RESEARCH PAPER

ADHERENCE AND PHARMACO-CARE INTERVENTIONS AMIDST HIV PATIENTS ON COMBINED ANTIRETROVIRAL THERAPY IN NIGERIA

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Present study examines the level of adherence and pharmaceutical care interventions among HIV patients on combined antiretroviral therapy in Nigeria. Adherence to cART among 297 patients was determined using pill counting method. The levels of patient adherence were evaluated at baseline and then re-evaluated at three, six, and nine months. The subjects were also followed up with drug counseling at 3 months interval of the hospital visit for prescription refills. More than one-half of them were on cART between 2 and 3 years. At baseline, the adherence level obtained from pill counting was 85.9%. Following the patient-focused interventions, the adherence level steadily increased to 97%. Before the intervention, patients most adhered to Tenofovir + Emtricitabine + Efavirenz followed by Zidovudine + Lamivudine + Efavirenz. After the intervention, there was an improvement in adherence level to all the regimens of drugs used for the patients. In treating HIV-infected subjects on combined antiretroviral therapy, application of pharmaceutical interventions and continual monitoring are essential to heighten adherence and promote survival.

Key words: Pharmaceutical care, Adherence, Line regimen, Pill counting, Antiretroviral therapy.

INTRODUCTION

Some HIV-infected patients do not gain from combined Antiretroviral Therapy (cART) due to non-adherence and this poses long-term threat for the efficacy of cART (Adefolalu and Nkosi, 2013). The success of cART depends on sustainable superior levels of adherence (National Consolidated Guidelines, 2015). Whether the patient is treatment inexperienced or treatment experienced, the chance of adherent diminishes over time (Hornschuh *et al* 2017). Pill count method of adherence however, involves physical counting of patient remaining pills by the pharmacist, nurse, physician or other health-care practitioners. There are beneficial effects of adherence to therapy in HIV-infected patients. There is a virologic failure among non-adherent patients when compared to adequately adherent patients. The increase in adherence leads to increase in CD_4 count. Non-adherence correlated with a longer stay on hospital admission and increased the frequency of hospitalization. Previously, various levels of adherence in many countries have been observed. In North America, adherence level was reported to be 55% while 72.9% was reported in sub-Saharan Africa (Reda and Biadgilign, 2012; Heestermans *et al* 2016).

In Nigeria, the level of adherence recorded in Kano by Muktar *et al* 2006 was 49.2% while in Benin City and Ilorin the levels were 58% (Erah and Arute, 2008) and 73.3% (Bello, 2011) respectively. This study examines the level of adherence and pharmaceutical care

interventions among HIV patients on combined antiretroviral therapy in Nigeria.

EXPERIMENTAL
Materials and Methods
The research was conducted in the Infectious Disease Clinic of University of Benin Teaching Hospital (UBTH), Benin City, Edo State, Nigeria. A prospective study was conducted between 15th October, 2012 and 3rd October 2013 following approval by the Ethics and Research Committee of UBTH (Protocol Number: ADM/E22/A/VOL. VII/833). Verbal and written informed consents were obtained from the patients before enrolment.
The case notes of 297 patients among those on cART for 2-8 years who were on first-line antiretroviral drugs (Zidovudine + Lamivudine + Nevirapine; Zidovudine +Lamivudine + Efavirenz; Tenofovir + Emtricitabine + Efavirenz; Tenofovir + Emtricitabine + Nevirapine) and second line combination (Zidovudine + Lamivudine + Lopinavir boosted Ritonavir; Tenofovir + Emtricitabine + Lopinavir boosted Ritonavir) were randomly selected from 10,440 patients.

Pill counting method of adherence measurement
In this method, the remaining pills brought to the pharmacy by the patient whenever visiting the hospital for a prescription refill was counted and matched against his/her prescription. Adherence level in percentage was determined by dividing actual pills actually consumed over a period with the pills prescribed to have been taken for the period and multiplying by 100.

Patient-focused intervention
The patients were followed-up for 9 months with drug counseling at 3 months interval they visited the hospital for prescription refills. All the patients were duly counseled on the beneficial effects and toxicities of cART. Also, the importance of adhering to cART and the possibility of drug resistance and therapeutic failure were emphasized.

Data analysis
The collected data of the study were analyzed with SAS software program version 9.2.

