Introduction

The Acquired Immune Deficiency Syndrome (AIDS) that hit the world in 1981 spread worldwide. Twenty million people have died from AIDS and every day fourteen thousand people thereabout contract the virus. Due to the use of medicines, studies that aim to eradicate the disease have been successful. However, these substances can harm the human body because they change the immune system and hematological system. Induced by low absorption of iron, folic acid and vitamin B12, the anemia is a risk factor that contributes to these alterations. The changes are seen when these values are compared to the reference values of the full blood count.

Keywords: AIDS; Anemia; Epidemiology.

Abstract

The Acquired Immune Deficiency Syndrome (AIDS) was recognized in 1981, in the USA, through the identification of a high number of male and homosexual patients that lived at San Francisco, who presented the typical characteristics of the disease: Kaposi's sarcoma, Pneumocystis carinii pneumonia, and immune system impairment [1].

The Human Immunodeficiency Virus attacks immune cells, mainly the CD4 cells. As a result, the person starts showing some symptoms such as loss of weight, bubo, fever, sweating, and loss of memory. Furthermore, the person is more likely to acquire other diseases. These diseases, named opportunistic infections, are responsible for leading the individual to death [2].

In Brazil the first confirmed cases of AIDS date from 1982, in São Paulo. Since the 80's there are around 600 thousand Brazilians infected by the human immunodeficiency virus. More than 80% of these people live at south and southeast region [3].

AIDS is a disease that represents one of the biggest health problems of the society nowadays. In Brazil, 506,499 cases of AIDS were registered since 1980 to June 2008. The total of death due to AIDS until 2007 is 205,409. In 2006, the disease reached 17.5/100,000 of the population, and the men/women proportion was 1.5/1 [1].

As a result of the 1% increase on the rate of infected women, the percentage of vertical transmission has grown. Around 1996-1997, 90.1% of pediatric AIDS cases were acquired during the perinatal period, and only 1.7% was acquired by blood transfusion or blood derivatives. In 1985, homosexuals leaded the ranking of HIV positives; followed by bisexuals, drug users and heterosexuals, whereas in 1997 heterosexuals occupied the first position, followed by homosexuals and drug users [4].

If a child gets the virus, all her body systems may be impaired. Since the beginning of the infection hematological changes with multifactorial etiology are noticed, and they become more severe and frequent over time. Anemia is the most common finding, followed by lymphocytopenia, leukopenia, hyposegmentation of neutrophils, thrombocytopenia, myelodysplasia, atypical and vacuolated monocytes [4].

The rate of anemia on HIV positive children varies from 16% to 94% and the microcytic (56%) and hypochromic (40%) forms are predominant. On the other hand, adults usually present the normocytic and the normochromic forms of anemia. When macrocytosis occurs, it is due to the use of AZT [4].

About 43% to 47% of the infected children present leukopenia and neutropenia. The variation in the rates of lymphopenia in these children is due to the different stages of development of the disease in the studied groups. It was presented by 50% of the patients on Sandhaus & Scudder work, 36% on Ellaurie et al (1990) work and on 78% according to Suarez et al. (1994) [5].

In children, thrombocytopenia may be an initial manifestation of...
HIV infection. It occurs between 8% to 33% of the cases [6].

Due to the suppressive effect of the virus, HIV infection may present a large number of hematologic abnormalities such as ineffective hematopoiesis, bone marrow's diseases, peripheral consumption post splenomegaly, or immune deregulation and nutritional deficiency [7].

Anemia is a very common finding on asymptomatic HIV positives that is seen on 30% of them. Looking at those who have any clinical manifestation of AIDS, anemia is presented by 80% of them. Usually, this is a multifactorial condition [2].

