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Exercise as Medicine in The Management of Type2 Diabetes Mellitus: An Overview

Danladi Ibrahim Musa*, Sunday Omachi
Department of Human Kinetics and Health Education, Kogi State University, Anyigba

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***Corresponding author:** Danladi Ibrahim Musa, Department of Human Kinetics and Health Education, Kogi State University, Anyigba.

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Abstract:

Type 2 diabetes mellitus is a complex and chronic metabolic disease characterized by high blood sugar levels with risk factors spanning behavioural, genetic and social dimensions. It is associated with serious complications and co-morbidities, including cardiovascular disease, metabolic syndrome, and limb amputation. Until the last two decades, the medical community only considered diet and medication to treat chronic non-communicable disease (CNCDs), including Type 2 diabetes mellitus (T2DM), as the first-line approach. In contrast, physical activity (PA) was considered a suggestion. But in the recent past, there has been a considerable accumulation of knowledge regarding the importance of physical exercise in preventing and treating T2DM. There is a growing body of evidence suggesting that physical exercise is not only effective treatment for T2DM but a standard part of medical care for the prevention and treatment of T2DM and other CNCDs. This review examines the efficacy of exercise in managing T2DM; the concept of exercise is medicine; exercise prescription based on the consensus public health recommendations on PA and exercise for managing T2DM. Suggestions are proffered for adopting an active lifestyle to control T2DM.

Key Words: exercise is medicine; health promotion; obesity, physical activity; T2DM

Introduction

Preservation and promotion of health and prevention of disease have been recognized since time immemorial. The use of physical activity (PA) to prevent or treat diseases is as old as recorded history. Indeed, during the ancient period, physicians like Susruta of India, Herodicus and Hippocrates of Greece and Galen of Rome at various periods used physical exercise to treat diseases and certain ailments (Tipton, 2014; Berryman, 2010). Until recently, the medical community only considered diet and medication in treating chronic diseases, including type 2 diabetes mellitus (T2DM), as the first-line approach, whereas PA was often considered a suggestion. In the past two decades, however, there has been a considerable accumulation of knowledge concerning the importance of physical exercise as the first-line treatment of chronic non-communicable diseases (CNCDs) (Pedersen & Saltin, 2015). Consequently, medical doctors and other biomedical scientists have come to recognize exercise as a cheaper and safer alternative first-line treatment for CNCDs (Lobelo, Stoutenberg & Hutber, 2014).

Type 2 diabetes mellitus is a complex and chronic metabolic disease characterized by hyperglycemia and abnormalities in glucose (GLU), fat and protein metabolism (Ozougwu Obimba, Belonwu & Unakalamba, 2013; Campbell, 2009). Its risk factors cut across behavioural, genetic and social dimensions. It is associated with serious complications and co-morbidities, including cardiovascular disease, non-alcoholic fatty liver disease, osteoarthritis, end-stage kidney disease, retinopathy and limb amputations (Temneanu et al., 2016). According to Pedersen and Saltin (2015), T2DM is due to insulin resistance (IR) in the skeletal muscle tissue and a beta cell defect that inhibits insulin secretion to compensate for insulin resistance.

Until recently, T2DM was regarded as a disease of adults and the elderly, but it is increasingly becoming a paediatric health problem,which has been linked partly with the worldwide increase in childhood obesity (OB) and physical inactivity (WHO, 2016). Other recognized risk factors include ethnicity, hypertension, dyslipidemia, acanthosis nigricans and family history (Phyllis et al., 2005). It has been reported that the presence of T2DM doubles the risk of mortality regardless of the presence or absence of cardiovascular disease (CVD) (Beckman et al., 2013). The World Health

Organization predicted the global prevalence of T2DM to be 350 million by the year 2030 (Wild, Roglic, Green, Sicree & King, 2004; WHO, 2003). This is because it has been reported that chronic diseases cause more than 80% of deaths in developing countries, and mortality rates from CNCDs in these countries are four times that of developed countries (Anderson & Durstine, 2019). This may be due to late diagnosis and poor health facilities. Research has demonstrated a negative association between PA, cardiorespiratory fitness and metabolic syndrome (MS), T2DM and other chronic diseases (Pedersen & Saltin, 2015). In a summary of review, Williams et al. (2020) reported that increased PA produced significant improvement in glucose control and glycated haemoglobin (HbA1c) in patients with T2DM. It has been reported that if T2DM patients increase their sedentary time by 60min/day, mortality risk could increase by 13% (Andersen & Durstine, 2019). This clearly shows that PA is beneficial to diabetic patients and a key player in primary health care.

