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# Nutritional therapy in metabolic changes in individuals with HIV/AIDS

## ABSTRACT

**OBJECTIVE:** To analyze the effect of nutritional treatment on metabolic changes caused by the use of antiretroviral therapy in adults with HIV/AIDS.

**METHODS:** A systematic review of literature was conducted in the PubMed, Lilacs and Cochrane databases, between 1996 and 2010, including crossover and randomized controlled clinical trials performed in adults with HIV/AIDS using antiretroviral therapy and without opportunistic diseases. The intervention of interest was oral nutritional supplementation and/or a change in lifestyle due to specific dietary treatment: dyslipidemia, insulin resistance, lipodystrophy and systemic arterial hypertension. The Jadad scale was used for a qualitative classification of articles.

**RESULTS:** A total of 385 articles were found, of which seven were included. The interventions used in these studies were as follows: diet, diet and physical exercises, diet and supplementation, and only supplementation. Dyslipidemia was the outcome assessed in all studies. Studies that assessed omega-3 supplementation found a significant reduction in triglycerides. The specific diet with omega-3 supplementation showed an increase in HDL-cholesterol. Chrome nicotinate supplementation did not have an effect on dyslipidemia. Changing one's lifestyle, including diet and physical activity, significantly reduced waist circumference, lipodystrophy and systolic blood pressure.

**CONCLUSIONS:** Reduction in tryglicerides with omega-3 supplementation was the nutritional intervention with the strongest scientific evidence. Prescribing a specific diet appeared to be the most adequate intervention to increase HDL-cholesterol. Inferences could not be made about the nutritional treatment of total cholesterol, LDL-cholesterol and insulin resistance. Changes in lifestyle can promote an improvement in lipodystrophy and blood pressure.

**DESCRIPTORS:** Antiretroviral Therapy, Highly Active, adverse effects. Dietary Supplements, utilization. HIV-Associated Lipodystrophy Syndrome, diet therapy. Dyslipidemias, diet therapy. HIV Long-Term Survivors. Review.

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## INTRODUCTION

The World Health Organization (WHO) estimated there were 33.4 million people infected with HIV in 2009, of which 2.7 million new cases, and 2 million were aids-related deaths.<sup>a</sup> The availability of *highly active antiretroviral therapy* (HAART) has had a major impact on HIV/AIDS mortality and morbidity in recent years. However, HAART has been associated with metabolic adverse

<sup>a</sup> Joint United Nations Programme on HIV/AIDS. World Health Organization. AIDS epidemic update. Geneva: UNAIDS/WHO; 2009. 100p.

events characterized by dyslipidemia, body composition changes / lipodystrophy, insulin resistance / glucose intolerance and hypertension. Living with HIV/AIDS has become a condition similar to other non-communicable chronic diseases requiring lifestyle changes and drug management for prevention of cardiovascular events, among others.<sup>b</sup>

The WHO recommends that nutrition interventions should be part of all HIV/AIDS control and treatment programs because adequate diet and nutrition can improve adherence to antiretroviral therapy (ART) and its effectiveness, as well as help tackling metabolic abnormalities in people living with HIV/AIDS.<sup>c</sup> However, there is no consensus on the effect of nutrition therapy in people living with HIV/AIDS (PLWHA) on ART.

The present study aimed to assess the effect of nutrition therapy on improving metabolic changes caused by the use of ART.

## METHODS

Systematic literature review using a search engine especially designed by the authors but not recorded in specific databases for systematic review. The following aspects were predefined: topic; inclusion criteria; search and selection strategies; quality assessment; data collection and analysis form; and presentation and interpretation of study results. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)<sup>12</sup> recommendations were used as an aid tool.

There were selected cross-over, randomized, controlled, blinded or open, clinical trials published between 1996 and November 2010, conducted in both female and male adults living with HIV/AIDS on ART and with no manifestations of opportunistic diseases. The lower data limit for published studies was set based on the year of introduction of ART. Studies in English, Spanish, Portuguese and French were selected.

Interventions of interest were nutrition therapies aiming to improve metabolic abnormalities through oral supplementation or specific dietary therapies plus lifestyle changes. Oral supplementation regardless of dosage, dosing interval and duration of treatment / intervention and interventions tested against placebo or no intervention were assessed. The following outcomes of these interventions were studied: dyslipidemia, insulin resistance or glucose intolerance; lipodystrophy / body composition changes; and hypertension.

Outcome measures in mmol/L, g/L, and mg/dL were converted into mg/dL according to the International System of Units to make them consistent and comparable.

Subjects requiring enteral or parenteral nutrition were not included in the study because they had different nutritional needs and required different approaches than those used for metabolic changes and they were likely to have opportunistic infections.

