidence of lung abnormalities,

often leading to a misrepresentation of disease prevalence. In a study of 52 patients with RA, high-resolution computed tomography (HRCT) abnormalities were identified in 67.3% with only 40% of patients having respiratory symptoms ***(Bilgici et al., 2005).***

Mortality is increased in patients with RA with extra-articular manifestations relative to those without extra-articular involvement, with cardiovascular disease, infection, and lung disease being the leading causes. Mortality in RA is greatest within the first 5 to 7 years after diagnosis and risk may be slightly higher in men than in women, with a mortality ratio of 2.07:1.97 respectively ***(Young et al., 2007)*** Lung disease alone accounts for 10% to 20% of deaths in patients with RA, and most of these are attributed to interstitial lung disease (ILD) ***(Thomas et al 2003).***

RA is a common disorder with a myriad of pulmonary manifestations. Although any compartment of the respiratory system is at risk, the ILDs cause the greatest concern. In its most severe form, affected patients can develop a fibrotic ILD with progression similar to that seen in IPF. Treatment is based on clinician opinion and there are no placebo-controlled trials. In order to effectively care for these patients, a better understanding is needed of the link between synovitis and pulmonary disease. Predictors of lung involvement, biomarkers to clinically phenotype patients, and well-designed treatment trials are urgently needed ***(Young et al., 2007)***.

Methotrexate has shown efficacy for the treatment of several diseases, especially rheumatoid arthritis (RA). Methotrexate has also been implicated as a causative agent in interstitial lung disease. Patients with RA may develop pulmonary manifestations of their disease and are at increased risk of respiratory infection. The aim of this study was to evaluate the risk of pulmonary disease among patients with RA treated with methotrexate ***(Rojas-serraano et al., 2012).***

AIM OF THE WORK

We delivered this study to

1. Determine any association between methotrexate and induction of any lung abnormalities for rheumatoid arthritis patients.
2. Find out whether these complications occur from the disease itself or drugs like methotrexate have a role in aggravate these lung diseases.