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RESEARCH ARTICLE

A COMPARATIVE STUDY ON THE ADVERSE EFFECTS OF ANTIRETROVIRAL DRUG REGIMEN ZLN AND TLE AS FIRST LINE ART

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ABSTRACT

Objective: Comparative study of the adverse effects of antiretroviral drug regimen ZLN and TLE as first line ART in the initial 3 months of starting of therapy in 300 patients in MBGH,Udaipur, Rajasthan. **Methods:** This was a retrospective observational study. Patient's records were obtained from ART Centre, MBGH Udaipur from starting of HAART to 3 months of treatment for clinical and laboratory evidence of toxicity as per NACO protocol. **Results:** Total 300 patients were observed. Most common side effect was anemia mostly associated with Zidovudine based regimens followed by drug hypersensitivity and hepatotoxicity which was with nevirapine based regimen. Least was neuropsychiatric side effects which was with Tenofovir and Efavirenz based regimen. Drug hypersensitivity seems to be the most serious of the early toxicities & is the most common causes for interruption in ART. **Conclusion:** With introduction of new NACO guidelines in November 2014, TLE regimen was chosen over ZLN in all new HIV patients. The reason for such an important step taken by NACO can be easily understood by the results and observation of this study as TLE regimen is superior to ZLN regimen.

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INTRODUCTION

HIV infection has become a global pandemic with more than 36.7 millioninfected throughout the world as of 2016 (1) http://www.unaids.org/en/resources/fact-sheet). India has the third largest burden of HIV related pathology (2) http://naco.gov.in/sites/default/files/Annual%20Report%202015-16_NACO.pdf). With an increasing number of patients being on HAART, the toxicity of antiretroviral therapy becomes an increasingly important issue in the management of patients with HIV. Adverse effects have been reported with virtually all antiretroviral drugs and are among the most common reason for switching or discontinuation of therapy and for medication non adherence, many such adverse reactions are poorly studied and analyzed and are under reported during the early stages of treatment (https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/31/adverse-effects-of-arv). Owing to side effects of ZLN (Zidovudine, Lamivudine, Nevirapine) regimen as first line regimen since start of ART programme, NACO in November 2014 decided to change the first line regimen to TLE (Tenofovir, Lamivudine, Efavirenz) to reduce the side effects, improve adherence to therapy without compromising the efficacy (https://aidsinfo.nih.gov/ guidelines/ html/1/adult-and-adolescent-arv-guidelines/31/adverse-effects-of-arv). This study is an effort to look upon the side effects profile of both ZLN and TLE regimen as first line ART within 3 months of starting of therapy as well as various predictors of toxicity which interferes with ART and lead to change/ substitution of a drug and cause for poor adherence.

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OBJECTIVES

Primary: Comparative study on the adverse effects of antiretroviral drug regimen ZLN and TLE as first line ART in the initial 3 months of starting of therapy.

Secondary: To study any possible associated underlying disease as a predictor of adverse effects.

MATERIAL AND METHODS

The study was done on 300 patients registered at ART centre MBGH and RNT Medical College, Udaipur Rajasthan. Two groups werestudied,150 patients in each group, one with ZLN based regimen and the other with TLE. It was a retrospective study. Records were obtained from starting of HAART to 3 months of treatment for clinical and laboratory evidence of toxicity as per NACO protocol.

Inclusion criteria: Patients being newly initiated i.e. for the first time on first line ART either ZLN from 1st March 2014 to 30th October 2014 and TLE from 1st November 2014 to 31st May 2015.

Exclusion criteria: Patientsalready enrolled before and after the provided time period and who have already received ART earlier from other ART centre or private institution. Alcoholic, Pregnant female, Patient on ATT, Patient with other medical disorders like Diabetes Mellitus.

