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Organotherapic Medicine Improves Blood Glucose Levels in AIDS Patients

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Authors' contributions

This work was carried out in collaboration between all authors. Author ARTP designed the study, performed the statistical analysis and managed writing of the manuscript, author MSJ performed the clinical evaluation and author LM managed the literature searches, collected data and conducted laboratory tests. All authors read and approved the final manuscript.

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Short Research Article

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ABSTRACT

Aims: To evaluate the effect of an organotherapic drug, produced from the pancreas of a young pig, on glycemic alterations in AIDS patients.
Methodology: Current study was carried out in a double-blind, placebo controlled and randomized design. AIDS patients who had high fasting glucose (>110 mg/dL) were selected so that the effect of the organotherapic drug could be evaluated. The patients were divided into two groups: Group I comprised patients who received the organotherapic drug diluted in $1x10^{12}$ alcohol/ water 8%, once a day, with a sublingual-administered fasting dose of 10 drops, during four months. Group II consisted of patients receiving placebo once a day at the same dosage. Glucose oxidase method and ELISA, following the manufacturer's instructions, respectively determined levels of glucose and insulin before treatment and monthly until four months after the start of treatment.
Results: Results registered hyperglycemia in 30% of the patients (60/200), higher than in the population at large (7-15%). This fact could be related to the time of infection (10.0±4.78 years) and treatment (9.3±3.76 years) of the patients. On the other hand, patients who underwent treatment with organotherapic medicine showed a significant reduction (p<0,001) in blood glucose

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levels (from 204.5±86.63 to 86.63±16) and lower insulin levels after four months of treatment (organotherapic group with 8.02±3.598 versus placebo with 23.83±3.670 p<0,001) within normality, regardless of age, time of infection and time of treatment. This fact suggests that the organotherapic drug was effective to stabilize blood glucose levels in patients.

Conclusion: Current study evidences that the organotherapic drug obtained from the pancreas of a young pig, diluted $1x10^{12}$ in alcohol/ water 8% improves blood glucose levels in patients with hyperglycemia keeping within the normal range after four months of treatment. Considering the HAART therapy that significantly increases the life expectancy of AIDS patients but with significant metabolic alterations this study shows the possibility of utilization of complementary and alternative therapies. Although results indicate a significant effect of the organotherapic drug, additional studies are needed to evaluate the long-term effects.

Keywords: Organotherapic medicine; HIV/AIDS; blood glucose; insulin level; complications.

1. INTRODUCTION

Metabolic disorders including insulin resistance, diabetes and dyslipidemia have been of significant concern to HIV-infected adults since the introduction of effective antiretroviral therapy. Further studies have shown that HIV-infected adults may be at the risk of accelerated atherosclerosis and cardiovascular disease [1,2,3,4]. While HIV infection and therapies have been associated with adipose tissue changes and glucose and lipid metabolism disorders that may prematurely increase cardiovascular disease risk, more recent data have suggested that immune activation and inflammation from chronic HIV infection might also play an important role [5,6].

HIV is also associated with various endocrine abnormalities. The increased accumulation of visceral fat and waste of subcutaneous fat noted in patients with HIV provokes higher levels of inflammatory cytokines such as TNFα. The latter in turn leads to diabetes or impaired glucose tolerance by increasing insulin resistance [7]. However, the major contributor to hyperglycemia in HIV/AIDS is iatrogenic. The past few decades have seen a remarkable improvement in the clinical outcome of HIV patients due to highly active antiretroviral therapy (HAART). On the other hand, HAART may also lead towards an increase in metabolic dysfunction, including insulin resistance, diabetes, dyslipidemia and lipodystrophy [8,9,10].

Regenerative medicine replaces or regenerates human cells, tissues or organs to restore or establish normal functions [11]. Diabetes represents an attractive candidate for cell therapy. Several studies have reported the production of insulin-secreting cells from embryonic and adult stem cells that normalized blood glucose rates when transplanted into diabetic animal models [12].

Organotherapic medicine, pharmacologically classified as Biotherapeutic, are medicinal preparations made from not chemically defined biological products, such as secretions, excretions, tissues and organs, products of microbial origin and allergens [13]. Current study evaluated the effect of an organotherapic drug, produced from the pancreas of a young pig, on the glycemic alterations in patients with AIDS.

