The potential effect of a nutritional supplement on the health status of HIV-positive/AIDS patients

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Abstract
The primary aim of the study was to assess the effect of a nutritional supplement on the clinical conditions of HIV-positive/AIDS patients using standard procedures. This clinical trial comprising 35 patients consisted of a baseline visit and three months of nutrient supplementation from April to September 2003. At baseline, pre-study examinations of the patients were done and patients who satisfied the inclusion criteria were included in the study. At baseline, the physical and clinical conditions of the patients were noted and reported by a physician. This was followed by nutrient supplementation for three months under adequate supervision. The physical and clinical examinations were repeated monthly and at the end of the study. It is believed that the supplement probably played a contributory role in improving the clinical conditions, improvement on the physical appearance and quality of life. However, the positive effects of the supplement on the clinical conditions of the patients cannot be confirmed in this study. This is because the patients were also treated for different clinical conditions during the course of supplementation. Further studies are needed to confirm the effect of the supplement. The study was limited by small sample size, short duration of study and the late stage of HIV infection of the patients.
Key words: Potential effect, nutrition, supplement, health status, HIV-positive/AIDS patients.
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Introduction

In recent years, the importance of nutrition in human health has received growing attention. Therapeutic and preventive supplementations with vitamins and minerals have been used successfully for a long time for various clinical conditions[1, 2]. These include vitamin A for maintenance of vision, beta-carotene in erythropoietic protoporphyria, vitamin C in scurvy and niacin in pellagra. As the HIV/AIDS pandemic enters its third decade, the number of cases continues to increase. Definitive cures have not been found nor has an effective vaccine been developed. It is therefore time to examine other approaches to reducing the effect of HIV infection. Nutritional intervention may be one of such approaches, especially in a developing country such as South Africa. It is against this background that the potential effect of a nutrition supplement on the clinical conditions of HIV-positive/AIDS patients was examined.

Methodology

This was an open-ended, multiple-dose clinical trial consisting of 35 HIV-positive/AIDS volunteers. Of the 35 patients recruited at baseline, only 29 completed the study (2 dropped out while 4 died). Approval was obtained from the Ethics Committee (ETOVS 32/03) of the Faculty of Health Sciences, University of Free State and all patients signed the informed consent forms before being included in the study (the signing of patient's consent forms and medical examinations were done at Tsepo House (home-based care) and Medi Inn Clinic). The criteria for inclusion were: male and female patients between 18 and 65 years of age that are HIV-positive, not on antiretroviral therapy, who are willing to undergo pre-and post-study physical and medical examination, are found within the range of clinical acceptability in medical history and physical examination, have a $CD4^+$T-cell count of 100-350 cells/mm3 and are able to comprehend and willing to sign the statement of informed consent.

The study was conducted in two separate clinics, namely Tsepo House and Medi Inn clinic, both in Bloemfontein. The patients seen at Medi Inn clinic were patients from the South African Red Cross (home-based care) Bloemfontein, and were transported to the Medi Inn clinic by arrangement and in agreement with the Red Cross management with the consent of the patients. The study involved a baseline visit and 3 monthly visits for three months to Medi Inn clinic and Tsepo House from April to September 2003. At baseline the patients were examined for various physical and clinical conditions and findings were documented. The medical examinations were repeated monthly for 3 months and after supplementation. The CD4+T-cell count and viral load of the patients were determined at baseline and at final visit using flow cytometry and polymerase chain reaction (PCR) respectively. The duration of this study is similar to the one reported on by Allard *et al*[3].

Supplementation of patients

Following the physical and medical examination, $CD4^+$T-cell count and viral load determination at baseline, the patients were given 7.5 ml of the test supplement (Africa's Solution) twice daily (between 07:00-09:00 and 16:00-19:00 hours). The daily intake of the supplement by patients was monitored by members of the South African Red Cross Society, Bloemfontein and the medical staff at Tsepo House.