RESULTS AND DISCUSSION
All the HIV patients were on at least three cART drugs, of which Zidovudine-Lamivudine-

Nevirapine combination; a first-line regimen was mostly used. Second-line regimens (Zidovudine + Lamivudine + Lopinavir / ritonavir and Tenofovir + Emtricitabine + Lopinavir / Ritonavir) were reserved for patients who defaulted in their treatment and these accounted for 22 (8.5%) (**Table 1**). Greater than half of HIV patients had been on cART between a period of 2 and 3 years. The median of the duration on cART was 3.4 years. Only limited patients that were on cART reported minimal side effects, particularly body weakness. No one among the patients was on herbal medicines during the investigation period. The preferred method of medication-taking behavior among the patients was self or alarm reminder (**Table 1**). At baseline, the adherence level obtained from pill counting was 85.9%. Following the patient-focused interventions, the adherence level steadily increased to 97% (**Figure 1**). Prior to intervention, adherence to cART drugs recorded among the patients was much higher (85.9%) than those of earlier studies such as that of (Erah and Arute 2008) where adherence level of 58% was reported. This variance in adherence level can be explained based on the advancement in the WHO 2014 antiretroviral therapy treatment guideline, free cART drugs and patient-focused interventions provided on medications and disease treatment.
Prior to pharmacist intervention, the HIV-infected patients were mostly adhered to Tenofovir + Emtricitabine + Efavirenz followed by Zidovudine + Lamivudine + Efavirenz. After intervention, there was advancement in adherence to all drug regimes (**Table 2**). The commonest reasons for inapt adherence to cART medication at baseline were drug fatigue, wrong drug information and religion constraint (**Figure 2**). Furthermore, no one among the patients was on herbal medicines; therefore, consuming traditional drugs could contribute to inapt drug adherence. Besides, this study validates with the earlier findings (Mini *et al* 2012) that poor knowledge about patients' disease stage and appropriate therapy was the cogent reason for low level of adherence.
The regression analysis revealed that greater drug adherence was only associated with the duration on cART in HIV-infected patients [OR 2.1; 95% confidence interval 1.0-1.4, p < 0.05]. The longer a patient is on cART, the better the adherence level (**Table 3**). However, adherence was still below the minimum level of 95% (Lam and Fresco, 2015).
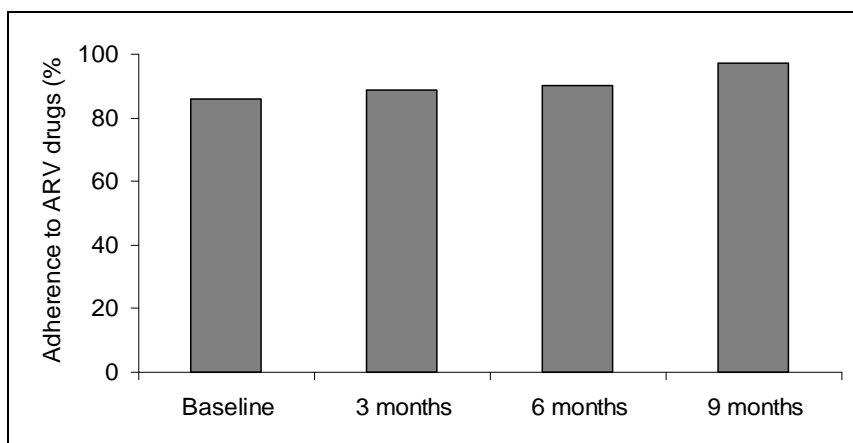
Fig. 1. Adherence to cART by HIV-infected patients following pharmacist's patient intervention

Table 1. Treatment characteristics of HIV-infected patients on cART

Characteristics	Frequency (%)
Combined Antiretroviral Therapy (cART)	
Zidovudine + Lamivudine + Nevirapine (ZLN)	211 (70.6)
Zidovudine + Lamivudine + Efavirenz (ZLE)	20 (6.9)
Zidovudine + Lamivudine + Lopinavir/ritonavir (ZLA)	13 (4.5)
Tenofovir + Emtricitabine + Efavirenz (TEE)	25 (8.5)
Tenofovir + Emtricitabine + Nevirapine (TEN)	16 (5.5)
Tenofovir + Emtricitabine + Lopinavir/ritonavir (TEA)	12 (4.0)
Duration on cART (years)	
2-3	156 (52.8)
4-5	85 (28.3)
6-8	56 (18.9)
Antiretroviral Side Effects	
Body weakness	85 (28.6)
Fever	85 (28.6)
Insomnia	64 (21.4)
Persistent headache	32 (10.7)
Infertility	21 (7.1)
Amenorrhoea	10 (3.6)
Prompter of Drug Administration	
Use of alarm/self-reminder	215 (72.4)
Spouse	40 (13.3)
Family member	23 (7.8)
Adherence counselor	12 (4.1)
NTA news	7 (2.4)
Herbal Medicines	
Patients on herbs	0 (0)