The following was reviewed and analyzed in the articles selected: author; year of publication; country; follow-up duration; methods; type of population; sample size; type of intervention; comparability between intervention and control groups at baseline; quality of outcome measurements; outcome results in intervention and control groups; treatment adherence; and adverse effects.

The Jadad scale<sup>9</sup> was used to independently and blindly assess methodological quality of studies. Two researchers assigned scores (zero to five) to the studies selected based on the following criteria: method of randomization (sequences and subject randomization criteria); use of blinding (subjects and investigators); and description of lost-to-follow-up proportions.

Two independent blinded researchers conducted the process of searching and selecting articles to avoid selection bias. When there was no agreement whether an article should be included or not in the study, this decision was made by a third researcher. The authors were not contacted at all.

The literature search was performed in PubMed, LiLACS, and Cochrane electronic databases (The Cochrane Central Register of Controlled Trials – CENTRAL) using a combination of three actions:

*- [(life and style and intervention or life and style and supplementations or nutritional and support or nutrition and therapy or exposure and dietetics or dietary and intake or food or food and consumption or eating or energy and intake or nutrient or diet)] AND [(lipodystrophy or hiv and associated and lipodystrophy and syndrome or body and fat and distribution or body and fat and redistribution or lipoatrophy or lipohypertrophy or body and composition or hypertension or insulin and resistance or glucose and intolerance or diabetes and mellitus or dyslipidemias or hypertriglyceridemia or hyperlipidemia or hypercholesterolemia or metabolic and syndrome or metabolic and abnormalities)] AND [(antiretroviral and therapy, and highly and active or haart)] AND Species=Humans.*

<sup>b</sup> Brazilian Ministry of Health. Recomendações para terapia antirretroviral em adultos e adolescentes infectados pelo HIV 2007/2008. Brasília: Ministério da Saúde; 2008. 229p

<sup>c</sup> World Health Organization. Nutrient requirements for people living with HIV/AIDS. Reports of a technical consultation. Geneva: WHO; 2003. 31p.

Search filters (“humans” and “all adults”) were used to increase specificity. References in review and consensus articles and in articles retrieved using the search strategy were searched manually to ensure the inclusion of all articles relevant to the topic. No contact was made with medical researchers to check for ongoing research.

## RESULTS AND DISCUSSION

A total of 385 non-duplicate articles were retrieved. Seven were included after eligibility criteria were applied (Figure).

The articles retrieved while searching for insulin resistance were the same ones retrieved while searching for glucose intolerance.

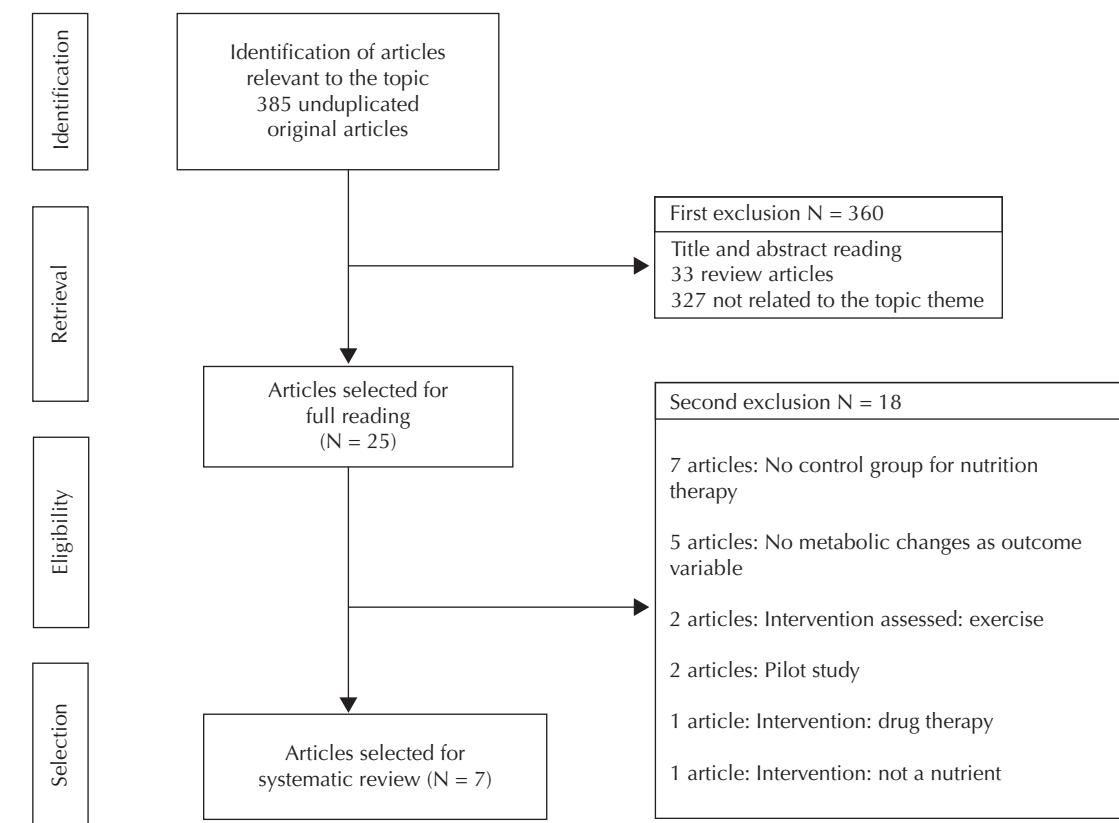
Of the seven studies included, four were conducted in the United States,<sup>8,17,18</sup> two in Canada,<sup>1,2</sup> one in France,<sup>16</sup> and one in Australia.<sup>4</sup> They were published from 2005 to 2009 (Table 1).

