# Advanced pharmacology essay

Health & Medicine, Disease

The Human Immunodeficiency Virus (HIV) poses a serious threat to the well-being of people in different parts of the world. When the virus infects, body cells of a healthy individual, it weakens the immune system and makes an individual vulnerable to contracting to AIDS. In essence, this paper covers many aspects of the HIV virus including its pathophysiology, genomic factors, prevention, treatment, a comprehensive literature review among others.

## Pathophysiology of the Disease Processes

Usually, the HIV causing virus binds itself onto cells often classified as CD4 alongside a co-receptor enclosed by a set of glycoproteins (Hammer & Squires, 2010). Notably, replication of DNA is dependent on an unreliable process, which is characterized by remarkable mistakes. More specifically, transcriptase enzyme is central to the replication process that is marked with mutations because of the integration mistakes prevalent at this stage. The resistance to infection in some individuals can be explained by the mutations that take place.

Dormancy of the virus for a considerable amount of time within the cell is common during the infection process. In response to the human immune responses, the virus takes advantage of the internal cellular processes to multiply(Hammer & Squires, 2010). The virus reproduces in a process that utilizes the mechanisms of the host cells and releases the mature replicates of itself through the plasma membrane.

According to Palella et al., (2011), the virus has the ability to multiply quickly to increase their chances of survival within a short time. The body immune system is pertinent to curbing the multiplication of the virus. During this

process, the relative density of the virus in the blood decreases. Noticeably, a higher proportion of the CD4 cells in response to the immune response entail one of the observable changes at this stage. The body immune system succeeds in the prevention of viral multiplication by creating a retractile mechanism dependent on antibodies that lessen the intensity of the viral particles.

HIV infection entails a continuum of progressive destruction of the immune system. Noticeably, the time it takes for the virus to manifest and traverse through the infection spectrum ranges from 12months or less in some individuals to almost 20 years in others (Peter et al., 2009). The age continuum for the HIV infection is significant in identifying laboratory tests that are essential to treatment decisions and for prognosis. Moreover, the age continuum is instrumental to determine the co-factors that retard or increase the rate of HIV progression. Furthermore, the age continuum is pertinent to developing HIV immune-based therapies.

## The Genomic Issues Inherent in the HIV Disease Process

Notably, there are individuals who are resistant to HIV infection even with repeated exposure to the virus. Some of the factors that explain this relate to the disease process, which entails the genomics as the basis for understanding what happens throughout the HIV manifestation spectrum. In essence, CD4 is the principal receptor for the HIV infection. Typically, CD4 is described as an extracellular receptor, which is enclosed by a membrane and used by immune cells including monocytes, dendritic cells, macrophages and T helpers to assist in detection of foreign cells in the human body. Specifically, the CD4 cell facilitates the amplification of the action of T-cell

receptors upon stimulation with the histocompatibility complex (Wei et al., 2009). Usually, the HIV virus binds to a protein on the surface of the cell and the CD4 once the virus locates a cell having a CD4 receptor. The protein to which the HIV virus attaches itself serves as a receptor (CCR5 ORCXCR4) with an ability to identify immune signals (Wei et al., 2009). In fact, the HIV virus is only able to infect the host cell once it has established an attachment to either the CD4 or the chemokine receptor protein. For some individuals, their immune signal receptor is slightly truncated and assumes a different shape because of mutation. Impliedly, the HIV virus finds it difficult to attach itself to such signal receptor, a situation that prevents the viral infection. Evidently, researchers have been successful in establishing the function of chemokine receptors that are the co-receptors for the Human Immunodeficiency Virus. In respect to this, evidence suggests that individuals having mutations in the alleles coding for the chemokine receptors are resistant to the Human Immunodeficiency Virus (Wei et al., 2009. Specifically, the chemokines entail well-known chemical messengers, which pass across activation signals to the recipient host cells. Pertinently, studies have found that chemokines are effective in inhibiting the Human Immunodeficiency infection. On the other hand, the CCR-5 describes the receptor for CC chemokines, and it represents a crucial co-receptor for M-tropic (macrophage tropic) strains of HIV-1 (Suzanne & Goudsmit, 2010). Essentially, the M-tropic strains are the ones, which establish infection as well as predominate during the elementary stages of HIV infection. As usual, these strains target both the CD4+ lymphocytes and the macrophages. at the later stages of HIV infection, the T-tropic strains become predominant

