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Research Article

A STUDY ON ADVERSE DRUG REACTIONS IN HIV INFECTED PATIENTS AT A ART CENTRE OF TERTIARY CARE HOSPITAL IN GUWAHATI, INDIA

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ABSTRACT

BACKGROUND: Currently Anti-Retroviral Therapy (ART) regimens suppress viral replication, provide significant immune reconstitution, and have resulted in a substantial and dramatic decrease in AIDS related opportunistic infections and deaths in both adults and children. These medicines are often associated with adverse effects, with both short and long term treatment. OBJECTIVES: This study was conducted to assess the incidence and causality of ADRs in HIV infected patients receiving ART. METHOD: The cross-sectional study was carried out in nodal ART centre of Assam situated at Government hospital in Guwahati. The ADRs reported by physician were collected, analyzed and causality assessment was done. RESULTS: In the present study, (13.13%) gastritis, (8.75%) rashes, (8.13%) anemia, (7.5%) maculopapular rashes, (6.87%) giddiness, (6.87%) anorexia and (3.75%) parasthesia of legs were commonly reported ADRs. Out of 160 ADRs, 50 (31.06%) ADRs were belonging to gastrointestinal system. Zidovudine+Lamivudine+Nevirapine (ZDV+3TC+NVP) regimen use reported majority of ADRs. 102 (63.7%) ADRs were possible by Naranjo causality assessment scale. CONCLUSION: Gastritis was the commonly reported ADR from ART. The findings of this study suggest that there is a need of intensive monitoring for ADRs in ARTs centres of Assam.

Keywords: ART, ADRs, Assam, Gastritis

INTRODUCTION

In India, National AIDS Control Organization (NACO) under the aegis of Government of India, Ministry of Health and Family welfare has established Anti-Retroviral Therapy (ART) centres in various Government hospitals of India to provide free antiretroviral treatment to the people living with human immunodeficiency virus (HIV) [1]. Thus, with the easily availability of generic Highly Active Anti-Retroviral Therapy (HAART), an increasing number of HIV infected individuals in India are now receiving therapy. A successful ART regimen involves a combination of at least three drugs. Unfortunately, upto 25% of patients discontinued their initial HAART regimen because of treatment failure (inability to suppress HIV viral replication to below 50 copies/µl), toxic effects or noncompliance of therapy [2][3].

Most often adverse drug reactions (ADRs) go unnoticed or are not reported. The present study was conducted to know the status of ADRs caused due to ART in the nodal ART center of Assam situated at Government hospital in Guwahati. Assam does not fall in the high-risk category but the worrying part is that it is surrounded by Manipur, a very critical state in terms of HIV/AIDS and number of people living with HIV/AIDS has increased alarmingly in recent years. This study would be beneficial to the HIV infected patients, with the ultimate goal of improving the tolerability and effectiveness of HIV treatment by promoting the early recognition of potentially serious adverse effects. Therefore, this study was conducted to assess the incidence and causality of ADRs in HIV infected patients receiving ART in nodal ART centre of Assam.

METHOD

The observational and cross-sectional study was carried out in the outpatient setting of nodal ART centre of Assam situated in the Gauhati Medical College and Hospital (GMCH), Guwahati from august to december 2011. It is the largest and most advanced tertiary care Government hospital of the entire north-east region of India. The Institutional Ethical Committee permission was taken to conduct the present study. ADRs were identified and reported by physicians of ART centre, where collected and considered as an ADR. Patient's demographic character like age & sex, mode of transmission, and antiretroviral regimens were collected during the study period. The reported ADRs were assessed for causality by using the Naranjo's algorithm scale [4]. This scale categorizes the association between the reaction and the suspected drug into four categories: definite, probable, possible and unlikely. Descriptive statistical analysis was used in the present study.

RESULTS

In our study, 300 patients were included those who were receiving ART from the nodal ART centre of Govt. hospital during the study period. Out of theses, 208 were males and 92 were female. Of the 300 patients, 93 (31%) patients had experienced ADRs; comprising 70 (75.26%) male patients and 23 (24.73%) female patients. Among different age group, 70 (75.26%) patients had experienced ADRs who were belonged to age group of 21-40 years while 21(22.58) patients suffered from ADRs who were having ages ≥41years (table no.1). Heterosexual mode of HIV transmission was found in 262 (87.33%) patients followed by 10(3.33%) patients by blood transfusion, 7(2.33%) patients by injectable drug use, 5(1.67%) patients by homosexual mode of transmission and 16(5.33%) patients by unknown mode of transmission.

