

## EFFECT OF EXERCISE ON PERIODONTAL TISSUES OF DIABETES MELLITUS TYPE 2 PATIENT : A REVIEW

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**ABSTRACT :** Diabetes mellitus is one of the leading causes of death in the world. Type 2 diabetes mellitus is a combination of the inability of cells to respond to insulin (insulin resistance) and inadequate compensatory insulin secretion due to the relative failure of B cells. One of the non-pharmacological therapy for diabetes mellitus is exercise or physical activity. Some studies have concluded that exercise can improve blood glucose control and eliminate complications such as the effect of fat oxidation, blood pressure, cardiovascular disorders, mortality, and quality of life. No studies have reported the effect of exercise on periodontal tissue of type 2 diabetes mellitus patients. This study determines the effect of exercise on periodontal tissue of type 2 diabetes mellitus. Management of hyperglycemic in diabetes mellitus with exercise may result in the upregulation of antioxidant defense mechanisms in several tissues, including the periodontal tissue. Doing exercise regularly can induce elevated anti-inflammatory cytokine levels, resulting in an anti-inflammatory mechanism. On the periodontal tissue, blood flow increases, decreased the level of bone loss, repair periodontal tissue so the periodontal state of the patients becomes good.

**Key words :** Exercise, anti inflammatory, diabetes mellitus, periodontal disease.

### INTRODUCTION

Diabetes mellitus is one of the leading causes of death in the world. The prevalence of people with diabetes mellitus in the world today is 195 million people and will continue to increase every year. There are about 97% of people with type 2 diabetes. According to the Basic Health Research Results of the Indonesian Ministry of Health, in 2008 DM patients in Indonesia reached around 12 million people. Type 2 diabetes mellitus is a combination of the inability of cells to respond to insulin (insulin resistant) and compensating insulin secretions that do not meet the relative requirements of B cell compatible, thereby causing an increase in muscle and liver fusion (Kurniawan and Wuryaningsih, 2016).

The management of type 2 diabetes mellitus includes pharmacological therapy, meal planning, and counseling for diabetics by health advocates. Lack of pharmacological therapy for DM is a side effect that can be experienced by people with DM (Sudoyo *et al*, 2006; Rezkita *et al*, 2020).

One non-pharmacological therapy for diabetes mellitus is to do exercise or physical exercise. Some of the results of studies of several activities related to lipids, blood pressure, cardiovascular disorders, mortality and

quality of life (Gandini and Agustina, 2013).

Diabetes mellitus and periodontal disease are interrelated; that is, individuals suffering from diabetes are at high risk of developing diabetes. Exercise training is known to increase the success of diabetes mellitus therapy and overall immunological status. However, there are no studies that report on the effects of physical exercise on periodontal disease in patients with diabetes mellitus (Schulze and Busse, 2009).

The purpose of this paper is to review the effect of exercise on periodontal tissue with type 2 diabetes mellitus. So, it is hoped that this paper can provide practitioners with knowledge about the effects of exercise on periodontal tissue with type 2 diabetes mellitus and its mechanism.

### Diabetes mellitus

Diabetes mellitus (DM) is a state of chronic hyperglycemia accompanied by various metabolic disorders due to hormonal disorders, which cause various chronic complications in the eyes, kidneys, nerves, salivary gland and blood vessels (Narmada *et al*, 2019). According to ADA (2009), diabetes mellitus is a chronic disease due to the pancreas not producing enough insulin or the body