and only infect CD4+ lymphocytes while they utilize a different co-receptor called fusin instead of the macrophages.

In fact, most chemokine co-receptors such as fusin and the CCR-5 serve as secondary receptors, which facilitate the virus entry. Sometimes fusin is represented as CXCR-4 because of the nature of its chemokine ligand. In respect to the discovery that fusin comprises of a functional co-receptor, researchers derived an added pertinence to the initial finding that the C-C chemokines (RANTES and MIP-1-1 beta) are central to preventing infection of the CD4+ via M-tropic as opposed to the T-tropic HIV-1(Suzanne & Goudsmit, 2010).

Seemingly, CCR5 is necessary for non-syncitium inducing (NSI) Human Immunodeficiency strains. On the contrary, the CXCR4 is more preferable for SI (syncytium-inducing strains). Typically, the SI strain is more aggressive particularly in the aggressive stage of the disease process. However, the most common sexually transmitted strain of the HIV virus comprises of the NSI. Instead of infecting the T-cells, the NSI type of HIV virus often infects the macrophages, which are in most cases found in the mucous membrane and the skin. At first, the sexual transmission of HIV involves the establishment of the virus in the form of M-tropic virus which at a later stage develops into a T-cell-tropic in most individuals. While there is a lot of information on the SI and NSI strains, the conversion of the virus from an NSI to an SI strain in some individuals remains unclear for scientists and researchers (Peter et al., 2009). In essence, about 50% of persons who die because of HIV infection show a predominant NSI virus strain (Suzanne & Goudsmit, 2010). Notably, the SI strain of HIV is more likely to correlate with a more rapid disease

progression and is aggressive. With the aggressive nature of the SI strain, the anti- HIV medication tends to be less effective against the SI virus strains.

Upon the binding of the virus to the CD4+ cells, the CCR-5 receptor facilitates the penetration of the HIV-1 into the cell. In respect to this, the mutations that follow are responsible for making cells resistant to such infection. Besides, only a few individuals who have a homozygous condition for the CCR-5 allele have been found among the highly exposed seronegative individuals. In most studies, evidence suggests that lymphocytes from such people tend to be highly resistant to infection with the HIV-1 virus (Peter et al., 2009). In fact, since the first appearance of the infection to the present times, individuals with the homozygous mutant condition have not been found with the infection. In essence, researchers associate heterozygosity to a partial protection from the infection in the sense that persons with a single mutant copy comprising of the CCR-5 chemokine receptor tend to have some resistance to the invasion of the HIV virus. However, a large number of seronegative individuals lack a CCR-5 mutation but show some resistance to the virus. The explanation behind the resistance of such individuals remains unclear, and scientists or researchers have not managed to obtain a substantive elucidation (Peter et al., 2009). Alternatively, when a lot of chemokines is made by the action of the CD8+ cells, an infection may be prevented because of blockage of the path through which the CCR5 protein moves(Suzanne & Goudsmit, 2010). On the other hand, chances of infection are higher when the chemokine levels are low because the virus can access the CCR5 receptor, which facilitates

infection of the cells. Collectively, the consecutive discoveries with respect to the role of the CCR5 receptor and chemokines continue to unravel the mystery behind the HIV virus infection trajectory and serves as the foundation for explaining the differences in the disease process from person to person.

