Oxygen transport potential of blood of HIV patients on highly active antiretroviral therapy in Benin city, Nigeria

Richard Omoregie, Faith Huemomen Unuabonah and Ehijie Xavier Iyamah

Abstract

Aim: This study aimed to determine the effect of highly active antiretroviral therapy (HAART) therapy on the oxygen transport potential of blood of HIV patients. The impact of CD4 count and anaemia on the oxygen transport potential was also assessed.

Methods: Blood was collected from 255 subjects consisting of 207 HIV patients on HAART therapy for 3 – 6 months and 48 apparently healthy HIV seronegative individuals. Haematocrit, haemoglobin, whole blood viscosity, oxygen transport potential and CD4 T-lymphocyte count were determined using standard techniques.

Results: Haematocrit values and oxygen transport potential of blood of HIV patients were significantly lower than those of non-HIV individuals (p<0.0001 and p=0.0262, respectively). In relation to the CD4 count, only blood viscosity of HIV patients on HAART differed significantly between HIV patients with CD4 count <200 cells/μL and non-HIV subjects (p=0.0361), while oxygen transport potential did not differ between HIV patients with CD4 count ≥200 cells/μL and their non-HIV counterparts (p=0.0717). Anaemic state significantly lowered blood viscosity (p<0.0001) and oxygen transport potential (p=0.0217) of HIV patients on HAART without any significant effect (p=0.05) on the same parameters in non-HIV individuals.

Conclusions: Oxygen transport potential of blood is lower in HIV patients on HAART and is affected independently by anaemia and CD4 count. Measures to improve immunity and anaemic status of HIV patients on HAART are advocated.

Keywords: anaemia, CD4 count; blood flow, haematocrit-blood viscosity ratio, oxygen transport potential, highly active antiretroviral therapy (HAART)


Introduction

Transport of oxygen from the lungs to tissues is a principle function of red blood cells and anything that affects blood flow will affect this function. Previous research has indicated that in patients with human immunodeficiency virus (HIV) infections the blood flow is defective (1). Erythrocyte aggregation is a determinant of blood flow (2) and the haematocrit value affects the erythrocyte sedimentation rate which in turn affects erythrocyte aggregation and ultimately blood flow (3), leading to reports that haematocrit are lower in HIV patients (4).

Anaemia is the most commonly encountered haematological abnormality in HIV patients, and is a significant predictor of progression towards acquired immunodeficiency syndrome (AIDS) or death, with more than 70% of patients developing anaemia and requiring blood transfusions (5). Highly active antiretroviral therapy (HAART) entails treatment with a combination of two nucleoside reverse transcriptase inhibitors and potent protease or non-nucleoside reverse transcriptase inhibitors, and has generally been taken as the gold standard for the management of HIV patients (5). HAART has been reported to increase haemoglobin concentration and reduce the prevalence of anaemia (5,6). However, anaemia is still reported in this group of patients (6,7). In addition, the use of protease inhibitors has been reported to increase the risk of cardiovascular disease (8) and thus affect blood flow. In our Institution the HAART regime does not include protease inhibitors and thus provided the opportunity to investigate the oxygen transport potential of blood from HIV infected patients receiving HAART therapy. To our knowledge, the oxygen transport potential of blood of HIV patients on HAART has not previously been studied. In this study we report the oxygen transport potential of blood of HIV patients on HAART, including the effect of anaemia and CD4+ T-lymphocyte count on the oxygen transport potential.

Materials and methods

Study population

The study was conducted in the University of Benin Teaching Hospital, Benin City, Nigeria – a tertiary hospital with a referral status. A total of 255 subjects consisting of 207 HIV patients on HAART for 3 – 6 months and 48 apparently healthy HIV seronegative individuals, were recruited for this study. The age range of all subjects was 20 to 55 years. The HIV patients were out-patients and asymptomatic for any illness, especially ones that can affect their blood rheology. The non-HIV subjects were out-patients and asymptomatic for any illness, especially ones that can affect their blood rheology. The non-HIV subjects were out-patients and asymptomatic for any illness, especially ones that can affect their blood rheology. In our Institution the HAART regime of our HIV patients included zidovudine, reverse transcriptase inhibitors, and has generally been taken as the gold standard for the management of HIV patients. Highly active antiretroviral therapy (HAART) entails treatment with a combination of two nucleoside reverse transcriptase inhibitors and potent protease or non-nucleoside reverse transcriptase inhibitors, and has generally been taken as the gold standard for the management of HIV patients.
that of water. The ambient temperature of our laboratory was 25 ± 2°C during the period of the study.

The oxygen transport potential of blood specimens was calculated as the ratio of haematocrit to blood viscosity (11).

Statistical analysis
The parametric data were analyzed by student t-test while the non-parametric data were analyzed by Chi square ($\chi^2$) test and odd ratio analysis. The statistical software, INSTAT® (Graph Pad Software Inc., La Jolla, CA, USA) was used for all statistical analysis.

Results
Haematocrit values and oxygen transport potential of blood of HIV patients on HAART were significantly lower compared to that of non-HIV individuals (p<0.0001 and p=0.0262, respectively). However, blood viscosity did not differ significantly (p=0.0569) between both groups (Table 1).

Table 1. Haematocrit, blood viscosity and oxygen transport potential of HIV and non-HIV subjects

<table>
<thead>
<tr>
<th>Parameters</th>
<th>HIV patients (n=207)</th>
<th>Non-HIV subjects (n=48)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haematocrit (%)</td>
<td>34.14 ± 0.40</td>
<td>39.30 ± 0.75</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Blood viscosity</td>
<td>5.33 ± 0.08</td>
<td>5.81 ± 0.23</td>
<td>0.0569</td>
</tr>
<tr>
<td>Oxygen transport potential (%)</td>
<td>6.57 ± 0.08</td>
<td>7.15 ± 0.24</td>
<td>0.0262</td>
</tr>
</tbody>
</table>

Figures are mean ± SEM.