Components of the supplement

The contents of the supplement are extract of hypoxis (500 mg), grape fruit seed extract (4 mg), sitosterol & sitosterolin (28 mg), beta-carotene (1 mg), vitamin E (12.5 mg), vitamin B_6 (7.5 mg), vitamin B_1 (3.75 mg), vitamin B_2 (10 mg), vitamin B_{12} (3 µg), nicotinamide (5 mg), vitamin C (50 mg), olive green leaf extract (35 mg), folic acid (325 µg) and natural anti-oxidant (biocydin) (52 mg) and every 15 ml of the solvent contain the amount of ingredient as indicated above.

Follow-up Visits

The patients visited the clinic on a monthly basis. On each visit, physical and medical examinations were carried out on each patient by the clinical investigator in the study. The physical and medical examinations were repeated at the end of the study to determine the possible effect of the supplement on the health status of the patients. Compliance with the regime was ensured by counting the supplement units on a daily basis and at each visit, and by constantly reminding the patients of the need to follow the protocol. During the follow-up visits, clinical conditions that were identified in the patients (example tuberculosis) were treated.

Results

In Table 1, ten (28.6%) of the patients had ear infection at baseline and this decreased to 5 (17.2%) following treatment and supplementation. Eight (22.9%) of the patients had candidiasis at baseline and this decreased to 5 (17.2%) with supplement administration. Six of the patients (17.1%) had tuberculosis (TB) at baseline. At the end of the study, there was no incidence of TB reported but mainly due to treatment of the TB with drugs. Three of the patients (8.6%) had diarrhoea at baseline visit, which decreased to 2 (6.9%) by the end of study. Although, it cannot be categorically stated whether the decrease was due to the effect of the supplement or the treatment, it is suggested that the supplement could have contributed to the general well-being of the patients examined in this study. Liver enlargement was observed in 7 of the patients and it persisted during the study. Skin rashes decreased from 10 (28.6%) at baseline visit to 3 (10.3%) by the end of study. It was observed that 75.9% of the patients had lower blood pressure while 24.1% had normal blood pressure. Table 2 shows the viral load and $CD4^+$T-cell count of the whole patients at baseline and final visit. The viral load significantly (<0.002) decreased with time following supplementation for a period of three months. However, the supplement showed no positive effect on the CD4+T-cell count. Overall, the patients showed slight improvements in clinical condition as well as physical appearance and quality of life.

Discussion

Different types of infections and clinical conditions have been reported in HIV-positive/AIDS patients[4]. The type and severity of the infection depend on the nature of the immune defect. Secondly, the degree of immune suppression is important as HIV infection causes a progressive immune suppression in all patients who are not treated with antiretroviral therapy. As immunity decreases, patients become susceptible to a wider spectrum of infections[4]. In addition, organisms that are prevalent in the patient's environment will be responsible for a large proportion of the infections. This is perhaps the reason why HIV-associated infections in sub-Saharan Africa differ markedly in their incidence from those in industrialised countries4. These infections (in the sub-Saharan region) range from bacterial to fungal, parasitic and viral. The quality of life and lifespan of HIV-infected persons is affected by these (various) infections. In this study, a few opportunistic or HIV-related conditions/infections were identified and they are discussed below.

Few cases of HIV-related ophthalmological problems have been reported in HIV-positive/AIDS patients[5]. The patients examined in the current study reported a very low infection rate (2.9%), with no eye discharge (Table 1). It is worth noting that even the very low eye infection rate documented did not

Table 1: Physical and Clinical Conditions of HIV-positive/AIDS Patients before and after nutrient supplementation.

