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Review

HIV Management with Selenium

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Abstract: This review article examines the vital role of selenium, an essential trace element, in the management of Human Immunodeficiency Virus (HIV). Selenium's intrinsic role in human health is emphasized due to its involvement in the synthesis of selenoproteins, critical for antioxidant defense mechanisms, where it mitigates cellular damage and inflammation. A particular focus is given to how selenium levels, often found to be deficient in individuals with HIV, correlate with the progression and management of the disease. The deficiency has been associated with advanced disease states, heightened risk of mortality, and increased susceptibility to opportunistic infections. Correcting selenium levels emerges as a crucial strategy, complementing antiretroviral therapy (ART), not only controlling viral replication but also improving overall well-being in affected individuals. The broader implications of selenium include its role in reducing the risk of co-infections, drug resistance, cardiovascular complications, and other conditions associated with HIV. This article endeavors to explain the multifaceted benefits of selenium in HIV management, exploring its potential to improve the quality of life for those living with HIV and reflecting on its significance in evolving comprehensive HIV care strategies.

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Introduction

A significant global health issue that has impacted millions of people globally is the Human Immunodeficiency Virus (HIV). On the previous World AIDS Day, there were 38.4 million HIV-positive people worldwide. A total of 1.5 million persons contracted the disease for the first time in 2021, according to UNAIDS [1]. Acquired immune deficiency syndrome (AIDS) is the result of it attacking the immune system. Antiretroviral therapy (ART), the main form of HIV treatment, is still accessible, but managing the infection is still difficult. Investigating how micronutrients like selenium may help control the virus has garnered more attention in recent years. The body needs selenium, a trace element, to function properly. It is involved in a number of physiological functions, including the control of the immune system. Examining recent research on selenium's function in HIV care and its potential as a supplemental medicine is the goal of this study.

Selenium is a crucial trace element integral to maintaining human health and has emerged as a critical component in managing HIV. HIV systematically impairs the immune system, influencing the body to a numerous of infections and diseases. Extensive research has examined the interplay between selenium and HIV, uncovering selenium's substantial role in fortifying immune function and potentially delaying the progression of HIV-related complications [2]. Selenium is vital for the synthesis of selenoproteins, essential for antioxidant defense systems, contributing to cellular protection from oxidative damage and inflammation mitigation [3].

Observational studies have consistently reported diminished selenium levels in individuals with HIV, a deficiency correlated with accelerated disease progression and elevated morbidity and mortality risks [4]. Consequently, rectifying selenium deficiency has become a focal point in HIV management strategies, facilitating enhanced immune responses, diminished oxidative stress, and a potential reduction in opportunistic infections' incidence. The optimization of selenium levels is

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conceptualized as a complementary strategy to antiretroviral therapy (ART), targeting not merely the control of viral replication but also the enhancement of the overall well-being of HIV-affected individuals [5].

Furthermore, selenium's instrumental role in mitigating the risks of co-infections, drug resistance, cardiovascular complications, and other HIV-associated conditions emphasizes its comprehensive impact on improving the health outcomes of those with HIV [6]. This article explains how selenium helps in HIV care, improves the life quality of HIV patients, and its importance in overall HIV treatment strategies.

Selenium in the Body

Selenium is a vital micronutrient that the body needs in trace levels to function properly. It participates in a number of physiological activities, including as the synthesis of DNA, the control of the immune system, and the generation of antioxidant enzymes [7]. The muscles, liver, and kidneys are where the body accumulates the majority of its selenium.

Natural Source of Selenium

Selenium is a vital trace element found naturally in a variety of foods. It is integral part for human health due to its antioxidant properties and role in immune function. Brazil nuts are notably one of the richest sources of selenium; consuming just one to two of these nuts can meet the daily recommended intake [8]. Seafoods like tuna, halibut, and sardines are also high in selenium, along with meats such as turkey, chicken, and beef [8]. Additionally, grains like wheat germ and rice, as well as seeds, especially sunflower seeds, are excellent plant-based selenium sources [9]. Diversifying selenium sources is crucial as the selenium content in foods significantly depends on the selenium concentration in the soil where the plants grow or where animals graze [10]. For adults, a daily selenium intake of 55 micrograms is advised [11].

