Original Research Article

Clinical assessment of incidence of anaemia in patients undergoing Anti Retro viral treatment

Asha Kumari[1*], Amit Kumar Jha[2]

[1]Assistant Professor & H.O.D, Deptt. of Pharmacology, Darbhanga Medical College & Hospital, Laheriasarai, Bihar, India

[2]Associate Professor, Deptt. of Pharmacology, Darbhanga Medical College & Hospital, Laheriasarai, Bihar, India

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Abstract

Anti Retro viral agents are used against HIV infection. The present work was done to assess incidence of anaemia in patients undergoing Anti Retro Viral therapy. Value of Hb < 12gm/dl was taken as anaemia . 200 cases of people living with HIV were studied and compared with data. First line ART was availale and NNRTI, NRTI were included in study. Statistical analysis was done. Chi square evaluation was done. It was concluded that Zidovudine most commonly causes macrocytic anemia.

Key Words: Anti Retro Viral Drugs, Zido vudine, HIV infection

Introduction

It is estimated that 50-70% of individuals with HIV infection experience an acute clinical syndrome -3-6 weeks after primary infection. Varying degrees of clinical severity have been reported, and although it has been suggested that symptomatic seroconversion leading to the seeking of medical attention indicates an increased risk for an accelerated course of disease, there does not appear to be a correlation between the level of the initial burst of viremia in acute HIV infection and the subsequent course of disease. As far as typical clinical findings in the acute HIV syndrome is concerned, they occur along with a burst of plasma viremia. It has been reported that several symptoms of the acute HIV syndrome (fever, skin rash, pharyngitis. and myalgia) occur less frequently in those infected by injection drug use compared with those infected by sexual contact. The syndrome is typical of an acute viral syndrome and has been likened to acute infectious mononucleosis. Symptoms usually persist for one to several weeks and gradually subside as an immune response to HIV develops and the levels of plasma viremia decrease. Opportunistic infections have been reported during this stage of infection, reflecting the immunodeficiency that results from reduced numbers of CD4+ T cells and likely also from the dysfunction of CD4+ T cells owing to viral protein and endogenous cytokine-induced perturbations of cells associated with the extremely high levels of plasma viremia. A number of immunologic abnormalities accompany the acute HIV syndrome, including multiphasic perturbations of the numbers of circulating lymphocyte subsets. The number of total lymphocytes and T cell subsets (CD4+ and CD8+) are initially reduced.

*Correspondence

Dr. Asha Kumari

Assistant Professor & H.O.D, Deptt. of Pharmacology, Darbhanga Medical College & Hospital, Laheriasarai, Bihar, India.

An inversion of the CD4+/CD8+ T cell ratio occurs later because of a rise in the number of CD8+ T cells. In fact, there may be a selective and transient expansion of CD8+ T cell subsets, as determined by T cell receptor analysis (see above). The total circulating CD8+ T cell count may remain elevated or return to normal, however, CD4+ T cell levels usually remain somewhat depressed, although there may be a slight rebound toward normal. Lymphadenopathy occurs in -70% of individuals with primary HIV infection. Most patients recover spontaneously from this syndrome and many are lelt with only a mildly depressed CD4+ T cell count that remains stable for a variable period before beginning its progressive decline; in some individuals, the CD4+ T cell count returns to the normal range. Approximately 10% of patients manifest a fulminant course of immunologic and clinical deterioration after primary infection, even after the disappearance of initial symptoms. In most patients, primary infection with or without the acute syndrome is followed by a prolonged period of clinical latency or smoldering low disease activity.

Diseases of the Hematopoietic System Disorders of the hematopoietic system including lymphadenopathy, anemia, leukopenia, and/or thrombocytopenia are common throughout the course of HIV infection and may be the direct result of HIV, manifestations of secondary infections and neoplasms, or side effects of therapy. Direct histologic examination and culture of lymph node or bone marrow tissue are often diagnostic. A significant percentage of bone marrow aspirates from patients with HIV infection have been reported to contain lymphoid aggregates, the precise significance of which is unknown. Initiation of cART will lead to reversal of most hematologic complications that are the direct result of HIV infection.