## A review of the literature on the basics of the disease and its treatment

Admittedly, there has been a progressive increase in the global commitment in the recent years to combat the spread of the HIV virus. Besides, the concerted efforts to prevent the pandemic, the spread of the HIV virus have been on the increase in a manner that is alarming to nations throughout the world. By the end of 2010, about 50million people throughout the world were living with the HIV virus, which represents a notable increase from the 35million individuals infected with the virus in the year 2007 (Peter et al., 2009). While sub-Saharan Africa is the most affected region with the HIV virus, the spread of the virus in some parts of Eastern Europe and Asia is becoming increasingly alarming in the present times (Gant, Heath, & Ejikeme, 2009). In the year 2010 alone, close to 3 million AIDS deaths and about five million new infections occurred, figures that represent more deaths and new infections compared to the previous year 2009.

Besides the rapid spread of the HIV virus, significant milestones have been realized by many countries in curbing the transmission of the virus. Some of the diverse efforts that exemplify the extraordinary prevention of HIV include Uganda’s remarkable decrease in HIV prevalence, Thailand’s 100 percent condom program and syndromic management of sexually transmitted

infections from a community-based approach in Mwanza Tanzania (Gant, Heath, & Ejikeme, 2009).

Additionally, the development and efficient use of specific and highly sensitive HIV screening tests, which have been instrumental in eliminating the infection from the blood supply in the developed world represents one of the remarkable successes. Similarly, the current administration of short educative courses of nevirapine to newborns post-partum and mothers during labor is essential to reducing the risk of mother to child spread in a considerably higher percentage of about 47% (Peter et al., 2009). The recent data on HIV infections suggest that most of the short-term successes are likely to be achieved at the expense of resistance and the failure of the virus upon the introduction of treatment after delivery.

Because of the enormous advancements in the treatment regimens of the HIV virus, the natural history of the infection has been fundamentally altered in the sense that morbidity and mortality have been reduced in nations where the treatments for the virus are readily available. Noticeably, the use treatment of the HIV virus using anti-retroviral drugs in the late 1980s was instrumental in marking a revolution in the overall management of the infection and can be considered analogous to the elementary use of penicillin to treat bacterial infections especially in the year 1940. Moreover, the most notable advance towards curbing HIV is the combined approach of antiretroviral therapy.

According to Gebre & Jacksons (2012), the transmission of HIV occurs through three major mechanisms: perinatal transmission, sexual transmission and exposure to infected blood or in some cases exposure to

blood products. Often, the likelihood of spread of the HIV infection is influenced by environmental, cultural and social factors that differ markedly within and between countries and regions. Similarly, immunological, molecular, viral and host factors have been found to influence the likelihood of transmission of the Human Immunodeficiency Virus. Sexual intercourse is the most common mechanism of transmission, accounting for about 85% of the infections. For example, in sub-Saharan Africa alone, approximately 90% of the infections occur from unprotected sexual intercourse between a healthy and infected person (Gebre & Jacksons, 2012). Besides, studies reveal that a substantial number of persons continue to engage in unprotected sexual intercourse.

On the other hand, exposures to blood products or infected blood entail blood transfusion and drug use via injections. Sharing of the injection equipment such as needles and the subsequent frequency of the injections are significant correlates of the HIV virus transmission. Similarly, sharing of needles, especially at shooting galleries, represents an independent risk factor to the contraction of the HIV virus. In addition, an HIV-contaminated blood transfusion prevalence stands at 90% (Gebre & Jacksons, 2012). In respect to the large amount of HIV virus in a single contaminated transfusion, individuals who contract the virus rapidly develop AIDS. G3ebre, transfusion of contaminated blood products accounts for about 5 to 10% of the HIV infections throughout the world.