1. Selenium Enhances Immune Defense

Role in Immune Function

Selenium has a crucial role in the function of immune system [12]. It influences the body to respond to infection. Also, it is vital in regulating the immune response, even during conditions like viral infections, inflammation, and autoimmune diseases [13]. For instance, selenium deficiency has been linked to impaired immune function and increased susceptibility to infectious diseases due to reduced activity of selenium-dependent enzymes and proteins [14].

Role in Antioxidant Defense

Selenium also contributes significantly to our antioxidant defense systems. Antioxidants are compounds that inhibit oxidation, a chemical reaction producing free radicals, subsequently leading to cell damage. Selenium-containing enzymes, such as glutathione peroxidases, protect the cell components from oxidative damage, thereby reducing the risk of chronic conditions associated with oxidative stress, such as cancers, neurodegenerative diseases, and cardiovascular diseases [15,16].

2. HIV Increases Infection Risk

Impact on Immune System

HIV binds to CD4+ T cells, gains entry, and then integrates its viral RNA into the host DNA, subsequently hijacking the cell machinery to reproduce and destroy the host cell [17]. The progressive loss of CD4+ T cells leads to immunodeficiency, allowing opportunistic pathogens to exploit the weakened immune defenses and cause severe, often life-threatening illnesses [18].

Opportunistic Infections

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Opportunistic infections are illnesses caused by various organisms that usually do not cause disease in people with healthy immune systems. These infections can cause serious illnesses in people with weakened immune defenses due to HIV [19]. These infections, such as Pneumocystis pneumonia, and cytomegalovirus, can be severely devastating and can signify the progression to AIDS (Acquired Immunodeficiency Syndrome), the final stage of HIV infection [20].

Oxidative Stress

Reactive oxygen species (ROS) are molecules that contain oxygen and are highly reactive. In simpler terms, they are unstable oxygen molecules that are always looking to react with other molecules in our body. While they can be harmful in large amounts, causing damage to our cells. In smaller amounts, they play important roles in our body, like helping to fight off infections [21]. Oxidative stress arises from an imbalance between the production of reactive oxygen species (ROS) and our physiological ability to detoxify them or repair the resulting damage [22]. HIV infection elevates oxidative stress by stimulating excessive production of ROS and exhausting antioxidant defenses, thus contributing to the overall pathology and progression of the disease [23]. This increased oxidative stress may also play a role in the development of HIV-associated neurocognitive disorders and cardiovascular complications [24].

3. HIV Reduces Selenium Levels

Selenium Levels in HIV-Infected Individuals

Baum et al. (1997) indicated that the reduced levels of selenium in HIV-positive individuals are correlated with decreased immune cell counts and increased risk of mortality. The study concluded that selenium deficiency could contribute to the progression of HIV to AIDS. Reduced selenium concentrations in the body can affect the optimal functioning of the immune system, making the body more susceptible to opportunistic infections, which are frequent complications of HIV/AIDS.

Implications of Lower Selenium Levels

Having lower levels of selenium can have implications in the overall health outcomes of HIV-infected individuals. Selenium is crucial for the proper function of selenoproteins, which are important for protecting cells from damage due to oxidative stress [25]. Consequently, People with HIV who have low levels of selenium are more likely to be harmed by oxidative stress. This can make HIV worse faster and raise the chance of getting other related health problems. [26].

Selenium and HIV: Treatment Implications

Research has investigated the effects of selenium supplementation on individuals with HIV, highlighting its potential benefits when used in conjunction with Antiretroviral Therapy (ART). The study by Hurwitz et al. (2007), a randomized, double-blind, placebo-controlled trial, stands out in this regard. It revealed that daily selenium supplementation, when combined with ART, not only suppressed the progression of HIV-1 viral load but also improved immune cell counts. These findings underscore the role of selenium in potentially delaying HIV disease progression and reducing the morbidity associated with HIV/AIDS.

4. Antiretroviral Therapy (ART) and Selenium

Selenium and ART: Immune Function

The study by Rayman, 2000 observed that Selenium is a vital component for the synthesis of selenoproteins, which are crucial for maintaining optimal immune function and reducing oxidative stress in the body. Studies have indicated that adequate selenium levels can support immune health in HIV-positive individuals, possibly enhancing the efficacy of ART by contributing to the restoration and maintenance of immune system integrity [27].

