



Prevalence and Comparative Assessment of adverse Drug Reactions in Dots with Focus on HIV Negative patients in Karad Region

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Abstract:

TB is major public health problem in Asia especially in India. In India, annually more than 3,30,000 patients die due to tuberculosis (TB). Recently due to multiple drug therapy, cases of adverse drug reactions are increasing. Nowadays TB and Human immunodeficiency virus (HIV) are most common, and having high prevalence rate. Treatments to both diseases are having various multi-drug therapies; which may interact with each other. To find out adverse drug reactions induced due to Directly Observed Treatment, Short-course (DOTS),. A study was undertaken to assess the prevalence rate and pattern of adverse drug reactions (ADR) in DOTS with focus on HIV non reactive cases in Karad region, Maharashtra state. The incidence of adverse drug reactions was prospectively observed in 99 individuals treated for TB, all were HIV non reactive cases. 99 tuberculosis infected individuals received DOTS therapy. Adverse drug reactions were recorded in 13. The result of our study showed that adverse drug reactions appeared in 13.1% of the patients. Patients experienced skin hypersensitivity, gastritis, nausea, vomiting, arthralgia, fever, abdominal pain, constipation, vertigo and restlessness. Due to adverse drug reactions, patient adherence to treatment decreases; it may cause high risk factor for treatment discontinuation and Multi-drug-resistant tuberculosis (MDR-TB).

Keywords:

Adverse Drug Reaction, DOTS, India, Karad, Tuberculosis

Introduction:

Tuberculosis (TB) causes three million deaths each year that is declared to be 'global health emergency' by World Health Organization (WHO, 1996) ^[1] Tuberculosis (TB) is also considered as a major public health problem in India. India accounts for one-fifth of the global TB incident cases. Each year nearly 2 million people in India develop TB, of which around 0.87 million are infectious cases. It is estimated that annually around 3,30,000 Indians die

due to TB ^[2] Hence the government of India in collaboration with WHO and WORLD BANK launched RNTCP (Revised National Tuberculosis Control Programme) to ensure complete treatment and control of Tuberculosis as well as to reduce its social burden, but the anti-TB drugs cause higher incidence of Adverse Drug Reactions ^[3] Long duration of treatment for Tuberculosis patients with drugs like Isoniazid, Pyrazinamide, Rifampin, Ethambutol and Streptomycin – the drugs used above are potential to cause adverse drug reactions like arthralgia, headache, skin rashes etc ^[4] Patients with multiple drug therapy are prone to develop an adverse drug reactions due to alteration of drug or by synergistic effect. Multiple / intercurrent disease and multiple drug therapy are responsible for increased risk of developing an ADR ^[5] Anti-TB chemotherapy exhibit greater level of efficacy with an acceptable degree of toxicity, however combination treatment may produce severe adverse events. Important adverse effects are hepatitis, skin rash, gastrointestinal upset, hyperuricemia, peripheral neuropathy, visual disturbances. A few studies are reported on adverse effects of anti-TB drugs related to specific regimen of drug and risk factors for those adverse effects. So, we aimed to study the adverse drug reaction in DOTS treatment in patients without HIV. Tuberculosis in HIV is having high prevalence rate. HIV patients are receiving so many multiple drug therapies like ART as well as they are getting symptomatic treatment. Due to such combinations drug interactions are occurring. To avoid this confusion we have targeted only DOTS patients with HIV negative cases.

In this context the present study was carried out with an objective of assessment of adverse drug reactions in tuberculosis patients with HIV negative cases in Karad region.

Materials and Methods:

Study site: The study was conducted on the patients of DOTS with HIV non reactive cases at hospitals providing and monitoring DOTS in Karad region. Karad is the largest tehsil in Maharashtra state with a total population of 1630272.

Subjects: From 1st March 2010 to 31st October 2011, a prospective evaluation of DOTS (anti-tuberculosis drugs-induced side effects) in people was undertaken. A total of 99 newly diagnosed tuberculosis patients, who were tested for HIV at Venutai Chavan Hospital Karad, the patients with HIV non reactive reports were participated in study. 59 were attending at Venutai Chavan Sub-district Hospital, Karad and 40 patients attending at Primary Health Centre Vadgaon were included in the present study. Informed consent was taken from each patient enrolled in this study. After taking the consent of the patient, Case record form was filled. Patients were kept under observation during their whole treatment period. Patients were instructed to report any signs and symptoms they will come across during the treatment period as well as physicians observed adverse drug reactions. The patients with any kind of adverse drug reaction were focused and recorded into the adverse drug reaction form.

