Research Article

Profile of Adverse Drug Reactions in TB Patients Taking ATT

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ABSTRACT
INTRODUCTION - Tuberculosis treatment need more than one drug combination to eradicate tuberculosis bacteria². The use of multidrug regimens has been associated with increased incidence of adverse drug reactions of anti-tubercular drugs. Hence, there is a need to monitor the adverse effects of antitubercular drugs in a hospital set up.

METHODOLOGY - Information on any past or current occurrence of adverse effects due to the ATT drugs being administered to the patients was collected. Frequency distribution tables were prepared from the collected data.

RESULTS AND DISCUSSION - In our study Gastrointestinal symptoms like Anorexia, Vomiting, Nausea, abdominal pain were the most commonly reported ADRs followed by headache and tingling and burning sensation in hands and feet. Similar adverse effects were reported in other studies. Adverse drug reactions were more frequently and more severely reported among females and elderly patients (>60yrs).

CONCLUSION - Adverse drug reactions among patients taking anti tubercular treatment is common. So identification of such adverse effect and prompt management will definitely be very helpful for a successful anti tubercular chemotherapy.

INTRODUCTION
India is the second-most populous country in the world one fourth of the global incident TB cases occur in India annually. As per WHO Global TB Report, 2015, out of the estimated global annual incidence of 9.6 million TB cases, 2.2 million were estimated to have occurred in India¹. Tuberculosis treatment need more than one drug combination to eradicate tuberculosis bacteria. First line anti-tuberculosis drugs recommended by WHO are combination between isoniazid, rifampicin, pyrazinamide, streptomycin and ethambutol.² The use of multidrug regimens has been associated with increased incidence of adverse drug reactions of anti-tubercular drugs³. Under RNTCP, the doses of first line anti-TB drugs (Isoniazid, Rifampicin, Pyrazinamide, Streptomycin and Ethambutol) were consistent on the basis of body weight and were given different regimens. In initial intensive phase combination of 4-5 drugs is used for 2-3 months, aimed to rapidly kill the TB bacilli, bring about sputum conversion and to get symptomatic relief. This is followed by a continuation phase lasting 4-6 months, during which the remaining bacilli are eliminated so that relapse does not occur.⁴,⁵ As the treatment of TB almost always involves combinations of drugs that are to be taken for a prolonged period of time, the occurrence of ADR is quite likely. Moreover, the adverse effect of one drug may be enhanced by...
the associated drug used which is one of the major reasons for the faulty patient treatment. So, there is a need to monitor the side effects of anti tubercular drugs in a hospital set up.\(^8\)

In the course of anti tubercular treatment some patients may experience problems, usually due to the bulk of the drugs, a single day’s dose consisting of more than five drugs. Drug related side effects might be minor or major.\(^6\) In general, a patient who has minor side effects should be encouraged to continue the treatment with symptomatic measures such as antacids, anti histaminics, anti emetics, or analgesic. If major side effects occur, the regimen, or the offending drug, if identified, must be stopped. Further management depends on the nature of side effects and may have to be done in a hospital.\(^7\)

These side effects are regarded as one of the major causes of non-adherence to anti-TB treatment.\(^9\) Hence, comprehensive understanding of the various ADRs along with their management is mandatory for effective TB management.\(^10\)

**METHODOLOGY**

The study was done in SSMC Rewa. The target population was Tuberculosis patients undergoing anti tubercular treatment (ATT) with first line drugs. Any patient undergoing treatment at the time of study was included. Patients who were lost to follow up within one month, uncooperative or unwilling to be enrolled, or suffering from other co-morbidities were excluded. The study tool used was the Patient profile form which recorded all the information, such as name, age, sex, residence, life style factors and dietary factors. Information on any past or current occurrence of adverse effects due to the ATT drugs being administered to the patients was collected. Frequency distribution tables were prepared from the collected data.

**RESULTS AND DISCUSSION**

A total of 45 patients were included in the study. The demographic details of the patients receiving DOTS are shown in Table 1. 4 (9%) patients were less than 20 yrs of age, 31 (69%) individuals were of age in between 20 to 60yrs, and 10 (22%) individuals age were 60yrs and above. Out of 45 patients, 29 (64) % were male and 16(36) % were female.

