

Research Article

Adverse effects of antiretroviral treatment at a tertiary care hospital in India: a prospective observational study

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Received: 14 May 2013

Accepted: 21 May 2013

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ABSTRACT

Background: Data on adverse drug reactions (ADRs) related to antiretroviral (ARV) use in public health practice are few indicating the need for antiretroviral therapy (ART) safety surveillance in clinical care.

Methods: 143 patients on ART were studied prospectively over a period of two years. All patients were asked to visit the clinic if they developed any symptoms or on a monthly basis. They were screened clinically and investigated suitably for any ADRs.

Results: 143 HIV positive patients were analyzed. At least one ADR was seen in 87 (60.83%) subjects. The most common ADR observed was peripheral neuropathy in 54 (37.76%) patients, followed by lipodystrophy (13.98%), anemia (10.48%) and hyperlipidemia (6.29%). Patients with peripheral neuropathy and lipodystrophy were mainly on stavudine based regimes, while patient with anemia and hyperlipidemia were on zidovudine based regimes.

Conclusions: In spite of high ADRs, highly active antiretroviral therapy (HAART) is the only answer to HIV/AIDS. To optimize adherence and thus, efficacy of ART, clinicians must focus on preventing adverse effects whenever possible, and distinguish those that are self-limited from those that are potentially serious.

Keywords: Adverse drug reaction, Antiretroviral therapy, Acquired immune deficiency syndrome

INTRODUCTION

An HIV infected person can possibly live a normal lifespan today, provided she or he takes highly active antiretroviral therapy and takes it perfectly.¹ ARV drugs are associated with a broad range of toxicity, ranging from low-grade intolerance, which may be self-limiting, to life-threatening side-effects. Most of the toxicity/side-effects can be adequately co-managed with efficient clinical monitoring at all levels of the health care system.² The spectrum of adverse effects related to HAART in developing countries may differ from that in developed countries because of the high prevalence of conditions such as anemia, malnutrition, and tuberculosis and frequent initial presentation with advanced HIV disease.³

Consistent use is vital for HAART to be effective and to prevent emergence of resistance. However, ARV drugs are highly toxic and are associated with various adverse drug reactions (ADRs) due to which many patients require withdrawal of the drug or even discontinue the treatment resulting in treatment failure. Hence, monitoring and reporting of ADRs in HIV/AIDS patients receiving ART assumes great importance.⁴ Unfortunately, up to 25% of patients discontinue their initial HAART regimen because of treatment failure (inability to suppress HIV viral replication to below the current limit of detection, 50 copies/mL), toxic effects or noncompliance within the first 8 months of therapy.^{5,6} Several strategies have been implemented to improve treatment duration. While development of new

antiretroviral agents continues, efforts to maximize the effectiveness of currently available treatments include attempts to better understand and manage adverse effects.⁷ This prospective study was planned to evaluate the incidence of adverse drug reaction in individuals receiving ART.

METHODS

This study was carried out at SMIMER Hospital, Surat after the Ethical Committee approval from October 2009 to November 2011. This was a prospective, observational study. 143 HIV-positive cases who were already on ART and who were newly started on ART were included and were followed prospectively for the development of any ADRs. A detailed history of every patient was taken including past history of ART. We used the WHO definition of ADR as any response to a medicine which is noxious and unintended, and which occurs at doses normally used in man.⁸ A pre-designed and pre-tested Performa was used to record ADR keeping all the norms of confidentiality. Baseline laboratory investigations such as complete blood counts, liver function tests (LFTs), renal function tests (RFTs), lipid profile and blood sugar tests were carried out in all patients. Clinical examination along with appropriate lab investigations, histopathology, and radiodiagnosis were documented in the adverse reactions reported by the treating physician.

Patients received four first line regimens as per the NACO guidelines²:

I: Zidovudine, Lamivudine and Nevirapine (ZLN)

I (i): Stavudine, Lamivudine, and Nevirapine; (SLN)

II: Zidovudine, Lamivudine and Efavirenz (ZLE).

II (i): Stavudine, Lamivudine, and Efavirenz (SLE)

They were also screened for opportunistic infections (OIs) and drug toxicity in each follow-up visit during this two-year period. CD4 count was done every six months or more frequently if clinically indicated. In patients who were on zidovudine (AZT)-containing regimens, hemoglobin was measured before initiation and at 4, 8 and 12 weeks of therapy or in response to their symptoms. LFTs were done at 2, 4, 8 and 12 weeks in patients on nevirapine (NVP)-based regimens. Lipid profile and serum lactate, serum amylase was done whenever indicated.

