

COMPARATIVE STUDY OF EFFICACY OF TWO ANTIRETROVIRAL REGIMENTS (ZIDOUVDINE+LAMIVUDINE+NEVIRAPHINE VS STAVUDINE+LAMIVUDINE+NEVIRAPINE) IN HIV/AIDS PATIENTS

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ABSTRACT: BACKGROUND: AIDS, the acquired immunodeficiency syndrome, is the worst disease in the history of medicine due to HIV infection in many sexually active people. This disease is treated with two regimens of drugs in the ART centers at free of cost by the government. **AIMS AND OBJECTIVES:** To study and compare the efficacy of two antiretroviral regimens (zidovudine +lamivudine+ nevirapine) vs (Stavudine+ lamivudine +nevirapine) in HIV/AIDS patients. **Methods:** It is a longitudinal, prospective, observational study, carried at ART centers of siddhartha medical college, Vijayawada, AP and Guntur medical college, Guntur, AP from October 2006 to March 2008. **Results:** 650 patients were enrolled into study. Out of 650, 325 patients were received Tab.Zidovudine +Tab.Lamivudine+Tab.Nevirapine (Regimen A) and 325 patients were received Tab. Stavudine + Tab.Lamivudine + Tab. Nevirapine (Regimen B) in fixed drug combination. The study is designed for a Period of 12 months by recording observations at 0 months, 6months and 12months. All the cases enrolled had been studied prospectively at the ART centers and the data entered into the case sheets. The adherence to the ART is assessed by asking the patients to get the empty drug bottles and checking the number of remaining tablets. The chi-square test is applied for all the parameters after 6 months data and after 12 months data with degree of freedom (Df) of $>1=$ and $>P=$ value as 0.05 ($p=0.05$) and the level of significance as $\chi^2 > 3.84$. **CONCLUSIONS:** Stavudine containing regimen B is having better efficacy than zidovudine containing regimen A.

KEYWORDS: Acquired Immuno Deficiency Syndrome, Anti-Retroviral Therapy centers, Andhra Pradesh State AIDS Control Society, National AIDS Control Organization.

MeSHterms: Anti HIV agents (D27.505.954.122.388.077.088), HAART (E02.319.310.075)

INTRODUCTION: AIDS, the acquired immunodeficiency syndrome, is the worst disease in the history of medicine.⁽¹⁾ with 6800 people infected afresh and causing more than 5700 deaths everyday across the globe. In India more than 2.39 million people are suffering with HIV/AIDS.^(2,3,4) AIDS is caused by Human immunodeficiency virus (HIV) which belongs to retrovirus breaking down the body's immune system making the body to prone for many opportunistic infections and finally ensuing the death.^(4,5) So the WHO and UNAIDS instructed all countries to establish AIDS controlling organizations to curtail the prevalence of AIDS. Hence Govt. of India started National AIDS controlling organization (NACO) under which State aids controlling societies(SACS) are initiated in all states.⁽⁶⁾ The SACS started antiretroviral therapy (ART) centers through which HIV infected patients are diagnosed and treatment is initiated free

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of cost with the supplied drugs. In ART centers in India, NACO supplied 4-5 antiretroviral drugs which are given in two regimens of combination therapy, i.e. ZIDOVUDINE +LAMIVUDINE+ NEVIRAPINE as regimen A & STAVUDINE+LAMIVUDINE+NEVIRAPINE as regimen B for all HIV patients registered at ART centers.^(6, 7,8,9,10) So many HIV patients are flooding these ART centers and receiving these drugs continuously. There is little number of studies about the comparison of efficacy of these regimens in Indian population.⁽¹⁰⁾ In this scenario, this study is taken to compare the efficacy of these two regimens in terms of rise in CD4+T cell count, changes in the weight of patients and in reducing the frequency of opportunistic infections between the two regimens and to draw a conclusion which regimen is efficacious.

MATERIALS & METHODS: It is a longitudinal, prospective, observational study, carried at ART centers of Siddhartha medical college, Vijayawada, A.P and Guntur medical college, Guntur, A.P from October 2006 to march 2008, after the approval of college ethical committee. An informed consent was taken from each patient.

INCLUSION CRITERIA: Patients were declared as HIV +ve as per NACO guidelines in the VCTCs under the departments of Microbiology, Siddhartha Medical College, Vijayawada and Guntur Medical College, Guntur. Both males and female patients aged above 13 years. Patients enrolled at ART centers, Vijayawada and Guntur are included.

Patients with CD4 + cell count less than 200cells/cu.mm and between 200cells/cu.mm and 300 cells /cu.mm with symptomatic HIV disease.

