National Journal of Physiology, Pharmacy and Pharmacology

RESEARCH ARTICLE

An assessment of adverse reactions to antiretroviral therapy in a South Indian government hospital

Shrinivas R Raikar, Shivaraj B Patil, Venkata Rao Y, Raghuveer B

Department of Pharmacology, Kamineni Institute of Medical Sciences, Narketpally, Nalgonda, Telangana, India

Correspondence to: Shivaraj B Patil, E-mail: shivarajpatil85@gmail.com

Received: June 12, 2018; **Accepted:** July 11, 2018

ABSTRACT

Background: Adverse drug reactions (ADRs) can lead to non-adherence to antiretroviral therapy (ART) and are also the major causes of hospitalization and higher cost of treatment. **Aims and Objectives:** The aims of this study were to analyze the pattern of ADRs, causality, and severity among HIV-infected patients. **Materials and Methods:** It was a retrospective analysis conducted over 1 year from January 2017 to December 2017. ADRs due to antiretroviral drugs (ARVs) were collected from the Government District Hospital, Nalgonda, as part of pharmacovigilance program and analyzed. The WHO-UMC scale was used for assessing the causality and Hartwig–Siegel scale for severity of reactions. **Results:** A total of 113 ADRs due to ART were received. In that 68 were female patients. 83% ADRs were of mild grade of severity. Most of the ADRs were related to gastrointestinal system. Causality assessment of ADRs was probable in 62(54.9%) patients and possible in 51 (45.1%) patients. **Conclusion:** Maximum number of ADRs was of mild nature suggesting that the ART is well tolerated among the patients. Further studies need to be conducted to fully understand the determinants of ADRs due to ART in a statistically significant manner.

KEY WORDS: Adverse Drug Reactions; Antiretroviral Therapy; Human Immunodeficiency Virus; Pharmacovigilance

INTRODUCTION

As of 2016, around 36.7 million people worldwide are suffering from human immunodeficiency virus (HIV)[1], and in India, an estimated 21 lakh adults are suffering from HIV.[2] The advent of antiretroviral therapy (ART) in the management of human immunodeficiency virus infection was a boon to HIV patients which resulted in decreased morbidity and mortality as well as improved the quality of life of these patients. Furthermore, HIV infection which was earlier thought to be untreatable infection has become now a chronic treatable condition.[3] In India, also ART is given to HIV patients under national acquired immunodeficiency syndrome control program[4], and nearly one million people with HIV infection are on ART.[2]

Just like any other drugs which are taken for long duration, antiretroviral drugs (ARVs) also have documented side effects. These adverse drug reactions (ADRs) include both minor and serious reactions. These ADRs can lead to poor adherence or discontinuation or changes in ART regimens.[5-10] They are also the major causes of hospitalization and higher cost of treatment.[11]

The ultimate goal of selecting an appropriate ART regimen should be not only to maintain viral suppression but also to ensure that the regimen is safe so that the patient does not discontinue the therapy. This requires consideration of many factors; one such factor is toxicity profile of drugs. Very less data are available about the ADRs due to ART

Access this article online

Website: www.njppp.com

DOI: 10.5455/njppp.2018.8.0620811072018

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in developing countries like India, and the data may differ between developing countries like India and developed countries.[12,13] Thus, the aim of this study was to analyze the pattern, severity, and causality of ADRs among HIV-infected patients.

MATERIALS AND METHODS

It was a retrospective analysis of ADRs due to ARVs conducted over 1 year from January 2017 to December 2017. The data were collected as part of pharmacovigilance program and analyzed. These ADRs were collected from government district hospital, Nalgonda, Telangana, India. Permission from the Institutional Ethics Committee was taken before starting the study. Demographic details, medical history, details of ARVs, and other concomitant medications prescribed were collected. An expert committee which included pharmacologist and clinical expert assessed the causality of adverse reactions using WHO-UMC causality assessment system.[14] Two drug regimens were followed Efavirenz+Lamivudine+Tenofovir (E+L+T) regimen and Zidovudine+Lamivudine+Nevirapine (Z+L+N) regimen. Hartwig and Siegel scale was used for analyzing the severity of adverse events.[15] The data were analyzed and presented as numbers and percentages.

RESULTS

A total of 113 ADRs due to ARVs were received. In that 68 (60.2%) were females and the rest were male patients. Higher prevalence of ADRs was in the age group of 31–40 years [Figure 1]. Figure 2 shows the severity of ADRs. Regarding severity of ADRs, most of them were of mild nature. Majority of the ADRs were related to gastrointestinal system followed by dermatological system [details are provided in Table 1]. Majority of the ADRs were attributed to E+L+T regimen as compared to Z+L+N regimen. Only two cases of anemia were reported due to zidovudine, and skin rashes were reported more with efavirenz. Causality assessment of ADRs was probable in 62 (54.9%) patients and possible in 51 (45.1%) patients.

