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Prevention of Diabetes: Effects of a Lifestyle Intervention

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1. Introduction

Lifestyle is directly related to the incidence of type 2 diabetes mellitus (DM2), a risk dramatically elevated by obesity and inactivity. Sedentary lifestyle, inadequate eating habits, aging, educational backgrounds and the increased life expectancy observed in Brazil suggested to be the main culprits for the increased prevalence of DM2 seen in this country. Therefore, many epidemiologists have been emphasizing the importance of primary prevention for obesity and DM in Brazil (Sartorelli & Franco, 2003).

Some studies have shown that people consuming a diet rich in whole grains (Salmeron et al. 1997a; Salmeron et al. 1997b) and polyunsaturated fatty acids (Salmeron et al. 2001), combined with low intake of trans fatty acids and foods with low glycemic index (Salmeron et al. 1997a; Salmeron et al. 1997b; Salmeron et al. 2001; Burani &Longo, 2006), present lower risk for the development of DM2. Several studies have verified the benefit of educational interventions on the progression of impaired glucose tolerance (IGT) to DM2. Some of the interventions strategies utilized medication and diet, diet and/or physical exercise or the combination of diet and exercise, generally referred to a change in lifestyle (Pan et al. 1997; Tuomilehto et al. 2001; Knowler et al. 2002). The Finnish Diabetes Prevention Study showed that lifestyle counseling can be effective and feasible in routine health care (Tuomilehto et al. 2001; Lindstron et al. 2003; Absetz et al. 2009).

Brazilian studies evaluating the impact of DM2 on primary care or "at risk" populations are still scarce. Preliminary data from an intervention study for DM2 prevention among adults suggests that these programs are not only viable in Primary Public Health Care (Sartorelli et al. 2004) but also help to improve the health of the population. Since DM2 is one of the biggest problems in public health worldwide, it should receive special attention from health-related government entities.

In order to identify the effects of a 12-month nutritional education and lifestyle intervention program in a Brazilian urban community, on metabolic improvement, body composition and eating behavior, we evaluated subjects recruited primarily through 2 Diabetes Prevention Campaigns, carried out in November 2002 and November 2003 in a small urban Brazilian community. A total of 2043 individuals were screened for capillary glucose levels and among them 142 people presented fasting plasma glucose above 100mg/dL and also 2 risk factors for developing DM2 and cardiovascular disease (CVD). Fasting plasma glucose

and an oral glucose tolerance test were repeated in these subjects to confirm the diagnosis of impaired glucose tolerance and/or fasting glucose levels. A total of 67 subjects aged from 30 to 85 years were included in the study and were divided in two groups: compared (n=43) and intervention (n=24) group (CG and IG respectively). Availability to attend the group session was considered for including individuals in the IG. All individuals in both groups had their clinical, metabolic and dietetic profiles examined. The subjects in the IG were given detailed advice about diet, exercise and lifestyle modification through monthly individual visits and group meetings every two weeks for 12 months. An individual visit was offered to the GC at the beginning of the study and after 12 months. Dropout rates were 8.3% (n=2) in the IG and 31% (n=13) in the CG. Principles of the Declaration of Helsinki were followed. Subjects gave their informed consent for the study, which was reviewed and approved by the Medical Ethics Committee of the University of São Paulo. A paired *t* test was used to examine differences in the outcomes between baseline and 12 months. Statistical analyses were performed using the Bioestat program.

Baseline characteristics of the participants are given in Table 1. The IG patients achieved a weight loss of 5.10% ($p<0.001$) while the CG had an increase of 0.54% from their initial weight. IG patients reduced 3.3% ($p<0.05$), and 6.8% ($p<0.01$) of their waist circumference (WC) and body fat %, respectively. Fasting and postprandial glucose levels were reduced 13.5% ($p<0.05$) and 20.9% ($p<0.05$), respectively, in the IG. The assessment of dietary composition at the beginning and at the end of the study showed that cholesterol and caloric intake significantly decreased inside the IG patients (49.5% and 4.7%, respectively).