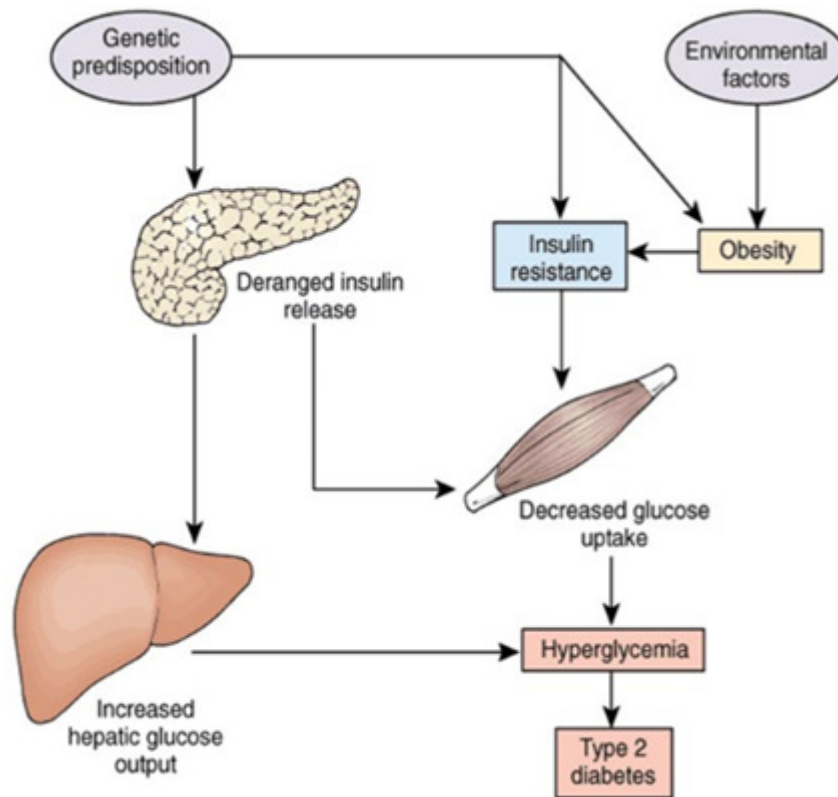


Fig. 1 : Etiology of DM Type 2 (Guyton and Hall, 1997).

cannot utilize the insulin produced effectively and causing increased blood glucose concentrations (Gandini and Agustina, 2013; Mansjoer *et al*, 2000).

The etiology of diabetes is in Insulin-Dependent Diabetes Mellitus (IDDM) or Insulin Dependent Diabetes Mellitus (DMTI) caused by the destruction of the B cells of the islets of Langerhans due to the autoimmune process (Fig. 1). Meanwhile, in Non-Insulin Dependent Diabetes Mellitus (NIDDM) or Diabetes Mellitus Dependent on Insulin (DMTTI) due to the relative failure of B cells and insulin resistance. Insulin resistance is the decreased ability of insulin to stimulate glucose uptake by peripheral tissues and to inhibit glucose production by the liver. B cells are not able to compensate for this insulin resistance completely, that means that there is a relative deficiency of insulin. This inability can be seen from the reduction in insulin secretion in glucose stimulation and glucose stimulation along with other insulin secretion stimulants (Mansjoer *et al*, 2000).

If there is insulin resistance, glucose cannot enter the cells, so glucose levels in the blood will increase or hyperglycemia occurs (300-1200 mg/dl). Glucose can not be used to produce energy (Suciadi *et al*, 2019). Glucose that accumulates in the body will be excreted in urine causing glycosuria. This is because the amount of glucose entering the kidney tubules in the glomerular filtration

process increases from normal levels. As a result, glucose can not be reabsorbed so that the glucose level in the blood is more than 180 mg/dl whereas if the blood glucose level is 300-500 mg/dl it means that the person has already suffered from severe diabetes because it was previously not treated, so the urine release every day will contain glucose in high numbers (Guyton and Hall, 1997).

The diagnosis of DM was initially thought to be with the symptoms of polydipsia, polyphagia, polyuria, weakness, and weight loss. Other symptoms that patients may complain of include tingling, itching, blurred eyes, and impotence in men and pruritus of the vulva in women (Sudoyo *et al*, 2006).

Acute complications can include hypoglycemia coma, ketoacidosis, nonketotic hyperosmolar coma. Meanwhile, chronic complications can include macroangiopathy of large blood vessels (heart arteries, peripheral blood vessels, cerebral blood vessels) and microangiopathy, regarding small blood vessels (diabetic retinopathy, diabetic nephropathy). As well as diabetic neuropathy, susceptible to infections, such as pulmonary tuberculosis, gingivitis, and urinary tract infections, diabetic feet (Mansjoer *et al*, 2000).

Diabetes management has the ultimate goal of reducing DM morbidity and mortality, specifically aimed

at achieving 2 main targets, namely: maintaining plasma glucose levels within the normal range and preventing or minimizing the possibility of diabetes complications (Sudoyo *et al*, 2006).

There are two approaches to managing diabetes, the first approach is without drugs and the second is the approach to drugs. A drugless approach can be in the form of diet and exercise regulation. Meanwhile, the approach to drugs is in the form of insulin therapy or oral hypoglycemic drug therapy, or a combination of both. Thus, it can be concluded that the main framework for DM management is food planning, physical exercise, pharmacological therapy and counseling or counseling in diabetics by health practitioners (Sudoyo *et al*, 2006; Ministry of Health Republic of Indonesia, 2015).

