A consequence of HAART:HIV associated-lipodystrophy syndrome

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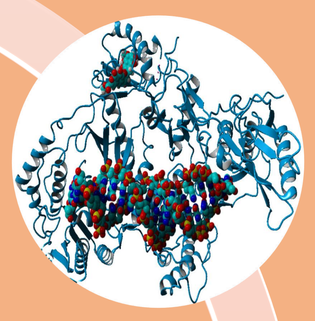
Introduction

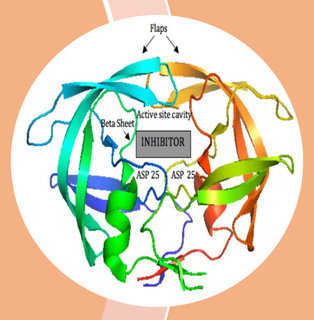
Antiretroviral therapy has changed human immunodeficiency virus (HIV) infection from a near-certainly fatal illness to one that can be managed chronically. The goal of therapy is to suppress HIV viral load, restore immune function, prevent HIV transmission, prevent resistance, and improve quality of life. The standard treatment consists of a combination of at least three drugs (often called “highly active antiretroviral therapy” or HAART) that suppress HIV replication. Three drugs present in HAART therapy are:

- Two-Nucleoside reverse transcriptase inhibitor(NTRIs)with either
- protease inhibitor (PI) or
- Non-nucleoside Reverse Transcriptase Inhibitors(NNRTI)

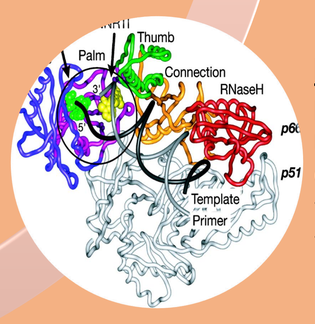
HAART



NRTIs- inhibit transcription of viral RNA into proviral DNA



PI- block the activity of the protease enzyme; used to break up large polyproteins into the smaller pieces required for assembly of new viral particles



NNTRI-binds to a hydrophobic pocket adjacent to the active site of reverse transcriptase and cause a conformational change that reduces the ability of nucleosides to be added to the growing DNA chain

Disturbance in lipid and glucose metabolism, along with body shape abnormality and alteration in fat distribution were the mostly described consequence of HAART and these clinical aspects are coined under a syndrome named as “**HIV associated lipodystrophy syndrome”**.

Lipodystrophy syndrome, characterized by selective loss of subcutaneous fat from the face and extremities and, in some cases, accumulation of fat around the neck, dorsocervical region, abdomen and trunk Lipodystrophy in HIV-infected (LDHIV) individuals is associated with metabolic complications such as dyslipidemia and insulin resistance. The dyslipidemia in LDHIV individuals is characterized by:

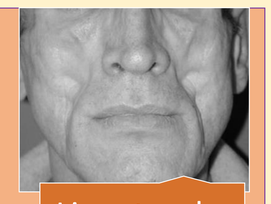
- ❑ Hypertriglyceridemia,
- ❑ Hypercholesterolemia and
- ❑ Low serum high-density lipoprotein cholesterol (HDL-C) levels

Clinical Signs

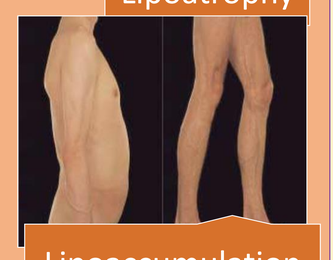
Lipodystrophy can develop in men, women or children

Lipoatrophy is most apparent in the face but is also visible in the arms, legs, buttocks and trunk.

Lipoaccumulation is characterized by a marked increase in VAT that enlarges abdominal girth. It can also result in increased dorsocervical fat tissue (buffalo hump) and/or unilateral or bilateral gynecomastia.

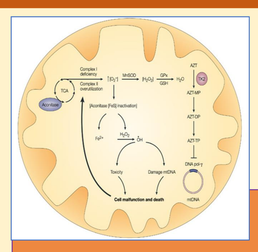


Lipoatrophy



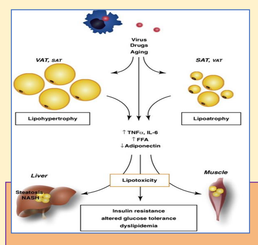
Lipoaccumulation

Pathogenesis



ROLE of NTRI

- NRTIs have an affinity for human mitochondrial DNA polymerase gamma and can cause a decrease in the content and quality DNA- **Mitochondrial Dysfunction**
- Loss of fatty tissue
- Hyperlactatemia and
- Lactic acidosis



ROLE of PI

- More strongly associated with metabolic abnormalities: hypercholesterolemia, hypertriglyceridemia & Insulin resistance
- PI induces adipocytes dysfunction by inactivating SREBP-1 (sterol-regulatory element binding protein 1) and GLUT 4

RISK FACTORS

- Age < 40
- Viral Load <100,000 copies/ml
- CD4 cell count > 350 cells/mm3
- Common in females
- Nutrition-elevated serum TG level

Role of Cytokines

The gain and loss of fatty tissue may be the result of a change in equilibrium between the genesis and death of cells.

Lipogenesis and lipolysis can be influenced by proinflammatory cytokines- TNF-α

Anthropometric parameters

- Weight, size and body mass index are important parameters while evaluating lipodystrophy.

Biological parameters

- serum cholesterol, triglycerides and insulin

Radiological parameters

- Ultrasonography, DEXA, CT and magnetic resonance imaging have all been used for the objective measurement of the fat composition of particular body regions in patients

Management

- **Exercise & Nutrition**
- **Minimizing drug exposure**
- **Cosmetic corrective treatment- Liposuction**

Conclusion

Several elements contribute to lipodystrophy syndrome, supporting a multifactorial etiology, Mitochondrial toxicity caused by NRTIs, metabolic changes induced by PIs, and immune system dysfunction resulting from a sustained elevation of proinflammatory cytokines are all involved in the pathogenesis of lipodystrophy but are modulated by other factors such as genetics, age, comorbidities, length of infection, established AIDS and the duration of antiretroviral therapy.

References

1.Baril, J.-G. et al. (2005). HIV-associated lipodystrophy syndrome: A review of clinical aspects. *Canadian Journal of Infectious Diseases and Medical Microbiology, 16*(4), 233-243.

2.Mallewa, J. E. et al (2008). HIV-associated lipodystrophy: a review of underlying mechanisms and therapeutic options. *Journal of Antimicrobial Chemotherapy, 62*(4), 648-660