The individuals in the IG showed a 5% weight loss at the end of the study and this was attributed to their participation in the nutrition intervention program. In parallel to weight loss, the IG also presented a significant decrease in body fat. Interventions to reduce the incidence of diabetes should aim at weight loss as the primary determinant of success (Hamman et al. 2006). The Finnish Diabetes Prevention Study (Tuomilehto et al. 2001) showed that a weight reduction of 5% or more can promote better metabolic control, prevent DM2 and improve quality of life. Interventions to reduce diabetes risk should primarily target weight reduction. The identification of abdominal obesity has become important due to its association with the risk for obesity-associated diseases, regardless of overall obesity.

After a 12-months follow-up, the IG presented a reduced intake of calories, saturated fatty acids and cholesterol. Qualitative assessment showed that eating habits of the individuals in both groups were within the dietary recommendations intake at the beginning and at the end of the study. The main objective of the nutritional counseling supplied by this study was not to encourage the individuals to adhere to a specific diet, but to encourage them to gradually change their diets as follows: eat smaller meals at more frequently intervals, select complex and whole carbohydrates; increase fiber, fruit and vegetable consumption; and increase unsaturated fatty acid intake by consuming olive oil and fish. Modifying the eating behavior of an individual is a complicated process since guidance needs to be on a personal level and individuals need to be encouraged to adhere to the process since people eat foods and not nutrients alone.

This study showed that a lifestyle modification program can reduce known risk factors for DM2 and CVD in a Brazilian urban community. This suggests that carrying out primary prevention of DM2 and CVD through lifestyle education, especially by emphasizing nutrition and physical activity, is very important in terms of public health and should be part of the routine of Health Care System. Further research is necessary to understand better

how to facilitate effective and efficient programs for the primary prevention of DM2 in developing countries.

	IG					CG				
	Baseline		12 months		P value	Baseline		12 months		P value
	Value	SD	Value	SD		value	SD	value	SD	
Weight (kg)	67.61	14.8	64.18	13.5	<0.001	75.78	15.2	76.20	16.3	0.43
BMI (kg/m²)	26.59	5.3	25.00	4.5	<0.001	28.46	4.5	28.60	5.2	0.98
WC (cm)	88.53	10.6	85.57	9.9	<0.05	91.19	17.0	92.50	18.1	0.34
Body fat (%)	33.36	9.61	31.10	9.51	<0.01	35.98	7.4	36.21	8.03	0.88
FPG (mg/dl)	105.0	21.6	90.83	14.2	<0.05	91.79	18.3	90.20	28.9	0.72
2-h PG (mg/dl)	138.0	40.8	109.17	27.4	<0.05	117.80	31.5	109.57	38.9	0.36
TC (mg/dl)	213.42	85.5	164.50	49.9	<0.05	170.43	62.7	163.73	45.1	0.60
Calories (kcal)	1 668.75	616.7	1 589.57	289.3	<0.05	1 445.16	686.7	1 785.75	552.5	0.04
Carbohydrates (g)	241.47	91.3	214.20	41.0	0.29	191.25	25.0	260.87	69.9	0.07
Proteins (g)	85.54	37.7	68.87	12.8	0.14	65.67	34.0	74.41	30.5	0.40
Lipids (g)	54.43	18.4	48.90	14.0	0.20	40.52	23.1	53.83	30.6	0.10
SFA (g)	18.32	10.2	8.51	1.4	0.18	9.91	6.5	10.98	8.3	0.71
Cholesterol (mg)	183.69	55.4	92.72	44.7	<0.001	155.01	81.0	118.25	81.7	0.15
Fibers (g)	12.23	5.7	12.13	5.5	0.94	7.72	10.7	7.93	7.8	0.93

IG = Intervention Group; CG = Compared Group; Values in Mean; SD = Standard Deviation; FPG = Fasting Plasma Glucose; 2-h PG = 2-hour Plasma Glucose; TC = Total Cholesterol; SFA = Saturated fatty acids.

Table 1. Changes in clinical, metabolic and dietetic characteristics from baseline and 12 months of the participants.