HIV patients with CD4 count <200 cells/μL had significantly lower haematocrit values than HIV patients with CD4 count ≥200 cells/μL (p=0.0014) and non-HIV subjects (p<0.0001). Similarly, HIV patients with CD4 count ≥200 cells/μL had lower haematocrit values than non-HIV subjects (p<0.0001). Blood viscosity were only significantly (p=0.0361) different between HIV patients with CD4 count <200 cells/μL (mean ± SEM: 5.13±0.22) and non-HIV individuals (mean ± SEM: 5.81±0.23). HIV patients with CD4 count <200 cells/μL had significantly lower oxygen transport potential of blood compared with HIV patients with CD4 count ≥200 cells/μL (p=0.0001) and non-HIV subjects (p=0.0001) (Tables 2 and 3).

Table 2. Effect of CD4 count on haematocrit, blood viscosity and oxygen transport potential of HIV patients

<table>
<thead>
<tr>
<th>Parameters</th>
<th>HIV patients with CD4 count (cells/μL)</th>
<th>Non-HIV subjects (n=48)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haematocrit (%)</td>
<td>29.95 ± 1.36</td>
<td>34.90 ± 0.38</td>
<td>0.0001</td>
</tr>
<tr>
<td>Blood viscosity</td>
<td>5.13 ± 0.22</td>
<td>5.36 ± 0.09</td>
<td>0.0217</td>
</tr>
<tr>
<td>Oxygen transport potential (%)</td>
<td>5.88 ± 0.17</td>
<td>6.68 ± 0.09</td>
<td>0.1601</td>
</tr>
</tbody>
</table>

Results are mean ± SEM.

Discussion
The major function of red blood cells is to transport oxygen from the lungs to the tissues and cells where it is used for energy generation. HIV patients have been reported to have lower haematocrit values and higher prevalence of anaemia than non-HIV individuals (4,6). HAART has been reported to improve haematocrit values and reduce the prevalence of anaemia (5), however, anaemia is still been reported among HIV patients on HAART (6, 7) and to date there is no report on the effect of HAART on oxygen transport potential of red blood cells of HIV patients.

The finding that HIV patients on HAART have significantly lower haematocrit values than non-HIV individuals agrees with a previous study (4). The cause of anaemia in HIV-positive patients is multi-factorial and includes infections, neoplasm, dietary deficiencies, blood loss, medications, inclusion of zidovudine in the HAART regimen and antibodies to antiretroviral agents (4,12). Zidovudine is among the HAART agents used in this study. The blood viscosity did not differ significantly between HIV and non-HIV subjects. Although haematocrit values affects blood viscosity (13), the non-significant difference in blood viscosity of HIV patients compared with their non-HIV counterparts is surprising. However, haematocrit values reflect both red cell number and dimensions (13) and HIV patients on HAART (zidovudine – containing HAART regime) have larger red blood cells as evidenced by higher mean cell volume (4). Therefore, the increase dimension of red blood cells may affect blood viscosity and may explain the findings in this study.

The oxygen transport potential of red blood cells of HIV patients on HAART was significantly lower than that of non-HIV individuals, indicating that HIV patients on HAART may still experience fatigue, loss of stamina and reduced quality of life.

Immunosuppression (CD4 count <200 cells/μL) resulted in significantly lower haematocrit values compared with HIV patients with CD4 count ≥200 cells/μL and non-HIV subjects. CD4 counts of <200 cells/μL has been reported to be associated with opportunistic infections (14). Our HIV patients were asymptomatic for any infection. However, asymptomatic infections have been reported among HIV patients on HAART with CD4 count <200 cells/μL (15) and some of these infections are associated with anaemia (15, 16). Infection has also been reported as one of the causes of anaemia in HIV patients (12). Immune competent HIV patients (with CD4 count ≥200 cells/μL) still have lower haematocrit values than non-HIV subjects.
This agrees with a previous report (4) and we surmise that antibody production against HAART agents may be responsible (4).

HIV patients with CD4 count <200 cells/μL had significantly lower blood viscosity than non-HIV subjects (p=0.0361) as well as lower oxygen transport potential than those with CD4 count ≥200 cells/μL and non-HIV subjects. This indicates that immunosuppression (defined as CD4 count <200 cells/μL) among HIV patients on HAART affects oxygen transport potential of their red blood cells. Thus, immune reconstitution may improve oxygen transport potentials. The HIV patients used in this study had been on HAART for 3 – 6 months. Perhaps, longer duration of HAART may improve immunity and ultimately oxygen transport potential. Further studies are required to verify this.

Anaemia significantly reduced the blood viscosity and oxygen transport potential of HIV patients. While among non-HIV subjects, anaemia did not significantly alter their blood viscosity and oxygen transport potential, the reason for this is unclear. However, anaemia was significantly associated with HIV status (HIV versus non-HIV: 72.46% vs. 14.58%; OR=15.41; 95%CI: 6.54- 36.35, p<0.0001) and is in agreement with a previous study(7). Like CD4 count <200cells/μL, anaemia affects oxygen transport potential of blood of HIV patients on HAART. But anaemia was not significantly associated with CD4 count <200 cells/μL (OR= 2.87; 95%CI: 0.95-8.63, p = 0.0847). This may indicate that anaemia and CD4 count <200 cells/μL independently affect oxygen transport potential of blood of HIV patients on HAART. Measures to improve immunity and anaemic status of HIV patients on HAART are advocated as they will ultimately improve oxygen transport potential.

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