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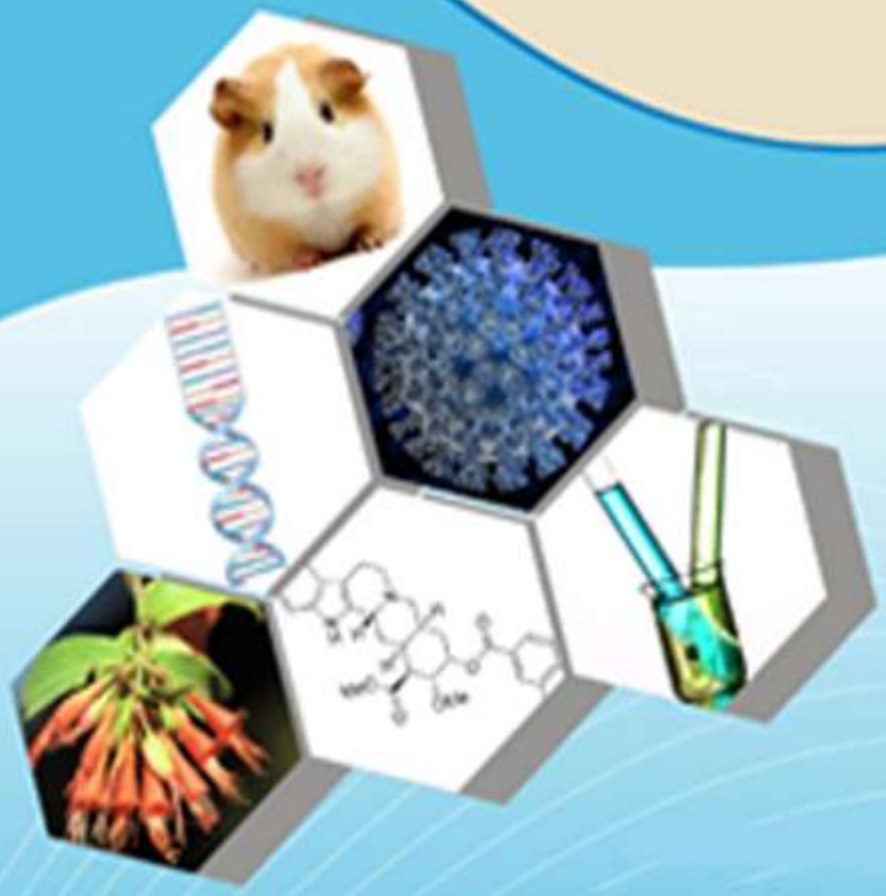

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# Extremely Rare Case of Fatal Lactic Acidoisis and Hepatitis Caused by Tenofovir and Lamivudine

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**ABSTRACT:** Analogs of nucleic acids may produce mitochondrial toxicity, which may result in lactic acidosis (LA). Due to its poor affinity for mt DNA polymerase, tenofovir-induced LA is relatively uncommon. We present a case of a seropositive patient with an obvious risk factor of extremely low CD4 count developing fatal hepatitis and lactic acidosis while taking tenofovir and lamivudine.

**Keywords**: HIV, Tenofovir, Severe lactic acidosis, Hepatitis

## I. INTRODUCTION:

One of the most effective first-line treatments for HIV-1 infection is tenofovir-based highly active antiretroviral therapy (HAART). However, research on the effectiveness and safety of Tenofovir-based treatment is scant. Potentially leading to lactic acidosis1, this nucleotide analogue has been shown to be harmful to mitochondria.Since it has a relatively low affinity for mitochondrial mt DNA polymerase, only around 1% to 2% of individuals treated with Nucleotide Reverse Transcriptase inhibitors (NRTIs) experience severe lactic acidosis.Lactic acidosis (LA) caused by tenofovir, a nucleotide analogue, occurs very rarely. We provide a case of a retropositive patient with a recognized risk factor of extremely low CD4 count developing acute hepatitis, lactic acidosis, and death after taking tenofovir and lamivudine.

## II. CASE SUMMARY :

With a CD4 level of 1, an ART Tenofovir based regimen (Tenofovir lamivudine and efavirenz) and co trimoxazole prophylaxis were started for a 31-year-old male with a retropositive diagnosis.The patient began experiencing significant stomach discomfort, nausea, and vomiting three weeks after beginning a tenofovir-based treatment program. It was determined that the patient's weight was 56.8 kg.The

Patient was alert, knew the time, location, and identity of caregivers; had a pulse of 122 beats per minute; had a blood pressure of 100 over 60 in the right arm while lying supine; breathed at a rate of 36 breaths per minute; was pale; and was severely dehydrated.The only unusual finding on a systemic check was some mild abdominal pain.

The results of the hematological analysis were as follows: 3550 white blood cells per microliter of blood, 150 000 platelets per microliter of blood, and a hemoglobin content of 9.4 g/dl.The levels of sodium, chloride, potassium, and bicarbonate in his blood were 132, 99, 5.11, and 11.2 mM, respectively.Serum creatinine was 0.8 mg/dl, urea was 29 mg/dl, and serum glucose was 115 mg/dl, indicating that his renal function was normal. Ketones were not detected in the regular urine analysis. Other anomalies detected in the lab were high levels of alkaline phosphatase (787 U/L) and gamma-glutamyl transferase (489.7 U/L), among others. Cholestatic hepatitis is likely given the elevated glutamyl transferase level of 786 U/L. The lipase and amylase levels in the blood were 272 and 136 U/L, respectively. Neither HBs ag nor anti-HCV were detected. Ultrasound of the abdomen showed a little fatty infiltration of the liver.High anion gap metabolic acidosis was detected in arterial blood gases (pH - 7.288, Pao2 114, PCO2).

