Evaluation of the effects of anti-retroviral drug regimen (Stavudine + Lamivudine + Nevirapine) on CD4 count, body weight, and haemoglobin of HIV positive patients: A retrospective study


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Abstract

Human immunodeficiency virus infection (HIV) has become a manageable disease due to antiretroviral therapy. Although many treatment schedules are effective in controlling the viral load, maintaining it for a long period is difficult due to many factors such as adverse effects, long-term toxicity, and dosing schedules, all of which may result in poor patient compliance, treatment failure and drug resistance. The evaluation of these treatment schedules in terms of their efficacy, duration, and acceptance is an important aspect for treating doctors, patients, and policy makers. Therefore, our objective is to evaluate stavudine, lamivudine, and nevirapine regimen in the management of HIV infection in our hospital. Methodology: An observational study was done in the ART centre of CG Hospital, Davanagere. The data were collected for the duration of 12 months (June 2012 to May 2013). Institutional ethics committee approval was taken before the initiation of the study. For inclusion in the study, the patients had to be antiretroviral (ARV) naive and receiving their ARV medication i.e., a combination of stavudine, lamivudine, and nevirapine therapy through the Government ART Program. Results: Among the 94 patients included, CD4 count after 6 months of treatment was 303 cells/mm³ as compared to the initial count of 163 cells/mm³. Likewise, an improvement was recorded in hemoglobin level and body weight by approximately 2g% and 3 kg, respectively. Conclusion: In the present study, there was a significant improvement in CD4 count, body weight, and haemoglobin level when compared to the initial, after 6 months of treatment with combination therapy of stavudine, lamivudine and nevirapine. However, there was no difference in response between the severe ill patients (CD4 count < 200 cells/mm³) when compared to the patients with CD4 count ≥ 200 cells/mm³. HIV infection can be tackled by a combined approach of multidrug therapy to prevent resistance and community based approach with good nutritional and dietary supplementation.

Key words: ART Regimen, CD4 Counts, Body Weight, Anaemia

Introduction

The human immunodeficiency virus (HIV) infection has become a manageable disease due to antiretroviral therapy (ART).

Improved the mortality, morbidity, and the quality of life among the HIV infected patients.

According to WHO estimate 1.1 million Asians are currently in need of the ART, but only 6%–7% having access to it. No doubt that the antiretroviral treatment has reduced AIDS-related
death. Approach to therapy is not universal, and the possibility of curative therapy and a successful vaccine are indeterminate.4

The implementation of the ART regimen has been plagued by certain serious pitfalls, amongst which the exorbitantly high costs, weak infrastructure, an utter lack of specialized care and human resources figure prominently.

Despite being a multitude of ART regimens with ability of lowering plasma viral loads below detectable limits, optimization of their durability, safety and ease of administration have hampered their implementation. Further, the toxicity seen with protease inhibitors (PI) use has propelled non-nucleoside reverse transcriptase inhibitors (NNRTIs) into the frontline as a part of the initial regimen.1

Nevirapine (NVP) in combination with stavudine (d4T) and lamivudine (3TC) has emerged as the most popular choice of the first line ART, in both the developed and the under-developed regions. Hence, this warrants that all the stakeholders so involved be aware of its anti-retroviral efficacy, durability, and safety profile.5

Therefore, our objective is to evaluate the combination of stavudine, lamivudine, and nevirapine in the treatment of HIV infection in our hospital.

Objectives
1. To evaluate the efficacy of the combination of Stavudine, Lamivudine, and Nevirapine of ART regimen in the treatment of HIV infection in our hospital.
2. To check the magnitude of response in severely ill patients and non-severely ill patients.

Materials and Methods
Study Design: This was a retrospective study. The study site was ART centre of CG Hospital, Davanagere. The data was collected for the duration of 12 months (June 2012 to May 2013). Ethics committee approval was taken before initiation of the study. Permission was also obtained from the officer in charge of the ART centre to access the records. Prescriptions of the patients were collected and the relevant information was entered in the preformed proforma and analysed.