2. MATERIALS AND METHODS

2.1 Organotherapic Medicine

Drug organotherapic produced from the pancreas of a young pig was obtained from the laboratory HN CRISTIANO, São Paulo, Brazil and diluted in $1x10^{12}$ alcohol/water 8%. The method used to prepare the drug has been described in the Brazilian Homeopathic Pharmacopoeia [14,15]. Healthy young pig was sacrificed and evaluated by a veterinarian. The pancreas of the animals were removed immediately and were washed three times in iced saline solution. The pancreas was kept in an ice bath and chopped into small pieces. It was then size reduction with equipment Vibratory Disc Mills Retsch RS200® triturated with lactose monohydrate P.A. at a ratio 1: 100 for 10 minutes. The homogenate was filtered through gauze and diluted in sterile mixture of 70% ethanol, water and glycerin (1: 1: 1). The organotherapic drug was left in the protected environment of the direct action of light and heat, shaking the container daily. It was filtered again on sterile gauze and diluted in water/ alcohol 70%. Being the solution of inventory that was used for preparation of the diluted drug organotherapic. All procedures were performed under aseptic conditions and sterile

equipment. Placebo medication was produced with lactose monohydrate and alcohol/ water 8% using the same method for preparation.

2.2 Subjects

HIV/AIDS patients treated at the Center for Studies and Support to HIV Patients of the State University of Maringá-Department of Basic Health Sciences. The Center attends to approximately 200 patients who freely seek the sector to participate in the project. All patients are evaluated clinically and laboratory tests are performed before participating in the projects, and examined monthly, for four months, after the start of the study.

2.3 Inclusion Criteria

Inclusion criteria were defined as glucose levels above 110.0 mg/dL and a good general health status, absence of acute metabolic complications or acute infections symptoms. These criteria were established by a careful study of each patient´s record and by a full clinical examination. After the explanation of the project, patients signed an informed consent approved by the Ethics and Research on Human Experimentation of the State University of Maringá, Maringá PR Brazil, and COPEP. CAAE n^{o} 0408.0.093.000-10/2011.

2.4 Study Model

Current study was carried out in a double-blind, placebo controlled and randomized design. AIDS patients who had high fasting glucose were selected so that the effect of the organotherapic drug could be evaluated. The patients were divided into two groups: Group I, comprised patients who received the organotherapic drug once a day, with a dose of 10 drops, administered sublingually and in fasting, for four months. Group II consisted of patients receiving placebo once a day in the same dosage. The groups were made by pairing age and gender.

2.5 Clinical and Laboratory Analysis

After an approximately 10-h overnight fast, 5 ml of venous blood was obtained from each patient. Levels of glucose were determined by glucose oxidase method (enzymatic colorimetric method) provided by GOLD ANALISA DIAGNÓSTICA LTDA and insulin levels were evaluated by ELISA (Active Insulin Elisa kit -Genway Biotechnology, USA), following the manufacturer's instructions. Overall clinical evaluation was performed and fasting serum glucose specific method was performed at each month up to the end of treatment, after four months. Clinical evaluation was performed monthly to assess the overall clinical state of the patient and patients were instructed to report any complications.

2.6 Statistical Analysis

Group-comparing statistics were performed with GraphPad Prism (GraphPad, San Diego, CA, USA), using Student's test. *P* rates at <0.05 were considered statistically significant.

3. RESULTS

Sixty patients, 32 males and 28 females, with glucose levels above 110.0 mg/dL, participated in current study. All were using HAART therapy for at least five years with mean 9.3±3.76 and average time of infection of 10.0±4.78 years. Patients´ age ranged between 35 and 50 years, with mean 43.53±6.107. Patients were divided into two groups (one group was treated with organotherapic drug and the other group by a placebo) with 30 patients each, 16 males and 14 females, in pairs for age and gender.

3.1 Effect of the Organotherapic Medicine on Fasting Blood Glucose

Table 1 shows the results of fasting blood glucose levels of patients undergoing treatment with organotherapic drug and compared to the placebo group.