In clinical practices, the most prevalent types of anemia are microcytic and hypochromic. Among them, we highlight iron deficiency anemia and anemia post chronic disease. Megaloblastic anemia is a normochromic and macrocytic form of anemia and it occurs as a result of changes in the metabolism of folic acid and/or vitamin B12. Although the low serum levels of vitamin B12 are presented by 1/3 of the adults, most of these individuals do not have megaloblastic anemia [7].

Anemia is a disease that causes some systemic manifestations. Considering that blood plays an important role at tissue oxygenation, it is extremely important that HIV-positive patients have frequent monitoring of hemoglobin levels, mainly because anemia is a very common disease in those patients and it may be one of the side effects of the medicines that they take, and it is a crucial factor for patients adherence to the treatment.

This is a literature review that aims to evaluate the full blood count of patients who have AIDS, taking into account that the medicines they use can intervene on iron, folic acid and vitamin B12 absorption, leading to anemia.

**Development**

**Human Immunodeficiency Virus--HIV**

HIV is a retrovirus with RNA genome, of the Retrovidae (retrovirus) family, Lentivirinae subfamily. It belongs to the cytopathic and non-pathogenic group that needs the reverse transcriptase to multiply. This enzyme is responsible for transcribing the virus RNA to a DNA copy that goes to the genome of the host [8].

The virus package has two glycoproteins: gp41 and gp120. The virus core contains three structural proteins: p24, p16 and p9. Protein p24 is a part of the virus capsid that stores two RNA strand and the virus enzymes. The genome has nearly 10000 nucleotides (10Kb) and is composed by the genes gag, env and pol, that encode respectively the structural proteins of the virus core, glycoprotein gp120 e gp41 (which helps the virus fix and enter the cell), and the enzymes Reverse Transcriptase (RT), integrase and protease. Furthermore, the genes tat and rev are essential to the virus replication, as well as to the virus transcription [9,10].

Some accessories genes contribute to the virus replication. They act on stages of the process, like the assembly procedure of the virus structure, the transportation of viral genome to the nucleus, modulation of the transduction signal. They also increase the infectious power of the virus and help the virus to get into the cells that have CD4 [11].

**HIV Etiology**

The first HIV infections started to be noticed during the half of the twentieth century. These clinical reports show that the disease came up on Central Africa, probably through mutation on monkeys' viruses. Some researchers try to explain how the transmission from monkey to human occurred, and it seems to be related to the close relationship between Africans and those animals. Biting, scratches, or the habit of eating monkey meat containing virus on its fluids contributed to the virus dissemination and then it was spread over the world [12,13].

The first relates of AIDS date from 1981, at USA. They occurred on adults, homosexuals, male individuals that died due to Kaposi's sarcoma and Pneumocystis carinii pneumonia, alongside with an important diminution at lymphocytes T CD4+ counting. However, other retrospective studies show that the human immunodeficiency virus had been isolated on Africa in a sample that dates from 1959 [14,15].

**HIV Physiopathology**

The human immunodeficiency virus has a preference for cells that show a CD4 molecule on their surface, mainly T-CD4 lymphocytes, T-helper and macrophages. The CD4 molecules acts as virus receptors and help them to get into the cell. However, other molecules as chemokine receptors CCR5 e CXCR4 play an important role at this procedure [16,17].

**HIV Transmission**

AIDS is classified as a STD (Sexually Transmissible Disease), so its main via of transmission is a sexual intercourse. A mother can also transmit the virus to a child during pregnancy, childbirth, breastfeeding. The contact with fluids that contain the virus (blood, semen, vaginal discharge) can also transmit the disease [10].

Even though the virus was found at saliva, urine and tear, researchers have found that it is impossible to acquire the virus by the contact with these fluids as well as by insect bites, non-sexual contact, aerosols, etc. [18]

**HIV Diagnosis and Prevention in Brazil**

The serological diagnosis of HIV is made in two stages. The first one is a screening through high sensibility tests (immunoassay), and in the second one the confirmation is obtained through high specificity tests (molecular tests). Those who were diagnosed with the virus are also submitted to a third stage in which their viral load is quantified [19].