2. Diet

In the last twenty years, Brazil and many other Latin American countries have experienced an accelerated demographic, epidemiological and nutritional transition. The so-called "nutritional transition," which refers to changes in secular nutritional patterns, that is, to structural dietary changes, is directly correlated to economic and demographic changes and health conditions (Kac, 2003; Ferreira et al., 2005).

As the nutritional transition advanced, the consumption of high-fat products increased, especially from animal fat and sugars. Additionally, the consumption of complex carbohydrates and dietary fiber is decreasing. This reduction has been pointed out as a critical factor for the increasing prevalence of obesity and its comorbidities.

The Diabetes Prevention Program (Tuomilehto et al. 2001) showed that it is possible to achieve primary prevention of type 2 diabetes by changing lifestyle (diet and exercise) in subjects with impaired glucose tolerance. The reduction in weight, in total intake of fat to less than 30 percent of energy, and in intake of saturated fat to less than 10 percent of energy, along with an increase in fiber intake to at least 15 g per 1000 kcal and physical activity, resulted in lost at least 5 percent of the initial weight, and reveals a cumulative incidence of diabetes 58 percent lower compared to individuals in the control group. The

Diabetes Prevention Program (Knowler et al. 2002) showed that lifestyle changes and treatment with metformin both reduced the incidence of diabetes in persons at high risk. The intensive lifestyle intervention aimed achieving and maintaining a weight reduction of at least 7 percent of initial body weight through a healthy low-calorie, low-fat diet, along with physical activity of moderate intensity. The lifestyle intervention reduced the incidence by 58 percent and metformin by 31 percent, as compared with placebo.

2.1 Carbohydrates, glycemic index and glycemic load

Diet is one of the main modifiable lifestyle factors and relates to the prevention of diabetes mellitus and/or its complications (Portero & Cattalini, 2005, Mclellan et al., 2007, Mclellan et al., 2009). Carbohydrates are responsible for postprandial hyperglycemia and insulin secretion (Bao et al. 2011), and are related to the etiology of many chronic diseases.

Epidemiological evidences show that a better choice of carbohydrates is promising for the nutritional therapy and metabolic control of people with DM (Willett et al., 2002; Sartorelli & Cardoso, 2006; AMB, 2005; Jenkins et al., 2008). Diets with low Glicemic Index (GI) and Glicemic Load (GL) are independently associated with a reduced risk of developing chronic diseases (Barclay et al., 2008). Increased consumption of fruits and vegetables, whole foods and products that have undergone less processing, as well as limited consumption of potatoes, white rice and white bread are measures that help to reduce dietary GI (Silva & Mello, 2006).

In the prospective epidemiological study called Nurses' Health Study (1997), which included 65173 American women aged 40 to 65 years, a positive association was found between the habitual consumption of a high-GI diet and incidence of DM after six years of follow-up (Salmeron et al., 1997a). Furthermore, the Nurses' Health Study II (2004), which included 91249 women aged 20 to 44 years, found that high GI values were associated with risk of DM after 8 years of follow-up (Schulze et al., 2004). Another prospective American study, the Health Professionals Follow-Up Study (1997), which included 42759 men aged 40 to 75 years, also observed a positive association between high dietary GI and incidence of DM after six years of follow-up (Salmeron et al., 1997b).

It is suggested that diets with low GI increase satiety, delay hunger and reduce the consumption of calories in subsequent meals. One of the main means of preventing DM and controlling metabolism is controlling the glycemic load. Blood glucose is modulated mainly by the speed in which carbohydrates enter the blood after meals, by its removal time determined by insulin synthesis and by the sensitivity of peripheral tissue to insulin. Thus, quantity and quality of carbohydrates have long been considered an important dietary factor involved in glycemic homeostasis (Ludwig, 2000; Sartorelli et al., 2006; Brand-Miller et al., 2003). According to the results of many studies, diets with low GI can in fact aid glycemic control and probably reduce the risks of DM complications.

GI is defined as the relationship between the area under the glycemic response curve two hours after the consumption of a test food containing 25 or 50 grams of carbohydrates, and the area under the glycemic response curve corresponding to the consumption of the same amount of carbohydrates from a reference food, that is, glucose or white bread (refined flour) (Jenkins et al., 1981; Jenkins et al., 2002; Sartorelli e Cardoso, 2006; Foster-Powell et al., 2002; Silva e Mello, 2006; Willett et al., 2002).