Table 1. Fasting glucose levels in the experimental groups. Levels of blood glucose (mg/dL) before treatment and glucose levels after four months of treatment

Group	Before treatment	After treatment
I (n=30)	204.5±108	86.63±16*
II (n=30)	197.2±107	218±128

*Each value corresponds to average of patients: Group I comprised patients who received the organotherapic drug once a day, at a dose of 10 drops, administered sublingually and while fasting, during four months. Group II consisted of patients who received a placebo once a day, in the same dosage; *p< 0.001 (Student´s t test)*

Fig. 1 shows the fasting blood glucose analysis. Fasting glucose was significantly lower after four months of treatment in subjects of Group I (n=30) treated with an organotherapic. Levels of blood glucose were gradually being reduced and remained stable within reference rates, after four months of treatment.

3.2 Effect of Organotherapic Medicine on Insulin Levels

Table 2 shows insulin levels of patients undergoing treatment with organotherapic drug after four months of treatment and compared to the placebo group.

Table 2. Plasma insulin levels in AIDS patients with hyperglycemia undergoing treatment with organotherapic medicine

Group	Insulin levels (3 -20µl U/mL)
I	8.02±3.598*
II	23.83±3.670

*Each value represents mean±SEM of insulin levels of AIDS patients with hyperglycemia, treated with organotherapic drug (Group I), and with a placebo (Group II). The treatment was continued for four months. (Student´s t test) *p<0.001*

Fig. 2 shows that indexes of insulin sensitivity obtained from the steady state (fasting) are normal in patients treated with the organotherapic drug (Group I), while the place bo (Group II) shows high levels of insulin.

4. DISCUSSION

As HIV treatment develops and access to therapy improves, the incidence of HIV-associated diabetes is bound to grow. The occurrence of diabetes has increased with the cumulative exposure to combination antiretroviral therapy [16,17,18]. Patients in this study had received HAART therapy for 9.3±3.76 years and the group underwent high exposure therapy.

Three subgroups of patients with diabetes and HIV may be identified: patients with preexisting diabetes who became infected with HIV; patients were diagnosed to have diabetes onset from HIV infection; patients who developed hyperglycemia after the start of therapy. Patients who participated in current study did not have diabetes before antiretroviral therapy treatment. Moreover, the group consisted of patients with at least a five-year-old positive diagnosis for HIV and treated with antiretroviral therapy, which made the study group have in common a relatively large exposure time to the effects of antiretroviral therapy. One may thus infer a significant effect of therapy inducing or exacerbating hyperglycemia.

Patients with HIV will certainly have the same rates of diabetes as reported in the background population. Owing to their relatively younger age, HIV patients may have a lower occurrence of preexisting diabetes when infected. However, as they grow older, they may develop diabetes in the normal course of events. Certain metabolic factors related to HIV and to HIV therapy may increase the occurrence of diabetes among them [19]. Current results reported hyperglycemia in 30% of the patients, which is higher than the percentage in the general population (5-15%) [10].

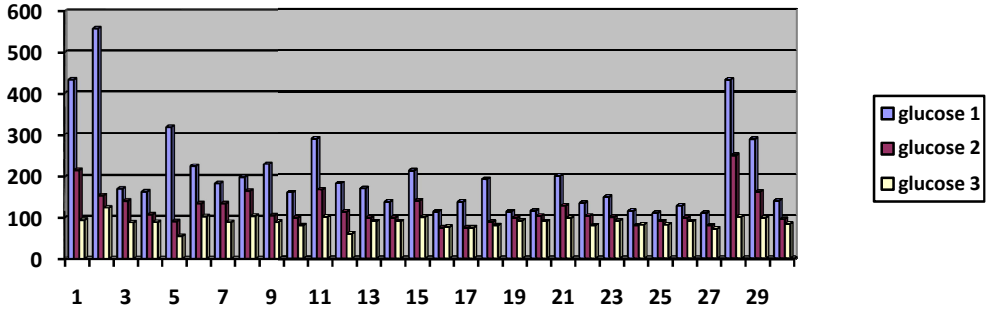

Fig. 1. Effect of drug organotherapic (produced from the pancreas of a young pig and diluted in $1x10^{12}$ alcohol/water 8%) on blood glucose levels in patients who received the organotherapic drug once a day, with a dose of 10 drops, administered sublingually. Glucose 1= before treatment, Glucose 2=after two months of treatment and Glucose 3=after four months of treatment. (n=30)

