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ORIGINAL ARTICLE

Adverse reactions among patients being treated for multi-drug resistant tuberculosis in Egypt from July 2006 to January 2009

Mohamed Awad Tag El-Din [a,*], Hesham Atef Abd-El Halim [a], Aboda Mahmoud El-Tantawy [b]

[a] *Faculty of Medicine, Ain Shams University, Cairo, Egypt*
[b] *Abbassia Chest Hospital, Cairo, Egypt*

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KEYWORDS

MDR-TB;
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Abstract *Background:* MDR-TB is regarded as a high-priority medical and public health issue, its treatment is frequently associated with prolonged illness and disability. Second-line TB drugs have a greater incidence of adverse reactions, which increases the morbidity as well as cost.

Objective: To assess adverse reactions of second-line TB drugs in patients treated for MDR-TB in Egypt from 1st of July 2006 to 1st of January 2009.

Methods: A retrospective study included 138 patients enrolled into the MDR-TB department at the Abbassia Chest Hospital during the study period. The patient was treated with 5 drugs according to results of the drug susceptibility test as follows: Any drug of the 1st line if not resistant, One of the injectable aminoglycosides (Kanamycin, Amikacin, Capreomycin or Streptomycin), Quinolones (Ofloxacin), Ethionamide, Cycloserine, and PAS. During the course of treatment, the patients were followed up by radiological and laboratory investigation and adverse reactions were determined by clinical and or laboratory criteria. Severity of adverse reactions was graded according to the National Tuberculosis Program.

Results: Majority of cases were cured (88.4%), one patient was lost to follow-up, 4 patients completed treatment and 7 patients died. There was a significant weight gain beginning from the 3rd month of treatment. There were statistically significant elevations of SGPT beginning from the 6th month, there were significant elevations of creatinine beginning from the 3rd month while there

Abbreviations: MDR-TB, multidrug resistant tuberculosis; DST, drug susceptibility test; NTP, National Tuberculosis Program; HIV, human immunodeficiency virus; DM, diabetes mellitus; PN, peripheral neuropathy; TSH, thyroid stimulating hormone; PAS, para-amino salicylic acid; IBS, irritable bowel syndrome.

* Corresponding author at: Pulmonary Medicine, Ain Shams University, 28C, Opera City compound, Sheikh Zayed, Giza, Egypt. Tel.: +20 2 38515201; fax: +20 1224474750.
E-mail address: heshamatef@med.asu.edu.eg (M.A.T. El-Din).

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were no significant changes in serum Potassium levels. Gastrointestinal manifestations were the most frequent adverse reaction, followed by PN, hypokalemia, IBS, Ototoxicity, Hypothyroidism, Skin manifestations, Hepatotoxicity then by nephrotoxicity. Hyponatremia and dizziness were the least adverse reactions, the majority of adverse reactions did not affect daily activity of the patients. There was a significant relation between smoking and peripheral neuropathy while there were no significant relation between smoking, DM and used antituberculosis drugs with the other adverse reactions.

Conclusion: The most common type of resistance was acquired resistance, There was a relation between both tobacco smoking and drug addiction, and MDR TB, The most common side effect of anti TB drugs was GIT manifestations and the least complication was dizziness. Adverse reactions did not negatively impact treatment outcome among individuals who were adherent to treatment.

Introduction

Tuberculosis (TB) is a medical, social and economic disaster of immense magnitude that occurrs all over the world [1]. The emergence of drug-resistant strains of Mycobacterium is a common consequence of inadequate therapeutic practice [2]. Strains of *Mycobacterium tuberculosis* that are resistant to both isoniazid and rifampicin with or without resistance to other drugs have been termed multidrug-resistant strains. Isoniazid and rifampicin are keystone drugs in the management of TB. While resistance to either isoniazid or rifampicin may be managed with other first-line drugs, multidrug-resistant TB (MDR-TB) demands treatment with second-line drugs that have limited sterilizing capacity, and are less effective and more toxic [3,4]. The treatment of MDR-TB is frequently associated with prolonged illness and disability. Second-line TB drugs have a greater incidence of adverse reactions, which increases the morbidity as well as cost [5]. Generally, these second-line agents must be administered more frequently than first-line agents, making compliance with medications more difficult. Many authorities have advocated that MDR-TB be regarded as a high-priority medical and public health issue and that these patients should be referred upon diagnosis to a specialized center for systematized and aggressive medical therapy [6]. The treatment of MDR-TB is a challenge which should be undertaken by experienced clinicians at centers equipped with reliable laboratory service for mycobacterial culture and in vitro sensitivity testing [1,4,7].

The aim of this study is to assess adverse reactions of second- line TB drugs in patients treated for MDR-TB in Egypt from 1st of July 2006 to 1st of January 2009.

Patients and methods

This was a retrospective study that included 138 patients enrolled into the MDR-TB department at the Abbassia Chest Hospital, Cairo, Egypt, between 1st July 2006 and 1st January 2009.

Patients were included in this study if they had active tuberculosis as evidenced by positive sputum for AFB and/or positive culture for *M. tuberculosis* in previously treated patients or new cases suspect to be MDR-TB, and had been documented as MDR-TB by the drug susceptibility test for 1st line anti-tuberculosis drugs done in the National Reference Laboratory. There were no exclusion criteria.

All cases were subjected to the following: Medical history with special attention to: whether primary or secondary resistance, special habits of medical importance, co-morbid diseases. clinical examination, initial laboratory investigation: serum potassium on admission then monthly while receiving an injectable agent, liver functions (SGPT), renal functions (Serum creatinine), HIV testing, and pregnancy test (for married women of childbearing age, and repeated if indicated). The patient was treated with 5 drugs according to results of the drug susceptibility test (DST) with dosage as follows: any drug of the 1st line if not resistant, one of the injectable aminoglycosides (kanamycin, amikacin, capreomycin or streptomycin), quinolones (ofloxacin), ethionamide, cycloserine, and Para amino-salicylic acid (PAS).

Follow up of patients

During the course of treatment, the patients were followed up by radiological and laboratory investigations such as: Sputum smear and culture; monthly until conversion then smear monthly and culture quarterly, Drug susceptibility test (DST) for patients who remains culture positive at the end of the intensive phase or after 8 months of treatment, Chest X-ray every 6 months or when indicated, Serum creatinine, monthly while receiving injectable drugs, Serum potassium monthly while receiving injectable drugs, Liver enzymes; periodic monitoring (every1–3 months), Thyroid stimulating hormone (TSH) every 6 months if receiving ethionamide or PAS and monthly for signs and symptoms of hypothyroidism, Audiometry, visual acuity and psychiatric disorders assessment, Hematological changes and allergic reactions when indicated.

Adverse reactions

Adverse reactions were determined by clinical and or laboratory criteria as follows: Ototoxicity: tinnitus, hearing loss confirmed by audiometry, presence of disequilibrium, Psychiatric disorders: presence of depression, anxiety, nightmares or psychotic symptoms, Gastrointestinal effects: nausea, vomiting, abdominal pain, haematemesis, melena, diarrhea, positive endoscopic findings. Arthralgia, arthritis: pain or swelling in