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REASONS FOR ART REGIMEN CHANGE AMONG PATIENTS ON HAART AT DURAME HOSPITAL, ETHIOPIA

RAZLOZI ZA PROMENU ANTIRETROVIRALNE TERAPIJE (ART) KOD BOLESNIKA KOJI SU PRIMALI VISOKO EFIKASNU ART U DURAM HOSPITAL BOLNICI U ETIOPIJI

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Key words

Regimen change, switch, highly active antiretroviral therapy (HAART), Reasons.

Ključne reči

promena terapije, zamena, visoko aktivna antiretroviralna terapija (HAART), razlozi

Abstract

Background: The Antiretroviral drugs, which are currently being used for the treatment of HIV/AIDS, can improve the quality of life of someone infected with HIV, helping them to stay well much longer than they otherwise would. Though the potent first line regimen is desired to last long, it is often changed or modified owing to various reasons.The objective of this study was to assess the reasons of antiretroviral therapy regimen modification in patients on HAART at Durame Hospital.
Methods: The study was conducted using a retrospective based cross sectional study by reviewing patient information sheet. All patients, who had changed their initial antiretroviral regimens within two years; from Jan25, 2011-Jan25, 2013, were included in the study.
Result: Out of 173 patientsassessed, 67.6% were females. The most common (52.0%) regimen before switch was D4T/3TC/NVP. The main reasons for regimen change were toxicity, co morbidity, treatment failure and pregnancy. The main types of toxicities that resulted in regimen change were: Metabolic disturbance in 62 (55.9%), peripheral neuropathy in 13 (11.7%), Anemia in 12 (10.8%) and Rash in 9 (8.1%).
Conclusion: Side effect (toxicity) was the main reason for modification of antiretroviral drugs among the study population. Metabolic disturbance (lipodystrophy) was the leading toxicity related cause for modification of HAART and it was associated mostly with D4T based regimens.

INTRODUCTION

HIV/AIDS, Human immune deficiency virus/Acquired immune deficiency syndrome (AIDS), continues to be a major global public health challengesince it first diagnosed in 1981 (1). Since the start of the epidemic, an estimated 36 million [30 million – 42 million] people have died of AIDS-related illnesses (2). According to the UNAIDS report on theglobal AIDS epidemic (3), an estimated 34.0 million [31.4 million–35.9 million] people worldwide were estimated to be living with HIV in2011. Sub-Saharan Africa remains most severely affected; accounting for 69% of the people living with HIVworldwide (3). Ethiopia is one of the heavily affected sub-Saharan African countries by the HIV epidemic.It has a large number of people living with HIV, approximately 800,000, withan estimated adult prevalence of 1.5% (4).

The antiretroviral drugs that are currently available can improve the quality of someone infected with HIV, helping them to stay well much longer than they otherwise would (5). After the introduction of potent combination antiretroviraltherapy (ART) in 1996, the overall AIDS related deaths and illnesses have been markedly decreased (1, 6). An estimated number of 265,174 people (out of 480,000 people eligible) were on ART treatment as of 2011 in Ethiopia (7).

Once antiretroviral therapy is initiated, patients generally remain on medications indefinitely (8). Though the potent first line regimen is desired to last long, it is often changed or modified owing to various reasons (9-11). A switch (modification) in the antiretroviral (ARV) regimenis often necessary because of acute and chronic toxicities, concomitant clinical conditions, poor adherence, a desire for pregnancy and development of virological failures (8).

Antiretroviral regimen change, however, should be done only when necessary to spare the future treatment options.The approach to patients who need to switch will defer depending on several issues, ART experience and available options [8]. Data on the reasons formodification of initial highly active antiretroviral therapy are limited among patients of Ethiopia. This study was therefore aimed to assess the causes for changing of ART among patients taking HAART in Durame Hospital, South Ethiopia.