In the case of prenatal transmission, there are two modes including transmission during breastfeeding and vertical transmission. Vertical transmission involves maternal viral load that has a marked association with

increased risk for spread of the HIV virus. Vertical transmission occurs at birth when the infected blood of the mother comes into contact with that of the baby. In Kenya, for example, a recent clinical trial revealed that maternal HIV RNA plasma levels were relevant in causing a fourfold increase in vertical transmission (Connor, Sperling, & Gelber, 2014). In respect to breastfeeding, the elevated viral load in the milk is responsible for the transmission of the virus to a newborn. Furthermore, recent data indicating high mortality among breastfeeding mothers has complicated decisions about breastfeeding. Moreover, the stigma associated with the HIV infection in most countries because of considering not breastfeeding as an indicator of having the HIV virus has complicated the collection of data with respect to the transmission of the disease through breastfeeding (Connor, Sperling, & Gelber, 2014).

Notably, developing vaccines for prevention of HIV has been difficult because of the mutation of the HIV surface proteins. Nevertheless, different vaccines are under study and some have revealed promising results in clinical trials. However, at the present, researchers have not found any effective vaccine for the HIV virus. Other prevention measures include public education, counseling for drug users, engaging in safe sex practices, screening of blood and organs, counseling of pregnant women and preexposure prophylaxis with antiretroviral drugs.

The treatment process of the HIV infection involves the use of antiretroviral drugs and prophylaxis to combat opportunistic infections. In essence, there are multiple antiretroviral drugs used to treat the HIV infection, according to their inhibitions. One class of drugs is pertinent to inhibiting the entry of the

HIV while the other inhibits one of the three HIV enzymes. The last class of drugs inhibits the reverse transcriptase by impairing RNA-DNA polymerase activity. While the retroviral drugs reduce severe symptoms, there is no permanent cure for HIV virus.

## Approach to Collecting This Information

In the initial stages, I conducted a search of all articles that were published in less than seven years ago and which were referring to Human Immunodeficiency Virus. The keywords included HIV virus, HIV treatment, HIV prevention, antiretroviral drugs and HIV genomics. In order to capture fine details on the HIV infection, I searched among technology, health and social science databases: CABI global health, web of science, PubMed, WHO technical reports, INSPEC and Google Scholar. The literature contained in the articles was classified into two categories: non-research and research. Some of the articles were excluded from the research because they lacked the detailed presentation of methods used in the investigation. All the other articles were used in the assessment of the HIV infection and in providing the relevant evidence to support the information presented in this paper.

## Approach to the Treatment of HIV Infection

Currently, the treatment approach for HIV virus is HAART, which entails giving three or more antiretroviral medication or drugs in a simultaneous manner (Gulick et al., 2009). Typically, drugs from different classes are used in combination to enhance their effectiveness depending on their functionality mechanisms. In respect to this approach, poor patient compliance has resulted in the failure of the treatment. Because of the need

to follow the treatment schedule, patients are often unable to follow the schedule, leading to the rebound of viral replication because of low drug levels in the body. Other approaches for treatment of the HIV virus include stem cell-based and the use of nanotechnology for antiretroviral drug delivery (Peter et al., 2009). The stem cell-based treatment modality entails the best approach towards combating HIV infection because it is essential for reconstituting the damaged immune system as well as eliminating the virus from the body.

## Follow-up treatment

The follow-up treatment for HIV infection is pertinent to curbing the transmission of the virus and ensuring that the infected persons can adhere to the treatment schedule. In essence, a physician should provide care for patients to help them remain in the treatment course. In addition, it is essential to educate and counsel infected individuals about the disease process to improve the quality of their life and prevent further spread of the infection. Furthermore, exercising and consumption of a nutritious diet are some of the follow-up approaches.

## Conclusion

HIV virus entails a serious threat to the health status of people of all ages, regions and countries. The pathophysiology of the HIV infection is somehow complex to understand, but it is essential for the development of immune based therapies to combat the disease. While there are various treatment approaches for the HIV infection, there is no conclusive treatment that has been known. Therefore, it is important for people to understand the spread

of the infection and restrain from unsafe practices to minimize the risk of contracting the virus.

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