Observations

In this study, total 300 patients were studied,150patients were in ZLN treated group and, 150 patients were in TLE treated group. In ZLN treated group102 (68%) were male and 48 (32%) were female while in TLE treated group 82 (54.6%) were male and 68 (45.3%) were female. In ZLN treated group number of patients belonging to age group 15 -45 years were 122 (81.3%) and in TLE treated group number of patients belonging to age group 15 -45 years were 131 (86.6%).. In ZLN treated group number of patients belonging to age group <15 yrs and >60 yrs were 03 (2%) &05 (3.3%) , while in TLE treated group 0 (0%) & 03 (2%). Overall in 300 patients mean age of patients studied was 35.8 years.

Among 150 ZLN treated patients number of patients had CD4 count 51-200 was 61(40.6%), CD4 count 201-350 was 60(40%), while number of patients had CD4 count >350 was 09(6%) , CD4 count <50 was 20(13.3%) . In contrast, among 150 TLE treated patients number of patients had CD4 count 201-350 was 60(40%) followed by CD4 count 51-200 was 56(37.3%). Number of patients14 (9.3%) had CD4 count <50 whereas 20(13.3%) patients had CD4 count >350. In 150 ZLN treated patients, 97 (64.6%) patients had hemoglobin 9- 12 gm% i.e. already anemic while 53 (35.3%) had hemoglobin >12 gm%. In 150 TLE treated patients, 79 (52.6%) patients had hemoglobin 9- 12 gm% i.e. already anemic while 54 (36%) had hemoglobin >12 gm%. Only 17 (11.3%) had hemoglobin below <9 gm%. Overall maximum patients 176 (58.6%) had hemoglobin 9- 12 gm% while minimum 17 (5.6%) patients had hemoglobin below <9 gm%. 107 (35.6%) patients had hemoglobin >12 gm%. In 300 patients before start of HAART 255 (85%) patients had normal serum transaminases level, 41 (13.6%) patients had high level of serum transaminases while in 04 (1.3%) patients had very high level of serum transaminases i.e. more than 3 times elevation. In 150 patients ZLN treated maximum number of patients 128 (85.3%) were having normal serum transaminases level. 21 (14%) patients had high level of serum transaminases while in 01 (0.6%)patients had very high level of serum transaminases i.e. more than 3 times elevation. In 150 patients of TLE treated group 127(84.6%) patients had normal serum transaminases level. 20 (13.3%) patients had high level of serum transaminases while in 03 (2%) patients had very high level of serum transaminases i.e. more than 3 times elevation. Side effects due to HAART was present in total 83 patients, out of total 300 patients. In ZLN treated group number of patients who had side effects were 79,while in TLE treated group number of patients had side effects were 04.Out of 79 patients (patients had side effects in ZLN treated group), regimen was

Table 1. Comparision between zln and tle treated groups

		ZLN Treated group n=150	TLE Treated Group n=150
Sex	Male	102(68%)	82(54.6%)
	Female	48(32%)	68(45.3%)
Age	<15yrs	3	0
	15-45 yrs	122	131
	46-60 yrs	20	16
	>60 yrs	5	3
Haemoglobin Value	>12 gm%	53(35.3%)	54(36%)
Before treatment	9-12 gm%	97(64.6%)	79(52.6%)
	<9 gm%	0	17(11.3%)
Serum Transaminase level Before	Normal	128(85.3%)	127(84.6%)
Treatment	High	21(14%)	20(13.3%)
	Very High(>3*UNL)	01(0.6%)	03(2%)
CD4 count before HAART	<50 cells/mm^3	20(13.3%)	14(9.3%)
	51-200 cells/mm^3	61(40.6%)	56(37.3%)
	201-350 cells/mm^3	60(40%)	60(40%)
	>350 cells/mm^3	09(6%)	20(13.3%)
Side Effect Present	Total	79	04
	Regimen Not Changed	44	04
	Regimen Changed	35	00
SideEffects	Anemia	69	0
	Rashes	3	0
	SJS	2	0
	Hepatotoxicity	5	0
	Lipid Abnormality	0	0
	Pancreatitis	0	0
	Renal Dysfunction	0	0
	Neuropsychiatric Manifestation	0	4
	Dysglycemia	0	0
	IHD	0	0
	Change In Bone Mineral Density	0	0

