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An Analysis upon Various Treatments for Prevention of Pre-Diabetes with Exercise

Lokendra Hada

M. Phil Physical Education, Fitness Expert

Abstract – Prediabetes is a condition that does not fall squarely into the primary or secondary prevention domain, and therefore tends to be inadequately addressed by interventions in either health promotion or disease management. Prediabetes is defined as having an impaired fasting glucose (fasting glucose of 100–125 mg/dL), impaired glucose tolerance (two-hour postprandial glucose of 140–199 mg/dL), or both. There is substantial evidence to suggest that even at these blood glucose levels, significant risk exists for both micro- and macrovascular complications.

It's easy to tell patients to modify their lifestyles to combat the development of diabetes, but getting them to do so is challenging. Here is specific direction on how to help them succeed. We examined the relationship between PD and objectively measured PA in NHANES 2003–2006 of 20,470 individuals, including 7,501 individuals between 20 and 65 yrs.We excluded all participants without IFG measures or adequate accelerometry data (final N = 1,317). Participants were identified as PD if FPG was 100–125 mg/dL (5.6–6.9 mmol/L). Moderate and vigorous PA in minutes/day individuals were summed to create the exposure variable "moderate-vigorous PA" (MVPA).

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INTRODUCTION:-

prediabetes is the term used to define individuals with slightly elevated blood glucose levels who are at higher risk for developing type 2 diabetes mellitus (T2D) over the next few years. Exercise has long been touted as an effective approach for preventing the transition from a state of prediabetes to overt T2D, but the exact types and intensities of physical activity needed have been a subject of debate.

As pointed out in the 2008 Canadian Diabetes Association (CDA) Clinical Practice Guidelines, lifestyle therapy that includes regular physical activity should be the first line of defence against T2D development from a state of prediabetes, although it is somewhat unclear who should be giving the prescription and what exactly the prescription should be. Another major barrier is that many individuals (and some health-care practitioners) may be somewhat "exercise naive," and patients may be particularly resistant to lifestyle changes. Although nutritional counselling is standard practice for patients in a clinical setting, an individualized prescription for the type, frequency, duration and intensity of exercise is much less likely to be given.

Effective physical activity prescription is contingent on an understanding of the underlying physiological adaptations and the differing responses to diverse modes and intensities of activity. Here we highlight the recent findings on the beneficial role of regular exercise in T2D prevention and provide an evidence-informed prescription for the type, intensity and duration of resistance and aerobic exercise for persons at risk for diabetes development.

Prediabetes is a condition in which blood glucose or A1C levels—which reflect average blood glucose levels—are higher than normal but not high enough for a diagnosis of diabetes. Prediabetes is becoming more common in the United States. The U.S. Department of Health and Human Services estimates that at least 86 million U.S. adults ages 20 or older had prediabetes in 2012.1 People with prediabetes are at increased risk of developing type 2 diabetes and CVD, which can lead to heart attack or stroke.

Prediabetes is a condition in which blood glucose levels are higher than normal but not in the diabetes range. PPOD and other health care providers can work with patients who are diagnosed as having prediabetes to help prevent them from progressing to additional health complications. Without intervention, people with prediabetes will progress to type 2 diabetes at a rate of 10% per year. Prediabetes also increases the risk of heart disease and stroke.1

Prediabetes is defined as impaired fasting glucose (IFG) of 100 to 125 mg/dl, impaired glucose tolerance (IGT) diagnosed by a post 75-gram glucose challenge (oral glucose tolerance test of >140 to

<200 mg/dl or both IFG and IGT), or a hemoglobin A1C of 5.7–6.4%. The Are You at Risk for Type 2 Diabetes? test, from NDEP, can help patients and providers assess individual risk for prediabetes.

The prevalence of pre-diabetes among US adults has increased markedly over the past two decades (*Karve & Hayward, 2010*). By current estimates, over 34% of nondiabetic US adults can be classified as pre-diabetic, 84% of whom meet the American Diabetes Association's criteria for impaired fasting glucose (IFG) (*American Diabetes Association, 2008*). Individuals with IFG and/or impaired glucose tolerance (IGT) are at increased risk for developing diabetes and cardiovascular disease (CVD) compared to those with normal fasting plasma glucose levels. In addition, IFG has been shown to be an independent predictor of CVD mortality after adjustment for age, sex, and other traditional CVD risk factors (*Barr et al., 2007*).