Anemia is the most common hematologic abnormality in HIV-infected patients and, in the absence of a specific treatable cause, is independendy associated with a poor prognosis. While generally mild, anemia can be quite severe and require chronic blood transfusions. Among the specific reversible causes of anemia in the setting of HIV infection are drug toxicity, systemic fungal and mycobacterial infections, nutritional deficiencies, and parvovirus BI9 infections. Zidovudine may block erythroid maturation prior to its effects on other marrow elements. A characteristic feature of zidovudine therapy is an elevated mean corpuscular volume (MCV). Another drug used in patients with HIV infection that has a selective effect on the erythroid series is dapsone. This drug can cause a serious hemolytic anemia in

patients who are deficient in glucose-6-phosphate dehydrogenase and can create a functional anemia in others through induction of methemoglobinemia. Folate levels are usually normal in HIV-infected individuals; however, vitamin B_{12} levels may be depressed as a consequence of achlorhydria or malabsorption. True autoimmune hemolytic anemia is rare, although -20% of patients with HIV infection may have a positive direct antiglobulin test as a consequence of polyclonal B cell activation. Infection with parvovirus B19 may also cause anemia. It is important to recognize this possibility given the fact that it responds well to treatment with IVIg. Erythropoietin levels in patients with HIV infection and anemia arc generally lower than expected given the degree of anemia. Treatment with erythropoietin may result in an increase in hemoglobin levels. An exception to this is a subset of patients with zidovudine-associated anemia in whom erythropoietin levels may be quite high.

Thrombocytopenia may be an early consequence of HIV infection. Approximately 3% of patients with untreated HIV infection and CD4+T cell counts >400/ µl. have platelet counts <150.000/ µI. For untreated patients with CD4+ T cell counts <400/µI, this incidence increases to 10%. In patients receiving antiretrovirals, thrombocytopenia is associated with hepatitis C, cirrhosis, and ongoing high-level HIV replication. Thrombocytopenia is rarely a serious clinical problem in patients with HIV infection and generally responds well to successful cART Clinically, it resembles the thrombocytopenia seen in patients with idiopathic thrombocytopenic purpura (Chap. 140). Immune complexes containing anti-gpI20 antibodies and anti-anti-gp 120 antibodies have been noted in the circulation and on the surface of platelets in patients with HIV infection. Patients with HIV infection have also been noted to have a platelet-specific antibody directed toward a 25-kDa component of the surface of the platelet. Other data suggest that the thrombocytopenia in patients with HIV infection may be due to a direct effect of HIV on megakaryocytes. Whatever the cause, it is very clear that the most effective medical approach to this problem has been the use of cART. For patients with platelet counts <20,000/µI, a more aggressive approach combining IVIg or anti-Rh Ig for an immediate response and cART for a more lasting response is appropriate. Rituximab has been used with some success in otherwise refractory cases. Splenectomy is a rarely needed option and is reserved for patients refractory to medical management. Because of the risk of serious infection with encapsulated organisms, all patients with HIV infection about to undergo splenectomy should be immunized with pneumococcal polysaccharide. It should be noted that, in addition to causing an increase in the platelet count, removal of the spleen will result in an increase in the peripheral blood lymphocyte count, making CD4+ T cell counts unreliable markers of immunocompetence. In this setting, the clinician should rely on the CD4+ T cell percentage for making diagnostic decisions with respect to the likelihood of opportunistic infections. A CD4+ T cell percentage of 15 is approximately equivalent to a CD4+ T cell count of 200/µI In patients with early HIV infection, thrombocytopenia has also been reported as a consequence of classic thrombotic thrombocytopenic purpura. This clinical syndrome, consisting of fever, thrombocytopenia, hemolytic anemia, and neurologic and renal dysfunction, is a rare complication of early HA' infection. As in other settings, the appropriate management is the use of salicylates and plasma exchange. Other causes of thrombocytopenia include lymphoma, mycobacterial infections, and fungal infections.

