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TO STUDY THE PATTERN OF ADVERSE DRUG REACTIONS (ADRS) OF ANTIRETROVIRAL DRUGS IN AIDS PATIENTS ATTENDING ART OUTPATIENT DEPARTMENT IN A TERTIARY CARE HOSPITAL - A PROSPECTIVE OBSERVATIONAL STUDY

Pharmacology

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ABSTRACT

Highly Active Anti-Retroviral Therapy (HAART) is fraught with a high risk of adverse drug reactions (ADRs) and consistent use is required to prevent viral drug resistance and meet treatment goals. We assessed 250 prescriptions of patients attending ART OPD (Out-Patient Department) in our hospital set up after Ethical and MDACS (Mumbai District AIDS Control Society) approval. The data related to drug reactions and relevant investigations were collected and then analysed statistically in Microsoft Excel 2013. Out of 250 prescriptions, drug reactions were observed in 108 prescriptions (43.2%). Most commonly affected patients were males, especially in the age group of 31-40 years. The most common reaction observed was anaemia in 44.4% patients caused due to Zidovudine and the least common was lipodystrophy in 2 % patients due to Stavudine. Thus other drugs of similar classes or different classes should be studied to develop a regimen with a better safety profile.

KEYWORDS

HAART, Adverse drug reactions, Anti-retro viral drugs, Anaemia, Zidovudine.

INTRODUCTION

ART (antiretroviral therapy) for the treatment of people living with HIV (Human immunodeficiency virus) and AIDS (Acquired Immunodeficiency syndrome) under NACO (National AIDS Control Organization) is freely available in designated ART centres and has contributed in prolonging survival. ART works by suppressing the viral load and restoring the immune system. The scientific community has come a long way from the first drugs available for HIV in 1986 as Zidovudine (AZT) and Didanosine (ddl) in the early 1990s to now an armatorium comprising of more than 25 drugs from six different classes. The introduction and availability of highly active anti-retroviral therapy (HAART) have translated to a significant reduction of AIDS-related morbidity and mortality. HAART involves using at least three different drugs from two different classes. It has been estimated that out of the 35.3 million worldwide, 10.6million received ART in 2012 and nearly 6.6 million AIDS-related death have been prevented with ART [1]

Nevertheless, challenges persist as HAART is fraught with a high risk of adverse drug reactions (ADRs) and consistent use is required to prevent viral drug resistance and meet treatment goals. A high percentage of ADRs deter the patients from taking regular medication, and drug withdrawal or discontinuation results in treatment failures. [2]

The success of the anti-retroviral treatment is highly dependent on the motivation of HIV positive individuals to adhere to complex ART regimens.[3] Unfortunately, Up to 25% of patients discontinue their initial HAART regimen because of toxic effects, noncompliance or treatment failure within the rest 8 months of therapy.[4] The occurrence of side effects can vary dramatically among different people.[5]Continuous evaluation needs to be done for the benefit of ART help to achieve the ultimate goal of making safer and more effective treatment to the patients.[6][7]Based on this information, we are conducting this study to evaluate the ADRs and find which anti-retroviral drugs are more safe and patient compliant.

MATERIALS AND METHODS

The study was conducted in a tertiary governmental teaching hospital in Mumbai, which provides Patients diagnosed with HIV infection based on the various clinical features and laboratory investigations visiting ART O.P.D of Sir JJ Hospital and started on ART. Age more than 18 years of either gender. Random 250 participants attending ART OPD were included in the study. The participants were recruited after obtaining written informed consent and the study was started Institutional Ethics Committee approval and MDAC approval. The data collection was done between November 2018 to February 2019. The data were obtained about the basic demographic details, diagnosis, duration of illness and treatment, current treatment regimen, per-capita family income, side effect due to drugs, whether the drug was stopped after the side effect and patient was treated as out-patient or was admitted in the hospital. Appropriate descriptive statistical analysis will be done using Microsoft Excel software. Results will be expressed in percentages and mean-standard deviation (SD).

RESULTS

Table No 1: Age- Gender Characteristics (N=250) Among The Study Population

Sr. No.	Age group	Male	Female	Total	Percentage
1	18-30	30	17	47	18.8
2	31-40	64	34	106	42.4
3	41-5	45	24	69	27.6
4	51-60	17	6	28	11.2
	Total	161	89	250	

Demographic assessment depicted that males are more affected by HIV than females. On comparing the age, it was found that maximum males affected falls in the age group of 31-40 (42.4%)

Table No 2: Socio – Economic Status Among The Study Population

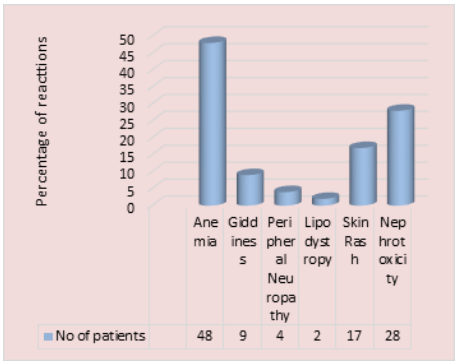
Sr. No	SES	Total Patients
1	26- 29	0
2	16-25	0
3	11-15	12
4	5-10	151
5	<5	87

Footnote: SES- Socioeconomic status. Modified Kuppuswamy score 26 – 29: Upperclass, 16-25: Upper middle class, 11-15: Lower middle class, 5-10: Upper lower, <5: Lower

Socio economic status of the patients was calculated by Modified Kuppuswamy scale. It was observed that maximum number of patients 151/250 in Upper lower-class category (42%).