## III. DIAGNOSIS AND INTERVENTION :

Patient was admitted to medical intensive care unit with provisional diagnosis of Type B lactic acidosis and hepatitis and pancreatitis which were secondary to Nucleotide reverse transcriptase inhibitors (NRTI). Patient was managed with intravenous and oral bicarbonate supplementation, high dose thiamine and other supportive measures. Highly Active Antiretroviral Therapy (HAART) was discontinued. But patient eventually succumbed to his illness.

## IV. DISCUSSION :

This instance of significant anion gap metabolic acidosis in an HIV-infected patient using Highly Active Anti Retroviral Therapy (HAART) with Tenofovir, Lamivudine, and Efavirenz is described. Clinical history and laboratory testing ruled out the most common causes of high anion gap acidosis, including diabetic ketoacidosis, uremic ketoacidosis, alcohol ketoacidosis, and the use of medications such as salicylates, isoniazid, metformin, and valproic acid.

There are two distinct forms of lactic acidosis.Anaerobic type A lactic acidosis results from a mismatch between oxygen demand and supply and is a hallmark of all shock states (septic, cardiogenic, and neurologic).

,cardiogenic,hypovolemic,obstructive), seizures/convulsions from regional ischemia (limb.mesenteric), and extreme instances of shivering. The absence of tissue hypoxia or hypoperfusion is a hallmark of Type B Lactic Acidosis.Although type B lactic acidosis is more uncommon than type A, both are caused by mitochondria's inability to absorb the large amounts of pyruvate that are supplied to them. As a consequence, the lactic acid cycle, an alternate mechanism for pyruvate metabolism, is triggered, leading to elevated lactate levels. Liver disease, malignancy, medication (metformin, epinephrine), TPN, NRTI therapy, thiamine deficiency, mitochondrial myopathy, congenital lactic acidosis, trauma, excessive exercise, diabetic ketoacidosis, and ethanol intoxication are all causes of type-B lactic acidosis.

**NRTI INDUCED LACTIC ACIDOSIS:**Severe Rarely is highly aggressive anti retroviral treatment (HAART) linked to type B lactic acidosis.An estimated 21 percent of NRTI-treated individuals have moderate hyperlactatemia, whereas only 1.3 to 20.9 instances per 1000 treated person years 3 experience symptomatic severe hyperlactatemia. Non-specific gastrointestinal symptoms are the most prevalent clinical manifestation of NRTI-induced lactic acidosis. Elevated transaminases and fatty infiltration of the liver were seen on USG, and the patient complained of nausea, vomiting, abdominal discomfort, fatigue, and difficulty breathing. Elevated lactic acid, serum amylase, and lipase, as well as a low bicarbonate concentration, are other characteristic symptoms. The most reliable method for identifying NRTI-related Muscle or liver biopsies revealing macro or micro vacuolar steatosis are indicative of mitochondrial damage, notwithstanding their infeasibility un a clinical situation. Biopsy was postponed in this patient due to the invasive nature of the operation and its poor expected and prognostic value. Toxic effects on mitochondria are considered to play a supporting role in NRTI-induced lactic acidosis. Depletion of kreb cycle substrates and reduced ATP synthesis occur as a consequence of impaired pyruvate oxidation, which results in the creation of lactate, and impaired oxidation, which results in the conversion of fatty acids to triglycerides that accumulate in the cytosol of myocytes and hepatocytes. There is evidence that NRTIs lead to mitochondrial DNA depletion through dysfunction of DNA polymerase, an enzyme necessary for mitochondrial DNA replication. Zalcitabine is thought to be more effective than didanosine, stavudine, lamivudine, zidovudine, and abacavir in inhibiting mitochondrial DNA polymerase gamma in cell culture. Due to its limited efficacy to produce mitochondrial toxicity4, there are relatively few case reports of lamivudine producing severe lactic acidosis. Obesity, female gender, pregnancy, liver injury, and a low CD 4 count all increase the likelihood of developing severe lactic acidosis after taking a NRTI. All of the documented cases included individuals with a preexisting condition that put them at increased risk for mitochondrial toxicity. Preexisting renal insufficiency, coadministration of didanosine, which has high affinity for mitochondrial DNA polymerase, and usage of diuretics were all risk factors in the case described by Murphy et al5. Hashim et al.6 reported a case of hypotensive episodes, bacteremia with E. coli, and underlying HCV infection. The extremely low CD 4 count in this instance is a recognizable risk factor.

## V. CONCLUSION:

This study highlights the need for vigilance while administering tenofovir and lamivudine, despite the fact that lactic acidosis generated by both drugs is uncommon. Clinicians need to be aware of the symptoms of Lactic acidosis in NRTI-treated HIV patients so they can begin therapy as soon as possible. Because of the high mortality rate (33–57%), treatment must be vigorous and include of things like stopping HAART, providing intravenous bicarbonate, and giving the patient supplements of things like thiamine, riboflavin, and carnitine.

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