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Antioxidant Role

Look et al., 1997 found that the antioxidant properties of selenium can have potential protective effects against the oxidative damage induced either by HIV itself or by some antiretroviral drugs used in ART. Oxidative stress is a known contributor to the pathogenesis of HIV/AIDS and addressing it through selenium supplementation can be beneficial in managing long-term complications of HIV and its treatment.

Safety and Efficacy

While the integration of selenium supplementation into Antiretroviral Therapy (ART) for HIV treatment presents encouraging potential, it is essential to proceed with caution. The addition of selenium, although beneficial in some aspects, carries a risk of toxicity if used excessively [28]. The potential for harm underscores the importance of precision in determining the appropriate dosage. In medical settings, particularly in the context of HIV treatment, the determination of a safe and effective dosage of selenium is a delicate balance. Clinicians and researchers must conduct thorough evaluations to establish the optimal level of supplementation. This involves a careful consideration of individual patient needs, the potential interactions with other medications, and the varying responses of different patients to selenium.

Moreover, regular monitoring is necessary to ensure that the selenium levels remain within a therapeutic range that provides benefits without causing harm. This approach necessitates a personalized treatment plan, where selenium supplementation is tailored to each individual's specific health profile and needs.

5. Immune Function and Selenium

Selenium in Viral Infections

Additionally, adequate selenium levels have been found to be crucial in viral infection defenses. Selenium deficiency can result in more severe outcomes following viral infections due to impaired immune responses. Studies have demonstrated that a selenium-rich diet can aid in controlling the progression of some viral infections, such as the influenza virus, by promoting immune system function [29].

Selenium and Chronic Conditions

Low selenium levels have been linked to a heightened risk of developing chronic conditions such as cancer, cardiovascular diseases, and autoimmune disorders, due to compromised immune responses and increased oxidative stress. Supplementation of selenium in individuals with selenium deficiency has been shown to enhance immune function and may contribute to reduced risks of these conditions [30].

6. Selenium and HIV Transmission

Impact on HIV Progression

Studies have revealed a correlation between selenium levels and the progression of HIV. Baum et al. (1997) found that selenium deficiency in HIV-positive individuals is associated with a higher risk of mortality and an accelerated progression from HIV to AIDS. Adequate selenium levels, on the other hand, are correlated with a slower progression of the disease and improved overall health outcomes for individuals living with HIV/AIDS.

Selenium and Mother-to-Child Transmission

Research focusing on pregnant women with HIV has shown the significance of selenium in preventing mother-to-child transmission of HIV. A study found that higher plasma selenium concentrations in pregnant women were associated with a reduced risk of mother-to-child

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transmission of the virus [31]. This is particularly crucial in regions where HIV prevalence is high, and interventions can significantly impact public health outcomes.

7. Selenium in Managing Co-Infections in HIV

People living with HIV (PLWH) are frequently faced with co-infections like tuberculosis, hepatitis, and fungal infections. These co-infections not only accelerate HIV progression but also complicate its management [32]. Furthermore, research by Baum et al., 1997 indicates a prevalence of selenium deficiency in PLWH, linking it to increased vulnerability to co-infections due to weakened immune responses.

Adequate selenium levels are vital for reinforcing the immune system and reducing the risks and impact of co-infections in PLWH. In this context, selenium supplementation emerges as a promising therapeutic approach. The study by Hurwitz et al., 2007 suggests that it can strengthen immune responses, alleviate oxidative stress, and potentially decrease the occurrence and severity of co-infections. Additionally, maintaining proper selenium levels, especially when combined with antiretroviral therapy, is crucial for the effective management of HIV and its associated co-infections.

8. Selenium and HIV-related Cancers

Enhanced Cancer Risk in HIV

Individuals with HIV are at an increased risk of several types of cancers due to immune deficiency, including Kaposi's sarcoma, non-Hodgkin lymphoma, and invasive cervical cancer [33]. The compromised immune system in HIV-infected individuals fails to combat cancer cells effectively, making them more susceptible to HIV-associated cancers.