The GL is a mathematical calculation based on the GI of a food and its carbohydrate content. It represents a global indicator of the glycemic response and insulin demand induced by a

serving of a food (Salmeron et al., 1997a; Salmeron et al., 1997b). The glycemic load of a food is calculated by multiplying the glycemic index by the amount of carbohydrates in grams provided by a food and dividing the total by 100 (Liu & Willett, 2002) When GI and GL are used together, they provide more tangible information about how the food affects blood glucose (Silva e Mello, 2006).
Glycemic index and glycemic load can be classified as low, medium or intermediate and high (Sampaio et al. 2007; Foster-Powell et al. 2002) as shown in Table 2.

	Glycemic index	Glycemic load
Low	≤55	≤10
Medium / Intermediate	56 to 69	11 to 19
High	≥70	≥20

Table 2. Classification of glycemic index and glycemic load

2.2 Dietary fiber

Fibers are classified as soluble and insoluble. Soluble fibers are represented by oat bran, pectin (fruits) and gums (oat, barley and legumes: beans, chickpeas, peas and lentils). Insoluble fibers are represented by cellulose (wheat), hemicellulose (cereals) and lignin (non-starchy vegetables). The recommended total fiber intake for adults is 20 to 30g/day, where 5 to 10g should be soluble (SBD, 2006).
Many studies have shown that diets rich in fibers, especially from whole grains, are associated with a significantly reduced risk of developing DM2 (Salmeron et al. 1997a; Salmeron et al. 1997b; Stevens et al. 2002; Montonen et al. 2003; Schulze et al 2004; Schulze et al. 2007). This is due to the production of short-chain fatty acids in the colon which increases hepatic insulin sensitivity (Schuze et al. 2007). Increased fiber intake may also improve insulin sensitivity (Behall et al. 2006; Weickert et al. 2006) and reduce systemic inflammation (Qi et al. 2006).
The soluble fibers found in fruits and legumes improve satiety by providing bulk and increasing digestion time (Institute of Medicine, 2002; Liu et al. 2000). The mechanisms that explain this action are related to the fact that dietary fibers are capable of reducing the speed in which glucose is absorbed, which in turn prevents glycemic and insulin peaks (Slavin, 2008). Studies show that a diet rich in fibers (>30g/day) can change biochemical parameters, reduce the likelihood of developing DM2 and reduce the risk factors associated with the development of cardiovascular diseases (ADA, 2002; Weickert et al. 2006; Qi et al. 2006).
Intervention studies done by Tuomilehto et al. (2001) and Knowler et al (2002) combined lifestyle changes with increased fiber consumption, which resulted in adults having a reduced risk of developing DM2 and IGT.
There are many factors related to the development of DM2, such as obesity, physical inactivity and genetic factors. Data from observational and intervention studies indicate that high-fiber diets improve glucose metabolism and reduce the risk of developing DM2, especially among high-risk individuals (Meyer et al. 2000; Liu & Willett, 2002; Liu, 2002; Priebe et al. 2008). A multi-ethnic study done in Hawaii with 75,512 individuals found that fiber intake was associated with reduced development of DM in men and women. High fiber intake reduced the risk of developing DM by 10% in the study individuals. High intake of fibers from non-starchy vegetables and fruits reduced the risk of DM by 22% in men (Hopping et al. 2010).

The prospective epidemiological study Nurses' Health Study followed 7822 American women with diabetes and investigated whether fiber intake affected mortality and cardiovascular risk. The study found a positive association between fiber intake and reduced mortality and cardiovascular diseases in diabetic women. This study shows the potential effect of fibers in the prevention of mortality and risk of cardiovascular disease in diabetic patients (He et al. 2010).