Compared with pre-diabetes, type 2 diabetes is associated with even greater risk for adverse cardiovascular health outcomes. Therefore, preventing the progression from pre-diabetes to diabetes is a critical link in our efforts to improve cardiovascular outcomes regardless of impact on other cardiovascular risk factors.

Investigations into the relationship between physical activity and insulin levels unequivocally demonstrate that high levels of sedentary time, low levels of daily movement, and little moderate to vigorous physical activity are associated with poor glycemic control (*Colberg, 2012*). Insulin resistance is a fundamental attribute of both IFG and IGT, and the inverse relationship between physical activity and insulin resistance is amply documented in both healthy individuals and those with pre-diabetes. Additionally, there is strong evidence that a dose–response relationship exists between insulin sensitivity and exercise "dose" (a combination of intensity, duration, and frequency) (*Dube et al., 2012*). Individuals with pre-diabetes have been shown to benefit significantly from intensive lifestyle intervention programs that include modified diets, increased physical activity, or a combination of the two . In 2002, a randomized clinical trial (The Diabetes Prevention Program [DPP]) demonstrated that lifestyle intervention reduced the incidence of Type 2 diabetes by 58% among those at high risk for developing the disease, including participants deemed to be pre-diabetic. However, while intensive lifestyle intervention may prevent the progression from pre-diabetes to diabetes, once a patient is diagnosed with type 2 diabetes, interventions such as diet, exercise, and weight loss do not appear to be effective in reducing cardiovascular morbidity and mortality. Additionally, the most effective behavioral intervention techniques aimed at increasing physical activity among Type 2 diabetics have yet to be elucidated (*Kinmonth et al., 2008*).Nonetheless, early lifestyle intervention in those with pre-diabetes may represent a window of opportunity for health improvement before the irreversible effects of diabetes set in.

TREATMENT OF PREDIABETES WITH LIFESTYLE

Since individuals with prediabetes are characterized by defects in both insulin secretion and sensitivity, interventions that enhance beta cell function and counteract insulin resistance are the most effective in preventing the progression of prediabetes to overt T2D. Typically, these individuals are sedentary and have excess adipose mass, both in the visceral region and within skeletal muscle and the liver. Given that excess adiposity potentiates the complex underlying pathology of metabolic dysfunction, lifestyle interventions that combine caloric restriction with increased physical activity are thought to be the best approach.

Interestingly, in animal models of the disease, regular exercise corrects both hepatic and skeletal muscle insulin sensitivity and increases beta cell function without a significant effect on body weight or fat mass. Although diet alone is effective in decreasing body weight, the concurrent reductions in body fat (subcutaneous and visceral) and increases in lean mass that occur using physical activity interventions result in a higher resting metabolic rate, more enhanced insulin sensitivity and a more improved cardiovascular risk profile. A recent meta-analysis of randomized controlled trials has shown that lifestyle improvements that include increased physical activity are at least as effective as drug treatment in preventing T2D.

The management of prediabetes and T2D requires a multidisciplinary approach that targets the treatment of not only blood glucose levels, but also associated cardiovascular risk factors, including dyslipidemia, blood pressure, inflammation and hypercoagulability. It is important to note that many antihyperglycemic agents (sulfonylureas, thiazolidinediones, D-phenylalanines and meglitinides) and insulin promote weight gain, which may then require additional intervention or increased drug dosing, whereas weight loss through lifestyle intervention can correct these disorders often without the need for any pharmacological intervention. Even if weight loss is not achieved by exercise, improvements in insulin sensitivity and cardiovascular risk factors can be achieved.

WHAT FORM OF PHYSICAL ACTIVITY IS BEST?

In general, physical activity comes in two forms—aerobic and anaerobic—and evidence is mounting that both forms have numerous beneficial effects on metabolism in a number of tissues and organs,

including skeletal muscle, adipose, liver, pancreas and even brain.

Several large-scale clinical trials have established that about 150 minutes of accumulated aerobic activity per week, such as brisk walking, with no more than one or two days off in a row, reduces the T2D risk by about 60%, about double the effectiveness of metformin as a prevention strategy.