In this study, 160 suspected ADRs were detected in 93 patients. As per the distribution of various organ systems affected by ADRs, 50 (31.25%) ADRs were related to gastrointestinal system, 38 (23.75%) ADRs were related to skin, 26 (16.25%) ADRs were related to central nervous system, 19 (11.87%) ADRs were related to blood and cardiovascular system, 15 (9.37%) ADRs were related to musculoskeletal system, 2 (1.25%) ADRs were related to hepatic abnormalities and 10 (6.25%) ADRs were belonged to other organ systems. The most commonly reported ADRs were (13.13%) gastritis, (8.75%) rashes, (8.13%) anemia, (7.5%) maculopapular rashes, (6.87%) giddiness, (6.87%) anorexia and (3.75%) parasthesia of legs (table no.2). According to Naranjo causality assessment scale, 102 (63.75%) ADRs were found to be possible and 58 (36.25%) ADRs were probable (table no. 4).

It was also observed that, 60 (37.50%) ADRs were reported from the regimen ZDV+3TC+NVP followed by 56 (35.0%) ADRs were from STV+3TC+NVP, 20 (12.5%) ADRs were from STV+3TC+EFV, 19 (11.87%) ADRs were from ZDV+3TC+EFV, 3 (1.87%) ADRs were

from TDF+3TC+EFV and 1(0.62%) each ADR was from TDF+3TC+LPV/r and TDF+ZDV+LPV/r (table no.3).

TABLE 1: DISTRIBUTION OF PATIENTS WITH RESPECT TO GENDER & AGE

CHARACTERS	TOTAL NO. OF PATIENTS, N=300	NO. OF PATIENTS WITH ADRS, N=93(%)
Gender		
Male	208	70(75.26)
Female	92	23(24.74)
Age (year)		
1-20	7	2(2.15)
21- 40	230	70(75.26)
≥41	63	21(22.58)

TABLE 2: ORGAN SYSTEM WISE DISTRIBUTION OF ADRS

ADRS	NUMBER OF ADRS,N=160
Gastrointestinal system (50)	
Gastritis	21
Anorexia	11
Increased appetite	1
Flatulence	2
Nausea	4
Vomiting	1
Pain abdomen	4
Epigastric tenderness	1
Abdominal cramps	1
Dysphasia	1
Diarrhea	1
Gastric intolerance	1
Fullness of abdomen	1
Central Nervous System(26)	
Insomnia	4
Giddiness	11
Headache	1
Peripheral Neuropathy	1
CNS problems	2
Tingling sensation	1
Drowsiness	2
Numbness	2
Disorientation	1
Tremors of hands	1
Skin(38)	
Rashes	14
Macula popular rashes	12
Mild retro auricular rashes	1
Erythematic popular eruptions	2
Acne form skin eruptions	1
Itching	4
Steven-Johnson syndrome	2
Photosensitivity reaction	1
Pigmentation of nails	1
Musculoskeletal system(15)	
Parasthesia of legs	6
Generalized weakness	4
Shoulder ache	1
Body ache	1
Muscular pain	1
Muscle cramps	1
Leg weakness	1
Liver(2)	
Increased liver enzyme levels	1
Jaundice	1
Blood & cardiovascular system(19)	
Moderate increase in BP	1
Anemia	13
Pallor	3
Palpitation	2
Other ADRs(10)	
Acute pancreatitis	2
Facial Lipodystrophy	2
Fever	2
Decreased vision	1
Increase frequency of Micturition	1
Weight loss	1
Itching eyes with lacrimation	1

TABLE 3: NUMBER OF ADRS WITH RESPECT TO ART REGIMENS

ART REGIMENS	NO. OF PATIENTS, N=300 (%)	NO. OF ADRS, N=160 (%)
Zidovudine+Lamivudine+Nevirapine (ZDV+3TC+NVP)	102 (34)	60 (37.5)
Stavudine+ Lamivudine+Nevirapine (STV+3TC+NVP)	196 (65.33)	56 (35)
Stavudine+ Lamivudine +Efavirenz (STV+3TC+EFV)	90 (30)	20 (12.5)
Zidovudine+Lamivudine +Efavirenz (ZDV+3TC+EFV)	25 (8.33)	19 (11.87)
Tenofovir+ Lamivudine +Efavirenz (TDF+3TC+EFV)	9 (3)	3 (1.87)
Tenofovir+Lamivudine+Lopinavir/Ritonavir (TDF+3TC+LPV/r)	1 (0.33)	1 (0.62)
Tenofovir+Zidovudine+Lopinavir/Ritonavir (TDF+ZDV+LPV/r)	1 (0.33)	1 (0.62)