Diet, diet and exercise, diet and supplementation and supplementation only were the most common nutrition

interventions used. Two studies<sup>8,18</sup> used diet as study intervention. One<sup>8</sup> followed the National Cholesterol Education Program-Adult Treatment Panel Guidelines (NCEP III)<sup>4,d</sup> and the other one<sup>18</sup> had no reference. Diet was used in an attempt to equate the intervention group (IG) and controls before implementing the intervention being tested.<sup>4,16</sup> Food supplements included chromium nicotinate and omega 3. Omega 3 was tested in five studies, with doses ranging from 3 g to 9 g/day (Table 1).

The number of subjects included in each group (IG and controls) ranged from five to 62. All studies but one analyzed data from those who completed the study (completers). Truchis et al<sup>16</sup> (2007) also included an intention-to-treat analysis. Lost-to-follow-up was reported in six studies.<sup>1,2,4,8,16,17</sup> The follow-up period ranged from 13 weeks to six months (Table 1).

Two were randomized, controlled and double blind studies,<sup>1,4</sup> two were randomized cross-over,<sup>2,16</sup> and three were randomized controlled trials.<sup>8,17,18</sup> (Table 1). Intraevaluator and interevaluator reliability as well as measures of association were not reported in the articles.



**Figure.** Flowchart of identification, retrieval, eligibility, and selection of clinical studies for review.

<sup>d</sup> National Cholesterol Education Program (US). Third Report of the National Cholesterol Education Program (NCEP). Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Bethesda (MD): National Heart, Lung, and Blood Institute (US); 2005. 48 p. (NIH publication; no. 02-5215).

**Table 1.** Description of intervention, study population, follow-up duration, methods, and outcome measures. 2005–2009.

Author/ Year of publication/ Country	Follow-up duration and methods	Study population Intervention group (IG) Controls (CG)	Intervention	Outcomes assessed	Jadad scoring
Aghdassi et al, <sup>1</sup> 2009 Canada	16 weeks randomized controlled, double- blind trial	IG: 23 HIV-infected CG: 23 HIV-infected + calcium phosphate	Chromium nicotinate (400 mg/day)	Triglycerides Total cholesterol LDL, HDL Body composition Insulin resistance	5
Woods et al <sup>18</sup> 2009 USA	13 weeks randomized, controlled trial	IG: 21 HIV-infected CG: 26 HIV-infected + regular diet	Diet (25% lipids, fiber ≥ 40 g/day, low glycemic index) + omega-3 (3 g/day)	Triglycerides Total cholesterol LDL, HDL	3
Baril et al <sup>2</sup> 2007 Canada	24 weeks crossover, randomized, controlled trial	Randomized double-blind phase IG: 26 HIV-infected CG: HIV-infected Open phase: IG: 26 HIV-infected CG: 31 HIV-infected and omega-3 after 12 weeks	Omega-3 (3 g/day)	Triglycerides Total cholesterol LDL, HDL	3
Truchis et al <sup>16</sup> 2007 France	16 weeks crossover, randomized, controlled double- blind trial	Randomized double- blind phase IG: 58 HIV-infected + hypertriglyceridemia CG: 62 HIV-infected + hypertriglyceridemia Placebo – paraffin oil. Open phase: IG: 55 HIV-infected + hypertriglyceridemia CG: 56 HIV-infected + hypertriglyceridemia	Equating groups with AHA <sup>a</sup> dieta for 4 weeks and then omega-3 (6 g/day)	Triglycerides Total cholesterol HDL	5
Carter et al <sup>4</sup> 2006 Australia	14 weeks randomized controlled, double- blind trial	IG: 5 HIV-infected CG: 6 HIV-infected + olive oil	Equating groups with nutritional counseling following the National Heart Foundation Guidelines for 6 weeks and then omega-3 (9 g/day)	Triglycerides Total cholesterol	4
Fitch et al <sup>8</sup> 2006 USA	6 months randomized controlled trial	IG: 12 HIV-infected CG: 16 HIV-infected + nutritional counseling	Lifestyle changes Nutritional counseling (NCEP <sup>b</sup> III + DDP + AACE <sup>c</sup> ) + diet <sup>e</sup> + exercise	Triglycerides Total cholesterol LDL, HDL Body composition Blood pressure	3
Wohl et al <sup>17</sup> 2005 USA	16 weeks randomized controlled trial	IG: 22 HIV-infected CG: 19 HIV-infected Counseling on diet and exercise according to AHA recommendations throughout follow-up	Omega-3 (3 g/day)	Triglycerides Total cholesterol LDL, HDL	3