Study Population: Patients belonging to different age groups, visiting the HIV clinic between the periods from 1 January 2010 to 30 September 2012 were included in our study. Only the patients who were either the ART naïve or receiving the combination of stavudine, lamivudine, and nevirapine (SLN) through the government ART program were included in our study. Further, in the case of the patients on SLN regimen, only those subjects who were compliant for a period of six months were included in our study. Exclusion criteria involved unreliable data on baseline characteristics and ART history as well as initiation of a second ART regimen on admission and unavailability of baseline CD4 values.

Study Setting: Outpatient at ART centre of CG Hospital, a tertiary care centre in Davanagere.

Sample Size: During the period of 12 months (June 2012 to May 2013), 94 case sheets of the patients diagnosed to have HIV infection and meeting the inclusion criteria were studied.

Informed Consent: Informed consent of the patients was not taken (as it was a retrospective study) and the data obtained was kept confidential.

Statistical methods
In this study, the data was analysed using Descriptive Statistics. Analysis to check for the changes after 6 months of the treatment in the parameters such as CD4 counts, haemoglobin, and body weight was carried out. Wilcoxon matched pairs signed rank test was applied to compare the CD4 counts. Paired t test was applied to compare the weight and the haemoglobin levels before the treatment and after 6 months of treatment. An unpaired t test was applied between the groups to check for the response.

Results
Demographic Profile of the Study Population: The Demographic characteristics of the patients are shown in Table 1. In this study, 94 case records were evaluated. Out of these 16 cases belong to paediatric age group (≤ 14 years) of which 9 were males and 7
females. Remaining 78 cases were of the age group between 15 and 65 years of which 18 were males and 60 females.

Table 1: Demographic characteristics of HIV infected individuals receiving the combination therapy – stavudine, lamivudine, and nevirapine (SLN)

<table>
<thead>
<tr>
<th>Age group</th>
<th>Total</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 14 years</td>
<td>16</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>15-65 years</td>
<td>78</td>
<td>18</td>
<td>60</td>
</tr>
</tbody>
</table>

Table 2: CDC classification of HIV infected individuals based on their baseline CD4 counts

<table>
<thead>
<tr>
<th>CD4 counts (cells/mm³)</th>
<th>Total</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;500</td>
<td>4</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>200-499</td>
<td>34</td>
<td>8</td>
<td>26</td>
</tr>
<tr>
<td>&lt;200</td>
<td>54</td>
<td>16</td>
<td>38</td>
</tr>
</tbody>
</table>

In the present study, we divided the patients into 2 groups based on the baseline CD4 counts < 200 cells/mm³ as group A and ≥ 200 cells/mm³ as group B.

The efficacy parameters in our present study are the response to treatment which can be evaluated by knowing the increase in the CD4 counts when compared to the baseline, the improvement in the Hb percentage, and the bodyweight.

In the present study, we divided the patients into 2 groups based on the baseline CD4 counts < 200 cells/mm³ as group A and ≥ 200 cells/mm³ as group B.

Another efficacy parameter assessed was the bodyweight and its median and IQR after the treatment was 45 (37 - 52) kg compared to 42 (32.75 - 50) kg at the baseline which was statistically significant (p < 0.0001).

The Hb percentage which we have considered as the efficacy parameter showed significant increase i.e., median and IQR 11.18 (9.8 – 12.12) g% after 6 months of treatment when compared to the baseline value 9.35 (8.11 – 11.18) g% which was statistically significant (p < 0.0001).

Both the groups were compared based on the three parameters – CD4 count, bodyweight, and Hb level. There was no significant difference between the two groups in response to the treatment that is in patients with CD4 counts < 200 cells/mm³ and ≥ 200 cells/mm³. By this, we can say that the severely ill patients respond equally to the treatment regimen with the combination of stavudine, lamivudine, and nevirapine.

