Egyptian Journal of Chest Diseases and Tuberculosis (2015) 64, 939–952

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

Adverse reactions among patients being treated for multi-drug resistant tuberculosis at Abbassia Chest Hospital

Mohammad A. Tag El Din [a,1], **Ashraf A. El Maraghy** [a,*], **Abdel Hay R. Abdel Hay** [b,2]

[a] *Chest Department, Ain Shams University, Cairo, Egypt*
[b] *Abbassia Chest Hospital, Cairo, Egypt*

Received 19 February 2015; accepted 5 March 2015
Available online 30 April 2015

KEYWORDS

Multi-drug resistant tuberculosis;
Abbassia Chest Hospital;
Adverse reactions

Abstract *Background:* Pulmonary tuberculosis is a major cause of morbidity and mortality worldwide, resulting in the greatest number of deaths due to any one single infectious agent. Drug resistance threatens global tuberculosis control efforts.

Objective: The aim of this study was to assess adverse reactions of second-line TB drugs in patients treated for MDR-TB at Abbassia Chest Hospital from 1st of January 2009 to 1st of January 2012.

Subjects and methods: This study included 107 patients admitted at Abbassia Chest Hospital; during the period from January 2009 to January 2012. The patients were resistant to at least Rifampicin and INH. All patients' files were analyzed and the following data were discussed: meticulous history taking, complete clinical examination, drug susceptibility testing, and initial laboratory investigations, adverse reactions were determined by clinical criteria and/or laboratory data, severity code, management of side effects and fate of treatment.

Results: 72.9% of the patients were males and 27.1% were females. The mean of age was 37.1 years. The special habits detected among the studied cases were tobacco smoking, drug addiction and alcohol intake. According to type of resistance, acquired resistance was 95.3% and primary resistance was 4.7%. The most common co-morbidities associated with MDR-TB in the studied cases were diabetes (29.9%) and chronic obstructive lung disease (11.2%). Side effects of drugs were; 57% GIT manifestations, 53.3% peripheral neuritis, hypokalemia 26.2%, irritable bowel syndrome 22.4%, ototoxicity 17.8%, skin reaction 10.3%, hypothyroidism 10.3%, hepatotoxicity 9.3%, hypoalbuminemia 5.6%, depression 3.7%, arthritis 0.9%, gynecomastia 2.8%,

* Corresponding author. Tel.: +20 01001770702.
E-mail addresses: mohamedawadtag@yahoo.com (M.A. Tag El Din), ashrafelmaraghy@yahoo.com (A.A. El Maraghy), abdelhay.ramadan@yahoo.com (A.H.R. Abdel Hay).
[1] Tel.: +20 01222172859.
[2] Tel.: +20 01000237687.

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

http://dx.doi.org/10.1016/j.ejcdt.2015.03.004

hyponatremia 5.6%, hypomagnesaemia 1.9%, dizziness 0.9%, nephrotoxicity 3.7%. Most of the drugs' side effects started to appear within the first 3 months of treatment. The frequency of nephrotoxicity, hepatotoxicity and hypoalbuminemia were significantly higher in diabetic than in non-diabetic cases. Elevations of liver enzymes began from the 3rd month after treatment and these elevations became statistically significant beginning from the 6th month. Also, elevations of creatinine levels began from the 3rd month after treatment and became statistically significant beginning from the 6th month, while there were no significant changes in potassium levels among the studied cases all through the follow up period. It was noticed that highly significant gain of body weight started from the 3rd month after treatment. 92.5% of the studied cases were cured, 6.5% died and 0.9% was defaulter. The predictors of patients' outcome were sputum conversion, number of previous TB treatment and associated co-morbidities.

Conclusions: There is a relation between both tobacco smoking and drug addiction, and MDR TB. The most common type of resistance is acquired resistance because of lack of adherence to treatment or inappropriate treatment. The most common co-morbidities associated with MDR TB are diabetes and chronic obstructive lung diseases. The most important predictors of patients' outcome are sputum conversion, number of previous TB treatment and presence of co-morbidities.

Introduction

Tuberculosis (TB) is an infectious bacterial disease caused by *Mycobacterium tuberculosis*, which most commonly affects the lungs. It is transmitted from person to person via droplets from the throat and lungs of people with the active respiratory disease [1].

Approximately 9.4 million new cases and 1.7 million deaths were encountered per year worldwide [2].

Morbidity and mortality are especially high in specific populations such as those with underlying immunosuppression or very young children [3].

Tuberculosis remains a public health problem in Egypt. Although Egypt is in the era of epidemiological transition from communicable to non-communicable diseases like many other countries, TB, still, must be addressed and handled as a health problem affecting large sectors in the society, especially the poor and the vulnerable [4].

Early diagnosis and immediate initiation of treatment are essential for an effective TB control program. Delay in diagnosis is significant to both disease prognosis at the individual level and transmission within the community. Most transmissions occur between the onset of cough and initiation of treatment. The diagnosis of pulmonary TB depends on clinical suspicion, response to treatment, chest radiographs, staining for acid fast bacilli (AFB), culture for TB, and, nucleic acid amplification (NAA) assays [5].

The most effective anti-TB drugs are Isoniazid (INH) and Rifampicin (RIF). Resistant Mycobacteria to at least one of these drugs are the cause of Multidrug-resistant tuberculosis (MDR-TB). This type of resistance is highly problematic due to limited sources of drugs as well as the high toxicity, low efficacy and high cost of second-line tuberculosis drugs [6].

Multidrug-resistant TB (MDR-TB) is caused by bacteria that are resistant to at least Isoniazid and Rifampicin, the most effective anti-TB drugs. MDR-TB results from either primary infection with resistant bacteria or may develop in the course of a patient's treatment [7].

In 2008, an estimated 390,000–510,000 case of MDR-TB emerged globally. Among TB cases, 3.6% are estimated to have MDR-TB. Twenty-two of 48 African countries reported first-line TB drug resistance, the estimated number of MDR-TB cases (primary and acquired) in 2008 was 69,000 (53,000–110,000). Although the rate of drug resistance is continuously increasing, only around 7% of estimated cases are detected. The control of drug resistant disease is difficult especially in high burden countries due to poor laboratory services and the slow nature of conventional drug susceptibility testing [8].

In Egypt, a nationwide drug resistance survey was carried out in 2002, in which a total number of 849 patients enrolled, 632 new and 217 old patients [4].

There are several ways that drug resistance to TB and drug resistance in general, can be prevented:

- Rapid diagnosis and treatment of TB.
- Completion of treatment.
- Patients with HIV/AIDS should be identified and diagnosed as soon as possible.
- Identify contacts who could have contracted TB: i.e. family members, people in close contact, etc.
- Research: Much research and funding is needed in the diagnosis, prevention and treatment of TB and MDR TB [9,10].

The emergence of multidrug resistant TB (MDR-TB), i.e. which is resistant to at least Isoniazid (INH) and Rifampicin (RIF), is of great concern, because it requires the use of second-line drugs that are difficult to procure and are much more toxic and expensive than FLDs [11].

Laboratory monitoring is required for patients receiving a regimen with second-line anti-TB drugs. Adverse effects can be occult (not obviously noted by taking the history of the patient or by physical examination). Note the following important aspects of laboratory monitoring for adverse effects:

- Renal toxicity monitoring
- Electrolyte monitoring
- Monitoring for hypothyroidism
- Monitoring liver toxicity
- Pregnancy testing
- Audiometry [12].