Patients who were initiated with highly active antiretroviral therapy (HAART) by two regimens i.e., Tab.Zidovudine +Tab.Lamivudine+ Tab.Nevirapine and Tab. Stavudine + Tab.Lamivudine + Tab. Nevirapine.

EXCLUSION CRITERIA: Children below 13 years, pregnant women. Patients already used/ using ART outside and attending ART clinic and Patients with chronic renal, hepatic and heart failure.

All patients were asked to visit ART centers if they developed any symptoms or on a monthly basis. They were screened clinically and investigated suitably for any opportunistic infections. Weights of patients were measured periodically. CD4 + cell count measured with machine made by Beckson and Dickinson company, made in USA and Beckson and Dickinson kits, available at Department of Microbiology, GMC, Guntur.

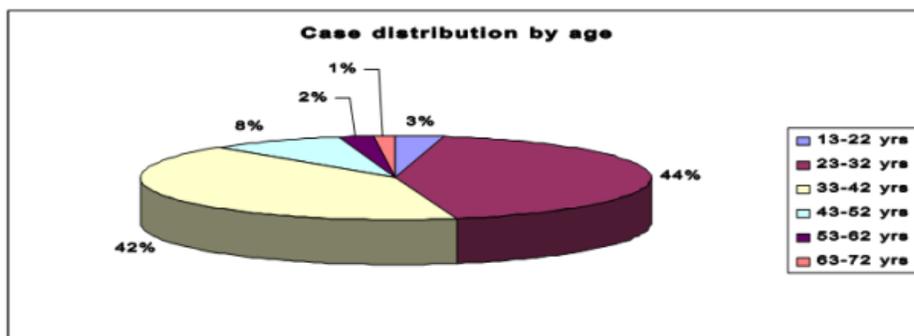
OBSERVATIONS: 650 patients were enrolled into study. Out of 650, 325 patients were received Tab.Zidovudine +Tab.Lamivudine+Tab.Nevirapine (Regimen A) and 325 patients were received Tab. Stavudine + Tab.Lamivudine + Tab. Nevirapine (Regimen B) in fixed drug combination.

The study is designed for a Period of 12 months by recording above observations at 0 months, 6months and 12months. All the cases enrolled had been studied prospectively at the ART centers and the adherence to the ART is assessed by asking the patients to get the empty drug bottles and checking the number of remaining tablets.

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The chi-square test is applied for all the parameters after 6 months data and after 12 months data with degree of freedom (df) of $>1=$ and $>P=$ value as 0.05 ($p=0.05$) and the level of significance as $\chi^2 > 3.84$.

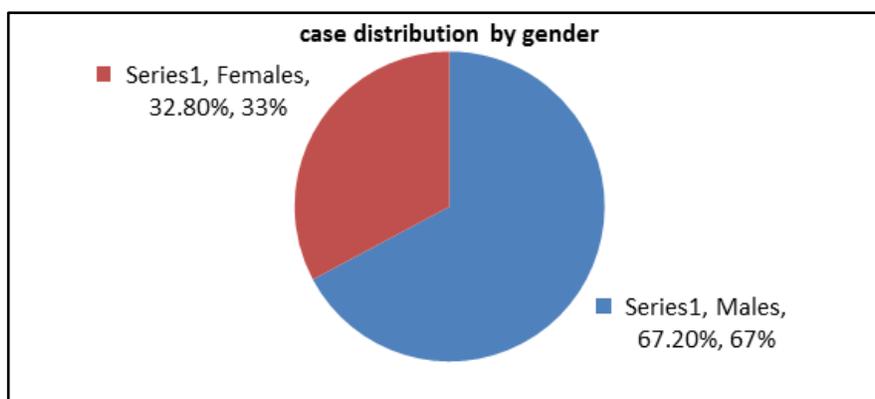
RESULTS: Distribution of cases according to age:



GRAPH NO. 1

Six hundred and fifty patients were enrolled into the study. Out of 650 patients, 3% ($n=19$) were belonged to 13-22 years, 43% ($n=279$) were belonged to 23-32 years, 42% ($n=273$) belonged to 33-42 years, 8.4% ($n=55$) were belonged to 43-52 years, 2.2% ($n=14$) were belonged to 53-62 years and 1.4% ($n=10$) belonged to 63-72 years. Maximum number of patients i.e. 43% ($n=279$) and 42% ($n=273$) belonged to 23-32 years and 33-42 years respectively.