### Meal planning

A good diet is key to successful diabetes management. The recommended diet is food with a balanced composition in terms of carbohydrates, proteins, and fats, according to the adequacy of good nutrition as follows: carbohydrates: 60-70%; protein: 10-15% and fat: 20-25%. Calorie counts are adjusted for growth, nutritional status, age, acute stress and physical activity, which are aimed at achieving and maintaining ideal body weight (Sudoyo *et al*, 2006).

### Physical exercise

The recommended exercise is CRIPE (Continuous, Rhythmical, Interval, Progressive, Endurance Training). As far as possible reach the target zone 75-85% maximum pulse rate (220-age), adjusted to the ability and condition of the patient. Some examples of recommended sports include walking or jogging, biking, swimming, and so on. Aerobic exercise is at least done for a total of 30-40 minutes per day, preceded by 5-10 minutes of heating and ending with cooling between 5-10 minutes. Sports will increase the number and increase the activity of insulin receptors in the body and also increase glucose use (Ministry of Health, Republic of Indonesia, 2015).

### Pharmacological therapy

In patients with type 1, DM can be given insulin therapy. Meanwhile, patients with type 2 DM can be given hypoglycemic drugs can be oral or injection. Based on its mechanism of action, oral hypoglycemic drugs can be divided into 3 groups (Sudoyo *et al*, 2006; Ministry of Health, Republic of Indonesia, 2015), namely:

- a) Medications that increase insulin secretion, including oral hypoglycemic drugs, sulfonylureas and glinides.
- b) Insulin sensitivity (drugs that can increase the sensitivity of cells to insulin), including hypoglycemic

drugs of the biguanide and thiazolidinedione groups.

- c) Carbohydrate catabolism inhibitors, including  $\alpha$ -glucosidase inhibitors which work to inhibit glucose absorption and are commonly used to control postprandial hyperglycemia (post-meal hyperglycemia).

### Exercise in Diabetes mellitus patient

The principle of physical exercise for diabetics is the same as the principle of physical exercise in general, which is fulfilling several things, such as frequency, intensity, duration and type. The frequency of exercise per week should be done regularly 3-5 times per week. The intensity of exercise can be mild and moderate (60-70% Maximum Heart Rate). Duration of exercise 30-60 minutes. Types of physical exercise endurance (aerobics) to improve cardiorespiratory abilities such as walking, jogging, swimming and cycling (Gandini and Agustina, 2013).

Sports and physical training have the CRIPE principle:

- 1). Continuous (continuous) is the exercise carried out continuously at a certain time.
- 2). Rhythmical (rhythmic) which is the type of exercise chosen is rhythmic, which is muscle contraction and relaxation regularly such as walking, running, swimming, cycling.
- 3). Interval (intermittent) is the exercise carried out intermittently between slow and fast motion, for example, the road or brisk walk interspersed with normal roads (provided that do not stop).
- 4). Progressive (increasing) is the exercise carried out gradually increasing according to ability from mild to moderate to reach 30-60 minutes.
- 5). Endurance, namely exercise should be aimed at endurance training to improve breathing and cardiac abilities. It can be done by walking, running, swimming or cycling (Gandini and Agustina, 2013). To do physical training, according to Sudoyo *et al* (2006) the following matters need to be considered :

#### a. Warm-up

This part of the activity is carried out before entering the actual exercise, to prepare various body systems such as raising body temperature, raising the pulse to near the intensity of the exercise. Warming up is also necessary to avoid injury from exercise. Warm-up is enough for 5-10 minutes.

#### b. Core Training (conditioning)

At this stage, the pulse is reached at the target heart rate, to get the benefits of exercise. If the target heart rate is not reached, then there will be no benefit of training.

#### c. Cooling down

After finishing physical exercise, cooling should be

done. This stage is done to prevent the accumulation of lactic acid which can cause pain in the muscles after physical exercise, or dizziness due to the accumulation of blood in the active muscles. If the exercise is in the form of jogging, then cooling should be done by continuing to walk for several minutes. When cycling, keep pedaling the bike, but without the burden. Cooling is done for about 5-10 minutes until the heart rate approaches the pulse at rest.

#### d. Stretching

This stage is done to relax and flex the muscles that are still stretched and make it more elastic. This stage is more useful especially for those who are elderly. Regular physical exercise is important for everyone's health because it can provide more power to make the heart stronger improve circulation and strengthen muscles.