System	Baseline visit n=35	V1 n=30	V2 n=32	V3 n=29
1. **Eyes**				
• Jaundice	0	0	0	0
• Discharge	0	0	0	0
• Infection	1 (2,9%)	1 (2,9%)	0	0
• Pupil Normal	29 (82,9%)	29 (96,7%)	29 (90,6%)	29 (100%)
2. **Ears**				
• Pain	6 (17,1%)	4 (13,3%)	3 (9,4%)	2 (6,9%)
• Infection	10 (28,6%)	8(26,7%)	6 (18,8%)	5 (17,2%)
• Discharge	7 (20%)	6 (20%)	5 (15,6%)	4 (13,8%)
3. **Nose**				
• Pain	0	0	0	0
• Ulcer	0	0	0	0
• Swelling	2 (5,7%)	0	1 (3,1%)	1 (3,4%)
4. **Mouth & Lips**				
• Pain	1 (2,9%)	0	0	0
• Ulcer	6 (17,1%)	5 (16,7%)	3 (9,4%)	1 (3,4%)
• Swelling	1 (2,9%)	2 (6,7%)	2 (6,3%)	2 (6,9%)
• Cracked lips	2 (5,7%)	2 (6,7%)	2 (6,3%)	1 (3,4%)
• Candidiasis	8 (22,9%)	7 (23,3%)	6 (18,8%)	5 (17,2%)
5. **Throat**				
• Pain	15 (46,9%)	12 (40%)	15 (46,9%)	13 (44,8%)
• Ulcer	3 (8,6%)	2 (6,7%)	2 (6,3%)	4 (13,8%)
• Infection	21 (60%)	20 (66,7%)	21 (65,6%)	16 (55,2%)
• Candidiasis	3 (8,6%)	4 (13,3%)	5 (15,6%)	5 (17,2%)
6. **Respiratory System**				
• Cough	13 (37,1%)	21 (70%)	17 (53,1%)	14 (48,3%)
• Shortness of breath/Dyspnoea	3 (8,6%)	3 (10%)	3 (9,4%)	1 (3,4%)
• Pain	7 (20%)	12 (40%)	9 (28,1%)	10 (34,5%)
• Haemoptysis	0	0	0	0
• TB	6 (17,1%)	5 (16,7%)	2 (6,9%)	0
• Abnormal breath sounds	5 (14,3%)	13 (43,3%)	13 (40,6%)	11 (37,9%)
7. **Neck**				
• Swelling	2 (5,7%)	2 (6,7%)	1 (3,1%)	1 (3,4%)
• Glands				
Submental	5 (14,3%)	6 (20%)	4 (12,5%)	1 (3,4%)
Jugular	13 (37,1%)	20 (66,7%)	18 (56,3%)	15 (51,7%)
Posterior triangle of the neck	5 (14,3%)	7 (23,3%)	6 (18,8%)	5 (17,2%)
Occipital	16 (45,7%)	17 (56,7%)	15 (46,9%)	11 (37,9%)
8. **Cardiovascular**				
• Swelling of legs/angles	2 (5,7%)	0	4 (12,5%)	1 (3,4%)
• Other Edema	1 (2,9%)	0	4 (12,5%)	1 (3,4%)
• Shortness of breath/Dyspnoea	4 (11,4%)	5 (16,7%)	3 (9,4%)	3 (10,3%)
• Cyanotic	0	0	1 (3,1%)	0
• Club fingers	0	0	0	0
9. **Blood forming organs**				
• Enlargement of spleen	0	0	0	0
• Glands in the neck	17 (48,6%)	20 (66,7%)	18 (56,3%)	16 (55,2%)
• Axilla	11 (31,4%)	17 (56,7%)	10 (31,3%)	11 (37,9%)
• Groins	10 (28,6%)	13 (43,3%)	9 (28,1%)	10 (34,5%)
10. **Digestive**				
• Weight loss/Malnutrition	20 (57,1%)	16 (53,3%)	11 (34,4%)	10 (34,5%)
• Eating well	17 (48,8%)	15 (50%)	17 (53,1%)	18 (62,1%)
• Normal bowel movement	26 (74,3%)	26 (86,7%)	28 (87,5%)	28 (96,6%)
• Diarrhoea	3 (8,6%)	3 (10%)	2 (6,3%)	2 (6,9%)
• Constipation	1 (2,9%)	1 (3,3%)	1 (3,1%)	1 (3,4%)
• Abnormal pain	2 (5,7%)	0	0	0
• Nausea/Vomiting	0	0	0	0
• Liver enlargement	7 (20%)	7 (23,3%)	7 (21,9%)	7 (24,1%)
• Spleen enlargement	0	0	0	0
11. **Genito-urinary**				
• Dysuria	6 (17,1%)	4(13,3%)	4 (12,5%)	4 (13,8%)
• Dysmenorrhoea	2 (7,41%)	1 (3,7%)	2 (7,41%)	1 (3,7%)
• Vagnila discharge	6 (22,2%)	11 (40,7%)	11 (40,7%)	10 (37,0%)
• Urethral discharge	0	0	0	0
• STI	2 (5,7%)	2 (6,7%)	2 (6,3%)	2 (6,9%)
• Penile discharge	0	0	0	0
• Swelling of scrotum	0	0	0	0
12. **Locomotor**				
• Pain	5 (14,3%)	5 (16,7%)	8 (25%)	3 (10,3%)
• Neuropathy	10 (28,6%)	12 (40%)	7 (21,9%)	9 (31%)
13, **Skin**				
• Rashes	10 (28,6%)	9 (30%)	8 (25%)	3 (10,3%)
• Ulcers	4 (11,4%)	5 (16,7%)	4 (12,5%)	4 (13,8%)
• Tumours	0	0	0	0
14. **Central Nervous**				
• Paralysis	0	0	0	0
• Normal state of consciousness	32 (91,4%)	30 (100%)	29 (90,6%)	25 (86,2%)
• Normal sensory system	32 (91,4%)	30 (100%)	30 (93,8%)	29 (100%)
15. **Vital Signs**				
• Temperature/Normal	31 (88,6%)	30 (100%)	31 (96,9%)	29 (100%)
• Blood pressure/Normal	7 (20%)	3 (10%)	5 (15,6%)	7 (24,1%)
• Pulse rate/Normal	21 (60%)	21 (70%)	18 (56,3%)	17 (58,6%)

