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Research Paper

Biochemical Disturbances During Hiv Infection

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SUMMARY
Biochemical disturbances are due to the direct effect of the virus, opportunistic infections, and/or the cumulative toxicity of antiretroviral drugs. They are frequent and affect carbohydrate, lipid and protein metabolism. Insulin resistance, glucose intolerance and diabetes have been described and are frequently associated with lipid disorders. These abnormalities are aggravated by antiretroviral treatment which causes hypertriglyceridaemia, often moderate, and hypercholesterolaemia characterised by low HDL cholesterol and high LDL cholesterol. Protein levels are increased secondary to polyclonal hyper-gammaglobulinaemia, while major hypo albuminaemia is noted.
Serum ferritin concentration is increased. It is considered a marker of disease progression. Serum enzyme activity is increased as a result of viral liver damage, opportunistic infections and drug toxicity. Increased serum creatinine and proteinuria are the most common abnormalities and are associated with several fluid and electrolyte disorders.
KEY WORDS: *Infection, HIV , Biochemical disturbances , Metabolic disorders*

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I. Introduction:

HIV infection affects multiple organs and systems and manifests itself with a wide range of clinical and biological symptoms. Several biochemical disturbances are observed during the different stages of the infection. They are due to the direct effect of the virus, but above all to opportunistic infections secondary to the state of immunodepression, the ageing of people living with HIV and the cumulative toxicity of antiretroviral drugs. These disturbances affect the metabolic functions of the liver, but also the kidney (1).

Metabolic disorders :
These disturbances affect carbohydrate, lipid and protein metabolism.

Carbohydrate metabolism :
The viral load and stress caused by HIV infection are thought to elicit complex hormonal and immunological responses in patients, which modify various biochemical pathways, including glucose metabolism (2) The role of pro-inflammatory cytokines (tumour necrosis factor alpha, interleukin-6) has been raised in the development of insulin resistance. The latter would be linked to the reduction of stimulation by insulin of the GLUT4 glucose transporters by inhibiting their translocation (3,4)

In addition to the direct impact of HIV, highly effective antiretroviral therapy containing one or more nucleoside reverse transcriptase inhibitors, with or without protease inhibitors, exposes patients to significant metabolic side effects such as insulin resistance characterised by low HDL-cholesterol and high LDL-cholesterol, which is seen in about 20% of patients (5,6,7).

All of these metabolic disturbances are responsible for a lipodystrophy syndrome and are potentially atherogenic. This may partly explain the increased risk of cardiovascular disease observed in these patients. Hypertriglyceridaemia also contributes to the development of a cachectic state and dementia is favoured by disturbances in cholesterol metabolism (5)

Protein metabolism :
Serum protein disturbances are marked essentially by a major hypo albuminemia associated with polyclonal hypergammaglobulinemia (8). The energy deficiencies resulting from alterations in lipid and carbohydrate catabolism lead to an increase in protein catabolism. In addition, during the natural history of HIV

infection, there is a progressive collapse in androgen levels and an increase in glucocorticoid levels which promote protein catabolism. Glutamine is also used as a substrate for immune cells and is used for the synthesis of inflammation proteins under the influence of certain cytokines, including IL-1

Problems of malnutrition, malabsorption, as well as the acceleration of intestinal transit are accompanied by a decrease in protein levels. The inflammatory syndrome associated with the infectious syndrome at the AIDS disease stage is responsible for a polyclonal increase in immunoglobulins (A,G,M), the C3 fraction of complement, haptoglobin and orosomucoid. On the other hand, certain proteins such as albumin, pre-albumin, retino-binding protein are decreased. This decrease can be explained by the inflammatory syndrome under the action of IL6, by protein leaks often of digestive origin or by hepatocellular insufficiency (8) C-reactive protein is usually normal and the inflammatory syndrome is generally moderate despite the presence of opportunistic infections and malignant tumours. This state is secondary to a deficient hepatic response to inflammatory stimuli (9).