2.3 Dietary fat intake

The dietary pattern of the Brazilian population has been changing (Levy-Costa et al. 2005; Molina et al. 2007). Data from household budget surveys from 1974 to 2003 that showed time-trends in metropolitan areas indicating a decline in the consumption of traditional food (rice and beans); noticeable increases in the consumption of processed items such as cookies and soft drinks (Mondini & Monteiro, 1994; Monteiro et al. 2000); a continued excessive consumption of sugar; and a continued increase in total fat and saturated fat content in the diet (Levy-Costa et al. 2005).

The type and amount of dietary fat intake has been associated with insulin sensitivity (Storlien et al. 1991), monounsaturated or polyunsaturated fats appear to have beneficial effects on insulin action, whereas saturated fats and diets with high total-fat content appear to decrease insulin sensitivity in studies with animal (Storlien et al. 1991; Lardinois & Starich, 1991) and human (Vessby et al. 2001). Changes in dietary fatty acids may influence insulin action in the body through many mechanisms such as by affecting membrane lipid composition, metabolism, signal-transduction pathways, and by the direct control of gene expression (Vessby 2003).

Prospective studies such as the Nurses' Health Study suggest the role of specific types of fat in the development of DM2 mellitus (Salmeron et al 2001) and weight gain (Field et al 2007). There was an inverse association between development of diabetes and intake of vegetable fat and polyunsaturated fat, and a positive association for *trans*-fatty acids. The investigators found no association for total fat in the diet and development of diabetes (Salmeron et al 2001). Field et al (2007) investigate the association of dietary fat and weight gain among 41,518 adult women in the Nurses' Health Study. The results showed that the percent of calories from fat had a weak positive association with weight gain, and the percentage of calories from animal, saturated fat, and *trans*-fatty acids had stronger associations.

The Finnish prospective cohort study, with a 4 years follow-up, assessed the association of serum fatty acid composition and the development of impaired fasting glycemia (IFG) or DM2 in a cohort of middle-aged normoglycaemic men (n = 895). The results showed that a high proportion of linoleic acid in plasma fatty acids, indicating a high intake of dietary linoleic acid, had a lower risk of developing DM2 and showed lower increases in serum insulin and blood glucose over the follow-up period (Laaksonen et al. 2002). These findings are compatible with other studies (Vessby et al. 1994; Feskens, 2001), which indicated that individuals with a low proportion of linoleic acid or vegetable fat in the diet have an increased risk of developing DM2.

3. Medication

Although long term studies demonstrated that changes in lifestyle could prevent or retard the development of IFG or IGT to clinical diabetes, in practice, the achievement of changes in lifestyle for most of individuals are not easily observed indicating that the early

intervention with pharmacological in addition to diet and exercise, could improve the success of preventing or delaying the incidence of the disease. To solve this difficulty, several randomized placebo-controlled clinical trials specifically designed to demonstrate the efficacy and potential disadvantages of precocious pharmacological intervention to prevent the progression of prediabetes to diabetes were performed using different anti-diabetic drugs, specially agents that improve insulin sensitivity.

3.1 Metformin

The two major studies that had included metformin were the DPP study performed in United States and the IDPP-1 study in India. In the DPP trial 1073 participants with IGT were allocated to 850 mg of metformin twice a day and 1082 to placebo that were followed-up for a median period of 2.8 years. At the end of the study metformin reduced the incidence of DM2 by 31% compared to placebo being metformin more effective in individuals who had baseline Body Mass Index (BMI) of 35 kg/m² or more in whom incidence of diabetes was reduced in 50% and in individuals younger than 60 years (Knowler et al, 2002). The weight loss was 1.7 kg in metformin group compared with a weight gain of 0.3 kg in placebo group. However, in comparison to the study arm that changed only lifestyle (LSC), the reduction of incidence of diabetes at the end of the study in individuals using metformin (Met) was significantly less pronounced (LSC: 59% vs. Met: 31%). After the end of the original study a 10 years follow-up was offered to the active participants that continued to follow the original study protocol. A total of 88% of the participants (n= 2766) enrolled for and additional median follow up of 5.7 years. Diabetes incidence in 10 years since DPP randomization was reduced by 37% in the LMC group and 18% metformin group in comparison to placebo. The study confirmed that prevention or delay of diabetes with LSC or metformin can be maintained for at least 10 years (Diabetes Prevention Program Reasearch Group, 2009). The IDPP-1 study showed a 25% relative reduction in 120 patients who used metformin 250 mg twice a day. The beneficial changes were similar to those observed with LSC and also showed that the combination of LSC with metformin did not have an additional benefit (Ramachandran et al, 2006). A Chinese study randomizing 70 participants with IGT to receive placebo and metformin at a dosage of 250 mg 3 times a day for a period of 12 months and observed a beneficial effect of metformin in reducing diabetes incidence in comparison to placebo (Met: 16.2% vs. Pbo: 3%) (Li et al, 1999). A meta-analysis of 31 randomized studies including 4570 participants of at least 8 weeks of metformin use showed that the incidence of DM2 was reduced by 40% with an absolute risk reduction of 6% (Sally, 2008).