<sup>a</sup> American Heart Association (AHA) diet: 15%-18% protein, 45%-55% carbohydrates and 30%-35% lipids and no alcohol

<sup>b</sup> NCEP III: National Cholesterol Education Program-Adult Treatment Panel Guidelines; DPP: Diabetes Prevention Program, AACE: American Association of Clinical Endocrinologists

<sup>c</sup> 35% lipid diet (less than 10% saturated fat, more than 10% polyunsaturated fat with emphasis on the consumption of omega-3 plus more than 20% of monounsaturated fat, 25 g to 35 g of soluble and insoluble fiber).

Dyslipidemia was reported in all studies,<sup>1,2,4,8,16-18</sup> lipodystrophy / body composition changes in two,<sup>1,8</sup> and insulin resistance / glucose intolerance<sup>1</sup> and hypertension<sup>8</sup> in one (Table 1).

The quality assessment of studies using the Jadad scale<sup>9</sup> showed that all had good methodological quality: two scored five,<sup>1,16</sup> one score four,<sup>4</sup> and four score three.<sup>2,8,17,18</sup> Most studies did not use blinding.<sup>2,8,17,18</sup>

The three double-blind studies<sup>1,4,16</sup> used supplementation as nutrition intervention, including placebo and blinding; one of them<sup>4</sup> did not provide information on the method of randomization.

The effects of each intervention by the outcomes dyslipidemia, body composition changes / lipodystrophy, insulin resistance / glucose intolerance and hypertension are presented in Tables 2, 3 and 4.

### Effects on dyslipidemia

Five studies examined the effects of supplementation with omega-3 on dyslipidemia in PLWHA on ART.<sup>2,4,16-18</sup> Omega-3 fatty acids can promote a reduction in plasma triglycerides by decreasing hepatic synthesis of VLDL-cholesterol in the general population and may have other cardiovascular effects. At high doses (4 to 10 g/day), they can reduce triglycerides and slightly increase HDL-cholesterol, but may increase LDL-cholesterol. Omega-3 can be administered as adjuvant therapy in patients with hypertriglyceridemia,<sup>6</sup> but its effects on PLWHA on ART is unknown.

Woods et al<sup>18</sup> (2009) conducted an intervention study using more specific dietary supplementation with omega-3 (3 g/day). They found more

significant reductions in triglycerides in IG than controls. HDL-cholesterol significantly increased in IG at the end of the study compared to baseline, but there was no significant difference between IG and controls. Total cholesterol in IG was significantly lower compared to baseline and was lower than controls at week 3 of a 13-week follow-up. No significant differences were seen in LDL-cholesterol.

Supplementation with omega-3 (3 g/day) was also used in Baril et al study.<sup>2</sup> There was a significant reduction in triglycerides in IG compared to controls in the first phase of the study, but no significant reduction compared to baseline. Total cholesterol was reduced in IG. There was no significant change in either LDL-cholesterol or HDL-cholesterol.

Dietary changes were not evaluated, although all subjects were instructed not to change their diet and level of physical activity. A limitation of this study is its open design, though the authors claimed the study scenario matched a real-life one where patients and physicians are aware of their treatment.

Truchis et al<sup>16</sup> (2007) conducted a randomized study in patients with hypertriglyceridemia following a 4-week diet as proposed by the American Heart Association.<sup>10</sup>