The purpose of this paper is to review the current literature concerning the use of exercise as medicine in the prevention and treatment of T2DM. The paper focused on the concept of exercise is medicine (EIM); the pathophysiology of T2DM; exercise for preventing and treating T2DM, and exercise prescription for T2DM patients.

The concept of Exercise is medicine

Although modern-day physicians and biomedical scientists have come to recognize exercise as a less expensive and safer alternative first-line treatment modality, the concept of EIM is not just a new initiative but has roots in antiquity (Tipton, 2014). Physicians from India, Greece and Rome used exercise to treat various diseases and ailments during the ancient civilizations. Other Physicians like Hippocrates and Galen also used diet and exercise to treat various diseases during this period (Tipton, 2014; Berryman, 2010; Snook, 1984).

Recognizing the beneficial role of PA in health care, the American Medical Association (AMA) and the American College of Sports Medicine (ACSM) established the EIM initiative in 2007 to make PA a standard part of medical care for the prevention and treatment of CNCDs (Lobelo et al., 2014). The EIM in the USA was cascaded in seven centres across the globe in the six continents to help spread the EIM initiative globally. McCrory (2006) defines EIM or sports and exercise medicine (SEM) as the use of exercise as a therapeutic modality in treating and preventing diseases.

Exercise is considered an effective evidence-based medicine which should be prescribed for specific chronic diseases. This initiative recommends that physicians who are not well grounded in exercise prescription should make referrals to skilled allied health practitioners, including accredited exercise physiologists and physiotherapists (Green, Engstrom & Friis, 2018). In a commentary, Green et al.(2018) reported the position of several international sports and exercise medicine organizations on the need for physicians to play a vital role in SEM by asking about PA participation just as they do for other chronic diseases during consultation. This helps in assessing the health status of patients. It has been documented that individuals achieving 150min/wk of moderate-to-vigorous physical activity (MVPA) have a risk reduction of 25% to 50% for many major chronic diseases. In this regard, the Canadian Academy of Sport and Exercise Medicine (CASEM) (Thornton et al., 2016) has advised that physicians should apply the 5As approach during a consultation with patients as follows:

1. Ask: about physical activity
2. Assess: days/week and min/day of at least moderate physical activity (MPA)
3. Advice: gradual increase to achieve at least 150min of MVPA/wk
4. Assist: written specific exercise prescription
5. Arrange: referral and follow-up

The concept of EIM has made it clear that PA is an effective and inexpensive modality for combating many chronic diseases affecting humans. Therefore, health care professionals, especially doctors, should prescribe PA for its health benefits.

Pathophysiology of T2DM

Type 2 diabetes mellitus is characterized by derangement in the balance between plasma glucose levels and glucose uptake by the tissues resulting in hyperglycemia, the hallmark or common denominator of the disease. The critical pathophysiological features of the T2DM are impaired insulin secretion and decreased insulin sensitivity at the peripheral tissues, notably the liver, skeletal muscle and adipose tissue (Shakoor et al., 2021; Ohiagu, Chekezie & Chikezie, 2021).

The causes of T2DM are multi-factorial and include genetic and environmental (poor diet and physical inactivity) that affect pancreatic beta cell function and insulin sensitivity (Shakoor et al., 2021). In T2DM, either the pancreas does not produce enough insulin or the cells fail to use insulin properly, that is, insulin resistance. As the need for insulin increases, the beta cells of the pancreas, due to excessive stress can no longer maintain insulin production leading to dysfunction and eventual failure. Insulin resistance and pancreatic dysfunction results in hyperglycemia which eventually leads to T2DM and its adverse consequences.