METHODS

A retrospective cross sectional study was conducted by reviewing patient cards at ART clinic of Durame Hospital, which is located 360km away from the capital city, Addis Abeba, in southern Ethiopia. Thehospital is a general government hospital and the ART services is provided free of charge. A total of 173patients, whohad changed their initial antiretroviral regimens within two years; from Jan 25, 2011-Jan 25, 2013, were included inthe study. Pretested data collection format was used to collect data on the demographic conditions, the starting and the new regimen, duration of initial therapy, CD4 count, World Health Organization (WHO) stage of the disease, and reasons for changing the regimens. Prior to the beginning of the study, ethical clearance was obtained from of Jimma University Ethical Review Board. An official letter was written to DurameHospital from Jimma university pharmacy department. Officials at different levels in the study area were communicated to get permission for data collection. Patient card number was used instead of patient's name, to keep confidentiality of the patients' information.

RESULTS

One hundred seventy three patient records were assessed at DurameHospital. The rate of treatment change was 17.52% in two years. The mean age of the patients was 28±2 years. Majority (27.7%) of the patients were between the ages of 26-30 years. Females accounted for 117(67.6%) (Table 1).

Majority (38.7%) of the patients in the study had a body weight in the range of 40-50kg. Eighty four (48.55%) patients had a CD4 count in the range of 51-200 cells/mm³on initiation of ART. Eighty six(49.7%) of the patients were at WHO clinical stage III at the initiation of treatment (Table 2).

Majority of the patients were on D4T based regimen before they got their regimen changed. From a total of 69.3% on this regimen, 52.0% were on D4T/3TC/NVP and 13.3% were on D4T/3TC/EFV regimen. The rest were on AZT/3TC/NVP (16.2%), AZT/3TC/EFV (5.2%), TDF/3TC/EFV (6.9%) and TDF/3TC/NVP (2.3%) (Table 2).

Drug side effect (toxicity) was the most common (64.2%) cause for ARV change (Table 3). From all toxicities reported for patients in this study, metabolic disturbance (lipodystrophy) which accounted 55.9% was the most common, followed by peripheral neuropathy 11.7% and anemia 10.8 %. From a total of 62 patients who changed their treatment regimen due to metabolic disturbance, modification for 50 patients was made after 2 years (Table 4).

Table 1: *Socio-demographic characteristics ofthe patients*

Variable	Frequency (173)	Percentage (%)
Sex		
Male	56	32.4
Female	117	67.6
Age		
18-20	3	1.7
21-25	40	23.7
26-30	48	27.7
31-35	29	16.8
36-40	28	16.2
41-45	10	5.8
≥45	15	8.7
Marital status		
Married	84	48.6
Widowed	34	19.7
Unmarried	28	16.2
Divorced	27	15.6
Educational status		
Illiterate	28	16.2
Primary	56	32.4
Secondary	73	42.2
Tertiary	16	9.2

Table 2*: Clinical characteristics of the patientsat the initiation of ART*

Characteristics	Frequency (n=173)	Percentage
Baseline body weight Kg)		
<40	23	13.3
40-50	67	38.7
50-60	61	35.3
>60	22	12.7
CD4 count at baseline(cells/mm^3)		
<50	21	12.14
51-200	84	48.55
>200	50	28.9
Not written	18	10.41
WHO Clinical Stage		
Stage I	29	16.8
Stage II	35	20.2
Stage III	86	49.7
Stage IV	23	13.3
Initial ART regimen		
D4T/3TC/NVP	90	52
D4T/3TC/EFV	30	17.3
AZT/3TC/NVP	28	16.2
AZT/3TC/EFV	9	5.2
TDF/3TC/NVP	4	2.3
TDF/3TC/EFV	12	6.9

Table 3: *Reasons for modification of initial ART treatment regimens*

Reasons	Initial treatment regimens, N (%)						Total, N (%)
	D4T/3TC/NVP	D4T/3TC/EFV	AZT/3TC/NVP	AZT/3TC/EFV	TDF/3TC/NVP	TDF/3TC/EFV	
Drug side effect	65(37.6)	18(10.4)	18(10.4)	7(4)	0	3 (1.7)	111(64.2)
Co morbidity	18(10.4)	2(1.2)	5(2.9)	0	2(1.2)	1(0.6)	28(16.2)
Treatment failure	3(1.7)	0	3(1.7)	2(1.2)	2(1.2)	4(2.3)	14(8)
Pregnancy	1(0.6)	8(4.6)	1(0.6)	0	0	3(1.7)	13(7.5)
Poor adherence	0	1(0.6)	0	0	0	1(0.6)	2(1.2)
Illness	2(1.2)	0	0	0	0	0	2(1.2)
Others	0	2(1.2)	1(0.6)	0	0	0	3(1.7)
Total	90(52)	30(17.3)	28(16.2)	9(5.2)	4(2.3)	12 (6.9)	173(100)