TABLE 4: CAUSALITY ASSESSMENT OF ADRS BY NARANJO ASSESSMENT SCALE

CAUSALITY	SCORE	NO. OF ADRS (%)
Definite/highly probable/certain	9	0
Probable	4 to 8	58(36.25)
Possible	1 to 4	102(63.75)
Unlikely	0	0

DISCUSSION

In our study, the prevalence of ADRs was high in males as compared to female patients. In contrast to this finding, Rajesh *et al.* [5] has found high prevalence of ADRs in females, when compared to males. The reasons for these sex differences in adverse drug reactions might be due to differences between men and women in body mass index and fat composition, hormonal effects on drug metabolism, or genetic constitutional differences on the levels of various enzymes. In our study most of the patients were belonged to the age group of 21-40 years and ≥41 years; therefore we might have detected majority of ADRs from this group.

It was observed that, 31% of patients experienced ADRs to ART during the study period. This incidence rate was less than the study of Ghate *et al.* [6] in which 35.32% patient experienced ADRs whereas Rajesh *et al.* reported 43.85% of ADRs which was high as compare to our study. These variations in the incidence rate of ADRs may be because of concurrent medications used for treating opportunistic infections and other co-morbid conditions which may results in increase of ADRs incidences. Among the various organ systems, (31.25%) gastrointestinal system and (23.75%) skin was most predominantly affected organ system by ADRs. Similarly, in the study of Khalili *et al.*[7] gastrointestinal toxicity was most prominent with incidence rate of 63.7% whereas Singh *et al.*[8] have found skin related toxicity with the incidence rate of 15.83%.

In our study, nevirapine use was observed as a high risk factor for gastritis. Similarly, the previous studies have also shown high prevalence of gastritis [9], maculopapular rashes [10] and hepatotoxicity [11] by nevirapine use. Steven Johnson Syndrome (SJS) is the most severe medical emergency which is seen with nevirapine use. Here, we have found 2 cases of SJS due to nevirapine where the patients were having diffuse, exfoliating exanthema with generalized bulbous eruptions all over the body. We have also observed significant association between the use of zidovudine and anemia in the patients, similar to the study of Moyle *et al* [12]. Stavudine use was observed as a risk factor for facial lipodystrophy and peripheral neuropathy. Although, our study has reported only 1 ADR of peripheral neuropathy but the studies conducted by Von

Giesen *et al.*[13] and Scarsella *et al.*[14] have shown significant association in the nevirapine use and occurrence of peripheral neuropathy. In our study, efavirenz use was observed as a risk factor for insomnia, parasthesia and central nervous system problems in patients. Fumaz *et al*. [15] and Subbaraman *et al*. [16] have also reported similar kind of ADRs with the efavirenz use. It was also seen that most of the ADRs were reported from regimen ZDV+3TC+NVP and STV+3TC+NVP consisting of zidovudine and nevirapine. Rajesh *et al*. has also found that those patients who received regimen containing zidovudine and nevirapine were reported maximum number of ADRs.

Causality assessment of ADRs by Naranjo scale showed that most of the (63.75%) ADRs were possible while remaining (36.25%) ADRs were probable. None of the ADRs were definite and unlikely. These results are in contrast to the study conducted by Rajesh *et al*. were majority of (63.5%) ADRs were probable.

The present study has some limitations. The study was conducted in only one nodal ART centre of Government hospital in Assam. These may exclude the actual number of HIV infected patients who were on ART and experienced ADRs. We have lack to identify the potential predictors of ADRs to ART in HIV infected patients. Furthermore, we have not shown statistical significance among the parameters and large study sample must be needed for interpretation of results and to arrive at a definite conclusion. However, gastritis was the most commonly reported ADR from ART and those patients who received regimen containing zidovudine and nevirapine were more likely to suffer ADRs. Thus, the findings of our study suggest that treating physicians must focus on early detection and prevention of ADRs in HIV infected patients of ART centres.

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