Out of 45 patients, 30 patients (66.6%) belonged to category I and 15 patients (33.3%) belonged to category II. The study showed that 89 % of the patients experienced adverse effects, among which 60% of the patients had multiple adverse drug reactions.

Table 2 shows the frequency distribution of adverse drug effects of ATT drugs in Category I and Category II TB patients. Among category I drug users 19 (64%) patients had anorexia/vomiting/nausea, 6 (20%) patients had dermatological manifestations, 6 (20%) patients had joint pain, 15 (50%) patients had abdominal pain, 6 (20%) had burning sensation, 9 (30%) patients had headache, 3 (10 %) patients had no side effects.

Among category II drug users 08 (53%) patients had anorexia/vomiting/nausea; 06 (40%) patients had abdominal pain; 02 (12%) patients had dermatological manifestation, 4 (26%) got burning sensation, 03 (20 %) had joint pain. 1 (6%) patient reported no side effect.

Out of 16 female patients 15 (94%) female patients reported adverse effect, and most common were anorexia, nausea and vomiting. In age group > 60 years, 9 out of 10 (90%) patients had adverse drug effect.

Table 1: Demographic details of the patients receiving DOTS

| Demographic variables | No. of patients | % |
|-----------------------|-----------------|---|
| Age ( in years)       |                 |   |
| <20                   | 4               | 9%|
| 20-30                 | 10              | 22%|
| 30-40                 | 7               | 15%|
| 40-50                 | 8               | 18%|
| 50-60                 | 6               | 13%|
| >60                   | 10              | 22%|
| Sex                   |                 |   |
| Male                  | 29              | 64%|
| Female                | 16              | 36%|
| Alcohol               |                 |   |
| Alcoholic             | 12              | 26%|
| Non Alcoholic         | 33              | 74%|
| Smoking               |                 |   |
| Smoker                | 19              | 42%|
| Non smoker            | 26              | 58%|
| Sputum smear          |                 |   |
| Positive              | 25              | 55%|
| Negative              | 20              | 45%|
Table 2: Frequency distribution of different categories of drug and its adverse effects

| Adverse drug effect                                      | CAT I n | CAT II n | Total n |       |
|---------------------------------------------------------|---------|----------|---------|-------|
| Anorexia/Vomiting/Nausea                                | 19      | 08       | 27      | 60%   |
| Abdominal pain                                          | 15      | 06       | 21      | 47%   |
| Dermatologic manifestation                              | 06      | 02       | 08      | 16%   |
| Tingling and burning sensation on hands and feet        | 06      | 04       | 10      | 22%   |
| Headache                                                | 09      | 04       | 13      | 29%   |
| Joint pain                                               | 06      | 03       | 09      | 20%   |
| Fever                                                   | 07      | 02       | 09      | 20%   |
| No adverse drug effect                                   | 03      | 01       | 04      | 08%   |

In our study Gastrointestinal symptoms like Anorexia, Vomiting, Nausea, abdominal pain were the most commonly reported ADRs followed by headache and tingling and burning sensation in hands and feet. Similar adverse effects were reported in other studies. As per study by Nishant P et al,11 Gastrointestinal intolerance, arthralgia & itching with or without rashes were most common ADRs.

Adverse drug reactions were more frequently and more severely reported among females and elderly patients (>60yrs). Out of 16 female patients 15 (94%) female patients had adverse effect, and most common were anorexia, nausea and vomiting. In age group > 60 years, 9 out of 10 (90%) patients had adverse drug effect. As similar to our findings studies by Nishant P al,11 Yee et al 12 and Shakya et al13,14 showed that Female gender was found to be a significant risk factor for developing Adverse drug reaction. It might be because they pass through life stages like pregnancy, menarche, etc., which modify the drug response.15 Studies from the UK and Canada also reported females to have a significantly higher incidence of ADRs due to ATT drugs.12 This suggests the need for special precautions while prescribing ATT drugs to females.

A study conducted by Daphne et al16 reported that most of the side effects occurred in patients above the age group of 60 years, same findings were noted in our study also.