3.2 Thiazolidenidione

Since experimental and clinical evidences indicated that TZDs could improve insulin sensitivity and restore pancreatic B cell function, this class of agent have been used in several clinical trials to evaluate the prevention of DM2. Troglitazone was the first of this drug class tested in the Trogliazone in Prevention of Diabetes Study (TRIPOD) in women with story of gestational diabetes. In a medium follow up of 30 months it was observed a risk reduction of 55% and the effect of treatment was found to persist months after the drug withdrawal (Buchanan et al, 2002). An open labeled 3 years follow up study for pioglitazone entitled Pioglitazone in Prevention of Diabetes (PIPOD) showed similar results to those observed with troglitazone (Xiang, 2006). In the DPP trial troglitazone was prescribed in 585 participants with IGT for 9 months before its withdrawal due to

hepatotoxicity, being observed a remarkable reduction of 75% of clinical DM2 in a relatively short period (Knowler et al, 2002). Rosiglitazone was tested alone in 2 randomized studies: the Diabetes REduction Assessment with Ramipril and Rosiglitazone Medication (DREAM trial) and the Canadian Normoglycemia Outcomes Evaluation (CANOE). The Dream Trial, one of the largest multicentric study demonstrated in 5269 patients recruited with IFG, IGT or both that rosiglitazone was highly effective in reducing the incidence of DM2 by 60% in comparison to placebo (Gerstein et al 2006). The CANOE Study randomly assigned in 207 patients with IGT to receive either a combination of rosiglitazone (2mg) and metformin (500 mg) twice daily for a median period of 3.9 years matched for placebo showed a effective reduction of incidence of DM2 (Zinman et al, 2010). Pioglitazone use to prevent progression of diabetes was observed for a average off 3.75 years in the randomized-placebo controlled study ACT NOW in which 602 patients with IGT received either 45 mg/day pioglitazone or placebo. Patients randomized to pioglitazone treatment showed a reduction 82% reduction in progression in comparison to those treated with placebo (DeFronzo et al, 2009). Despite there are no evidences of association of pioglitazone to cardiovascular risk and hepatotoxicity related respectively to rosiglitazone and troglitazone (that caused their withdrawal of the market), one must also consider the drug´s long term adverse effects like edema, weight gain, increased risk to heart failure and osteoporosis could be a limitation for the drug for diabetes prevention (Nissen et al, 2007).

3.3 Acarbose

Acarbose, a α-glicosidase inhibitor, was tested for its potential to prevent diabetes in persons with IGT in the Study to Prevent Non-insulin dependent Diabetes (STOP-NIDDM) in 1429 participants randomized either to 100 mg of acarbose or placebo, 3 times a day for a mean period of 3.3 years. A relative reduction of 35.8% was seen with acarbose group when compared to placebo. However one third of those in the acarbose group could not complete the study because of gastrointestinal side effects. The study also showed a 49% relative risk reduction in cardiovascular events (Chiasson et al, 2002).

3.4 Other antidiabetic drugs

Meteglinide a rapid acting insulin secretor and valsartan, a angiotensin receptor blocker, were tested to their potential to prevent the development of diabetes and cardiovascular in 9306 participants with IGT in the Nateglinide and Valsartan Improved Glucose Tolerance Outcomes Research (NAVIGATOR) study in a median follow up period of 4 years. Neither the drug or the combination reduced the incidence of diabetes progression or cardiovascular disease (Navigator Study Group, 2010).

