Egyptian Journal of Chest Diseases and Tuberculosis (2015) 64, 109–113

HOSTED BY

The Egyptian Society of Chest Diseases and Tuberculosis

Egyptian Journal of Chest Diseases and Tuberculosis

www.elsevier.com/locate/ejcdt
www.sciencedirect.com

ORIGINAL ARTICLE

Tuberculosis chemoprophylaxis in rheumatoid arthritic patients receiving tumor necrosis factor inhibitors or conventional therapy

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Received 8 August 2014; accepted 23 November 2014
Available online 19 December 2014

KEYWORDS

TB;
Anti-TNF therapy;
Latent TB;
Rheumatoid arthritis;
Chemoprophylaxis

Abstract *Introduction:* Patients with rheumatoid arthritis (RA) have increased susceptibility to infection. The risk of acquiring infection including tuberculosis (TB) in RA may be increased in patients receiving any immuno-suppressive medication including anti-TNF therapy, which is used successfully for treating patients with rheumatoid arthritis. The aim of this work was to assess the risk of TB in RA patients on anti-TNF therapy compared to conventional disease modifying anti rheumatic drugs when screening for latent TB and TB chemoprophylaxis was applied.

Patients and methods: This study conducted on (235) RA patients indicated for either conventional therapy or anti-TNF therapy from 1-1-2010 to 1-10-2013. Assessment was done before RA treatment and included medical history, clinical examination, plain chest X-ray, HRCT chest QuantiFERON®-TB Gold in-tube (QFT-GIT) test and microbiologic investigations for tuberculosis when indicated. All patients with positive QFT-GIT received chemoprophylactic treatment for TB.

Results: The studied rheumatoid arthritic patients were divided into two groups; group (A) included (105) RA patients on conventional disease modifying anti rheumatic drugs (DMARDs) with mean age (51 ± 12) and group (B) included (130) RA patients on anti-TNF therapy with mean age (48 ± 13). This study showed no significant increase of tuberculosis among patients on anti-TNF therapy (group B) compared to patients on (DMARDs) (group A). Chemo-prophylaxis in patients on anti-TNF therapy leads to prevention of reactivation of latent TB.

Conclusion: There was no significant increased risk for tuberculosis among RA patients receiving anti-TNF therapy when screening and chemoprophylaxis was applied, so screening of RA patients before anti-TNF therapy for latent tuberculosis and TB chemoprophylaxis should be done.

Introduction

Patients with rheumatoid arthritis (RA) are reported to have an increased susceptibility to infection [1]. Studies of a specific

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Peer review under responsibility of The Egyptian Society of Chest Diseases and Tuberculosis.

http://dx.doi.org/10.1016/j.ejcdt.2014.11.027
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susceptibility to tuberculosis (TB) in patients with RA have produced contrasting results. For example in the USA, an increased incidence of TB in patients with RA was not observed [2]. In contrast, a substantial increase in the risk of acquiring TB in RA has been reported in Europe and Asia [3,4]. The risk of acquiring TB in RA may be increased in patients receiving oral glucocorticoid therapy or the use of therapeutic agents that neutralize tumor necrosis factor (TNF) [5,6].