Exercise in the prevention and treatment of T2DM

The benefits of physical exercise for patients with T2DM are well documented, and the American Diabetes Association (ADA), in its position statement, recommended exercise as one of the three critical modalities in the treatment of diabetes along with diet and medication (Colberg et al, 2016). Indeed, exercise has continued to receive more attention in the management of T2DM from health care providers because of its accessibility and cost-effectiveness (Yang, Yang, Li & Han, 2019). Physical inactivity is considered one of the most important health problems of this century, and it is listed as the fourth leading risk factor for global mortality, responsible for an estimated 3.2 million deaths globally (WHO, 2010). Indeed, it has been reported that the global economic burden of physical inactivity is about 53.8 billion US Dollars (O'Regan, Pollocl, D'Sa & Niranjan, 2021). As late as the 1950s, most people around the world lived on farms or villages and hamlets with agriculture as the main source of livelihood. But with increased mechanization and its attendant rural-urban migration, the use of remote-control television sets, elevators and escalators in our modern buildings, driving and excessive commuting by many is common place today. These labour-saving devices have made many people unfit and sedentary. This sedentary lifestyle lives many people prone to CNCDs including

diabetes. There is substantial evidence that PA is effective for preventing and managing chronic diseases, including CVD, T2DM, some forms of cancer and mental illness (Jones, Brooks & Wylie, 2013). Indeed, Susrata was the first documented physician to prescribe moderate exercise to treat diseases like diabetes mellitus (Snook, 1984).

Mechanism of action of physical activity in T2DM

Before presenting the evidence-based relationship between PA and T2DM, it is important to describe the mechanism by which PA attenuates the complex abnormality of T2DM. In a review of the literature, some scholars (Yang & Kwon, 2020; Yang et al., 2019; Pedersen & Saltin, 2015;) highlighted the mechanism of action of PA to include:

1. Increases insulin sensitivity in trained muscle
2. Stimulates muscle contraction-induced blood glucose uptake in the muscles through increase post-receptor insulin signaling
3. Increased glucose transporter (GLUT4) in skeletal muscles resulting in improvement of GLU metabolism.
4. Increased glucose synthesis activity and lower release and higher clearance of free fatty acid (FAA).
5. Increased transport of GLU to the muscles as a result of enlarged muscle capillary network and blood flow.
6. Increased capacity of mitochondrial oxidase and regulation of the lipid content of mitochondria, which lead to improvement of mitochondrial function to ustilize glucose effectively.
7. Significant increase in strength of skeletal muscles and their cross-sectional areas resulting in increased number of insulin receptors and improvement in insulin sensitivity.
8. Protection of pancreatic beta cells and improvement in general pancreatic function. This is possible through utilization of accumulated glucose and lipid which reduces the glucotoxicity and lipotoxicity on beta cells. There is also reduction in pancreatic inflammation and oxidative stress.
9. Increased production of some hormonal mediators like cytokines by the skeletal muscles. Some cytokines such as myokine irisin, osteokine osteocalcin and adipokine adiponectin play important roles in regulating energy metabolism, improving insulin synthesis and reducing insulin resistance.
10. Significant elevation in serum levels of alpha ketoglutaric acid (AKG) leading to fat loss and muscle hypertrophy. With enlarged muscle, there is increase in insulin receptors resulting in improvement in insulin sensitivity. Consequently, there is a decrease in blood GLU which alleviates T2DM.

Evidence-based physical exercise intervention.