According to Gandini and Agustina (2013), the benefits of exercise by diabetics include :

- 1) Energy consumption increases and if it is accompanied by eating arrangements, weight loss occurs. This is very beneficial for diabetics who are overweight.
- 2) Will reduce insulin resistance so that insulin can be improved.
- 3) Blood circulation will be more smooth with regular exercise.

In type 2 diabetes, physical exercise can improve overall glucose control, as evidenced by a decrease in HbA1c concentrations, which is sufficient guidance to reduce the risk of diabetes complications and death. In addition to reducing risk, physical exercise will have a good effect on body fat, arterial blood pressure, baroreflex sensitivity, vasodilation of endothelium-dependent vessels, blood flow to the skin, the results of a comparison between heart rate and blood pressure (both at rest and active), hypertriglyceridemia and fibrinolysis. The morbidity and mortality rate in people with active diabetes is 50% lower than those who are relaxed (Sudoyo *et al*, 2006).

#### Periodontal disease

Periodontal disease is a multifactorial disease that has been linked to several risk factors. This disease is triggered by the accumulation of dental plaque. The clinical picture is caused by the inflammatory response and the resulting immune response. There are two diagnostic categories of periodontal disease, namely gingivitis and periodontitis. Gingivitis is the presence of gingival inflammation which results in reversible destruction of gingival tissue. Gingivitis is characterized by gingival redness, edema, bleeding, contour changes, loss of tissue adaptation to teeth, and increased flow of

GCF (Gingival Crevicular Fluid). Whereas, periodontitis is inflammation at the site where junctional epithelial migration occurs to the root surface with loss of connective tissue and alveolar bone. Clinically, periodontitis is usually characterized by a pocket, loss of attachment, and bleeding on examination with a probe (examination of bleeding on probing), the existence of suppuration and there is tooth sway. Radiographically it is characterized by bone loss horizontally and/or vertically (Al-aysa and Majevea, 2008).

This disease is a multifactorial disease. Some related risk factors include bacteria such as *Aggregatibacter actinomycetemcomitans*, *Porphyromonas gingivalis*, *Prevotella intermedia*, *Tannerella forsythia*, *Fusobacterium nucleatum* and *Peptostreptococcus micros*. Systemic factors such as Diabetes Mellitus, HIV, and neutropenia. Genetic, gender and ethnic factors. Environmental factors: oral hygiene, smoking, psychological stress. Local risk factors: such as the anatomical shape of teeth, restoration of teeth and habitual factors (Greenwell *et al*, 2004).

Periodontal disease starts from the accumulation of plaque and microbes on the tooth surface. Then, microbial enzymes, bacterial products, and components attach to epithelial cells in the sulcus (Fig. 2). The body responds by producing pro-inflammatory cytokines and other chemical mediators. This causes an inflammatory response in the gingiva. Gingiva becomes oedematous because of fluid accumulation and cell infiltration (Al-aysa and Majevea, 2008). Inflammatory cells will produce matrix metalloproteinase 8 (MMP-8) which causes connective tissue damage. Next, attachment between the

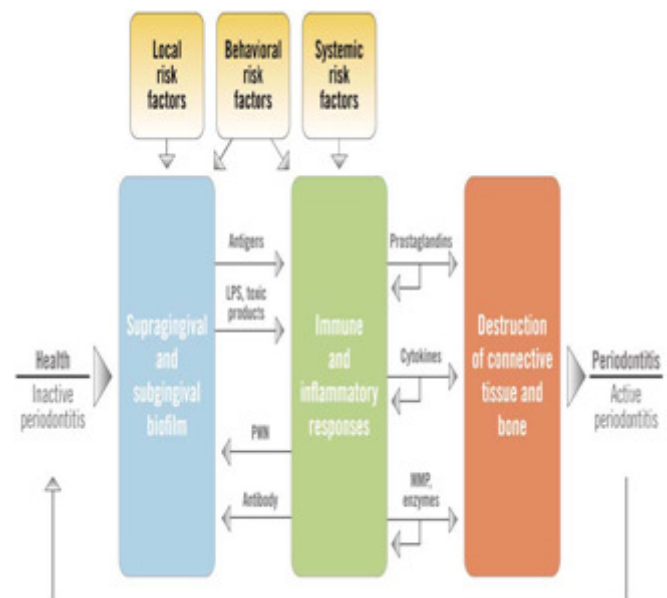


Fig. 2 : Pathogenesis of periodontitis.

periodontal ligament and the tooth is lost and a periodontal pocket is formed. Production of Interleukin 1 $\beta$  (IL-1 $\beta$ ), Tumor Necrosis Factor  $\alpha$  (TNF- $\alpha$ ), and Prostaglandin 2 (PGE-2) will increase in response to bacterial infections and cause bone resorption (Mealey and Rose, 2008).