V1 (visit one) • V2 (visit two) • V3 (visit three)

progress as the study proceeded.

In this study, 28.6% of the patient population had an ear infection (table 1). Observation revealed that the ear infections decreased to 17.2% following supplementation. The patients were treated on recognition of infections, therefore it makes it difficult for us to say with certainty whether the supplement had a positive effect on the clinical conditions nonetheless, the supplement probably aided the healing or recovery process.

Studies[6, 7, 8] have demonstrated the prevalence of oral infection due to Candida species in patients with HIV/AIDS. Greenspan[9] reported that candidiasis is one of the most common oral infections in HIV patients. The most frequent species producing oral infection is Candida albicans, but other species are occasionally found which infect the oral mucosa[9]. Both oral (22.9%) and throat (8.6%) candidiasis (table 1) were diagnosed among the studied patients. It was observed that oral candidiasis decreased following supplementation and treatment. However, throat candidiasis did not decrease during supplementation and treatment. The reason for this is not known, but drug resistance may be responsible. Fluconazole resistance in *Candida albicans* has been reported recently in HIV/AIDS patients, especially those with $CD4^+$T-cell counts of less than 200 cells/mm^3[3, 6]. Our patients had inclusion criteria of $CD4^+$T between 100-350 cells/mm^3. The mean $CD4^+$T-cell count of the patients at baseline and the final visits were between 203-164 cells/mm^3. Furthermore, a recent study revealed that dysfunctional $CD4^+$T-cells and $CD8^+$T-cells may be associated with inadequate defence against oral and oropharyngeal candidiasis in patients with HIV/AIDS[10]. As observed in the present study, the $CD4^+$T-cell count decreased significantly ($P<0.03$) (table 2), indicating a dysfunction in $CD4^+$T-cells. The significant decrease in the $CD4^+$T-cell count is a reflection of the severity of the patients' immune system and not due to an adverse effect of the supplement on the immune system. The decrease also shows that although the viral load decrease significantly (statistically) but does not reflect clinical significance. This could be another reason for the non-improvement in candidiasis following supplementation, but then it cannot be confirmed whether this mechanism (association between low $CD4^+$T-cell count and candidiasis) contributed to the clinical picture in regard to candidiasis. This needs further investigation.