Results:

A total of 99 cases during 1st March 2010 to 31st October 2011 for the period of 20 months were included in the study. Among the studied 99 cases of tuberculosis mean average age was 40.44 years (Fig. 2), 59 males were with mean average age 40.77 years and 40 females with mean average age 39.95 years (Fig. 1,4). Rural patients were 40 and urban 59 (Fig. 3).

Total No. of patients participated in study were 99. In between them 79 were cured successfully. 12 patients were dropped from study without completion of treatment so they are named as defaulter from study. 6 patients were died. And 2 patients could not be cured due to treatment (Fig. 5).

Adverse drug reactions were recorded in 13 patients. The study showed that 13.1% of patients reported they had experienced at least one type of adverse drug reaction. However, most of the reactions were minor and required no modification of treatment. The result of our study showed the adverse drug reactions appeared in 13.1% of the patients (Fig. 6).

In this study, 4 patients (31%) experienced skin hypersensitivity. 2 patients (15%) experienced gastritis, nausea, vomiting. 2 patients (15%) experienced joint pain and inflammation (arthralgia). 2 patients (15%) experienced fever. 1 patient (8%) experienced abdominal pain and constipation. Also vertigo was experienced by 1 patient (8%). Restlessness was experienced by 1 patient (8%) (Fig.7).

Fig. 1. Female-Male average age

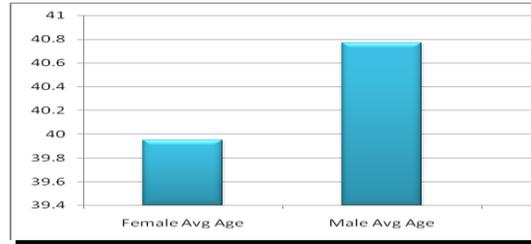


Fig. 2. Mean age

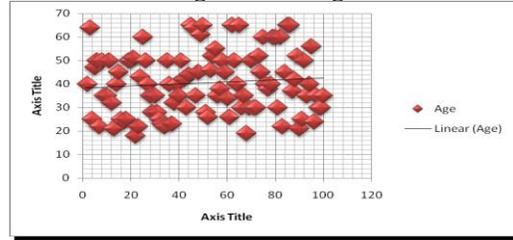


Fig. 3. Rural and urban distribution

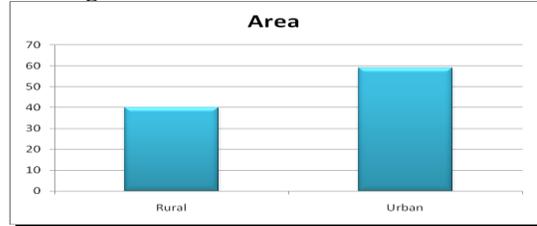


Fig. 4. Male and female distribution

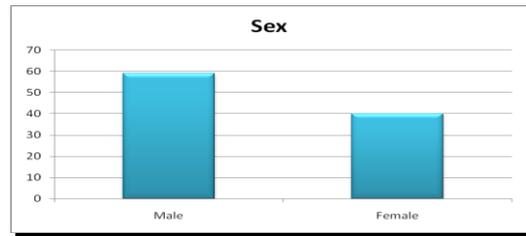


Table 1. Outcome of treatment

Total No. Of Patients	99
Cured	79
Defaulter	12
Death	6
Failed	2

Fig. 5. Outcome of treatment

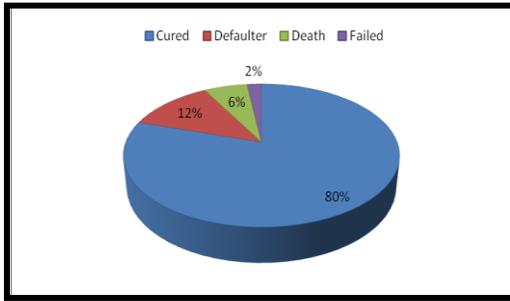


Table 2. Comparative assessment of ADR against Non ADR cases

Total No. Of Patients	99
No. Of Patients with ADR	13
No. Of Patients without ADR	86