Table 2. Reason for Change of Art Regimen in Zln Treated Patients

Reason	No. Of patients(n=35)
Anaemia (Hb below 9gm %)	28(80%)
Rash	03 (8.5%)
Steven Johnson syndrome	02 (5.7%)
Hepatotoxicity	02 (5.7%)
Total	35(100%)

Table 3. Comparision between regimen changed and regimen not changed groups

		Regimen Changed n=35	Regimen Not Changed n=48
Sex	Male	20(57.1%)	33(68.7%)
	Female	15(42.8%)	15(31.2%)
Age	<15yrs	0	01(2%)
	15-45 yrs	30(85.7%)	41(85.4%)
	46-60 yrs	03(8.5%)	05(10.4%)
	>60 yrs	02(5.7%)	01(2%)
Haemoglobin Value	>12 gm%	07(20%)	33(68.7%)
Before treatment	9-12 gm%	28(80%)	15(31.2%)
Serum Transaminase level Before Treatment	Normal	26(74.2%)	42(87.5%)
	High	02(5.7%)	00
	Very High(>3 upper limit)	07(20%)	06(12.5%)
CD4 count before HAART	<50 cells/mm^3	8(22.8%)	6(12.5%)
	51-200 cells/mm^3	16(45.7%)	16(33.3%)
	201-350 cells/mm^3	10(28.7%)	23(47.9%)
	>350 cells/mm^3	01(28%)	03(6.2%)
SideEffects	Anemia	28	41
	Rashes	3	0
	SJS	2	0
	Hepatotoxicity	2	3
	Lipid Abnormality	0	0
	Pancreatitis	0	0
	Renal Dysfunction	0	0
	Neuropsychiatric Manifestation	0	4
	Dysglycemia	0	0
	IHD	0	0
	Bone Mineral Density	0	0

Table 4. Biochemical changes onzln regimen changed group

Hb Level Before Start of ZLN Regimen >12gm% n=7	Decrease but below<9 gm%	4
	Decrease but above 9 gm%	2
	Increase	1
Hb Level Before Start of ZLN 9-12gm% n=28	Decrease but below<9 gm%	24
	Decrease but above 9 gm%	3
	Increase	1
Change in Serum transaminase Level n=35	Improvement	3
	Asymptomatic worsening	1
	Hepatotoxicity	2
	Normal	29

changed in 35 patients due to significant toxicity while in 44 patient regimen not changed due to absence of significant toxicity. Among TLE treated group 4 patients had side effects due to HAART, regimen was not changed in any of the patientsinthis group. In ZLN treated 150 patients, regimens was changed in 35 patients. The most important reason for changed regimen was anemia (Hb below 9gm %), 28 (80%) patients. Drug hypersensitivity in form of rash and Steven Johnson syndrome was present in 03 (8.5%) & 02 (5.7%) respectively. Hepatotoxicity was seen in only 02 (5.7%) patients. In regimen changed& ZLN treated group, number of patients belonging to age group 15 -45 years, were 30 (85.7%),age group 40-60 year were 03(8.5%), age group >60 year were 02 (5.7%), age group <15 year were 0(0%), Among 35 patient treated with ZLN and regimen changed, 20 (57.1%) were male and 15 (42.8%) were female. In 35 regimen changed & ZLN treated patients number of patient had CD4 count 50-200 was 16 (45.7%), number of patients had D4 count >350 was 01 (2.8%). 10 (28.5%) and 08 (22.8%) patients had CD4 count 200-350 and <50 respectively.In study total number of patients had toxicities were 83,and among these, in 48 patients regimen was not changed(44 patients of ZLN treated group,4 patients of TLE treated group).Out of 41 patients with anemia as side effect, maximum numbers i.e. 20 (48.7%) of patient had CD4 count 201-350. Number of patients had CD4 count >350 were i.e. 03 (7.3%). Similarly, Out of 3 patients with hepatotoxicity as side effect, numbers of patient had CD4 count 201-350 were 02 (66.6%), number of patients had CD4 count 51-200 were 01 (33.4%). Out of 4 patients with Neuropsychiatric symptoms as side effect 02 (50%) were having CD4 count 201-350, while number of patients i.e. 01 (25%) each had CD4 count 51-200 had 201-350. In 35 regimen changed with ZLN treated patients, before start of HAART 28 patients were already anemic i.e. Hb 9-12 gm%. With ZLN for 3 months, 24(85.7%) out of 28 had hemoglobin level below 9 gm%. 03(10.7%) patients had decrease in hemoglobin values but not below 9 gm%. Only 01/28 (3.5%) patient had increase in hemoglobin level.