In sub-Saharan Africa, *Mycobacterium tuberculosis* (TB) is seen as a frequent secondary infection to occur in HIV-infected patients[11, 12]. The development of TB in HIV-infected patients has a poor prognosis and a high mortality rate[13]. HIV/AIDS patients also have a significantly higher risk of contracting TB infection owing to the underlying immune deficiency[14]. TB infection is a public health problem in South Africa, especially among the lower socio-economic group of society[15]. The prevalence of TB in this study was not very high, occurring in 17.1% of the patient population (table 1). The clinical conditions improved with treatment and supplementation. From observation, TB does not seem to be a major infection in this group of patients. It is also worth noting that viral load increases with TB infection, and the fact that the viral load in this study decreased significantly in the presence of TB infection, demonstrates the positive effect of the supplement and indicates the importance of supplementation in HIV-infected persons, especially those infected with HIV and TB.

Swelling or enlargement of glands, especially near the neck, was observed in HIV-positive/AIDS patients[4], but the severity and frequency of the swellings depended on the immune responses and the stage of HIV infection. In this study, clinical observation showed that the prevalence of swelling was higher around the jugular vein and it did not show improvement with supplementation (table 1).

Pathological abnormalities in the central nervous system have been reported in 70-90% of patients dying of AIDS[16, 17]. Cognitive dysfunction is said to be common as well. Immune deficiency may result in opportunistic infections of the central nervous system (CNS), causing specific neurological dysfunction[18]. The patients examined showed a normal state of consciousness (91.4%) and all demonstrated a normal sensory system. Ten (28.6%) of the patients examined, (table 1) had neuropathy at baseline and showed no consistent sign of improvement with supplementation. The technique employed in the diagnosis of neurological problems was limited, thus certain abnormalities that could have been identified may have been left undiagnosed.

Malnutrition and body weight loss are commonly documented in HIV infection[19, 20]. Malnutrition associated with HIV/AIDS is known to be the result of several processes, but the degree to which nutrition therapy can positively alter the course of HIV disease among HIV-positive/AIDS patients in Africa is largely unknown[21]. Malnutrition in HIV/AIDS patients includes symptoms such as weight loss, loss of muscle and subcutaneous fat, vitamin and mineral deficiencies, reduced immune competence and increased susceptibility to infection. Conditions that could lead to malnutrition include lack of appetite, poor nutrient intake, limited food availability, chronic infection, malabsorption, metabolic disturbances, fever, nausea, vomiting and diarrhoea, depression and the side-effects of drugs[22, 23]. The medical history and medical examination of patients in the current study showed that 57.1% of the patients (at baseline) reported weight loss/ malnutrition. This condition improved with supplementation, falling to 34.5%. The result therefore tends to indicate that there was a gain in weight with supplementation. This is understandable since there was a significant decrease in the viral load. A decrease in the viral load is expected to result in a decrease in metabolic activities. We are of the opinion that the supplement partly contributed to this observed improvement in malnutrition. Another factor that could have contributed to the improvement of malnutrition is the fact that patients reported good appetite. Clinically, nausea and vomiting were not noted. This perhaps improved the nutritional status of the patients as well.