Discussion

The present study was intended to evaluate the efficacy of the combination stavudine, lamivudine, and nevirapine in the community without the consideration of coexisting illnesses. A multitude of reasons, including enhanced potency of drugs, better tolerability, and compliance have ensured a greater viral suppression rates with the existing ART regimens in comparison to the other host of initial multi-drug therapies. In clinical trials, 70% of the patients recorded sustained periods of viral suppression with the ART regimens. The efficacy parameter considered for the analyses was CD4 counts, which is one of the important parameters utilized for monitoring the patient on ART treatment. Along with this, the hemoglobin level and the bodyweight were considered for the evaluation of efficacy. In our study, we have observed...
an improvement in the CD4 counts after 6 months of ART therapy with increase in hemoglobin level. There was also increase in the body weight in the treatment group.

A study revealed that the SLN regimen is associated with the increased durability of anti-retroviral activity and better immunological response in patients with advanced HIV infections. A switch to another drug can mitigate the concerns with the long-term safety of stavudine by an appropriate time. However, this strategy needs a further evaluation.6

Another study done by Desakorn V et al., showed that the SLN regimen had increased the CD4 cell count and the bodyweight with reduction in opportunistic infections. Thus, they concluded that the SLN regimen had both clinical and immunological benefits but one third of the patients had adverse effects.7

One more study by Getahun A showed that the SLN was well tolerated and effective in increasing the CD4 counts and suppressing plasma viremia in the advanced HIV infections during the 48-week follow-up periods.8

A Nigerian study revealed that the SLN regimen had produced excellent viral suppression, enhanced immunological response, and a relatively better quality of life for the patients over the 12-month treatment period.9

The efficacy of SLN regimen received a shot in the arm from the results of a study conducted in the United States of America, which showed that the SLN remained effective irrespective of prior treatment or baseline viral loads.10

An optimal virucidal efficacy, durability of its anti-retroviral action, easy tolerability, least possibility of adverse effects with minimal drug-drug interactions are the hallmarks of an ideal initial ART regimen. In regions with recorded ZDV resistance, d4T can be used instead. Some of the commonly observed adverse effects include peripheral neuropathy, lipoatrophy, steatohepatitis and hyperlactaemia. 3TC use is associated with a host of adverse effects like anaemia, gastrointestinal upset, myalgia, and very rarely pancreatitis. Further, its efficacy may be hampered by the presence of a single M184V gene mutation, which has been observed to confer a high level of resistance.5

NNRTIs score over PIs, in terms of their better safety profile, pharmacokinetic features, and ease of administration. However, a single gene mutation rendering the NNRTIs impotent is a serious drawback associated with its use. Furthermore, the fatal hepatotoxicity associated with NVP use requires that close tabs be kept on the initial treatment regimen.5

Despite these above-mentioned factors, the SLN has remained as the cornerstone around which the World Health Organization (WHO) guidelines for ART in resource-starved settings have been built. A recent study carried out in Cameroon revealed that the SLN treatment produced undetectable viral load in 80% of the study subjects. Additionally, the SLN was well tolerated, with treatment being withdrawn in only one patient due to the development of a cutaneous adverse reaction following NVP administration.5

Since the current strategies formulated by WHO are voluntary counselling and testing and provider initiated testing and counselling which is inadequate for the control of this communicable disease, there is a need to develop new strategies by the government. The reason for no improvement in weight to an optimal level may be the post HIV depression where one of the signs of depression is the loss of weight and another reason is cachexia associated with HIV infection.

Limitations

This was a retrospective study. After reviewing the records, we could capture data consistently until 6 months. After 6 months, i.e., at 1-year, 2-year we had planned to capture the efficacy parameters. Mostly patients were not adherent to the treatment in our hospital but they were referred to higher centres. Since HIV RNA is not a part of the ART program, the data could not be captured.
Conclusion

In the present study, there was a significant improvement in the CD4 counts, the body weight, and the haemoglobin level when compared to the baseline, after 6-month treatment with the combination therapy of stavudine, lamivudine, and nevirapine. However, there was no difference in response between severe ill patients (CD4 counts < 200 cells/mm³) and patients with CD4 counts ≥ 200 cells/mm³.

Bibliography


