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SERONEGATIVE CONVERSION OF AN HIV POSITIVE SUBJECT TREATED WITH *NIGELLA SATIVA* AND HONEY

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Abstract

Background: There are many documented roles of *Nigella sativa* and honey in treatment of diseases but the least expected are the potentials in curing HIV infection.

Materials and Method: A 27 years old HIV infected woman was diagnosed during ante-natal care (ANC) at General Hospital (EIA) and confirmed with Western blot in 2004 at National Institute of Medical Research, Lagos (NIMR). She could not benefit from free antiretroviral therapy because her CD4 count was above 200 cells/ μ L (350 cells/ μ L) thus herbal therapist commenced her on *Nigella sativa* and honey therapy (60: 40 respectively) of 10mls thrice daily for a year.

Result: The repeat serology tests for HIV infection (EIA and Western blot) since 2005 were negative with undetectable viral (HIV-RNA) load. The woman had 3 children (2007, 2010 and 2012) that were breastfed without any of the children infected with HIV and none of the repeat CD4 count was less than 750 cells/ μ L.

Conclusion: It was concluded by this report that HIV infection in this 27 years old woman completely sero-reverted by a year therapy of *Nigella sativa* and honey.

Key word: HIV infection, *Nigella sativa*, honey, serology tests.

Introduction

Since 1980's when Human immunodeficiency virus (HIV) was isolated from patients with opportunistic infections and Kaposi sarcoma there are millions of people living with this dreadful virus (Barre-Sinoussi et al, 1983; Gallo et al, 1983 and UNAIDS 2010). It was estimated that no infectious organism has claimed more lives in history than HIV (UNAIDS 2010). Although the prevalence of HIV infection is reducing globally, many factors had been associated with this gain. Advent of highly active antiretroviral therapy (HAART) and vigorous campaign on sexual behaviours considerably have reduced the loss of lives to HIV infection. However, HIV infection is still believed to be incurable and can only be managed with HAART. Numerous research works had been done, and still on going to determine the effective curative agent for HIV infection. Presently, there is no publicly documented effective HIV vaccine. Interestingly, seroreversion has been reported in some HIV patients placed on HAART at early stage of HIV infection (Coyne et al, 2007; Jurriaans et al, 2004 and Kassutto et al, 2005). The 'Berlin patient' and 'Mississippi child' are also very few publicly declared patients that were functionally cured of HIV infection (Hutter et al, 2009; Lampton 2013; Tobin and Aldrovandi 2014; Saez-Cirion et al, 2013).

The potential HIV curative agents that had been documented are bone marrow transplantation, some vaccines, cytotoxic agent, early commencement of HAART and some herbal remedies (Abalaka 2004; Hutter et al, 2009; Jurriaans et al 2004; Lampton et al 2013; Lu et al 1997). However, none of these agents had been considered to be effective HIV curative agent. Bone marrow transplantation is expensive and risky. The vaccines content and procedures were scantily documented or available to the public (Abalaka 2004; Metadilogkul et al, 2009)). Likewise not all HIV patients that were commenced on HAART early became sero-reverted (Kassutto et al, 2005).

The role of herbal remedies as defined by World Health Organisation (2002) as herbs, herbal materials, herbal preparations and finished herbal products, that contain as active ingredients parts of plants, or plant materials, or combinations thereof used to treat a multitude of ailments throughout the world is not doubtful. Like HAART, some herbal remedies have been documented to inhibit viral replication. For example, *Ancistrocladus korupensis* (tropical liana plant) inhibits reverse transcriptase and HIV induced cell fusion while *Calophyllum lanigerum* was rated as non-nucleoside reverse transcriptase inhibitor in potency and pentosan poly-sulphate (carbohydrate derivate) inhibits HIV tat regulatory protein (p14) that strongly activates transcription of proviral DNA (Matthee et al, 1999; Watson et al, 1999; Dhamaratne et al, 2002). But curative role of herbal remedy is yet to be full elucidated perhaps due to low expectation or scientific recognition among others.

Although it was initially documented that some traditional Chinese Medicines caused sero-reversion in HIV infected patient in 1990's but duration of effectiveness and content of the drug had been main concern since almost two decades when it was documented (Lu et al, 1997). *Nigella sativa* and honey are widely available in many countries in the World. The role of honey as antimicrobial agent is not ambiguous but its effectiveness when combined with *Nigella sativa* in HIV infection was scantily documented. *Nigella sativa* and honey (main constituents of α - zam) was initially documented to have caused increase in CD4 count and decrease in viral load in HIV patients (Onifade et al, 2011).