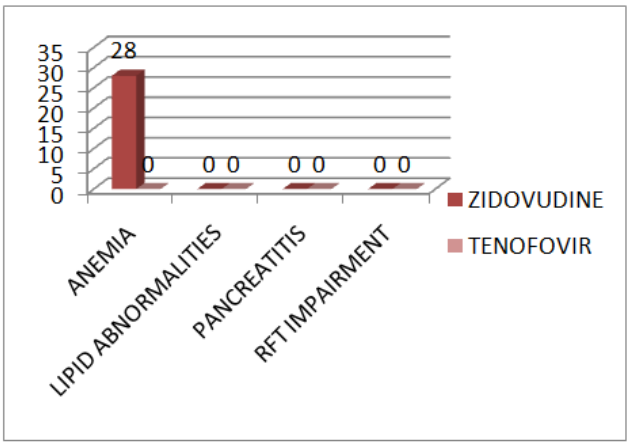

Figure 1. Comparative presentation of adverse effect due to zidovudine and tenofovir regimen changed group (n=35)

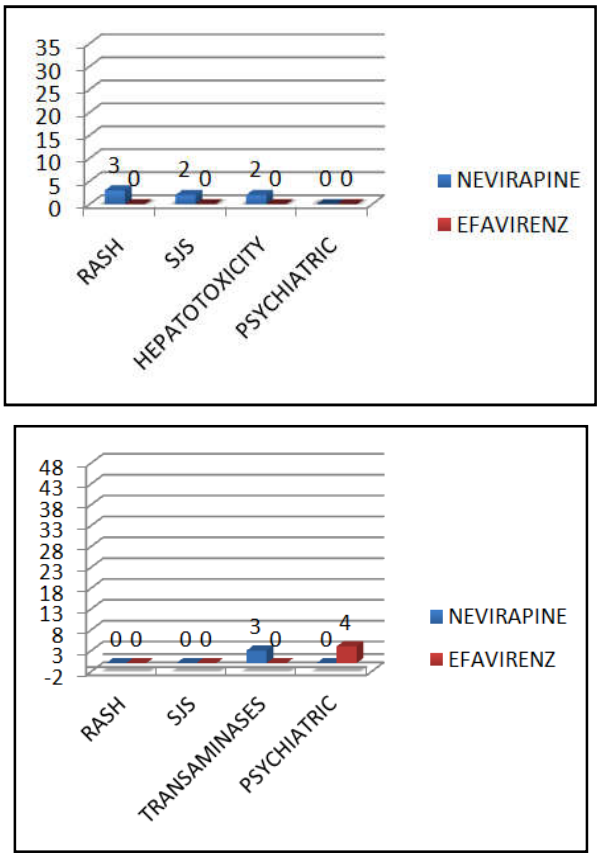

Figure 2&3. Comparative presentation of adverse effects due to nevirapine and efavirenz in regimen changed (n=35) and regimen not changed group (n=48)

In 7 patients with normal level of hemoglobin out of 35 regimen changed patients, 04(57.1%) had significant drop of >3 gm% and had their hemoglobin below 9 gm%. 02(28.5%) had decrease in hemoglobin but was above 9 gm%. Only 01/07(14.2%) patient had increase of hemoglobin from previous value. In 35 regimen changed patients 29/35 (82.8%) patients had normal serum transaminases level. 03/35 (8.5%) patients had improvement while 02/35 (5.7%) had significant toxicity while 01/35 (2.8%) patient had asymptomatic mild increase in serum transaminases.