The ACSM and ADA joint statement (Colberg et al., 2010) on the positive effect of exercise on health, updated by ADA position statement on physical activity/exercise and diabetes (2016) recommended mild-to-moderate intensity exercise as capable of improving insulin action and, thus, glucose control from two to 72 hours post-exercise. The document also considered a combination of aerobic and resistance training as better than either training method separately in the treatment of patients with T2DM. This is because of the synergistic effect due to specific training adaptations. For instance, aerobic training produces enhanced peripheral insulin action, while resistance training results in augmented glucose storage. Furthermore, aerobic training results in a substantial reduction in body weight, waist circumference and fat mass, while resistance training elicits a substantial increase in lean body mass, especially in overweight subjects. A combination of aerobic and resistance exercise leads to a greater reduction in HbA1c, fasting glucose, triglycerides, diastolic blood pressure and increased high-density lipoprotein cholesterol (Williams et al., 2020). The statement recognizes improvements in the disease prognosis of T2DM patients as a result of exercise training. Some specific training-induced adaptations include enhanced activity of proteins involved in blood glucose metabolism and insulin signalling, improved capacity for lipid oxidation, muscle hypertrophy and reduction in HbA1c. However, the ADA position statement (2016) reported that the challenges related to blood glucose management vary with the type of diabetes, PA type, and presence of diabetes-related complications. Thus, PA recommendations should be tailored to meet specific needs of individuals.

According to Thyfault and Bergouignan (2020), acute physical exercise improves the disposition index, defined as the product of insulin sensitivity multiplied by amount of insulin secreted in response to glucose. These scholars reported that acute exercise leads to increased GLU production by reducing insulin secretion and increasing glucagon secretion. In T2DM, exercise improves insulin sensitivity and pancreatic beta cell function, that is, the disposition index.

In a study involving 92 Danish diabetic patients, McDonald et al. (2020) randomly assigned participants into three exercise groups and a control group (standard care). The experimental groups consisted of low volume (178 min/week), intermediate volume (296 min/wk) and high volume (380 min/wk) exercise. The exercise group trainded for 12 months. Findings indicated significant improvements in cardiovascular disease risk factors such as HBA1c, fitness, two-hour glucose and triglyceride levels among the intermediate and upper tertiles but not in the lower tertile and the Standard Care groups. Furthermore, exercise volume was associated with discontinuation of glucose-lowering medication in a dose-response manner. That is, the higher the volume of exercise, the lower the need for drugs. This study clearly underscores the positive effect of exercise on glycemic control among diabetic patients.

Kessler et al. (2012), in a meta-analysis, observed that high-intensity interval training (HIIT) ranging between two weeks to six months improved aerobic fitness and insulin sensitivity significantly. In their report, a minimum of 12 weeks wasrequired for improvement in fasting glucose.

Exercise prescription for T2DM

Type 2 diabetes mellitus is mainly a result of resistance of several tissues such as the striated muscle, liver and adipose tissue to insulin action, thereby limiting utilization of GLU by these tissues. Glycemic control should be the major goal of treatment in T2DM. Regular PA has demonstrated a beneficial effect on glycemic control, with best results in patients with higher HbA1c values (Rijal et al., 2019).

When prescribing exercise for patients with T2DM, physicians

should use the WHO 2020 Guideliness on PA and Sedentary Behavior (Bull et al., 2020) as a general guideline before proceeding to the specifics.The WHO Guidelines (Bull et al., 2020) emphasized exercise duration, frequency, mode and intensity, focusing on three age groups: 5-17 years old, 18-64 years old, 65 years and above and pregnant and postpartum women (table 1). Individuals meeting these guidelines, to a great extent, should be able to improve and maintain optimal health, all else being equal. Physical inactivity or sedentary behaviour is a big threat to health promotion, not only because of its adverse effect on health but also the economic consequences on society.

Age group	Duration (min)	Intensity	Frequency	Mode
5-17y	60	MVPA	Daily	Aerobic
	60	VPA	3 d/w	Muscle and bone-strengthning aerobics
18-64y	150 75	MPA MVPA	2-3 d/w Weekly	Muscle-strengthning aerobics aerobic
≥ 65y	150 75	MPA MVPA	Weekly Weekly	Aerobic Aerobic
	75	MPA	3 d/w	Strength training and functional balance PA
Pregnant and postpartum	150	MPA	daily	Aerobics muscle-strengthening and mild stretching PA

Adapted from: WHO (2020). Guidelines on physical activity and sedentary behaviour
MPA = moderate physical activity; MVPA = moderate to vigorous physical activity; d/w = days per week