Honey is widely available and generally used for wound dressing and as medication (Osuegbo et al., 2012, Beicher 2013; Johnson et al, 2014). Unlike honey, *N. sativa* is widely available in Asia and Mediterranean regions. *N. sativa* was documented to increase T helper cell and other leucocytes (Bamosa et al, 1997; El-Kadi and Kandil, 1986). *Nigella sativa* was documented to be potent antimicrobial agent on bacteria, fungi, protozoa and viruses (Alijebre et al, 2005; Akhtar and Riffat, 1991; Morsi 2000; Topozada et al, 1965).

Previous studies and presentations of a herbal remedy (α - zam) that contained *Nigella sativa* and honey as the main constituents, other auxiliary constituents were not declared for public use by the herbal therapist (Onifade et al 2011; Onifade et al 2012; Onifade et al 2013). Further studies with other herbal therapists suggested that *Nigella sativa* and honey alone may be effective in HIV infection. This was confirmed with the outcome of this reported case study.

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Methods

Herbal preparation

Six kg of dried seed of *Nigella sativa* purchased from market in Kano (Northern part of Nigeria) was grounded to fine powder with pestle and mortar. 4 litres of newly harvested honey (pure honey) was poured into a clean large open container of about 20 litres for mixing. The 6kg of grounded fine powder of *Nigella sativa* was mixed with 4 litres of pure honey with stirrer. The paste formed is stored in another clean container with cover for daily dispensing of 30 millilitres per day in three divided doses (10mls t. d. s)

Herbal administration

The medication was commenced at third trimester (31-week gestational age) with 10mls of paste formed (from well mixed *Nigella sativa* powder and honey) was taken three times daily. She took the medication for 1 year (third trimester inclusive).

Patient's monitoring

The patient was monitored weekly until after delivery and monthly until 2 years then every 6 month until 10th year. CD4 count, viral (HIV-RNA) load and Enzyme Immunoassay/Western blot were repeated yearly after sero-reversion

Results

The result obtained of serial CD4 count, viral (HIV-RNA) load and Enzyme Immunoassay (EIA)/Western blot is tabulated below

Table 1: CD4, Viral load, EIA/Western blot and Child delivery of HIV infected patient

	CD4 count	HIV (RNA)	EIA & Western blot	Delivery of new-born baby
0 th	350	-	Positive	
3 rd month	-	-	-	Baby boy
6 th month	500	-	Positive	
1yr	750	≤50	Negative	
2 nd year	820	≤50	Negative	
3 rd year	850	≤50	Negative	New child
4 th year	850	≤50	Negative	
5 th year	880	≤50	Negative	
6 th year	900	≤50	Negative	New child
7 th year	860	≤50	Negative	
8 th year	920	≤50	Negative	New child
9 th year	840	≤50	Negative	
10 th year	900	≤50	Negative	

Discussion

HIV infection had generated many interests since about 3 decades when it was discovered. The general dogma that HIV infection is not curable had been questioned in recent years with reported cases of 'Missisipi child', 'Berlin patient' and sustained sero-reversion and complete recovery of HIV infected patients (Hutter et al, 2009; Onifade et al, 2012; Onifade et al, 2013; Onifade et al, 2014; Saez-Cirion et al, 2013). The potential effective therapeutic agents documented were associated with problems of cost, availability and reproducibility (Blanco, 2013). In fact some of the proffered solutions (eg bone marrow transplantation) are not applicable to all HIV patients because of the associated risk of the procedure (Tobin and Aldrovandi 2014). This patient and other documented cases questioned the dogma that HIV/AIDS is not curable.

Some herbal remedies had been documented to induce sero-reversion in HIV patients (Lu et al, 1997; Onifade et al, 2012; Onifade et al, 2013; Onifade et al, 2014). Although *Nigella sativa* herbal concoction had been earlier documented to induce sustained sero-reversion and complete recovery in some HIV patients, however the herbal therapist did not declare the full content and procedure of producing the concoction. The herbal therapist of the earlier documented *Nigella sativa* concoction only declared that the main active constituents are *Nigella sativa* and honey (Onifade et al., 2011; Onifade et al., 2012; Onifade et al., 2013; Onifade et al., 2014). From the result of this patient and herbal therapist procedure of producing the medication, this may be a lead drug which can be researched further for possible sterile cure of the dreaded infection/disease.

Since there is no HIV infection vaccine (pre or post exposure) and this HIV infected patient did not declare taking any other medication since diagnosis was confirmed, the only acceptable explanation is that the therapeutic agent (*Nigella sativa* and honey therapy) taken by the patient induced sustained seroreversion. Although pre-treatment viral (HIV-RNA) load test would have been preferred in diagnosis, however gradual increase in CD4 count despite seropositivity with EIA and Western blot confirmed the initial diagnosis of HIV infection in this patient. Aviraemia, double fold increase in CD4 count and sero-negativity recorded in this patient at the end of a year therapy on *Nigella sativa* and honey therapy is not strange because it was documented earlier that HIV patients became sero-reverted and recovered completely with advanced HIV infection after 5-month therapy (Onifade et al, 2012).