DISCUSSION

One of the important determinants of the success of an ART regimen is compliance & one of the major hurdles to compliance is toxicity .As per New NACO Guidelines in November 2014 on selection of first line HAART regimen, ZLN is no longer considered to be the first line regimen. Now the first line regimen in every newly initiated HAART is TLE in place of ZLN as well as patient with toxicity to ZLN is to be changed to TLE.

Effect of age, sex, base line cd4 count, other drug and chronic medical conditions

From data obtained we can deduce that in our study age, gender distribution is similar to National HIV population data, but age,sex,base line CD4 count ,and other drug given to patient ,do not have any association with occurrence of side effects . Out of 83 patients with side effects one patient had hypertension and diabetes both .No association seen between these two chronic medical condition and occurrence of side effects and no association seen between opportunistic infections and occurrence of side effects.

Hemoglobin at Intiation in Patients Studied

The mean hemoglobin level at baseline in 300 studied patients from both ZLN and TLE treated group was 11.6 gm%. The range was 2.4 to 17.4gm%. Out of 300 patients 58.6% were having haemoglobin between 9 to 12gm% i.e. anemic level while 35.6% had hemoglobin >12gm%. 5.6% patients had very low hemoglobin i.e. <9gm% (TLE treated). This finding is consistent with the study conducted by Damodhar Bhaschaniet al[4] who found hemoglobin of less than 10gm% in 36% of studied patients. Also, in 35 patients with significant side effects & in whom regimen was changed 80% were having haemoglobin between 9 to 12gm% i.e. anemic level while 20% had haemoglobin>12gm%. Conversely, out of 48 patients with mild side effects & regimen not changed maximum patients 31.2% were having haemoglobin between 9 to 12gm% i.e. anemic level while 68.7% had haemoglobin>12gm%. In 300 patients from both ZLN and TLE treated group, 54 patients had drop of haemoglobin below 12gm%. All these patients were receiving ZLN as Initial HAART. Out of these 54 patients with haemoglobin below 12gm% 37 patients had drop in haemoglobin within 1 month of therapy, 8 patients had drop in haemoglobin in 1-2 months of therapy while 9 patients had drop in haemoglobin in 2-3 months of therapy Out of these 54 patients, 28 patients had haemoglobin<9gm% because of Zidovudine toxicity and thus it was substituted with Tenofovir as per NACO guidelines. In these 24 regimen changed patients 24 patients already had haemoglobin between 9-12 gm% i.e. already anemic and only 4 patients haemoglobin between >12 gm%. Maximum 22 patients had CD4 count below 200mm (Sharma, 2008).

Similarly in rest 26 patients in whom regimen was not changed 18 patients have haemoglobin>12gm% while only 8 patients had haemoglobin between 9-12 gm% i.e. already anemic. In these 26 patient drop in haemoglobin was not so significant <9 gm% so that in these individuals regimen was not changed. From above data & observation, we can deduce that, in 35 patients with significant side effects because of anemia due to ZLN regimen the Zidovudine was changed to Tenofovir in 28 patients. Among these 80% have hemoglobin already in anemic range, so haemoglobin level fall was greater in this group which is already anemic i.e. median baseline haemoglobin level 9-12 gm%. This observation was found to be highly significant (p valve =0.0098). With above data and observations we can conclude that already anemic population

and CD4 count less than 200mm (Sharma, 2008). Had more chances of developing Zidovudine toxicity. There were no other associations found between baseline characteristics and Anaemia including gender, age, baseline CD4 count and concurrent tuberculosis treatment. This is not enitirely different from the findings of a study done by Kenneth A. Lichtenstein et al in USA[5]; the factors associated with an increased incidence of anemia included Female gender. Three other factors were associated in above study baseline low Hemoglobin median value (p= 0.0098), baseline CD4 count <200 cells/mm^3 and Zidovudine use (p= 0.0001). In our study also all of these 3 factors are found to have significant association.