**Table 2.** Results of clinical trials of nutritional intervention for dyslipidemia. 2005-2009.

Author/Year of publication/ Country	TG	Resultados encontrados		
		TC	LDL	HDL
Aghdassi et al <sup>1</sup> 2009 Canada	↓ TG in IG compared to baseline (-48 mg/dL)	NS	NS	NS
Woods et al <sup>18</sup> 2009 USA	↓ TG in IG compared to baseline (-70 mg/dL) and to CG (-70 mg/dL vs. +30 mg/dL)	↓ TC in IG at week 3 compared to baseline (-22 mg/dL) and to CG (-22 mg/ dL vs. +5 mg/dL)	NS	↑ HDL in IG at week 13 compared to baseline (+5 mg/dL)
Baril et al <sup>2</sup> 2007 Canada	↓ TG in IG compared to CG (-97mg/dL vs. +27 mg/dL) – double-blind phase  (-100 mg/dL) and compared to CG (-100 mg/dl vs. +10 mg/dL) – double- blind Phase	↓ TC in IG compared to baseline (-15 mg/dL) – double-blind phase	NS	NS
Truchis et al <sup>16</sup> 2007 France	↓ TG in CG at the end of double-blind phase (-150 mg/dL) - open phase <sup>a</sup>	NS	NA	NS
Carter et al <sup>4</sup> 2006 Australia	↓ TG in IG compared to CG (-269 mg/dl vs. -61 mg/dL)	NS	NA	NA
Fitch et al <sup>8</sup> 2006 USA	NS	NS	NS	NS
Wohl et al <sup>17</sup> 2005 USA	↓ TG in IG at week 4 compared to baseline (-155 mg/dl) and to CG (-155 mg/dl vs. +11 mg/dl) ↓ TG in IG at week 16 compared to baseline (-157 mg/dl)	NS	↑ LDL in IG at week 16 compared to baseline (+26 mg/dl)	NS

<sup>a</sup> All subjects received the intervention in the open phase of the study. TG: triglycerides; IG: intervention group; CG: control group; TC: total cholesterol; HDL: high-density lipoprotein; LDL: low-density lipoprotein; NS: not significant; NA: not assessed.

**Table 3.** Results of clinical trials of nutritional intervention on body composition changes and lipodystrophy. 2005-2009.

Study (author/year of publication/country)	% total fat	% fat in the trunk	% fat in the arms	% fat in the legs	% lean body mass	CC	Lipodystrophy score
Aghdassi et al <sup>1</sup> 2009 Canada	↓ total fat compared to baseline (-0.96%)	↓ fat in the trunk in IG compared to baseline (-1.05%)	↓ fat in the arms in IG compared to baseline (-0.55%)	↓ fat in the legs in IG compared to baseline (-0.74%)	↑ lean body mass in IG compared to baseline (+0.83%)	NS	NA
Fitch et al <sup>8</sup> 2006 USA	NA	NA	NA	NA	↓ WC in IG compared to CG (-2.6 cm vs. +1.2 cm)	↓ lipodystrophy in IG compared to CG (-1.2 vs. +0.9)	

WC: Waist circumference; IG: intervention group; CG: control group; NS: not significant; NA: not assessed.

**Table 4.** Results of clinical trials with dietary intervention for insulin resistance and hypertension. 2005-2009.

Study (author/year of publication/country)	Resultados encontrados	
	Insulin resistance	Hypertension
Aghdassi et al <sup>1</sup> 2009 Canadá	↓ insulin resistance compared to baseline (-0.43)	-
Fitch et al <sup>8</sup> 2006 USA	-	↓ systolic pressure in IG compared to CG (-13 mm Hg vs. +4 mm Hg)

IG: intervention group; CG: control group.

IG received omega-3 (6 g/day). There was a significant reduction in triglycerides in IG compared to controls and also a significant reduction in the first phase of the study compared to baseline in the intention-to-treat analysis and completers. There was also seen a reduction in triglycerides in controls in the open phase of the study compared to the last double-blind phase. There was no statistical difference for total cholesterol and HDL-cholesterol.

Carter et al<sup>4</sup> (2006), in an attempt to equate adult male patients, provided them with dietary counseling following the National Heart Foundation guidelines<sup>13</sup> for six weeks and then they were randomized to receive omega-3 (9 g/day). A significant reduction in triglycerides was seen in IG compared to controls. There was no significant difference in total cholesterol between the two groups. Although it was a randomized, controlled, double-blind study, the sample size was small.

Wohl et al<sup>17</sup> (2005) assessed supplementation with omega-3 (3 g/day) for 16 weeks. All subjects (IG and controls) were instructed to reduce their consumption of trans fatty acids, increase their fiber intake and engage

in a daily aerobic exercise program. There was a significant mean reduction in triglycerides in IG compared to baseline at week 4 to week 16. At week 16, there was significant reduction in triglycerides in IG compared to controls. LDL-cholesterol significantly increased in IG compared to baseline. Total cholesterol and HDL-cholesterol did not change significantly in either group. Supplementation with omega-3 significantly reduced triglycerides in IG compared to controls in at least one time point during the study.<sup>2,4,16-18</sup> This reduction was not dependent on the supplementation dosing (3, 6 or 9 g/day), dieting and exercising. The only study using a supplementation dose of 9 g/day of omega-3 showed the greatest reductions in triglycerides.<sup>4</sup> While it evidences a positive effect of supplementation on triglycerides, the amount of supplementation prescribed (9 g/day) may hinder adherence to treatment. Thus, the ability of patients to tolerate it in high doses in the long run remains unknown.