During the course of the study, various Adverse drug reactions (ADR's) like Anaemia, Giddiness, Peripheral Neuropathy, Lipodystrophy etc. were observed in 108 patients out of 250 patients that were evaluated for drug reactions being treated with ART regimen. Prevalence of ADR observed 43.2%. It was observed that the Incidence of Anaemia (44.4%) was higher compared to other drug

reactions observed in 48 patients whereas the incidence of Lipodystrophy (1.85%) was the least ie. 2 patients.



Graph No 1: Incidence – Prevalence Of ADRs Among The Study Population

Table No 3: Different Classes Of ART Drugs Causing Drug Reactions

Sr. No	Drug Name	Class	Type of ADR	Treatment Stopped
1	Zidovudine	NRTI	Anaemia	Yes
2	Efavirenz	NNRTI	Giddiness	Yes
3	Atazanavir	PI	Peripheral Neuropathy	Yes
4	Stavudine	NRTI	Lipodystrophy, peripheral neuropathy	Yes
5	Nevirapine	NNRTI	Skin Rash	Yes
6	Tenofovir	NTRTI	Nephrotoxicity	Yes

Footnote: Various classes of anti-retroviral drugs – NRTI – Nucleoside Reverse Transcriptase Inhibitors; NNRTI – Non-nucleoside Reverse Transcriptase Inhibitors; PI – Protease Inhibitors; NTRTI – Nucleotide Reverse Transcriptase Inhibitors.

During the course of the study, various ART drugs like Zidovudine, Efavirenz, Atazanavir, Stavudine, Nevirapine and Tenofovir were found to be associated with adverse reactions. Anaemia being the most common drug reaction was associated with the zidovudine-based regimen. Tenofovir was associated with the development of nephrotoxicity. Skin rashes were observed with nevirapine use. Efavirenz was associated with giddiness. Atazanavir and Stavudine were associated with peripheral neuropathy. Case of lipodystrophy with stavudine use was reported only in 2 patients.

Drug reactions like anaemia, skin rashes, lipodystrophy and nephrotoxicity were diagnosed by routine investigations (CBC, RFT, LFT, Viral load) done during the regular follow up. Reactions like giddiness and peripheral neuropathy were described by patients during the visit. During the course, Causality assessment of the reactions was done by WHO causality assessment scale and modified Hartwig and Siegel's scale was used for severity assessment. Once the ART drug causing the drug reaction was identified, the offending agent was stopped, and the regimen was changed.

DISCUSSION

Our study aimed at studying the pattern of Adverse Drug Reactions (ADRs) of Antiretroviral Drugs in AIDS patients and finding the drug causing a particular kind of side effect and the most common side effect observed. It was done because challenges persist as HAART is fraught with a high risk of adverse drug reactions (ADRs) and consistent use is required to prevent viral drug resistance and meet treatment goals. High percentage of ADRs deter the patients from taking regular medication, and drug withdrawal or discontinuation results in treatment failures. [2]

In our study, we observed that the most common age group suffering HIV was 31-40 years (42%) which co-related with the study conducted by Nirav Patel et al [8] as in their study maximum patients also fell under 31-40 years age group around 50%. On comparing the gender most commonly affected by HIV it was observed that Males were more affected 64.4% which very well co-related with the studies conducted by Nirav Patel et al (60% Males),[8] Swati Patil et al (52%).[9] The demographic association with Nirav et al [8] and Swati Patil et al [9] can be explained as the studies were conducted in the same ecological zone of Gujarat and Mumbai respectively.

In our study, the most common incidence of drug reactions was anaemia associated with Zidovudine which co-related with the study conducted by Swati Patil et al (58.6%),[9] McNeil Ngongondo et al (33.2%).[10] Raymond Tetteh et al also stated anaemia as the most common drug reaction observed in their study.[11] These patients diagnosed with anaemia were prescribed tablet ferrous sulphate 20 mg bd and were constantly monitored through regular CBC monitoring which was done once in every two weeks.

We observed nephropathy in 25.93% patients associated with tenofovir and 17% patients developed skin rashes due to nevirapine which was also observed in the studies conducted by Margaret Lartey et al,[12] Rita Kumari et al [13] and Swati Patil et al.[9] the least common side effect of lipodystrophy due to stavudine i.e. 2% correlated with the study conducted by Margaret Lartey et al,[12] but they also observed stavudine associated peripheral wasting.

These drug reactions become the commonest in our as well as other studies conducted across India because the drugs prescribed for HIV remains similar through out country prescribed as per NACO guidelines.

CONCLUSION

The study revealed that incidence as well as the prevalence of drug reactions of various classes of anti retro viral drugs has been increasing and the most commonest drug reaction (Anaemia) still remains the same. Thus other drugs of the similar classes or different classes not being prescribed commonly should be studied to develop a regimen with a better safety profile.

LIMITATIONS

The major limitation was being a single-centric with a limited number of participants.

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