CONCLUSION

Adverse drug reactions among patients taking anti tubercular treatment is common and these adverse drug reactions contribute to non adherence of treatment that leads to treatment failure and drug resistance. So identification of such adverse effects and prompt management will definitely be very helpful for a successful anti tubercular chemotherapy.

REFERENCES

1. TB India 2016 Revised National TB Control Programme Annual Status Report. New Delhi: Central TB Division, Directorate General of Health and Family Welfare, Nirman Bhavan; 2011. Available from: http://www.tbcindia.nic.in/showfile.-php?id=318.
2. WHO. Treatment of tuberculosis Guidelines. In. 4th Edition ed: World Health Organization; 2010.
3. Banu Eris- Gulbay OUG, Oznur Akkoca Yıldız, Zeynep Pınar Onen, Ferda Oner Erkekol, Ayse Baccıoglu, Turan Acıcan. Side effects due to primary antituberculosis drugs during the initial phase of therapy in 1149 hospitalized patients for tuberculosis. Journal Respiratory Medicine 2006;100:1834-42.
4. Gholami, K., E. Kamali, M.I. Hajiabdobaghiand and G. Shalviri. Evaluation of anti-tuberculosis induced adverse reactions in hospitalized patients. Pharmacy Practice. 2006;4: 134-138.
5. Koju. D, B.S. Rao , B. Shrestha, R. Shakya, R. Makaju. Occurrence of side effects from anti tuberculosis drugs in urban Nepalese population under DOTS.
treatment. Kathmandu University J. Science, Engineering and Technol. 2005;1:1-8.
6. Nader, L.A., A.A. Mattos, P.D. Picon, S.L. Bassanesi, A.Z. Mattos and M.P. Rodriguez. Hepatotoxicity due to rifampicin, isoniazid and pyrazinamide in patients with tuberculosis: is anti-HCV a risk factor?. Annals of Hepatol. 2010;9:70-4.
7. Xia, Y.Y., D.Y. Hu, F.Y. Liu, X.M. Wang, Y.L. Yuan and D.H. Tu. Design of the anti-tuberculosis drugs induced adverse reactions in China national Tuberculosis prevention and cotroscheme study. BMC Public Health. 2010;10: 267-76.
8. Rahman MM, Mishuk A, Halder S, Kabir AKL. Comparative Analysis of Adverse drug Reactions in Directly Observed Treatment Short Course (DOTS) in TB Patients. Global Journal of Medical research. 2013;6:6-10.
9. Awofeso N. Anti-tuberculosis medication side-effects constitute major factor for poor adherence to tuberculosis treatment. Bull World Health Organ. 2008;86:B-D.
10. Kaona FA, Tuba M, Siziya S, Sikaona L. An assessment of factors contributing to treatment adherence and knowledge of TB transmission among patients on TB treatment. BMC Public Health. 2004;4:68.
11. Nishant P. Dalal, Yogita S. Karandikar, Vijaya A. Pandit. Safety evaluation of directly observed treatment short course (DOTS) regimen in a tertiary care hospital, Pune. Int J Basic Clin Pharmacol. 2014;3:369-76.
12. Yee D, Valiquette C, Pelletier M, Parisien I, Rocher I, Menzies D. Incidence of serious side effects from first-line antituberculosis drugs among patients treated for active tuberculosis. Am J Respir Crit Care Med. 2003;167:1472-7.
13. Shakya R, Rao BS, Shrestha B. Management of antitubercular drugs-induced hepatotoxicity and therapy reintroduction strategy in a TB clinic of Nepal. Kathmandu Univ Med J (KUMJ) 2005; 3: 45-9.
14. Shakya R, Rao BS, Shrestha B. Incidence of hepatotoxicity due to antitubercular medicines and assessment of risk factors. Ann Pharmacother 2004; 38: 1074-9.
15. Wilson K. Sex-related difference in drug disposition in man. Clin Pharmacokinet 1984;9:189-202.
16. Daphne Y, Marthe P et al., Incidence of serious side effects from First-line antituberculosis drugs among patients treated for Active Tuberculosis, Am J Resp Crit Care Med. 2003;167:1472-1477.