Distribution of cases according to gender:



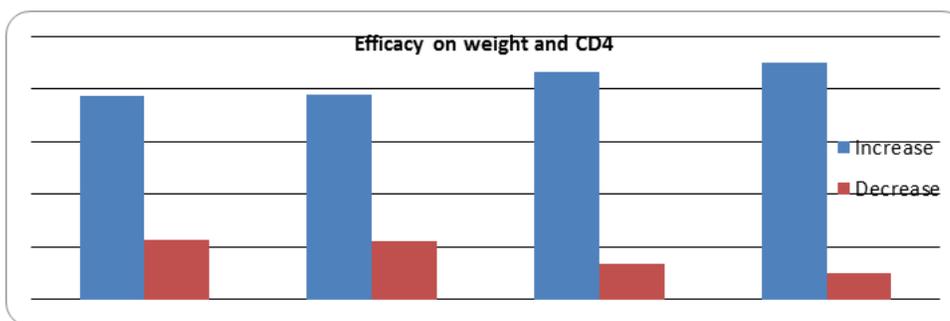
GRAPH NO: 2

Out of 650 patients, 67.2% ($n=437$) were males and 32.8% ($n=213$) were females. So more no. of males were attending ART center.

Assessment of efficacy after six months of treatment: (Df =1, P value =0.05, $\chi^2 \square 3.84$)

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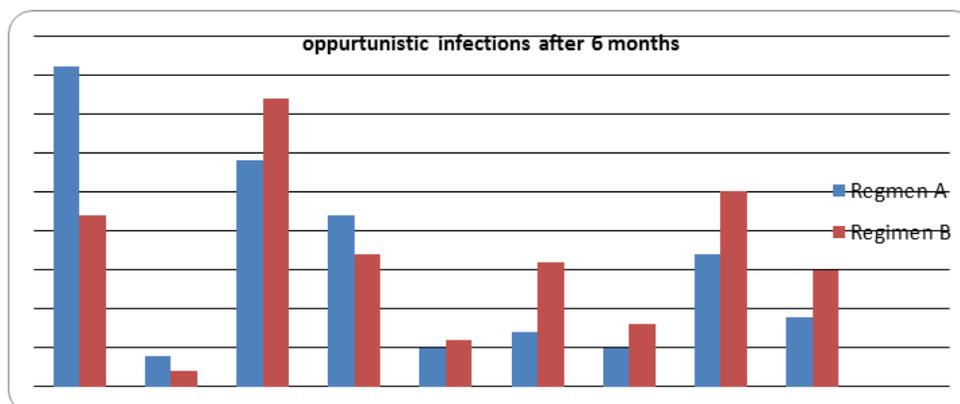
Efficacy on weight and CD4 count:



GRAPH NO. 3

In the first 6 months of treatment, 4%⁽ⁿ⁼¹³⁾ deaths and 6%⁽ⁿ⁼²²⁾ lost for follow ups (LFPs) on regimen A and 3%⁽ⁿ⁼¹⁰⁾ deaths and 6%⁽ⁿ⁼¹⁹⁾ LFPs on regimen B were lost as deaths and LFPs. So 290cases in regimen A and 296cases in regimen B were available for evaluation. After 6 months of treatment with regimen A, 77.4 %⁽ⁿ⁼²²⁵⁾ had increased weight, 86.2%⁽ⁿ⁼²⁴⁹⁾ had increased CD4+ count, After six months of treatment with Regimen B, 78 %⁽ⁿ⁼²³¹⁾ had increased weight, 90%⁽ⁿ⁼²⁶⁶⁾ had increased CD4+ count,

Assessment of opportunistic infections after 6 months:



GRAPH NO. 4

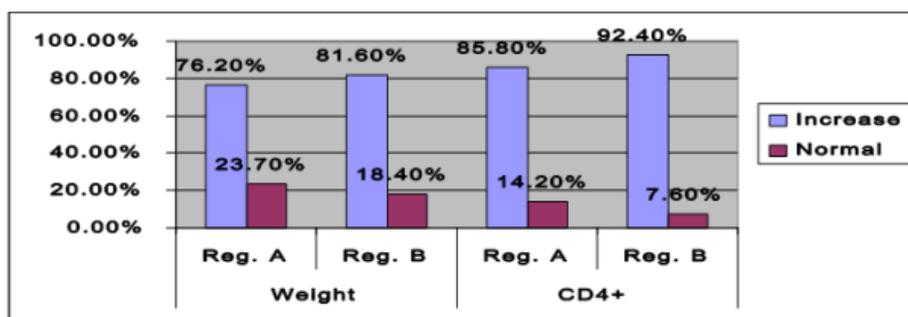
After 6 months of treatment with regimen A, 55.6%⁽ⁿ⁼¹³⁹⁾ had oppurtunistic infections and with Regimen B, 63.2%⁽ⁿ⁼¹⁵⁸⁾ had oppurtunistic Infections.