Acquired immune deficiency syndrome (AIDS) is caused by Human Immunodeficiency Virus (HIV). It is serious disorder of immune system in which normal defence of body breaks against infection leading to life threatening condition. AIDS was first recognised in United States in summer of 1981 among homosexuals since then HIV pandemic is being increased worldwide exponentially[1]. As per William Osler; a person who takes medicine must recover twice. Once from disease and once from the complications of medication. With their benefit antiretroviral treatment (ART) also comes along with adverse events[2]. ARV drugs are associated with a broad range of toxicity, ranging from low grade intolerance, which may be self-limiting, to lifethreatening side-effects. So, it is important to look for the potential side effects of antiretroviral therapy. Most of the toxicity/side-effects can be adequately co-managed with efficient clinical monitoring at all levels of the health care system[3].Among those side effects; our interest is to study the prevalence of anaemia in patients taking anti retro viral therapy.

Material and methods

The study was done between April to May 2021 in the department of Pharmacology of DMCH. The study was conducted in people living with HIV. Total 200 individuals were included in this study. First line ART was available and NNRTI, NRTI were included in our study.

a) Inclusion Criteria

1. Patients reactive for HIV-1 and/or HIV-2 antibodies.
2. Patients fulfilling above criteria and started on ART.
3. Patients presented with anaemia during trial.
4. Age more than 18 years.

b) Exclusion criteria

1. Patients non-reactive for HIV-1 or HIV-2 antibodies.
2. Patients who reactive to HIV1 and/or HIV2 antibodies but not on ART.

Complete blood counts were done. Patients having Haemoglobin <12 gm/dl were labelled as anaemia. Further, patients with gastrointestinal bleed and patients on drugs which may lead to bone marrow suppression were excluded. Baseline Hemogloin before starting ART was measured.

Table 1 showed Total 70 patients with anaemia. Out of which 58 patient were on ZLN while 12 patients were on ZLE.

Art Regime	Number of Patients
Zln	58
Zle	12

Table 2 showed number of females (n=45) were more as compared to number of males (n=25).

These values are statistically significant with Z=2.68 and p<0.01.

Gender	Number of Patients
Female	45
Male	25

Table 3 showed correlation between anaemia and CD4. Among patients of anaemia, CD4 Count <200 was seen in 26 patient, 200-350 in 24 patients and >350 in 20 patients.

Cdd4 Count	Number of Patients
<200	26
200-350	24
>350	20

Table 4 showed study among 70 patients of anaemia, peripheral smear showed macrocytosis in 55% (n=38) patients, normocytic morphology was seen in 30% (n=21) patients, microcytosis was seen in 15% (n=11) patients. Macrocytosis was common among patients of zidovudine induced anaemia. These values was statistically significant. Chi square=51.54, DF=3 and P< 0.01.

Rbc Morphology	Number of Patinents
Macrocytic	38
Normocytic	21
Microcytic	11

Discussion

In total there were 70 patients with anaemia. Out of which 58 patient were on ZLN while 12 patients were on ZLE. i.e. all the regimens were zidovudine based as it causes marrow suppression. Agrawal D et al. studied over 1259 patients receiving zidovudine and found that 213 (16.2%) patients on AZT regimen developed anaemia (<9 g/dL). A In our study CD4 counts in patients of anaemia were as follows: count <200 in 26 patients, count 200 to 350 in 24 patients and > 350 in 20

patients. Dash K et al[5]. stated that patients with low CD4 count were more prone to developing severe anaemia. Females (45) were more prone to develop anaemia than males (25).These values are statistically significant. Agrawal D et al[4]. studied over 1259 patients receiving zidovudine and found that females were more prone to develop anaemia. Santosh NH et al[6]. in their study found that among the 21 patients of Zidovudine induced anaemia, majority (13 patients) were females. Sharma SK et al[7]. found female gender to be a risk factor for zidovudine induced anaemia. On the basis of RBC morphology we found that peripheral smear of majority of anaemic patients showed macrocytosis (n=42). 21 patients had normocytic morphology while microcytosis was found in 8 patients and dimorphic picture was seen in 2 patients.

Conclusion and results

Anaemia was more common in zidovudine based regimen. Most common age group affected was fourth decade. Females were more prone to anaemia than males and it is statistically significant. Patients with CD4 count less than 200 /ul were at more risk of anamia. Macrocytosis was commonest peripheral blood picture.

Ethical considerations

Ethical issues (including plagiarism, consent misconduct. data fabrication and /or falsification, double publication and / or submission, redundancy etc.) have been completely observe by the other. Ethical clearance to conduct the study was obtained from ethical committee of Darbhanga Medical Collage and Hospital Laheriasarai, Bihar, India.

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