DISCUSSION

Pharmacovigilance in India is still in infancy. Reporting of ADRs due to ART is very poor, especially in government hospitals except those associated with medical colleges. This study becomes even more important because most HIV patients are treated in government hospitals than in private hospitals. ADRs are one of the most common reasons for poor compliance or noncompliance to treatment; hence, analysis of adverse reactions may help government hospital physicians in initiating appropriate dosage regimens.

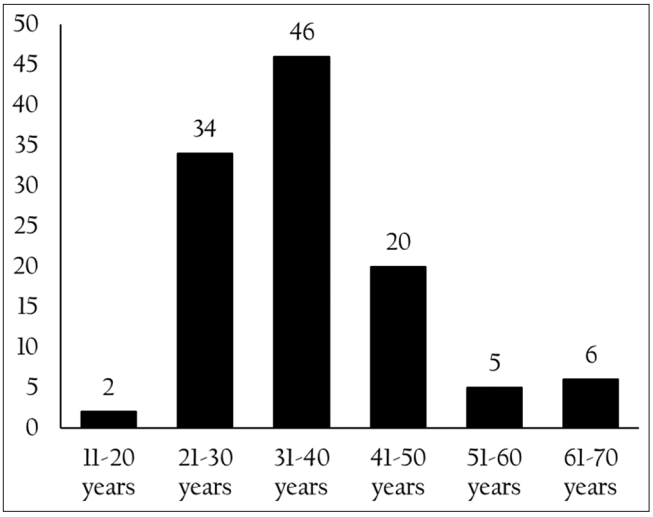

Figure 1: Distribution of the patients according to age

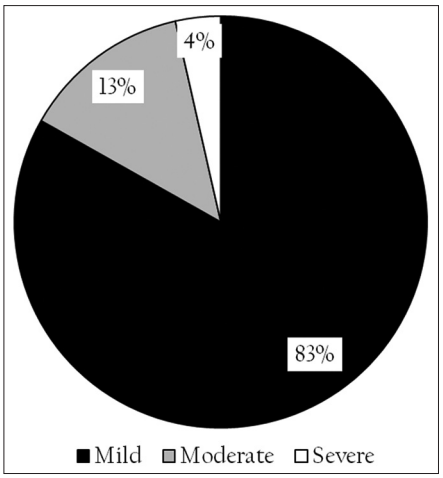

Figure 2: Severity of adverse drug reactions

Table 1: Systems affected by ADRs due to ARVs regimens

Systems affected	E+L + T regimen	Z+L + N regimen	Total *n* (%)
Gastrointestinal system	28	8	36 (31.9)
Dermatology	24	9	33 (29.2)
Central nervous system	14	5	19 (16.8)
Musculoskeletal system	6	4	10 (8.8)
Others	8	7	15 (13.3)

E+L + T regimen: Efavirenz+Lamivudine+Tenofovir regimen, Z+L + N regimen: Zidovudine+Lamivudine+Nevirapine regimen, ARVs: Antiretroviral drug, ADRs: Adverse drug reactions

In the present study, the majority of patients suffering from ADRs were females which match to results of previous study conducted in South Africa.[16] Prevalence of ADRs due to ART was more in the age group of 31–40 years which is in concordance to previous studies conducted in Kadapa[17] and Dhule.[18] This could be probably due to higher prevalence of HIV infection in this age group since they are economically productive and sexually more active.

Majority of the ADRs were of mild severity and did not require any specific treatment. This indicates that ART is mostly well tolerated.

In the present study, the most common systems affected by ADRs due to ART were gastrointestinal system followed by dermatological system and central nervous system. It was in line with previous studies.[13,19] Causality assessment of ADRs was "probable" in most of the cases followed by possible category as per the WHO causality assessment scale. Rechallenge was not done for any ADRs; hence, no ADRs were classified as definite. Another reason could be alternate causes cannot be excluded due to higher incidence of polypharmacy. In contrast, other studies have reported causality assessment as possible in the majority of cases but authors followed Naranjo's causality assessment scale.[18,20]

This kind of studies on ADRs will definitely help the physicians in selecting appropriate drug regimen which is effective as well as safe for the HIV patients. It also serves as a pilot study for conducting larger trials. There were few limitations in the present study. The analysis was based on voluntary reporting of ADRs, so there could be chances of underreporting. We did not go into the details of the frequency of prescription of individual drug regimens. More comprehensive and large-scale studies have to be conducted to overcome the limitations of the present study.

CONCLUSION

The success of ART depends on the treatment adherence, and one of the most common reasons for poor compliance is occurrence of ADRs. The present study found that ADRs due to ART were more common in females. Most of the ADRs were of mild nature suggesting that the ART is well tolerated among the patients. Further studies need to be conducted to completely understand the various factors affecting the occurrence of ADRs due to ART in a statistically significant manner.

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How to cite this article: Raikar SR, Patil SB, Venkata Rao Y, Raghuveer B. An assessment of adverse reactions to antiretroviral therapy in a South Indian government hospital. Natl J Physiol Pharm Pharmacol 2018;8(10):1405-1408.

Source of Support: Nil, **Conflict of Interest:** None declared.