Assessment of efficacy after twelve months of treatment: (df =1, P value =0.05, $X^2 \geq 3.84$)

In the second 6 months of treatment, 6%⁽ⁿ⁼¹⁷⁾ deaths and 8%⁽ⁿ⁼²⁵⁾ LFPs in regimen A and 7%⁽ⁿ⁼²⁰⁾ deaths and 10%⁽ⁿ⁼²⁶⁾ LFPs in the regimen B occured. So 248cases in regimen A and 250cases in regimen B were available for evaluation.

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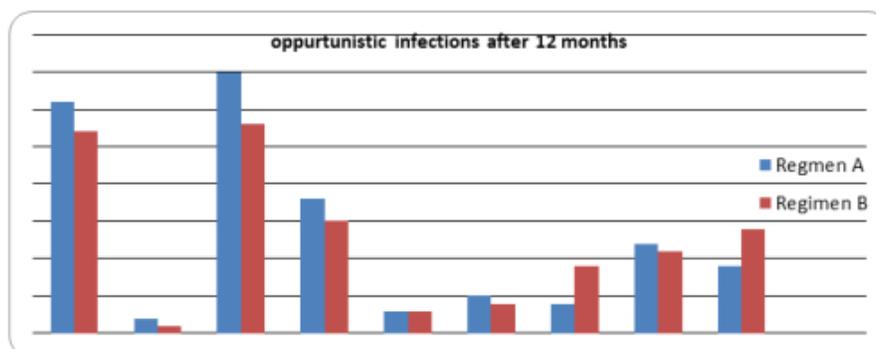
Efficacy on weight and CD4 count:



GRAPH NO: 5

After twelve months of treatment with regimen A, 76.2 %⁽ⁿ⁼¹⁸⁹⁾ had increased weight, 85.8 %⁽ⁿ⁼²¹³⁾ had increased CD4+ count, with Regimen B, 81.6 %⁽ⁿ⁼²⁰⁴⁾ had increased weight, 92.4 %⁽ⁿ⁼²³¹⁾ had increased CD4+ count,

Assessment of opportunistic infections after 12 months:



GRAPH NO: 6

After twelve months of treatment with regimen A 41 %⁽ⁿ⁼¹¹⁹⁾ had opportunistic infections and with regimen B 112%⁽ⁿ⁼¹¹²⁾ had opportunistic infections.

CONCLUSION: National Aids Control organization (NACO) is offering antiretroviral drugs for the needy HIV/AIDS patients all over India through established ART centers(6). Most common ART regimens offered by NACO are AZT +3TC+NVP & d4T +3Tc + NVP (9). The introduction of HAART has led to significant reduction in AIDS related morbidity and mortality (1, 10). In this scenario, pertained to the available resources at our center, we sought to study efficacy and compare these ART regimens for a period of one year.

This study shown an improvement in CD4+ cell count, weight gain and decreased opportunistic infections with Stavudine containing regimen B, which is slightly better than Zidovudine containing regimen A. During this study, there are 60 deaths and 92 lost for follow ups (LFPs) which is a serious problem. 23.3 %⁽ⁿ⁼¹⁵²⁾ patients losing in the form of deaths and LFPs

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was highly significant. David A. Kessler,⁽¹¹⁾ FDA commissioner reported that the increase in CD4 count was observed in 75% patients with azidothymidine regimen and 90% patients with stavudine regimen. While in this study an increase in CD4 count was observed in 85.8 %⁽ⁿ⁼²¹³⁾ patients and 92.4%⁽ⁿ⁼²³¹⁾ patients, an increase in weight was observed in 76.2 %⁽ⁿ⁼¹⁸⁹⁾ patients and 81.6 %⁽ⁿ⁼²⁰⁴⁾ patients with regimen A and regimen B respectively. The incidence of opportunistic infections was observed in 41 %⁽ⁿ⁼¹¹⁹⁾ patients and 37 %⁽ⁿ⁼¹¹²⁾ with regimen A and regimen B respectively. The cause of deaths and LFPs could not be found as it was beyond the scope of this thesis. So we could not investigate. But yet the reasons could not be ignored and left unexplained. The possible reasons might be the disease itself, due to non-adherence, increased opportunistic infections, lack of nutrition, again non-adherence due to ADRs and drug resistance etc. So the death enquiry and auditing should be done. To conclude based on above observations stavudine containing regimen B is having better efficacy, than zidovudine containing regimen A.

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