Patients on lipid lowering drugs were included in the sample but no analysis was carried out to differentiate the effect of the drug from the nutrition intervention, which may have been a major bias. The same was seen in two other studies.<sup>2,17</sup>

There is no evidence supporting an effect of specific diets or dietary counseling and exercise on hypertriglyceridemia in PLWHA on ART. Wohl study<sup>17</sup> (2005) investigated nutritional counseling, recommendations on physical activity, and supplementation with omega-3, and found the greatest reduction in triglycerides among studies investigating the use of omega-3 at a dose of 3 g/day. A set of actions including a specific diet, daily exercise, and supplementation with omega-3 may be the more suitable approach for treating hypertriglyceridemia in these patients.

No significant reduction in total cholesterol was seen in three<sup>4,16,17</sup> of five studies.<sup>2,4,16-18</sup> Two studies<sup>2,18</sup> found a significant reduction. One of them<sup>2</sup> found a reduction compared to baseline. Omega-3 may reduce total

cholesterol, but the results are inconsistent. Of three studies<sup>2,17,18</sup> evaluating LDL-cholesterol, two<sup>2,18</sup> did not find any significant reductions and one<sup>17</sup> found a significant increase compared to baseline.

HDL-cholesterol did not significantly increase in three<sup>2,16,17</sup> of four studies.<sup>2,16-18</sup> A study<sup>18</sup> showed a significant increase in HDL compared to baseline. In this study, in addition to omega-3 a specific diet low in total and saturated fat, high in fiber and omega-3 and with low glycemic index was prescribed as part of the intervention.<sup>18</sup>

High levels of triglycerides was an eligibility criterion in some studies; in one study, these criteria included high levels of triglycerides or abnormal quantitative insulin sensitivity check index.<sup>18</sup> Except for one study,<sup>4</sup> all studies did not find any significant differences between the intervention group and controls at baseline.

Two<sup>4,16</sup> of five studies<sup>2,4,16-18</sup> assessing the effect of supplementation with omega-3 on dyslipidemia included placebo in controls. These same two studies provided nutritional counseling before supplementation in an attempt to equate the intervention and control groups. In another study, subjects (IG and controls) were provided with counseling on diet and exercise throughout follow-up.<sup>17</sup>

There is no evidence to indicate that any treatment has significant effects on reducing total cholesterol and LDL-cholesterol and increasing HDL-cholesterol. Further studies are needed, but it has been suggested that a customized food plan with specific recommendations on dyslipidemia is the most effective approach to reduce total cholesterol and increase HDL-cholesterol because it has no unfavorable, deleterious effects.

Supplementation with chromium nicotinate 400 mg/day was evaluated in a 16-week study with significant reduction in triglycerides in IG compared to baseline.<sup>1</sup> Chromium is an essential nutrient of glucose and lipid metabolism as it enhances insulin action.<sup>5</sup>

The authors pointed to their study limitations including a heterogeneous sample of patients regarding to metabolic parameters, duration of HIV infection, duration of HAART and other drug therapies, as well as inaccuracies in evaluating dietary chromium intake. The population studied included predominantly male subjects, which may have been a bias in the study.

There were not evaluated any differences in the effect of the intervention between IG and controls at the end of the study. Statistical analyses were performed only in each individual group at baseline and at the end of the study and no intention-to-treat analysis was performed.

Supplementation with chromium showed significant results, but they were not quite remarkable when

compared to the reductions seen with omega-3. A single study investigating supplementation with chromium is not enough to support whether chromium should be used or not.

One intervention study included lifestyle changes with no supplementation.<sup>8</sup> This study comprised patients with metabolic syndrome were randomly distributed between IG and controls. The IG received counseling on healthy diet and physical activity throughout the study. Sociodemographic and clinical characteristics of subjects in both groups were compared at baseline and no significant differences were found. After 16 weeks of follow-up, there were no significant effects on triglycerides, total cholesterol, HDL-cholesterol and LDL-cholesterol.

The study limitations were small sample size and short follow-up, which may have affected the results. Unlike studies that evaluated the effect of supplementation with omega-3 on dyslipidemia, this study<sup>8</sup> did not include high levels of triglycerides as an eligibility criterion.