Table 1: WHO Guidelines on Physical Activity for Health

Exercise training is considered to be one of the cornerstones of diabetes care. Exercise for diabetics must be individualized according to medication schedule, presence and severity of diabetic complications. Food, especially carbohydrates with a high glycemic index, must be available during exercise. Furthermore, provision should be made for adequate consumption of water during and after exercise. According to Perdersen and Saltin (2015), exercise is contraindicated in the following situations:

1. Blood GLU levels are greater than17 mmol/l or less than 7 mmol/l.
2. Presence of eye problem, especially retinal haemorrhage.
3. Illness such as hypertension or infections.
4. Foot or lower extremity sores.
5. Extreme environmental temperature, for example, hot, humid or cold weather.

Prior to starting an exercise programme, the diabetic patient should undergo some preliminary investigations for the purpose of medical clearance. Two areas to evaluate are health and fitness. Results of these preliminary evaluations can guide the exercise specialist in testing and prescribing appropriate exercise based on the condition of the patient. The purpose of this evaluation is to detect the presence of other conditions that may lead to adverse effects during exercise participation. It must also be emphasized that exercise for diabetic patients should be under medical supervision

The purpose of exercise prescription is to enhance physical fitness, promote health by reducing the risk of development or recurrence of disease and to ensure safety during exercise (ACSM, 2018). Before initiating an exercise programme for the diabetic patient, there are certain factors to consider, and they include the following:

1. Exercise frequency: days of participation in exercise in a week, e.g., 3 to 5 days/week
2. Exercise intensity: hardness or difficulty of the exercise, Levelof exertion.
3. Exercise duration: time of participation per session, e.g., 30 to 60 minutes
4. Exercise mode: type of exercise, e.g., walking, running, swimming.

Details of exercise programming for diabetic patients are presented in Table 2.

Mode	Goal	Intensity/frequency/duration	Time to goal
Aerobic large muscle activities	To increase fitness, reduce blood sugar, BP and other CVD risk factors	40% to 60% HRR/ 150 min/wk 3 to 5 day/week 20 to 60 min/session	4 to 6 months
Resistance: free and machine weights	To improve strength/ muscle mass	2 to 4 set/muscle group 8 to 10 repetition/set 75% to 85% of one rep max 2 to 3 day/week	4 to 6 months
Flexibility/stretching	To maintain and increase range of motion		4 to 6 months

ACSM. (2018). ACSM guidelines for Exercise Testing and Prescription

Table 2: Exercise prescription for Type 2Diabetes Mellitus

As shown in Table 2, the types of exercise effective for managing T2DM are aerobics (brisk walking, jogging, cycling, skating, rowing, swimming), resistance training (workouts with free weights, e.g., dumb bells, machine weights, e.g., multigym, cybex, nautilus, pull-up, push-up, sit-ups) and stretching exercises (dips, alternate toe touching, trunk twists, arm swings). These activities should take place between 20 to 60 minutes, three to five days a week regularly for a period of at least six months for maximum benefits.

Conclusion

The global surge in T2DM among adults and youth is becoming a public health problem, especially in developing countries. Weight disorders, especially overweight and obesity, plus physical inactivity are the major risk factors underlying T2DM. Epidemiological evidence has indicated that exercise is an effective medicine in the prevention and treatment of diabetes, with few side effects compared to orthodox medicine. Such exercise should be prescribed on an individual basis, under medical supervision and consistent with the consensus public health recommendations on PA for managing T2DM. Physicians in developing countries should begin to play an active role in exercise prescription. This can be possible if courses in exercise prescription are incorporated in the curriculum of medical students as it is done in developed countries.

Suggestions

Based on the available evidence in support of exercise as an effective modality in the management of T2DM, the following suggestions are proffered:

1. Persons diagnosed with T2DM should be made to adopt regular exercise as part of their lifestyles in order to improve glycemic control and minimize the severity of T2DM.
2. Aerobic exercise complemented with resistant exercise should be the cornerstone of exercise training programmes for patients with T2DM. Such activities should be conducted based on appropriate intensity, frequency and duration.
3. Exercise training programmes for diabetic patients should last for a minimum of four to six months for optimal benefits to accrue.

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