Selenium and Cancer Prevention

Several studies have explored the potential role of selenium in preventing cancers in individuals with HIV. Research by Hurwitz et al., 2007 has shown that selenium supplementation can improve immune function and reduce oxidative damage, potentially leading to a lower incidence of cancers. Although conclusive evidence is still pending, maintaining adequate selenium levels might be associated with reduced cancer risk among people living with HIV.

9. Selenium Inhibits HIV Replication

Mechanism of Action

Selenium affects the replication of HIV by being a crucial component of selenoproteins, which play a significant role in reducing oxidative stress and maintaining cellular function. HIV-1 encodes a gene (the *tat* gene) which interacts with a cellular protein called selenoprotein W, inhibiting its activity. Look et al., (1997) found that when the activity of selenoprotein W is inhibited, it leads to elevated oxidative stress and promotes HIV replication.

Laboratory Studies

Laboratory studies have shown that increasing selenium concentration can inhibit the replication of HIV-1. For instance, a study conducted by Look et al. (1997) found that selenium supplementation inhibits the replication of HIV-1 in vitro by reversing the inhibition of selenoprotein W, subsequently reducing oxidative stress and HIV replication. This finding implies that maintaining optimal selenium levels could potentially restrict the replication and progression of HIV.

Implications for Therapy

Although in-vitro studies have demonstrated promising results, translating these findings to effective clinical interventions requires extensive research and clinical trials. However, Hurwitz et al.,

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(2007) observed these laboratory studies indicate that selenium supplementation could be an adjunctive therapy in managing HIV, potentially delaying disease progression and improving overall health outcomes for people living with HIV.

10. Selenium Deficiency Boosts HIV Resistance

The association between selenium deficiency and increased risk of drug resistance in HIV-positive individuals underscores the critical role of this essential trace element in managing HIV/AIDS. Drug resistance in HIV can lead to treatment failure and limits the options available for effective antiretroviral therapy, thus, identifying factors contributing to drug resistance is crucial.

Clinical Observations

Clinical studies have observed that HIV-positive individuals with low selenium levels tend to have a higher likelihood of developing drug resistance. One study explained that selenium deficiency is correlated with the emergence of drug-resistant strains of HIV, highlighting the importance of adequate selenium levels in preventing drug resistance [34].

Importance of Adequate Selenium Levels

Ensuring adequate selenium levels might help in maintaining the effectiveness of antiretroviral drugs and delaying the progression of HIV/AIDS. Hurwitz et al., (2007) informed adequate selenium levels might enhance immune function, reduce viral replication, and minimize the emergence of drug-resistant strains.

Potential Interventions

Selenium supplementation can be considered an adjunctive strategy in managing HIV-positive individuals, especially those exhibiting selenium deficiencies. However, it is essential to approach selenium supplementation with caution. Also, it should be balanced to avoid toxicity. Clinical trials and further research are needed to determine the optimal selenium levels and to establish guidelines for selenium supplementation in HIV-positive individuals.

11. Selenium Deficiency Elevates Cardiovascular Risks in HIV

Mechanism of Selenium in Cardiovascular Health

Selenium is crucial for cardiovascular health, as it is integral to the function of selenoproteins that protect the cardiovascular system from oxidative stress and inflammation [35]. A selenium deficiency can impair the activity of selenoproteins, leading to increased oxidative stress and inflammation, which are key contributors to cardiovascular diseases.

Cardiovascular Risks in HIV

Individuals with HIV are already at a heightened risk for cardiovascular complications due to persistent inflammation, immune activation, and the side effects of antiretroviral therapy (ART) [36]. The presence of selenium deficiency in this population can thus compound these risks, contributing to the development of cardiovascular conditions such as atherosclerosis and cardiomyopathy.

HIV, Selenium, and Heart

Studies have found that lower selenium levels in HIV-positive individuals are associated with a higher incidence of cardiovascular complications. A study by Freiberg et al. (2013) observed that HIV-positive individuals with lower selenium levels had a higher prevalence of cardiovascular diseases compared to those with adequate selenium levels. This association highlights the importance of maintaining selenium levels within the recommended range. It can mitigate cardiovascular risks in HIV-positive individuals.