Although intestinal hormone GLP-1 and incretin-mimetics drugs have been showed to preserve β cell function in animal models, the role in human β cell preservation remains to be established. Clinical studies using for exanatide and liraglutide have presented significant reduction in body weight and in glucagon secretion reduction and insulin secretion and improvement of insulin secretion in short and median term studies but no specific long term randomized studies designed to demonstrate the efficacy of preventing the progression of diabetes was already published (Blonde et al, 2006; Buse et al, 2009). In a similar way DPP-4 inhibitors, despite being demonstrated to improve glucose control with minimal side effects need to be tested in specific studies to demonstrate the advantage of its use precociously in DM2 to prevent β cell deterioration.

3.5 Other drugs

Besides anti-diabetic drugs, other pharmacologic agents as angiotensin converting enzyme inhibitors, calcium channel blockers, thiazides diuretics, beta-blockers, angiotensin receptor blockers were tested in several randomized studies for their potential benefits in reducing diabetes incidence, but evidences were insufficient to demonstrate their efficacy in reducing diabetes (Yussuf et al 2000, Fonseca, 2006; Padwal & Laupacis, 2004). In one study named Xenical in the Prevention of Diabetes in Obese Subjects (Xendos Study) an antiobesity agent, orlistat (Xenical), in comparison to placebo was tested for prevention of Diabetes and CVD (Torgerson et al 2004). Although it was observed in comparison to placebo a reduction in incidence of diabetes from 9 to 6% and a mean weight reduction of 2.8 kg, the results were not conclusive because the high attrition rate (57%).

Despite that experimental and clinical data based in long term randomized studies have demonstrated that the precocious pharmacological intervention of insulin sensitizing drugs metformin and TZD can reduce diabetes progression of IGF to clinical diabetes, their clinical systematic recommendation is still debated considering their superior efficacy and safety observed with lifestyle modifications, the coexistence with possible long term effect side effects associated to the drug use and difficultly to determine which kind of subjects will have real future benefits from the precocious drug intervention. Based on this concerns, organizations involved to diabetes study and care as the American Diabetes Association (ADA) and the Brazilian Diabetes Society (SBD) have not, until now, endorsed any recommendations to introduction of pharmacologic intervention in patients with prediabetes.

4. Future research / perspective

Despite the significant increase in DM2 prevalence and in the risk factors for metabolic syndrome, preventive intervention is still limited, as much in primary as in secondary care. Nutritional intervention programs and lifestyle changes can benefit the population at risk for developing chronic diseases such as DM2 and CVD (Ratner et al. 2005; Jörgensen et al. 2006), becoming therefore these programs strongly noteworthy.

Structuralized programs that emphasize lifestyle changes, including nutritional counseling, reducing fat intake (less than 30% of the total energy intake) increasing whole grain, fruit and vegetable intake, together with regular physical activity, are important for a better quality of life and prevention of DM2.

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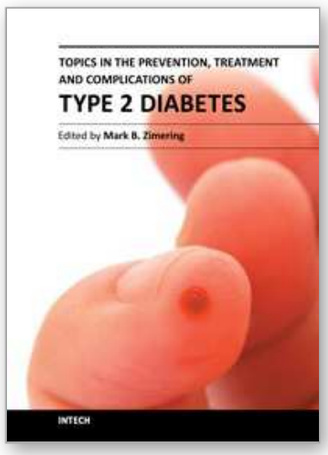

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Type 2 diabetes is estimated to affect 120 million people worldwide- and according to projections from the World Health Organization this number is expected to double over the next two decades. Novel, cost-effective strategies are needed to reverse the global epidemic of obesity which is driving the increased occurrence of type 2 diabetes and to less the burden of diabetic vascular complications. In the current volume, Topics in the Prevention, Treatment and Complications of Type 2 Diabetes, experts in biology and medicine from four different continents contribute important information and cutting-edge scientific knowledge on a variety of topics relevant to the management and prevention of diabetes and related illnesses.

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