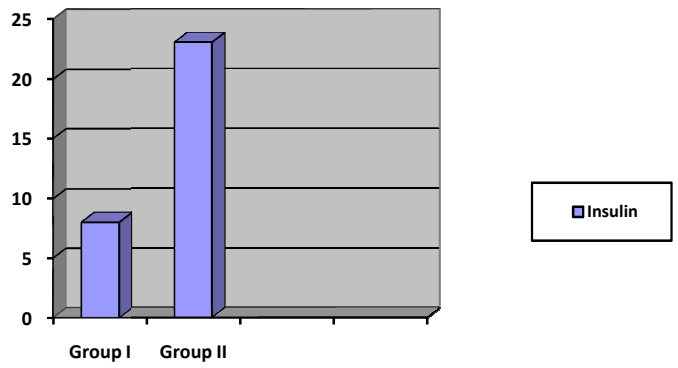

Fig. 2. Effect of drug organotherapic (produced from the pancreas of a young pig and diluted in 1x10^{12} alcohol/water 8%) on blood insulin levels in patients who received the organotherapic drug once a day, with a dose of 10 drops, administered sublingually (Group I, Mean, n=30) and patients who received placebo once a day, with a dose of 10 drops, administered sublingually (Group II, Mean, n=30) *P<0,001*

This fact might be related to the time of infection (median 15 years) and treatment (mean 5 years) of the patients. On the other hand, patients who underwent treatment with organotherapic medicine showed a significant reduction in blood glucose levels regardless of age, time of infection and time of treatment. The above suggests that the organotherapic drug was effective to stabilize blood glucose levels in patients. This is evident by results in Fig. 1. Extremely high blood glucose levels in patients were reduced, after a four-month treatment, to normal rates, in the same way as those in patients with moderate or mild hyperglycemia whose blood glucose also decreased until reaching normal levels.

Impaired glucose tolerance and insulin resistance precede weight loss inpatients with HIV [20,21,22,23]. Insulin resistance, rather than insulin deficiency, is usually implicated in the pathogenesis of diabetes in HIV-infected patients, According to earlier reports, evidence of islet cell autoimmunity, or beta cell destruction, has not been detected in HIV patients [24]. Autoimmune diabetes, however, has been reported to develop in some HIV-infected patients after immune restoration during HAART [25,26]. The results of current study (Fig. 2) clearly show a reduction in insulin in all patients treated with the organotherapic drug.

The drug used was formulated in ultradiluted form (1x10^{12} in alcohol/ water 8%) which may be similar to the production of nanoparticles. Medicinal nanoparticles stimulate a complex adaptive response in the organism that begins in the allostatic stress response network, with cascading indirect consequences over tie across the entire self-organizing organism [27].

The maintenance of blood glucose homeostasis is crucial to decrease the risk of metabolic complications in patients. From this point of view, organotherapic medicine demonstrated a beneficial effect because it maintained blood glucose homeostasis. This fact has been proven by insulin levels within normal levels, unlike those in patients treated with placebo.

5. CONCLUSION

Current analysis evidences that the organotherapic drug obtained from the pancreas of a young pig and diluted in 1x10^{12} alcohol/ water 8% improves blood glucose levels in patients with hyperglycemia keeping within the normal range after four months of treatment. Considering the HAART therapy that significantly increases the life expectancy of AIDS patients but with significant metabolic alterations this study shows the possibility of utilization of complementary and alternative therapies. Although results indicate a significant effect of the organotherapic drug, additional studies are needed to evaluate the long-term effects.

CONSENT

Not applicable.

ETHICAL APPROVAL

Ethical clearance was sought for and obtained from the Ethics Committee of the State University of Maringá, Maringá PR Brazil. The protocol was approved according to Resolution n° 196/96 and additional CNS / MS in 210th deliberative meeting of COPEP. CAAE n° 0408.0.093.000-10/2011.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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