Fig. 6. Comparative assessment of ADR against Non ADR cases

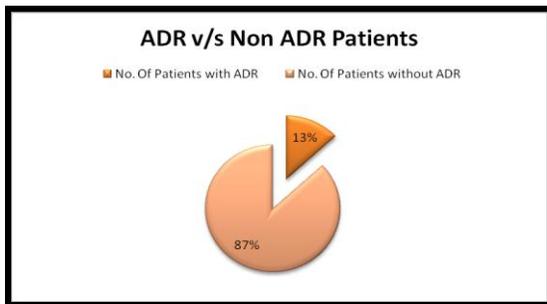


Fig. 7. Various pattern of ADR

Skin Hypersensitivity	4
Gastritis	2
Joint Pain and inflammation	2
Fever	2
Constipation	1
Vertigo	1
Restless	1

Discussion:

DOTS and ADR in TB treatment

The World Health Organization (WHO) has defined ADR as "A response to a drug which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function." [6]

We have focused to study only DOTS patients without any concomitant disease because we were interested in assessing adverse drug reactions occurred due to DOTS drug regimen. Previously few studies were referred by us. Previous studies have assessed incidence rate of adverse drug reaction in all DOTS patients but there are chances of drug interactions to occur. So we have focused to avoid drug interactions of other drugs with DOTS and study only adverse drug reaction or adverse drug effects in DOTS without HIV cases.

Incidence of ADR in HIV and non HIV patients in Anti TB treatment

HIV-infection increases the risk of hepatotoxicity during standard multidrug treatment of active TB. Why HIV-infected TB patients have an increased risk of Antituberculosis drug-induced hepatotoxicity (ATDH) is still a matter of debate. HIV patients with acute illnesses have altered activities of oxidative pathways, which may partly explain their increased risk of Antituberculosis drug-induced hepatotoxicity. Concurrent therapy of TB/HIV co infections requires concomitant use of two to four different antituberculosis drugs and at least three antiretroviral drugs. Unfortunately, combined TB/HIV treatment is often complicated by overlapping toxicities and drug-drug interactions. Nevirapine is the most hepatotoxic non-nucleoside reverse transcriptase inhibitor (NNRTI). The majority of the nucleoside reverse transcriptase inhibitors (NRTI) are potentially hepatotoxic (e.g. didanosine and stavudine) and hepatotoxicity has been described for some protease inhibitors (e.g. ritonavir, indinavir and saquinavir). The incidence of hepatotoxicity during highly active antiretroviral therapy (HAART) ranges from 2% to 18%. Drug toxicity, including hepatotoxicity, has been implicated as a major cause of TB or HIV treatment interruption during treatment of TB/HIV co infection. Therefore, HAART is often delayed in HIV-infected TB patients. The concomitant use of antifungals (e.g. fluconazole) which is often seen in HIV-infected patients, is also a risk factor for ATDH [7]

Prevalence of ADR in Karad region:

In this study, 4 patients (31%) experienced skin hypersensitivity - the drugs, which are responsible for this side effect, may be pyrazinamide, rifampicin and isoniazid. 2 patients (15%) experienced gastritis, nausea vomiting - the drugs, which are responsible for these side effects, may be pyrazinamide and rifampicin. 2 patients (15%) experienced joint pain and inflammation (arthralgia) - the drug, which are responsible for these side effects, may be pyrazinamide, ethambutol. 2 patients (15%) experienced fever - the drug, which is responsible for this side effect, may be rifampicin. 1 patient (8%) experienced abdominal pain and constipation - drugs, which are responsible for these side effects, may be pyrazinamide, rifampicin and isoniazid. Also vertigo was experienced by 1 patient (8%) - drug, which is responsible for this side effect may be streptomycin. Restlessness was experienced by 1 patient (8%) - the drug, which is responsible for this side effect, may be isoniazid.^[8,9]

Conclusion

The DOTS patients specifically HIV negative cases are having high incidence of adverse drug reaction which is 13.1%. Due to adverse drug reactions, patient adherence to treatment decreases, ADR is a major cause and a high risk factor for treatment discontinuation and Multi-drug-resistant tuberculosis (MDR-TB). So in future it is necessary to monitor DOTS with special reference to ADR events occurred during their due course for their success in non reactive cases.

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