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Risk of Fractures in Older Adults Living with HIV

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Recently, the impact of human immunodeficiency virus (HIV) in older patients has begun to be observed, creating a field that has not been explored at its fullest by infectologists and geriatricians. The complications associated with the pathogenesis of the disease and the antiretroviral therapy have a great impact on bone disease, specifically the risk of suffering bone fractures.

The aim of this article is to make a compilation of the most recent evidence that supports the relation of the repercussions that the pathogenesis of HIV, the highly active antiretroviral therapy (HAART) medication and the social aspects has with the increased risk of bone fracture on HIV+ elder individuals.

Introduction

The highly active antiretroviral therapy (HAART) has exponentially increased life expectancy in people with HIV. This caused a change in the epidemiology of HIV [1]. Currently, 50% of people that live with this disease in the United States of America are older than 50 years [1, 2]. The success of the HAART is partially affected due to the higher than expected prevalence of associated complications with age: cognitive impairment, loss of bone density, falls. These conditions increase the risk of bone fractures and can lead to a poor quality of life this group of patients [2].

Fractures in elderly people represent a major challenge for health systems because of the significantly increased complications related to the injury, morbidity, and total or partial disabilities and the. In 2014, our country health system reported an average of \$97 million USD cost for hip fractures [3], an important type of disabling injury that is rising among old patients due to osteoporosis and fragility syndrome.

Around 20% of patients in their eight decade of life with this type of fractures, die due to complications. Half survive with sequels. Costs rise significantly and progressively with age as a consequence of comorbidities and incapacities. It is estimated that in Mexico, 1 out of 12 women older than 50 years and 1 out of 20 men older than 50 years will suffer a fracture [3]. Other factors that increase the risk of suffering an important fall are fragility syndrome, comorbidities just as HIV and its treatment.

Age

The possibility of a fracture increases with age, just as in men with HIV+ as the ones that don't. In the study "An increased rate of fracture occurs a decade earlier in HIV+ compared with HIV-men", Andaa Gonciulea observes that their weren't differences in the incidence of fractures in men who here between 40 and 50 years old [4], but a higher one was observed in men between 50 and 60 years old. This concludes that HIV reshaped the effect on age in all

type of fractures, including traumatic fracture and associated with fragility.

These results promote current available guidelines that recommend dual-energy X-ray absorptiometry (DEXA) screening as the gold standard for HIV+ men from 50 years and older [4].

Fragility and falls

Falls are very important in older patients with HIV+ due to a major prevalence of loss of bone mineral density (BMD) and fractures, compared with non infected population [5].

Falls in adults HIV+ can take place at medium age with an incidence nearly to the ones in elder people (> 65 years), increasing with every additional comorbidity as hypertension [4]. It was found that non incidental fractures and fractures associated with fragility are two times most likely to occur in patients living with HIV [6]. Another important finding is that the risk of fracture also increases almost three times in patients both HIV+ and hepatitis C virus infection [7].

Population studies with similar groups, found that the risk can be directly related to use of drugs with a higher probabilities of traumas, falls and nutritional deficiencies [4].

From the same stem cells, bone and muscle develop [8] so the metabolic pathways are similar, involving growth hormone and insulin like growth factor, so they are being affected in a related way [9]. The decrease of bone mineral density and low body weight are strongly related [10]. Therefore, a loss of lean body mass leads to a loss of bone mineral density (BMD) that is observed at the beginning of the HAART treatment and decreases in subsequent months [11].

On the other hand, studies have proven that some patients with low mineral bone density and low lean body mass already had a deficient physical function or fragility. The deficient physical function represents an important element for the danger of falls and adding each positive fragility phenotype criteria (Fried), the probabilities of suffering a fall increased three times [12].

For a better understanding of the relation between sarcopenia, fragility, falls and risk of fracture in older adults HIV+, a series of interventions can be given to prevent and treat these entities from a more integral view in these group of patients.

Neurocognitive disorder

Hypothesis suggest that aging increases the probability of cognitive impairment in patients HIV+. Evidence show that the fact of being HIV+ does not leads to risk of falls. However, comorbidities along that damage cognitive function just as depression, neuroleptic drugs, neuropathies, and cognitive complaints, do increase the risk.

Modifiable risk factors that jeopardize cognitive function and can lead to falls are substance abuse (marijuana, alcohol, cocaine) and multiple active drugs por nervous central system. These drugs and substances produce excessive sedation, dizziness,

gait impairment, unsteadiness, impaired judgment or cognition [12]. The combined use of these substances can escalate the drug concentrations on blood, take to metabolic disturbances and increase adverse effects of other medications, and aggravate comorbidities [13]. The use of opioids without prescription are associated with falls and fractures. The consume of marijuana is considered the keystone to evaluate falls in older adults population.

A study evaluated the risk of falls in HIV+ women aging. It was found that the use of multiple drugs and central nervous system active drugs (antipsychotics, anticonvulsants, antihypertensives and opioids), simultaneously increased the risk of falls [12]. These evaluated drugs had anticholinergic activity that were related with a poor cognitive function, besides of gait impairment and unsteadiness in older adults. This is especially important considering the dangers of polypharmacy in the elderly and the medication used in HIV.

Bone mineral density

Regardless of age, bone mineral density decreases by 2 to 6% within 1 or 2 years after the starting of HAART, leading to and increase risk of fracture [14].

This loss of bone mineral density is because of the own virus's proinflammatory cytokines [15] just as the damage to the immunologic system. It is seen that the CD4 <50 cell/mm³ count [16] and AIDS-defining illnesses have increased the fracture rate due to a loss of bone mineral density [4].

Some of the drugs that are used such as Efavirenz are related to a decrease of the 25-hydroxyvitamin D; Tenofovir is associated to secondary hyperparathyroidism, leading to an elevated bone turnover [17]; keeping in mind that these are first line drugs, this creates a complicated outlook on the early management of infected patients. The side effects of some of the antiretroviral therapy, as protease inhibitors, and the main pathogenesis of the illness, cause kidney failure that is associated with proteinuria, leading to a low bone mineral density and elevated risk of fracture [18].

Low bone mineral density provoked by pathogenesis of HIV and HAART treatment, it is exacerbated by the risk factors that are usually related with the infection: low physical activity, smoking, use of alcohol and drugs [19].

Some studies found that despite an adequate Vitamin D supplementation, men with advanced age with the virus that have received HAART, have alterations in the trabecular cortical bone microstructure associated to a greater bone resorption [19], increasing the risk of suffering a hip, vertebrae or forearm fracture [20-26].

Conclusion

The population of people infected by the human immunodeficiency virus is having a longer life expectancy, thanks to HAART therapies. As a result of this situation we are facing a new

scenario in geriatrics and infectology. The pathogenesis of the virus, the comorbidities in this group of patients and HAART therapy with its complications are increasing the probability of suffering a fracture. This can cause a disability in patients and enormous cost in public health system, making the management of this group more complex. Definitely we need more research in this topic, especially studying the factors that increase the risk of fracture in HIV+ older adults, and screening tests for the prevention of them. It is needed an integral attention and work with geriatricians and infectologists to improve the quality of life of these patients.

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Conflict of Interest

No conflict of interest.

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