RESULTS

A total of 143 HIV patients (88 were males and 55 were females) were enrolled. The study group had a mean age of 37.58 ± 19.5 years. At least one ADR was seen in 87 (60.83%) subjects. The most common ADR observed was peripheral neuropathy in 54 (37.76%) patients, followed by lipodystrophy (13.98%), anemia (10.48%) and hyperlipidemia (6.29%). Anemia was observed in 15

(10.48%) patients who were on zidovudine based regime and severe anemia (grade IV, Hb < 6.5 g/dL) was observed in 4 patients. Skin rashes were found in 5.59% and patients. Rash was observed with nevirapine-based regimen. Abnormal liver function tests (LFT) were observed in five cases (3.49%). Among 87 patients, 36 had severe (grade-3 and grade-4) ADRs, whereas 51 patients had mild to moderate ADR (Grade-1 and Grade-2). Peripheral neuropathy and lipodystrophy were seemed to be caused mainly by stavudine. Anemia, hyperlipidemia and hyperglycemia found mainly with zidovudine based regimes. Nausea, vomiting and abdominal pain found in 15.38%, 8.39% and 12.58% patients respectively.

Table 1: No. of males and females on individual regime.

Regime	ZLN	SLN	ZLE	SLE	Total
Male	53	31	04	00	88
Female	19	32	01	03	55
Total	72	63	05	03	143

Table 2: ART regimes and adverse effects.

	ZLN	SLN	ZLE	SLE	Total	%
Peripheral Neuropathy	21	31	00	02	54	37.76
Lipodystrophy	03	12	02	03	20	13.98
Anemia	14	00	01	00	15	10.48
Hyperlipidemia	05	04	00	00	09	6.29
Skin rash	06	02	00	00	08	5.59
↑liver enzymes	02	03	00	00	05	3.49

DISCUSSION

One hundred and forty-three cases were observed over a period of two years. ADRs were observed in 87 of them (60.83%) while a Swiss cohort⁹ reported ADRs in 74% of their cases. In Singh et al¹⁰ study adverse effects were seen in 86% of cases. In our study the most common ADR observed was peripheral neuropathy in 54 (37.76%) patients. Similarly the most common ADR reported was peripheral neuropathy (31.64%) in Singh et al¹⁰ study. In Sharma et al¹¹ study the most common ADRs were cutaneous (44.4%), peripheral neuropathy (22.2%) and anemia (20%). In a study by Kumarasamy et al¹² the most common ADRs were PN, anemia and nail hyper pigmentation. Anemia found in 10.48% patients in current study while in Sharma et al¹¹ study anemia was seen in 20% of the cases. Lipodystrophy was observed in 13.98% patients in our study, which closely resembles Sharma et al¹¹ (14.5%) study. Singh et al¹⁰ and Balakrishnan K¹³ studies documented lipodystrophy in 20.04% and 14.5% of their cases respectively. Maximum (46.5% of their cases) lipodystrophy were reported in Thierry Saint Marc study.¹⁴ Liver enzymes elevation found in 3.49% patients in current study while Sharma et

al¹¹ and Singh et al¹⁰ reported 15.5% and 7.5% of their cases. Dyslipidemia found in 6.29% in our study which closely resemble Singh et al¹⁰ study (6.67%). 12.58% patient had complained abdominal pain in our study while in Jena A et al¹⁵ study 16% cases of abdominal pain documented. Sharma et al¹¹ and Maniar et al¹⁶ reported very few cases of abdominal pain (2.2% and 0.7% respectively).

This study has some limitations. The study included patients who had initiated ART before active surveillance of ADR commenced. Though this provided information on long term adverse effects, we may have missed early onset ADR from these patients. The small sample size of patients on different regimen limits our ability to compare ADR reported by other studies with different regimens. Also the ADR screening tool was structured and thus, does not allow details of unknown ADR to be captured and graded, thus the study was confined to report on known ADRs only.

CONCLUSIONS

As eradication of the HIV infection is currently not possible, significant problems related to compliance and long-term toxicity can be anticipated with decade-long therapies. Patient compliance can be improved with proper education and counseling regarding the disease process and inherent but innocuous side effects of HAART. More field based studies in resource constrained settings should be conducted. This will provide valuable insight in the incidence, prevalence and type of ADRs associated with ARVs. Finally more research is needed for generation of more efficacious and less toxic drugs.

Funding: None

Conflict of interest: None declared

Ethical approval: Approved by Institutional ethical committee

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DOI: 10.5455/2320-6012.ijrms20130805

Cite this article as: Vaghani SV, Gagiya AK, Shukla DK, Patel VP. Adverse effects of antiretroviral treatment at a tertiary care hospital in India: a prospective observational study. *Int J Res Med Sci* 2013;1:xx-xx