A new study shows that tuberculosis infection (TB) is 10 times more common among male patients who have rheumatoid arthritis than it is in the general population, and that risk appears to be elevated by treatment with any immunosuppressive medication, including anti-TNF therapy, which was used successfully for treating patients with rheumatoid arthritis. Drugs such as infliximab, adalimumab, and etanercept have been important treatment advancements because they allow the direct targeting of the inflammatory cytokine tumor necrosis factor alpha (TNF-α), which is elevated in the blood and tissue of RA patients [7]. The FDA monitors the safety of newly licensed products, such as infliximab, adalimumab and etanercept. Infliximab (Remicade) is a mouse-human (chimeric) antibody against tumor necrosis factor alpha, intravenous infusion of infliximab can be administered in a single dose (5 mg/kg), a monthly regimen, the loading regimen for all approved indications occurs at weeks 0, 2, and 6 then every 8 weeks at a clinic or hospital. The half-life of infliximab is 10 days, and its biologic effect persists for up to 2 months. Infliximab is supplied as a sterile, white, lyophilized (freeze dried) powder 100 mg dose and must be reconstituted [8]. Adalimumab, (HUMIRA, Abbott) is a fully human monoclonal antibody that binds to TNFα, preventing it from activating TNF receptors. HUMIRA (''Human Monoclonal Antibody in Rheumatoid Arthritis'') is marketed in both preloaded 0.8 mL syringes and also in preloaded pen devices (called Humira Pen), both injected subcutaneously, typically by the patient at home [9]. Etanercept (Enbrel, Pfizer), is a TNF receptor-IgG fusion protein. A single-use 50 mg auto injector ''pen'' was used subcutaneously once weekly [10,11]. Evidence about the benefits of these drugs is accumulating. However, they are not risk-free, and evidence of their risks primarily infection especially TB is also mounting so preventive actions are advised [12].

The aim of this work was to assess the risk of TB associated with the use of anti-TNF therapy compared to disease modifying anti rheumatic drugs (DMARDs) in RA patients when screening for latent TB with TB chemoprophylaxis was applied.

Patients and methods

Study design

A prospective study conducted on (235) rheumatoid arthritic patients indicated for either conventional therapy or anti-TNF therapy from 1/1/2010 to 1/10/2013 at the King Fahd Hospital in Al Madenha Almonoura, Kingdom of Saudi Arabia and Dallah and Nagd hospitals. RA was diagnosed according to established classification criteria [7] by rheumatologists.

The studied patients were divided into two groups; group (A) included (105) rheumatoid arthritic patients on conventional disease modifying anti rheumatic drugs (DMARDs) with mean age (51 ± 12) and group (B) included (130) rheumatoid arthritic patients on biological therapy with mean age (48 ± 13) as(55) patients on infliximab, (32) patients on adalimumab, and (43) patients on etanercept.

Before starting treatment for RA patients they underwent:

(1) Complete medical history.
(2) Clinical examination.
(3) Routine laboratory investigations.
(4) Plain chest X-ray (CXR).
(5) QuantiFERON®-TB Gold in-tube (QFT-GIT; Cellestis Limited, Carnegie, Australia) done according to the manufacturer instructions.
(6) High resolution computed tomography (HRCT) chest if chest X-ray (CXR) has any abnormality.
(7) Microbiological investigations to exclude active pulmonary tuberculosis in clinically suspected cases (AFB smear, mycobacterial Tuberculosis culture, and real time polymerase chain reaction).
(8) All patients with positive QFT-GIT received chemoprophylactic treatment for TB with INH 5 mg/kg body weight for 9 months [13] (after excluding active TB by medical assessment, chest radiography, as well as by other tests judged appropriate to identify active disease.

Follow up done monthly for:

(1) Any medical complaint especially suggestive of TB affection.
(2) Clinical examination: general and chest examination.
(3) Radiological and laboratory investigations for TB if the patient had new symptoms or signs suggestive of TB.
(4) Other investigations as needed e.g. excisional lymph node biopsy.

A patient was classified as a TB case when bacteriological confirmation of TB was done from any specimen obtained from a patient with an appropriate clinical picture [14].

Patients with active TB received anti TB medication, and Anti-tumor necrosis factor agents were stopped [15].

Exclusion criteria

Patients with active infection and patients with other immunosuppressive diseases were excluded.

Statistical analysis

All statistical analysis was performed using SPSS 12.0 for Windows. Results are expressed as mean and SD. Chi-square test for qualitative variables were used.

Results

This study was conducted on (235) rheumatoid arthritic patients. Patients were divided into two groups; group (A) included (105) RA patients on conventional disease modifying anti rheumatic drugs with mean age (51 ± 12) and group (B) included (130) RA patients on biological therapy with mean