Others: No reason, pill burden, out of stock

Table 4:*Number of weeks at which different toxicities caused change of treatment regimens*

Toxicity	Number of weeks at which treatment changed					Total (%)
	0-12	12-26	26-52	52-104	≥104	
Metabolic disturbance	3	5	2	2	50	62(55.9)
Peripheral neuropathy	2	0	3	2	6	13(11.7)
Anemia	7	2	3	0	0	12(10.8)
Rash	5	0	0	4	0	9(8.1)
CNS toxicity	1	0	0	1	3	5(4.5)
Nausea	0	0	0	1	1	2(1.8)
Diarrhea	0	0	0	0	1	1(0.9)
Others	5	0	0	1	1	7(6.3)
Total	23	8	7	11	62	111(100)

Others:Hepatitis, headache, breast cancer, jaundice

Table 5: *Toxicities reported as a reason for ART treatment change by ART treatment regimen*

Toxicity	Frequency (%) by Treatment regimen					Total Frequency (%) (n=111)
	D4T/3TC/NVP	D4T/3TC/EFV	AZT/3TC/NVP	AZT/3TC/EFV	TDF/3TC/NVP	
Metabolic disturbance	44(39.6)	14(12.6)	2 (1.8)	1(0.9)	1(0.9)	62 (55.9)
Peripheral neuropathy	12 (10.8)	1(0.9)	0	0	0	13(11.7)
Anemia	0	0	11(9.9)	1(0.9)	0	12(10.8)
Rash	4(3.6)	0	3 (2.7)	0	2(1.8)	9(8.1)
CNS toxicity	0	1(0.9)	0	4(3.6)	0	5(4.5)
Nausea	1(0.9)	0	0	1(0.9)	0	2(1.8)
Diarrhea	0	1(0.9)	0	0	0	1(0.9)
Others	4(3.6)	1(0.9)	2 (1.8)	0	0	7(6.3)
Total	65 (58.6)	18 (16.2)	18 (16.2)	7(6.3)	3 (2.7)	111(100)

Others: Hepatitis, headache, breast cancer, jaundice

Metabolic disturbance was most commonly, 71.0%, reported for patients on D4T/3TC/NVP regimen. Anemia was due to AZT containing regimens of AZT/3TC/NVP (91.7%) and AZT/3TC/EFV (8.3%) (Table 5).

Tuberculosis was the only co-morbid disease reported as the reason for modification of treatment regimenin16.35% of the patients. It was the reason for switching of 18 patients from D4T/3TC/NVP and 5 patients from AZT/3TC/NVP to EFV containing regimens.

Treatment failure, identifiedby immunological failure, was the reason for modification of treatment regimen in 8% of the patients. It was observed in all initial treatment regimens except D4T/3TC/EFV.

Thirteen (7.5%) of the patients changed their treatment regimen due to either planning for pregnancy or for being pregnant. Almost all modification due to this reason was from EFV regimen to NVP based regimen.

DISCUSSION

Majority (38.7%) of the patients in the study had a body weight in the range of 40-50kg. Eighty four (48.55%) patients had a CD4 count in the range of 51-200 cells/mm^3 on initiation of ART. Eighty six (49.7%) of the patients were at WHO clinical stage III at the initiation of treatment. These results indicate that most of the study patients were on advanced HIV illness when ART was initiated.

Majority of the patients were on D4T based regimen before they got their regimen changed. From a total of 69.3% on this regimen, 52.0% were on D4T/3TC/NVP and 13.3% were on D4T/3TC/EFV regimen. This study result is comparable with the research finding in south India [12], where 4T/3TC/NVP accounted for 63% and with that of coted'Ivoire[10] in which Stavudine-Lamavudine combination accounted for 58%. But it was much higher than the result of the study conducted in Assela and Shashamene[13] where D4T/3TC/NVP regimen accounted for 36%.