Table 2. Adherence distribution to cART according to drugs used

cART	Adherent patients Pre-intervention n (%)/total	Adherent patients Post-intervention n (%)/total
ZLN	22 (59.5)/211	62 (68.1)/211
ZLE	4 (10.8)/21	9 (9.9)/21
ZLA	2 (5.4)/13	4 (4.4)/13
TEE	5 (13.5)/25	9 (9.9)/25
TEN	3 (8.1)/16	4 (4.4)/16
TEA	1 (2.7)/11	3 (3.3)/11
Total	37/297	91/297

Z: Zidovudine, L: Lamivudine, N: Nevirapine, E: Efavirenz, E: Emtricitabine, A: Lopinavir/Ritonavir, T: Tenofovir
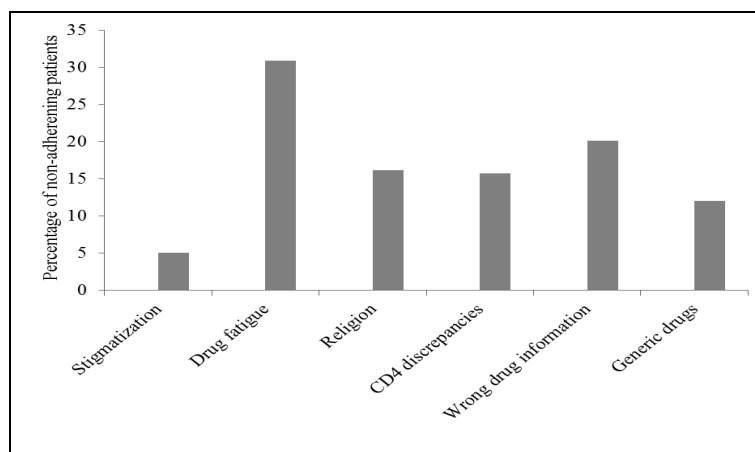
Fig. 2. Reasons for inapt adherence to cART drugs among the patients at baseline

Table 3. Logistic analysis for determinants of better adherence in HIV-infected patients on cART

Factor	OR (95% CI)	P-value
Age (years)		
20-30	2.416 (0.682-8.556)	0.172
31-40	1.114 (0.453-2.738)	0.814
41-50	1.117 (0.459-2.722)	0.807
50+	1.000 (0.192-2.012)	0.158
Gender		
Male	1.315 (0.755-2.288)	0.333
Female	1.000 (0.875-4.134)	0.365
Marital status		
Single	0.542 (0.211-1.394)	0.204
Married/ever married	1.000 (0.515-5.863)	0.511
Education		
Not educated	1.559 (0.414-5.863)	0.511
Primary school	0.688 (0.312-1.515)	0.353
Secondary school	0.858 (0.403-1.826)	0.691
Post-secondary	1.000 (0.111-0.349)	0.223
Occupation		
Unemployed/students	1.587 (0.622-4.051)	0.334
Employed/retired	1.000 (0.691-9.836)	0.157
cART regimen		
Zidovudine + Lamivudine + Nevirapine	1.061(0.309-3.644)	0.926
Zidovudine + Lamivudine + Efavirenz	0.666 (0.165-2.684)	0.568
Tenofovir + Emtricitabine + Efavirenz	0.938 (0.186-4.743)	0.939
Tenofovir + Emtricitabine + Nevirapine	1.881 (0.339-10.428)	0.470
Tenofovir + Emtricitabine + Lopinavir/Ritonivir	0.931 (0.194-4.469)	0.929
Zidovudine + Lamivudine + Lopinavir/Ritonivir	1.000 (0.145-4.902)	0.717
Duration on cART	1.180 (1.001-1.390)	0.048*

*Statistically Significant at $P < 0.05$, Z: Zidovudine, L: Lamivudine, N: Nevirapine, E: Efavirenz,
E: Emtricitabine, T: Tenofovir, A: Lopinavir/Ritonavir

The improvement in adherence level in the present research following intervention has been reported elsewhere (Mini *et al* 2012). Adherence to the medication was insignificantly affected by the gender, age, marital status, occupation, educational attainment and type of cART regimen in this study, similar to in Cross River State and in Sokoto State of Nigeria (Oku *et al* 2014; Agu *et al* 2013). In this research, however, duration of therapy with cART was appreciably correlated with better drug adherence (Talam *et al* 2008).

CONCLUSION

Prior to the intervention, the HIV-infected patients mostly adhered to Tenofovir + Emtricitabine + Efavirenz followed by Zidovudine + Lamivudine + Efavirenz. After the intervention, there was an improvement in adherence to all the drugs regimens utilized. In treating HIV-infected patients on combined antiretroviral therapy, application of the pharmaceutical interventions and continual monitoring are essential in improving adherence and promoting survival.

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