HIV prevention, as well as other sexual transmitted diseases, occurs basically by making the population aware about the disease...
and the preventive ways. Condom distribution, the addition of sexual education at schools, and the explanation about pathways of contamination other than sexual are measures that were taken to prevent the disease [20].

**HIV Treatment**

Studies regarding HIV replication cycle identified some macromolecules that work as a target that is susceptible to therapeutic intervention. The medicines, known as anti-retroviral medication, target two main enzymes: Reverse Transcriptase (RT) and Reverse Protease (RP). On both situations the medicine works as an enzyme inhibitor [21].

Reverse Transcriptase Inhibitors (RTI) are classified in nucleosides and non-nucleosides. In the first case, the inhibitors adhere to the virus’ DNA chain through Reverse Transcriptase and cause a failure at the chain, preventing the virus from reproducing. The main agents are Zidovudine (AZT), Abacavir, Didanosine (ddI), Lamivudine (3TC), Stavudine (d4T) and the association Lamivudine/Zidovudine. On the other hand, the non-nucleosides RTIs block the enzyme action and virus reproduction directly. The main agents are Efavirenz, Nevirapine, Etravirine and Delavirdine [22].

The Protease Inhibitor drugs (PI) act at the final stage of development of HIV, preventing Protease Inhibitor enzymes from dividing the protein chain that the cell produce into viral protein and enzymes that compose the nucleus of each HIV particle. The main agents of this group are Atazanavir, Darunavir, Fosamprenavir, Indinavir, Lopinavir/r, Nelfinavir, Ritonavir, Saquinavir e Tipranavir [23].

The monotherapeutic regime is taken as ineffective, thus a combination of antivirals that target HIV RP and RT is more suitable. This combination usually has two or three RTI and one RPI. It is popularly named “cocktail” and known as HAART (Highly Active Anti-Retroviral Therapy) [21,24,25,26,27,28].

**Anti-retroviral Medicines**

The knowledge regarding the human immunodeficiency virus had a huge evolution, especially on the anti-retroviral treatment. Originally, the drug of choice was Zidovudine (AZT) in a monotherapeutic regime. Nearby 1994 and 1996 a combination between two medicines was introduced. In 1996 protease inhibitor finally started to be used and we had a triple therapy. Through the new therapeutic techniques it has been possible to decrease or even make undetectable the HIV charge on patients and therefore the morbimortality related to AIDS reduced [24,29,30].

The insertion of the anti-retroviral therapy provides a huge progress on AIDS treatment. However, the side effects caused by all the medicines such as gastric intolerance, nausea, vomit and abdominal pain discourage patients to join the treatment in an effective way, harming the pharmacological effect of the drug and consequently decreasing the treatment effectiveness [8,31].

The use of the medicines combined to the pathology can enlarges the chances of a patient developing anemia. It occurs because the medicines have side effects that affect the food intake and nutrition of the patient and the pathology itself induces a reduction on iron, vitamin B12 and folic acid absorption [1].

Treatment with antiretroviral drugs brings many benefits to patients: increase survival and improve quality of life for those who correctly follow the medical recommendations. However, as the drugs must to be very strong to prevent the virus from multiplying in the body, will can cause some unpleasant side effects [23]. Some of these effects are shown in table 1.