This patient sustained sero-reversion, aviraemia and normal CD4 count confirmed the earlier herbalist's claim that the concoction contained mainly *Nigella sativa* and honey (Onifade et al, 2011; Onifade et al, 2012; Onifade et al, 2013). Based on the findings from this HIV patient and others

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earlier documented evidences, the inference is that *Nigella sativa* and honey are the main constituents and other non-disclosed components are accelerating separation media. There is no doubt that any agent that will induce sustained sero-reversion must have caused selective lysis of HIV infected cell (virucidal) because about 1% of HIV infected cells are at latent phase (not in replicative stage) thus escaping the inhibitory effect of highly active antiretroviral therapy (HAART) which acts by inhibiting one or more steps in HIV replication (Finci and Silicino 1998; Siliciano and Siliciano 2004). Furthermore, the persistence of HIV in latent or memory immune cells (although not in circulation) will evoke immune response of continuous antibody production thus sustained sero-positivity despite aviraemia. Thus, HIV infected individual is expected to be sero-positive for life because some cells are not within the reach of elimination of HAART (inhibitory agent).

The selective lysis (virucidal) effect of *Nigella sativa* and honey therapy could be an acceptable mechanism that eliminated all the HIV infected (circulatory or latent/memory) cells from the body resulting in sustained sero-reversion because the half-life of IgM and IgG are 24 hours and 23 days respectively thus non-existent HIV infected cell will not stimulate B or plasma cell to produce antibodies (Doan 2013). Although the patient was asymptomatic therefore the effectiveness of *Nigella sativa* and honey was only determined by laboratory assay of CD4 count and HIV-RNA load but the expectation was that the HIV infection should rebound after the therapy was stopped. This confirmed the earlier studies that there are agents that could selectively lysed HIV infected cells culminating in complete elimination of the dreadful virus from the body (Levin et al, 2010; Onifade et al, 2012; Onifade et al, 2013). Complete elimination of HIV infected cells by *Nigella sativa* could be the only explanation of non-rebound infection in this patient after a year therapy like the case of Berlin patient (Hutter et al, 2009).

Contrary to the mechanism of action of HAART, *Nigella sativa* and honey effect on HIV infection causes complete elimination of the dreadful virus. It was documented that HIV patients on HAART despite aviraemia still have the virus in their secretions (Lambert-Niclot et al, 2012). From this study, the child was not infected with HIV despite the seropositive mother (patient) practiced exclusive breastfeeding. The expectation was that subsequent pregnancy will induce immune-suppression thus non complete HIV elimination would result in rebound of the dreadful virus. Rebound HIV infection will induce HIV antibody production. However, there was no rebound HIV infection during subsequent pregnancies that culminated in delivery of new child at 3rd, 6th and 8th year thus confirming complete elimination of the virus from the body.

The effect of *Nigella sativa* on HIV infected cells is also different from HAART based on CD4 count measured in this patient. Unlike HIV infected patient on HAART, there is multiple folds increase in CD4 count within 6 month therapy, this was not found in this patient on *Nigella sativa* and honey therapy. The patient had increase in CD4 count but not multiple folds at the 6th month therapy. This confirmed the similar findings in other HIV patients on *Nigella sativa* concoction from the other herbal therapeutics (Onifade et al, 2011; Onifade et al, 2012; Onifade et al, 2013).

From the above result of this HIV patient on *Nigella sativa* and honey therapy alone, it confirmed the earlier studies that *Nigella sativa* is the main constituent of the concoction and other components served as separation vehicle that releases the active constituent of the herb (Onifade et al, 2011; Onifade et al, 2012; Onifade et al, 2013; Onifade et al, 2014). Unlike other patients that were at advanced stage of HIV/AIDS and recovered completely with sustained seroreversion after 4- 6 month therapy on *Nigella sativa* concoction, this patient took almost 12 months to achieve the same status. This showed that honey served as separation medium and other components of the concoction catalysed the release of active constituent. This confirmed that *Nigella sativa* has many constituents with antimicrobial functions if separated in appropriate media.

Conclusion

It is concluded that sustained sero-reversion and non transmission of HIV infection to any of the children in this patient could be attributed curative potentials of *Nigella sativa* and honey therapy

Limitation: This study is limited by inability to do in-vitro study of effect of *Nigella sativa* and honey on HIV infected cell
Further study. There will be further studies on more HIV infected patients and in vitro effect of different fractions of *Nigella sativa* on HIV cell lines

Declaration: There is no conflict of interest and no grant was given for this study

Recommendation: It is recommended this study should be repeated with many HIV patients

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