Different factors may cause modification of treatment regimens. Drug side effect (toxicity) was the most common (64.2%) cause for ARV change in this study. This result is comparable with the result of the study conducted in Addis Abeba[14], Assela and Shashemene[13], and southern

India[12] where toxicity caused ART change in 65%, 55%, and 64% of the patients respectively.

Metabolic disturbance such as lipodystrophy was the most common (55.9%) toxicity related reason for modification of the ART regimen followed by peripheral neuropathy (11.7%) and anemia (10.8%). This result is much higher than the finding of the study conducted in Mekelle[15] where lipodystrophy accountedfor only 27.7%. Metabolic disturbance and peripheral neuropathy were common in patients on D4T based regimens. On the other hand anemia was common on AZT based regimen as AZT is a known cause for Anemia.

Tuberculosis was the only co-morbid disease reported as the reason for modification of treatment regimen in16.35% of the patients. It was the reason for switching of 18 patients from D4T/3TC/NVP and 5 patients from AZT/3TC/NVP to EFV containing regimens. The reason for this NVP switch to EFV is the overlapping hepatotoxicity of NVP with anti-TB drugs and the potential drug-drug interaction between NVP and Rifampicin[16].

Treatment failure was the reason for modification of treatment regimen in only 8% of the patients in this study. All treatment failures identified in this study were determined by immunological failure alone. In resource limited countries like Ethiopia where there is no facility to determine virologic failure it is recommended to use clinical and, where possible, CD4 count criteria to define treatment failure [17]. Treatment failure was observed in all initial treatment regimens except D4T/3TC/EFV.

Thirteen (7.5%) of the patients changed their treatment regimen due to either planning for pregnancy or for being pregnant. Almost all modification due to this reason was from EFV regimen to NVP based regimen. This switch was mainly due to the teratogenic effect of EFV [8].

CONCLUSION

Drug side effect (toxicity) was the major reason for modification of antiretroviral drugs among the study participants. Co-morbidity, treatment failure and planning for pregnancy were the other reasons. Metabolic disturbance such as lipodysthrophy was the most common toxicity related cause for modification of the treatment regimen change.

CONFLICT OF INTEREST:
The authors declare that they have no conflict of interest.

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Sažetak

Uvod/Cilj: Atiretroviralni lekovi koji se trenutno koriste u lečenju HIV/AIDS-a mogu da poboljšaju kvalitet života osobe zaražene virusom HIV-a pomažući im da se osećaju dobro duže nego što bi to bio slučaj da ne koriste lekove. Iako je cilj da se lekovi koji se koriste kao prva linija odbrane primenjuju što duže, terapija se često menja ili modifikuje u zavisnosti od različitih razloga. Cilj ovog istraživanja bio je da se procene razlozi modifikacije antiretroviralne terapije u bolesnika lečenih HAART-om u Durame Hospital bolnici.

Meteode: U istraživanju je sprovedena retrospektivna studija poprečnog preseka uz korišćenje podataka iz kartona bolesnika. Svi bolesnici kojima je promenjena inicijalna antiretroviralna terapija u periodu od dve godine (od 25.01.2011-25.01.2013) bili su uključeni u studiju.

Resultati: Od 173 bolesnika uključenih u studiju 67,6% bile su žene. Najčešće korišćena terapija pre promene (52%) bila je kombinacija D4T/3TC/NVP. Glavni razlog promene terapije bila je toksičnost lekova, komorbiditet, neuspešno lečenje i trudnoća. Najvažniji tipovi toksičnosti koji su doveli do promene terapije bili su metabilički poremećaji u 62 (55,9%), periferna neuropatija u 13 (11,7%), anemija u 12 (10,8%) i osip u 9 (8,1%) bolesnika.

Zaključak: Neželjeni efekti (toksičnost) su bili glavni razlog promene antiretroviralnih lekova koji su korišćeni u lečenju bolesnika uključenih u studiju. Metabolički poremećaj (lipodistrofija) je bila vodeći uzrok koji je doveo do promene terapije (HAART-a) i bila je povezana uglavnom sa terapijom zasnovanom na DT4.

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