Iron balance :

Initially, HIV infection produces changes in iron metabolism similar to those described in inflammation Indeed, in the serum, there is a decrease in iron, transferrin and an increase in ferritin. This is the consequence of the sequestration of iron in the macrophages as a protective reaction of the organism against the infection since iron is an essential element for viral replication. Several mechanisms have been suggested to explain these different disturbances. On the one hand, cytokines increase the transcription of ferritin and on the other hand, there is an imbalance between IRE and IRP, proteins involved in the regulation of martial metabolism As the disease progresses, iron overload increases in many organs such as bone marrow, white matter, brain, muscle and liver. Serum ferritin concentration increases in parallel with the progression of the disease. This event preceded the fall in CD4 counts, resulting in a decrease in the body's defence capacity and the development of opportunistic diseases. It has also been reported that ferritin has a negative influence on T-cell immune function (10).

Increased serum ferritin levels appear to be an interesting marker for the progression of HIV infection. Hyperferritinemia is obviously not specific to this infection since it can also be associated with the inflammatory state or with cell lysis, whatever the origin (hepatic, globular or medullary) (11) A recent study of the aetiology of hyperfirritinemia in a hospitalized population indicates that 17% of cases report HIV infection (12).

Serum enzyme abnormalities :

HIV is not a hepatotropic virus, but clinical and biological findings suggest direct hepatic involvement by the virus. During primary infection, transaminases may be transiently increased up to 20 times normal with acute cytolytic hepatitis. This hepatitis occurs 5 to 25 days after the onset of symptoms and disappears within 10 weeks.Cholestasis and moderate hyper transaminasemia are noted in co-infections and opportunistic liver infections. On the other hand, liver damage secondary to combined antiretroviral treatment is likely to lead to an increase in transaminases or even clinical hepatitis (13)

Several physio-pathogenic mechanisms may be at the origin of ARV liver toxicity: immune restoration on introduction of ARVs, mitochondrial toxicity of nucleosides, immuno-allergy induced by certain molecules and direct dose-dependent toxicity of certain ARVs with hepatic metabolism Other mechanisms linked to the metabolic syndrome and insulin resistance can lead to steatohepatitis, the mechanism of which is still poorly understood (14).

Finally, disorders such as hemophagocytosis syndrome are associated with increased serum GGT activity and transaminases, biological cholestasis, hypertriglyceridaemia and hyperfirretinemia. Biliary disorders during HIV infection also lead to progressively worsening cholestasis, a moderate increase in transaminase activity and sometimes an increase in pancreatic enzymes.

Disturbances of the renal balance :

Renal disorders are very common in HIV infection. They can take many clinical and anatomopathological forms. Studies have reported that their prevalence is increased in comparison with the general population (15)

Indeed, the most recent epidemiological studies confirm this high frequency which varies between 15.5% and 38%. The risk factors for kidney disease found in most studies are age, high viral load, CD4 count, co-infection with hepatitis C virus, sub-Saharan ethnicity, diabetes and hypertension. Biologically, the most frequent abnormalities are increased serum creatinine and proteinuria. The increase in creatinine accompanies a CD4 count of less than 200/mm3 This increase must be interpreted in the clinical context, with the help of other investigations, and even a renal biopsy to establish the etiological diagnosis of this renal damage. The most frequent causes are functional renal failure, acute tubular necrosis and drug-induced tubulointerstitial nephropathy (16).

Proteinuria may exist even when renal function is normal. Here again, it is the renal biopsy that makes the etiological diagnosis.

Electrolyte disorders :

HIV infection may be accompanied by several electrolyte disorders caused by the infection or secondary to renal dysfunction or side effects of treatment. The most common abnormalities are yperuricemia, hypophosphatemia, and decreased bicarbonate levels Hyponatremia is common and is most often secondary to hypovolemia or inappropriate secretion of antidiuretic hormone. When the number of Cd4 is lower than 200/mm3 the serum calcium decreases. The causes of these abnormalities are poorly understood. But treatment with protease inhibitors is thought to be a significant risk factor for these disturbances (17).

II. Conclusion :

By affecting several systems and organs and by intervening in energy metabolism, HIV infection is the cause of multiple biochemical disturbances. These are generally interrelated and aggravated by opportunistic infections due to the state of immunodepression and the cumulative toxicity of the various therapies. The origin and mechanism of the majority of these abnormalities remain poorly understood.

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