Adverse effects other than Anemia

A total of 83 patients showed side effects, 79 from ZLN group and 4 from TLE treated group.In 79 ZLN treated patients 69 patients had anemia, 5 patients had drug hypersensitivity, hepatotoxicity in 5 patients. The toxicities observed were graded as Grade I in maximum 28 patients whereas Grade IV toxicity was seen 4 patients. Grade II toxicity was present in 2 patients while Grade III in only 1 patient. Sharma et al found 71% incidence of side effects in their study (3) https://aidsinfo.nih.gov/guidelines/html/1/adult-and-adolescent-arv-guidelines/31/adverse-effects-of-arv). In our study the incidence of side effects is 52.6% which is less to that of Sharma et al. The study conducted by Sharma et al included most patients on ZLN and also included nausea, vomiting, diarrhoea as side effects which constituted a significant toxicity. We did not take these as side effects in our study this may be reason for low incidence of side effects in our study. In a similar study in Thailand during a median observation period of 3.7 years, 142 Grade 3 or 4 toxicities occurred in 101 patients (24%) [65].The incidence in our study is somewhat similar, though ours was a short term study and looked at toxicities in only the first 3 months. In TLE treated 150 patients only 4 patients had side effects which were of Grade I and did not required change of regimen or discontinuation of therapy for any time period. May be due to nature of study being retrospective study subjective complaints which were included in study i.e. neuropsychiatric symptoms because of Efavirenz were recorded less as compared from the biochemical changes side effects in ZLN group.

Drug Hypersensitivity

A total of 5 reported drug hypersensitivity toxicities were observed among 300 patients . Rash developed in 3 patients with Grade I severity and 2 patients had Steven Johnson syndrome with Grade IV severity. All these patients were on Nevirapine based ZLN therapy. Out of 3 patients with rash, 1 patient developed this side effect in < 1 month of therapy while 2 patients developed same in 2-3 month of therapy. The patients with Steven Johnson syndrome developed within 1-2 months in 1 patient and within 2-3 month of therapy in other one. In all these patients on ZLN therapy regimen was changed to substitute nevirapine with efavirenz (ZLE/TLE). Because of Steven Johnson syndrome 2 patients were admitted in medical wards and HAART was stopped for nearly 2 weeks. . No mortality occurred though. Skin reactions seem to be the most serious of the early toxicities. Because of Drug hypersensitivity i.e. Rash in 3 patient & 2 patients with Steven Johnson syndrome Nevirapine component was changed to efavirenz. The incidence of drug hypersensitivity(rash) in our study was 3.3% whereas a study in Thailand reported rash in 34% of patients, who took Nevirapine or Efavirenz and only 6% of the patients developed rash in a study which was done in Uganda (Forna, 2007). The association of Nevirapine with occurrence of drug hypersensitivity in form of rash and Steven Johnson syndrome was found to be very significant (p value= 0.0241) Rash is relatively common. It can become serious & life threatening & needs close monitoring with a need for change in therapy.

Serum Transaminases Elevation

In 300 patients before start of HAART, maximum number 255 of patients was having normal serum transaminases level. 41 patients had high level of serum transaminases while in 04 patients had very high level of serum transaminases i.e. more than 3 times elevation. In 45 patients with high level of serum transaminases at the start of study, with HAART they had normalisation of serum transaminases. 255 patients had normal serum transaminases level, out of these only 5 patients (5 out 150 ZLN treated i.e. 3.3%) had elevated level of serum transaminases during initial 3 months of HAART. All of them were on Nevirapine based ZLN therapy & none of them was HBsAg or anti HCV positive. The elevation of serum transaminases was of Grade I severity in 3 patients and did not have any impact on treatment while 2 patients had significant elevations in serum transaminases level. One had grade III severity and another had Grade IV. In these 2 patients with significant hepatotoxicity lead to substitution of Nevirapine to Efavirenz based regimen (ZLE/TLE). This toxicity did not cause any temporary withheld of drug or mortality. This is different from a study done in Thailand, in which 6.7% patients had grade III or grade IV laboratory toxicity. In our study only 1.3 % patient had grade III or grade IV laboratory toxicity. This may be due to the fact that chronic hepatitis B or C co-infection was common in HIV-infected Thai patients (O'Brien, 2003). The association of Nevirapine with hepatotoxicity was found to be very significant (p value= 0.0241). But there were no association found between baseline characteristics and hepatotoxicity including gender, age, baseline CD4 and concurrent tuberculosis treatment. This was similar to the findings in other studies done in Uganda and South Africa (Chu, 2010).