### **Effect on body composition and lipodystrophy**

Lipodystrophy was first reported in 1998, two years after the introduction of ART.<sup>3</sup> Early controlled studies investigating how to minimize metabolic abnormalities caused by HAART dated back in 2006. Lipodystrophy is characterized by changes in body fat distribution including central lipohypertrophy, peripheral lipoatrophy and mixed lipodystrophy.<sup>3,7,11</sup>

Supplementation with chromium nicotinate significantly reduced total body fat and measures of body fat in the trunk, arms and legs compared to baseline.<sup>1</sup> There was an increase in total lean mass; however, a reduction in the percent of fat in the arms and legs did not result in any improvement in lipodystrophy. There was no significant reduction in waist circumference (WC).

Although IG and controls had similar physical activity profiles, changes in physical activity can affect body fat outcomes. This aspect was not investigated at the end of a 16-week follow-up. There is no clear evidence supporting the use of chromium nicotinate to treat lipodystrophy caused by ART.

Fitch et al<sup>8</sup> (2006) conducted a 6-month follow-up study with a lifestyle intervention including diet and exercise. Subjects in the IG had a significant reduction in WC and lipodystrophy compared to controls. They showed significant lifestyle changes compared to baseline while controls did not show significant changes.

The analyses between IG and controls at baseline and at the end of the study and the analysis of differences between IG and controls at the end of the study showed better results in IG than controls. One of the limitations of this study is the use of a wide variety of ARTs.

Based on the findings of the present review, it is suggested lifestyle changes including diet and exercise to reduce lipodystrophy and WC.

### **Effect on insulin resistance**

Insulin resistance can be caused by weight gain, changes in body fat distribution and use of retroviral protease inhibitors.<sup>1,14</sup> A single study<sup>1</sup> evaluated the effect of supplementation with chromium nicotinate on insulin resistance.

Aghdassi et al<sup>1</sup> (2009) found a decrease in insulin resistance in IG after supplementation with chromium nicotinate (400 mg/day). According to the Brazilian Society of Diabetes guidelines, supplementation with chromium may increase insulin sensitivity and improve glucose tolerance in individuals with type 2 diabetes or obese. However, there is no scientific evidence for this recommendation.<sup>e</sup>

As only a single study evaluated insulin resistance no recommendations can be made on nutrition interventions and/or supplementation to manage insulin resistance.

### **Effect on hypertension**

An intervention study carried out by Fitch et al<sup>8</sup> (2006) evaluated blood pressure in PLWHA on ART. The intervention was lifestyle change including a specific diet for metabolic syndrome control and physical activity. There was a significant reduction in systolic blood pressure in IG compared to controls.

The Sixth Brazilian Guidelines on Hypertension recommend that hypertension treatment include lifestyle changes.<sup>15</sup> This recommendation seems applicable to PLWHA on ART as lifestyle changes showed favorable results, even if only in systolic blood pressure. However, no further conclusions can be drawn as only a single study was reviewed.

### **FINAL CONSIDERATIONS**

One of the limitations of the present review is that only a small number of clinical trials were selected to assess

the effect of nutrition therapy in metabolic changes caused by the use of HAART. In addition, eligibility criteria for individuals with metabolic changes were inconsistent across the studies reviewed. The studies used different interventions and doses, making it difficult a comparison between studies.

Some studies did not meet key requirements for producing high-quality scientific evidence, especially blinding. However, it is well-known that blinding can be difficult to achieve in clinical trials including nutrition interventions with a diet plan or counseling on lifestyle changes.

There are little evidence of nutrition therapy for managing metabolic abnormalities in PLWHA on ART. The results are controversial and scientific information available is inconclusive.

There is strong evidence showing reduction in triglycerides after supplementation with omega-3. The prescription of a specific diet plus supplementation with omega-3 was the single intervention that resulted in increased levels of HDL-cholesterol, but this intervention was evaluated in a single study and requires further investigation.

No inferences can be made regarding the best intervention for reducing total cholesterol and LDL-cholesterol. Lifestyle changes including physical activity and healthy eating habits seem to help improving lipodystrophy and hypertension. Insulin resistance may be managed with supplementation with chromium nicotinate.

Randomized controlled studies are needed to further elucidate the effects of nutrition therapy on dyslipidemia, lipodystrophy, insulin resistance, and hypertension in PLWHA on ART. The scientific evidence available supports current recommendations for treating these abnormalities in non-specific population groups. Further research can help develop more reliable treatments for these patients and reduce the risk of cardiovascular morbidity and mortality and increase these patients' life expectancy.

<sup>e</sup> Sociedade Brasileira de Diabetes. Diretrizes da Sociedade Brasileira de Diabetes. Itapevi: SDC; 2009. 400p.