<table>
<thead>
<tr>
<th>Table 1: Side effects caused by antiretroviral drugs</th>
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<tbody>
<tr>
<td><strong>I- Kidneys</strong></td>
</tr>
<tr>
<td>Can be acute or chronic . Renal failure is caused by the most common toxic effects of antiretroviral therapy .</td>
</tr>
<tr>
<td><strong>II- Liver</strong></td>
</tr>
<tr>
<td>Antiretroviral can also cause liver damage and may even lead to its failure</td>
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<tr>
<td><strong>III- Bones</strong></td>
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<td>Can lead to osteoporosis , a disease that makes bones fragile , increasing the risk of fractures</td>
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<td><strong>IV - Neuropsychiatric disorders</strong></td>
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<td>Can trigger agitation, hallucinations , amnesia ( memory loss, temporary or otherwise ) , anxiety , mental confusion, seizures , depression, difficulty concentrating, irritability, insomnia, nightmares and vivid dreams . These neuropsychiatric disorders are more common among patients who drink alcohol and drug users .</td>
</tr>
<tr>
<td><strong>V-Gastrointestinal symptoms</strong></td>
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<tr>
<td>Among the most common are : diarrhea , vomiting , nausea , dry mouth, pain on swallowing , heartburn , constipation</td>
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<tr>
<td><strong>VI - Metabolism</strong></td>
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<tr>
<td>- Lipodystrophy: Poor distribution of body fat</td>
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<tr>
<td>- Diabetes: metabolic disorders may develop insulin resistance and , in some cases , the onset of diabetes mellitus</td>
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</tbody>
</table>
Anemia on HIV positive patients

The hematological changes presented by HIV positive patients are directly related to the severity of the disease. The cause is multifactorial, but we can cite the suppressive effect caused by the infection, autoimmune processes, bone marrow infiltration, nutritional deficiency and the toxic effect of the medicines used during the treatment [32].

Microcytic and hypochromic anemia are regularly found in clinical practice, specially iron deficiency anemia and megaloblastic anemia. The last one is defined as normochromic and macrocytic due to deficiency on vitamin B12 and/or folates metabolism [1].

Studies have demonstrated that HIV infection is accompanied by increased expression of proinflammatory cytokines, including biomarkers previously associated with inflammation and anemia aging [33].

Research shows that anemia is one of the most common hematological disorders found in HIV-infected patients. The prevalence varies from 63% to 95% among HIV positive patients, depending on their clinical condition. The development of anemia is related to a lower survival rate and a higher chance of evolution to AIDS, mainly in the severe forms where Hemoglobin is under 8g/dL [5,7].

HIV-infected individuals usually have an iron deficiency that in most of the cases is related to blood loss. They also have a problem with folates and vitamin B12 due to the malabsorption of these nutrients, or due to severe gastro-intestinal infections. Consequently, they are supposed to develop any type of anemia. Adults usually present normocytic, normochromic, and macrocytic anemia, while children are more likely to develop microcytic and hypochromic anemia. In both cases neutropenia and thrombocytopenia can be noticed [4,6,34].

HIV infection may contribute to activation immune aberrant that provides other causes of anemia. Studies have shown that the molecular similarity of erythropoietin (EPO), and the p17 protein of HIV-1 virus may lead to the production of autoantibodies to circulating endogenous EPO, blunting the normal physiologic cytokine response to anemia [35].

Some medicines that are used by HIV-infected patients are also responsible for the hematological problems. Here we can highlight AZT, which was the first among the anti-retroviral medicines and is the main cause of anemia [36].

Both, AZT (Zidovudine) and d4T (Stavudine) induce a failure in the metabolism of the erythrocyte precursor, what can be identified by an increase at MCV (mean corpuscular volume) [37]. However, AZT has a myelosuppressive effect (in vitro and in vivo) that induce an anemia that is probably related to the reduction of globin mRNA synthesis; in other words, it inhibits hemoglobin synthesis [38].

Conclusion

All in all, the rate of AIDS is still increasing. It targets all the social classes and in Brazil, due to the lack of public policies, the increasing rate occurs in all the provinces.

In this regard, information and prevention are crucial, mainly to the young population, which is the group that presents the higher risk of contracting the disease.

Medical sciences had a great progress alongside with the disease; however, the medicines are very strong and affect the immune system of the patients who have AIDS.

According to the research, the medicines used on AIDS treatment harm the human organism and contribute to the development of anemia due to iron, folic acid and vitamin B12 absorption deficiency.

References

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