Neuropsychiatric Symptoms: A total of 4 reported neuropsychiatric symptoms were observed in 300 patients studied. All were treated with Efavirenz based TLE regimen. Neuropsychiatric symptoms in form of insomnia or irritable behaviour of Grade I severity developed in initial 1 month of HAART. This is in contrast to the study done at Royal Free Hospital, London, UK73, where 6.4% of patients developed similar symptoms (Lodwick, 2008). Our study had less number of patients reported this adverse effect may be because it is retrospective study and this subjective complaint of Neuropsychiatric symptoms is often overlooked by patient as well as doctors unless given importance. None of these patients required change of regimen nor there was any interruption of treatment. This is in contrast to the findings of the study done by Royal Free Hospital, London, UK where most frequently reported toxicity which required a treatment change was central nervous system effects (22.9%) secondary to Efavirenz (Lodwick, 2008).

Other Side Effects: Zidovudine component of ZLN regimen had other side effects like pancreatitis and lipid abnormality.

None of the 150 ZLN treated patients had these side effects. Lipid profile was not measured as a baseline routine investigation in our centre may be a confounding factor. Tenofovir component of TLE regimen had side effects like renal dysfunction and bone mineral density defect. None of patients had these side effects probably it is long term toxicity of tenofovir therapy.

Conclusions

Toxicities observed with HAART: In the study following toxicities were observed in ZLN treated patients

- 54 patients had anemia.
- 5 patients had Drug hypersensitivity i.e. Rash in 3 patient & 2 patients with Steven Johnson syndrome.
- 5 patients had Hepatotoxicity

In the study following toxicities were observed in TLE treated patients

- Psychiatric symptoms in 4 patients

Toxicities: Timelines

- **Anemia :** 48 patients developed anemia in <1 month of therapy, 11 patients developed anemia within 1-2 months of therapy while 10 patients developed anemia within 2-3 months
- **Rash:** 1 patients developed rash in <1 month of therapy, 2 patients developed rash within 1-2 months.
- **Steven Johnson Syndrome:** 1 patient developed this toxicity within 1-2 months of therapy while another one developed within 2-3 months of therapy.
- **Hepatotoxicity:** 2 patients had elevated serum transaminase in <1 month of therapy, 2 patients had elevated serum transaminase within 1-2 months of therapy while 1 patients developed it within 2-3 months.

Toxicity: Grading of severity

- A total of 7 patients had Grade IV toxicity; 4 anemia, 2 Steven Johnson syndrome, 1 hepatotoxicity.
- Three patients had Grade III toxicity; 1 hepatotoxicity, 2 anemia.
- Seven patients had Grade II severity anemia.
- 28 patients had Grade I toxicity; 22 anemia, 3 rash, 3 hepatotoxicity

ART substitution due to Toxicities

- Anemia resulted in substitution of Zidovudine with Tenofovir.
- ART introduction along with anemia both Zidovudine&Nevirapine component was changed to tenofovir and efavirenzrespectively.
- Drug hypersensitivity i.e. Rash in 3 patient & 2 patients with Steven Johnson syndrome Nevirapine component was changed to Efavirenz.

Toxicities: Predictors

- No association was found with respect to age, gender, occupation and risk factor.
- Low initial haemoglobin level (Hb 9-12 gm %), baseline CD4 count < 200mm^3 was found to have association with occurrence of anemia.
- Nevirapine based regimens were significantly associated with skin reactions (p value= 0.0241) & Zidovudine based regimens were significantly associated with the occurrence of anemia (p value= 0.0001).
- Tenofovir and Efavirenz based regimen is seemed to have very less side effects.
- Drug toxicities are an important cause for treatment interruptions & noncompliance during the early period of ART.

Comparision of zln and tle regimen in terms of toxicities: In 300 studied patients, which included 150 patients each of ZLN & TLE treated side effects were present in 79 patients of ZLN as compared to 4 patients of TLE group. Also regimen changing was also not a problem in TLE group. Adherence was far better also.

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