Resistance exercise performed two or three times per week can provide benefits that complement aerobic exercise. Resistance training increases muscle mass, elevates resting metabolic rate, enhances muscular endurance, increases insulin sensitivity and attenuates muscle mass loss during caloric restriction and aging.

Based on published work, the greatest impact of resistance exercise on glycemic control (A1c) appears to be with fairly intense weight lifting—three sets at eight-repetition maximum (the maximum amount of weight you can lift eight times properly), three times per week for the major muscle groups (legs, arms, back, abdomen, chest). This sort of training may require initial instruction and periodic supervision from a qualified exercise professional.

LIFESTYLE MANAGEMENT OF PEOPLE WITH PREDIABETES

RCTs have confirmed the potential of lifestyle modification to approximately halve the risk of progression from prediabetes to Type 2 diabetes over a prolonged period. The following principles can help in providing advice to individuals:

Principles of initiating change -

- Changing eating and activity patterns and life-long habits is not easy
- Assess willingness to change
- Encourage people to make one change at a time
- Start with small achievable goals, especially those which might be expected to give the greatest benefit
- Ensure that people know what foods contain ‘sugar’ and hidden fat
- Encourage and congratulate even the smallest success
- Ensure that there is an agreed plan with the individual that includes follow up

Reducing weight -

- Weight reduction is the most important target for most people with prediabetes.
- Following healthy eating guidelines and increasing exercise will achieve weight loss in most people
- Assuming the patient is overweight or obese, aim for a weight loss of 0.5–1kg per week and a long-term loss of at least 5 per cent of initial weight - but acknowledge any degree of loss as a success
- Staying the same weight may be a meaningful achievement for some individuals

Follow the healthy eating guidelines -

- Eat three meals a day including 5+ serves of fruit and vegetables
- Reduce sugary foods and drinks by:

a) Substituting cakes, biscuits and snack foods with fruit

b) Drinking water instead of fizzy or sugary drinks

- Reduce fat by:

a) Using low-fat dairy products (e.g., skimmed or calci-trim milk, low fat yoghurts)

b) Limiting fried foods and takeaways to once a week or less

c) Avoiding food with hidden fat (e.g., pies, pastries, chippies)

- Have smaller portion sizes – use a smaller plate

Increase exercise -

- Consider a ’Green Prescription’
- Aim for 30 minutes of moderate intensity exercise such as brisk walking on most days - when possible increase exercise time to 60 minutes per day
- Help the individual find an activity that fits in with their lifestyle and is sustainable. Undertaking exercise with others is often more enjoyable

- Any increase in activity, however small, is a positive step. 'Snacks' of exercise, for example 3 x 10 minutes daily may have some value

- Reduce inactivity – avoid sitting for extended periods e.g., TV watching (even standing uses more energy)

Drug treatment -

Metformin is the only drug currently recommended for the routine management of prediabetes. It is an adjunct, not an alternative, and is less effective alone than lifestyle change. It is important to consider this in the context of CVR.

It is usually best to start with a low dose (500mg daily or twice daily with food) and increase gradually as tolerated, if required, to 1500–2000g/day in divided doses. Metformin should always be taken with food and, if patients are intolerant, can be initiated at a dose of 250mg/day.

Support to achieve lifestyle and weight loss goals should continue.

CONCLUSION

Although there are currently no consensus guidelines on the screening and treatment of prediabetes, the recent literature underscores the importance of screening, introducing the appropriate therapeutic regimens, and adopt- ing healthy lifestyle behaviors in order to delay or even prevent the onset of diabetes in prediabetes patients. The best way to screen for these individuals is with either a fasting glucose and/or an oral glucose tolerance test.

These individuals cannot be reliably identified from claims data unless the clinician codes for glucose intolerance, or possibly, metabolic syndrome. A DM program targeting this population will require the cooperation of its physician network in the identification process.

We believe that there will be additional compelling evidence that warrants further scrutiny of prediabetes as a condition to be considered for DM using a MI-based health coaching approach.

Our study was the first of its kind to use a large national database to examine the relationship between objectively measured physical activity and pre-diabetes. A significant strength of the current study was the use of objective measures of physical activity. However, variations in participant compliance with accelerometry wear time remain a potential source of sampling bias. Nonetheless, the close association between pre-diabetes and physical activity confirms that across the limited range of physical activity engaged in by US adults, diabetes can at least be postponed by relatively little extra activity.

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