Gastrointestinal infections include parasitic, bacterial and viral which contribute to diarrhoea, especially in AIDS patients. Gastrointestinal pathogens include opportunistic organisms that cause severe intermittent gastrointestinal disease, and non-opportunistic organisms that usually cause acute treatable diarrhoeal illness[24]. Clinical assessment of the patients in the present study indicated that diarrhoea (8.6% at baseline) was not a major illness among the patients. This may be related to the adequate care provided by the home-based care. The patients were taught about personal hygiene and given health education.

Vaginal discharge resulting from either candidiasis or sexually transmitted infections was diagnosed in the patients during the period of study. Vaginal candidiasis seemed to predominate and the prevalence increased through out the study. This might be related to the chronic nature of the infection. It is important to subject such diagnosis to laboratory testing. This should lead to the particular causative agent being detected and isolated and where applicable, the antibiotic sensitivity pattern being determined, and, ultimately appropriate treatment. Laboratory tests to isolate and identify potential pathogens are thus recommended in future studies.

Jeena[25] reported that over 80-90% of HIV-positive/AIDS patients have skin infections at some point during their illness. Local immunity of the skin is useful in determining the progression of HIV infection. With recurrent infections, it is known that there is impairment of the skin's immune system and primary HIV infection produces a typical infectious mononucleosis-like rash[25]. Also, secondary mucotaneous involvement is noted to be common with viral, bacterial, fungal and other miscellaneous infections[25]. In this study, 28.6% of the patients had skin rash at baseline but this decreased during the course of study. The percentage of patients with skin infections, as indicated here, may be related to the impairment of the immune status (dysfunctional immune system).

Conclusion

It cannot be confirmed in this study whether it was the supplement or the treatment or both that had positive effects on the clinical conditions of the patients. However, the supplement had a significant effect on the viral load. Therefore, it could be argued that the supplement probably played a contributory or an indirect role in improving the clinical/physical conditions and the quality of life of the HIV-positive/AIDS patients. Since combinations of antiretroviral therapies are generally limited to privileged persons for economic, social, political and sometimes religious reasons, consideration of the potential of this supplement remains important for developing countries, particularly those in sub-Saharan Africa where a majority of the populace can-

Table 2: Viral load and $CD4^+$T-cell count of HIV-positive/AIDS patients at baseline and final visit of the whole patients.

Variables	Baseline visit n=35			Final visit n=29			P-value
	Mean	SD	Median	Mean	SD	Median	
Total Tcell count/mm^3	1615	736.3	1543	1495.7	758.9	1400	0.07
$CD4^+$T-cell count/mm^3	203.9	83.5	176	188.2	96.9	164	<0.03*
$CD8^+$T-cell count/mm^3	1407.2	672.2	1254	1267.1	686.9	1228	0.09
CD4/CD8 ratio	0.2	0.1	0.2	0.2	0.1	0.2	0.7
Viral load/ml	374302	300299	292000	279367	244877.6	193000	<0.002*

SD (standard deviation)
The P-value tested the difference between both viral load and CD4+T-cell count at baseline and final visit.
*P<0.05. Parameters with the same superscript showed statistical difference.

not afford antiretroviral therapy. It could have an appreciable benefit, perhaps similar to the effect of vitamin A supplementation on childhood mortality in developing countries.

This study forms part of a comprehensive care system for the management of HIV-positive/AIDS patients. The supplement was well tolerated, hence no patient complained of any side-effects during and after the study. Observation showed that some of the patients improved physically and appeared healthier by the end of supplementation than before supplementation. Therefore, the benefit of the supplement may also extend to improved physical appearance and general well-being. Many vital questions, however, remain to be answered for one to understand fully the mechanism of action of the supplement and how best to utilize the supplement.

Limitation of the Study

This study was limited by small sample size, short duration and lack of a control group.

Acknowledgement

The Central University of Technology, Free State provided the main funding for the study. The financial assistance received from the HIV Council of the Free State Government and National Research Foundation of South Africa is acknowledged. Thanks to Pathcare laboratory for the analyses of blood samples, ProNutro supplied the porridge and Bermins provided the supplement.

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