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Therapeutic Implications

Addressing selenium deficiency through dietary intake or supplementation can be a potential strategy to reduce cardiovascular complications in people living with HIV. However, caution is necessary to avoid excessive selenium intake, which can lead to selenosis, a condition characterized by symptoms such as gastrointestinal distress, hair loss, and neurological damage.

12. Selenium Deficiency Elevates Liver Damage in HIV-Positive Individuals

Role of Selenium in Liver Health

Selenium acts as a cofactor for various antioxidant enzymes, which play an essential role in protecting the liver from oxidative damage [37]. The liver is particularly vulnerable to oxidative stress due to its role in metabolism and detoxification. Selenium deficiency may impair our antioxidant defenses, contributing to liver damage and diseases.

Liver Complications in HIV-Positive Individuals

Liver complications are prevalent in HIV-positive individuals due to various factors. These include the hepatotoxicity of antiretroviral drugs, co-infections with hepatitis viruses, and increased oxidative stress and inflammation associated with HIV infection [38]. In this context, selenium deficiency can intensify the risk of liver damage by exacerbating oxidative stress and impairing immune function.

Clinical Observations and Studies

Studies have found an association between low selenium levels and liver damage in people living with HIV. The study by Price & Thio (2010) highlighted that selenium deficiency in HIV-positive individuals is correlated with an increased risk of liver-related morbidity and mortality. This emphasizes the importance of maintaining adequate selenium levels to support liver health in people living with HIV.

Selenium: Liver Health

Managing selenium levels through diet or supplementation may be a crucial aspect of managing liver health in HIV-positive individuals. However, selenium supplementation needs to be approached with caution due to the narrow therapeutic window between adequacy and toxicity [39].

13. Selenium Deficiency Compromises Reproductive Health in HIV

Role of Selenium in Reproductive Health

Selenium is vital for reproductive health due to its role in the synthesis of DNA, protection against oxidative damage, and metabolism of thyroid hormones [40]. Selenium deficiency can potentially impair fertility and other aspects of reproductive health, due to increased oxidative stress and impaired thyroid function.

Impact on HIV-Positive Individuals

In HIV-positive individuals, compromised immune function coupled with selenium deficiency can lead to severe reproductive health complications. HIV-positive individuals are already susceptible to various infections, including sexually transmitted infections (STIs), which can impact reproductive health [41]. The presence of selenium deficiency can contribute to an enhanced risk of reproductive health issues due to its role in immune function and protection against oxidative damage.

14. Safety of Selenium Supplementation

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While it has been demonstrated that selenium supplements may be beneficial for those who have HIV, it's vital to remember that too much selenium can be hazardous [42]. 400 micrograms of selenium per day is the acceptable upper limit, and it is advised against exceeding this amount. Selenium overdose symptoms might include gastrointestinal issues, skin rashes, lethargy, and loss of hair and nails.

The fact that selenium supplementation may interfere with other drugs, such as antiretroviral therapy, should not be overlooked. Before beginning any new supplement, including selenium, people with HIV should speak with their healthcare physician [42].

Furthermore, crucial to keep in mind is the possibility of interactions between selenium supplementation and other drugs, such as antiretroviral therapy [43]. Before beginning any new supplement, including selenium, people with HIV should speak with their healthcare physician.

15. Conclusion

Selenium, a crucial trace element, is vital for managing HIV, particularly in resource-limited countries where HIV is prevalent. Its role in immune function and antioxidant defenses influences the overall health and quality of life of HIV-positive individuals. Maintaining adequate selenium levels is essential to curb HIV progression and transmission, minimize the risk of additional infections, and possibly avert HIV-related cancers. Combining selenium supplementation with antiretroviral therapy (ART) may improve immune responses and enhance ART effectiveness. However, balanced selenium intake is crucial to avoid adverse health impacts from its deficiency or excess.

There is a pressing need for extensive research to confirm these benefits and ascertain the ideal conditions and dosages for selenium supplementation, considering its interactions with ART. Existing studies, characterized by potential variability in design, populations, and methods, underscore the necessity for more generalized findings applicable across varied settings and populations, especially in countries with limited resources. Addressing these gaps will fine-tune our comprehension and utilization of selenium in managing HIV effectively.

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