## REFERENCES

1. Aghdassi E, Arendt BM, Salit IE, Mohammed SS, Jalali P, Bondar H, et al. In Patients with HIV-Infection, Chromium Supplementation Improves Insulin Resistance and Other Metabolic Abnormalities: A Randomized, Double-Blind, Placebo Controlled Trial. *Curr HIV Res.* 2009;7(6):1-8.
2. Baril JG, Kovacs CM, Trottier S, Roederer G, Martel AY, Ackad N, et al. Effectiveness and Tolerability of Oral Administration of Low-Dose Salmon Oil to HIV Patients with HAART-Associated Dyslipidemia. *HIV Clin Trials.* 2007;8(6):400-411. DOI:10.1310/hct0806-400
3. Carr A, Samaras K, Burton S, Law M, Freund J, Chisholm DJ, et al. A syndrome of peripheral lipodystrophy, hyperlipidaemia and insulin resistance in patients receiving HIV protease inhibitors. *AIDS.* 1998;12(7):F51-8.
4. Carter VM, Woolley I, Jolley D, Nyulasi JCI, Mijch A, Dart A. A randomised controlled trial of omega-3 fatty acid supplementation for the treatment of hypertriglyceridemia in HIV-infected males on highly active antiretroviral therapy. *Sex Health.* 2006;3:287-90.
5. Davis CM, Vincent JB. Chromium oligopeptide activates insulin receptor tyrosine kinase activity. *Biochem J.* 1997;36(15):4382.
6. Departamento de Aterosclerose da Sociedade Brasileira de Cardiologia. IV Diretriz Brasileira Sobre Dislipidemias e Prevenção da Aterosclerose. *Arq Bras Cardiol.* 2007;88(Supl 1):1-19.
7. Dong KL, Bausserman LL, Flynn MM, Dickinson BP, Flanigan TP, Mileno MD, et al. Changes in body habitus and serum lipid abnormalities in HIV-positive women on highly active antiretroviral therapy. *J Acquir Immune Defic Syndr.* 1999;21(2):107-13.
8. Fitch KV, Andersonb EJ, Hubbard JL, Carpentera SJ, Waddellc WR, Caliendod AM, et al. Effects of a lifestyle modification program in HIV-infected patients with the metabolic syndrome. *AIDS.* 2006;20:1843-50
9. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials.* 1996;17(1):1-12.
10. Krauss RM, Eckel RH, Howard B, Appel LJ, Daniels SR, Deckelbaum RJ, et al. AHA Dietary Guidelines. Revision 2000: A Statement for Healthcare Professionals From the Nutrition Committee of the American Heart Association. *Circulation.* 2000;102:2284-99.
11. Lo JC, Mulligan K, Tai VW, Algren H, Schambelan M. Buffalo hump in men with HIV-I infection. *Lancet.* 1998;351(9106):867-70. DOI:10.1016/S0140-6736(97)11443.
12. Moher D, Liberati A, Tetzlaff J, Altman DJ, PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. *Ann Intern Med.* 2009;151:264-69.
13. National Heart Foundation of Australia. The Cardiac Society of Australia and New Zealand. Lipid management guidelines - 2001. *eMJA.* 2001;175:S57-87. Disponível em: <http://www.heartfoundation.org.au/SiteCollectionDocuments/Lipid-management-guidelines.pdf>
14. Samaras K, Wand H, Law M, Emery S, Cooper D, Carr A. Prevalence of metabolic syndrome in HIV-infected patients receiving highly active antiretroviral therapy using International Diabetes Foundation and Adult Treatment Panel III criteria. *Diab Care.* 2007;30(1):113-9.
15. Sociedade Brasileira de Cardiologia. VI Diretrizes Brasileiras de Hipertensão. *Arq Bras Cardiol.* 2010;95(Supl 1):1-51.
16. Truchis P, Kirstetter M, Perier A, Meunier C, Zucman D, Force G, et al. Reduction in Triglyceride Level With N-3 Polyunsaturated Fatty Acids in HIV-Infected Patients Taking Potent Antiretroviral Therapy: A Randomized Prospective Study. *J Acquir Immune Defic Syndr.* 2007;44:278-285.
17. Wohl DA, Tien HC, Busby N, Cunningham C, MacIntosh B, Napravnik S, et al. Randomized Study of the Safety and Efficacy of Fish Oil (Omega-3 Fatty Acid) Supplementation with Dietary and Exercise Counseling for the Treatment of Antiretroviral Therapy-Associated Hypertriglyceridemia. *Clin Infect Dis.* 2005;41:1498-504.
18. Woods MN, Wanke CA, Ling PR, Hendricks KM, Tang AM, Knox TA, et al. Effect of a dietary intervention and n-3 fatty acid supplementation on measures of serum lipid and insulin sensitivity in persons with HIV. *Am J Clin Nutr.* 2009;90:1566-78.

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The authors declare no conflicts of interest.