The management of periodontal therapy aims to eliminate the main causes of periodontal disease as well as local factors that aggravate the periodontal disease. For this purpose, periodontal therapy is divided into four phases (Newman *et al*, 2006) namely:

- a. Phase 1, includes diet control, scaling, root planning, correction of restoration/prosthesis that is not good, antimicrobial therapy (local/systemic), occlusal therapy, splinting. Phase 1 is the initial therapy to eliminate etiological factors and predisposing factors.
- b. Phase 2, namely periodontal surgical therapy, such as curettage, gingivectomy, flap surgery, resective surgery, and regenerative bone surgery.
- c. Phase 3, namely reconstructive therapy, includes the final restoration of the teeth and removable / fixed prostheses.

Phase 4, maintenance therapy to maintain periodontal tissue health, by controlling infection and preventing recurrence of periodontal disease

### Cytokines

Cytokines are a group of proteins or glycoproteins (polypeptides) that are soluble and are produced by lymphocyte cells and other cells such as macrophages, eosinophils, mast cells, and endothelial cells. Cytokines function as intercellular signals that regulate almost all important biological processes such as activation, growth, proliferation, differentiation, cell inflammatory processes, immunity and tissue defense. Cytokines bind to specific receptors on the target cell membrane and trigger a signal-transduction pathway that changes the expression of genes in the target cell. Some cytokines bind to receptors on the membrane of cells that secrete them called autocrine action, which can also bind to target cell receptors that are nearby called paracrine action. And can also bind to target cells that are located far away called endocrine action. Cytokines regulate the intensity and duration of the immune response by stimulating or inhibiting the activation, proliferation and/or differentiation of various cells and by regulating the secretion of antibodies or other cytokines (Kindt *et al*, 2007).

### DISCUSSION

Diabetes mellitus is a risk factor for periodontal disease, and control of glycemia levels is an important factor in the relationship between these two diseases.

Patients with diabetes mellitus with poor glycemic control have a greater risk in the development of periodontal damage (Mealey and Rose, 2008).

The relationship between diabetes and periodontal disease is related to things that commonly occur in diabetes, such as resistance disorders, vascular changes, changes in oral microflora, and abnormal collagen metabolism. The mechanism of the effect of diabetes on periodontal tissue is illustrated by both microvascular and macrovascular complications because periodontal tissue is a tissue rich in vascularity (Pedersen, 2006).

The condition of hyperglycemia in type 2 diabetes mellitus causes the formation of Advanced Glycation End-products (AGEs). AGEs are a group of compounds that are highly oxidized and are formed through a non-enzymatic process of adding reduced sugars to free amino acids from proteins, fats, and nucleic acids. When binding to its receptors (RAGE), AGEs induce oxidative stress and secretion of pro-inflammatory cytokines (Golbidi *et al*, 2012).

Increased RAGE expression and increased interaction between AGE and RAGE in endothelial cells, causing changes in procoagulation, thrombus formation, increased activity of matrix metalloproteinases in the periodontal, and thickening of the basic membrane of the microvascular, resulting in microangiopathy. Microangiopathy also occurs in the gingival tissue of uncontrolled diabetic patients. Microangiopathy results in impaired cell exchange, oxygen, and metabolic products between intra and extracellular, which ultimately affects the host response and tissue repair (Al-Aysa and Majeva, 2008; Mealey and Rose, 2008). Furthermore, diabetes mellitus is also associated with chronic low-level systemic inflammation caused by increased TNF- $\alpha$  and specific cytokines. IL-6 often considered a cause of chronic inflammation in diabetes (Schulze and Busse, 2009).

Management of the condition for hyperglycemia in diabetes mellitus by exercise can produce upregulation of antioxidant defense mechanisms in various tissues, including periodontal tissues. Exercise is also useful by generating specific adaptations, such as increased antioxidant or enzyme activity that repairs oxidative damage, increases resistance to oxidative stress and decreases the level of oxidative damage (Al-aysa and Majeva, 2008).

Exercise also has a beneficial effect on insulin sensitivity both in healthy subjects and also in people with insulin resistance. Long-term training can potentiate the effect of exercise on insulin sensitivity through several adaptations to glucose transport. Improved glycemic

control can help improve HbA1c values. Weight loss can also be decreased due to higher energy expenditure, decreased insulin circulation and decreased therapeutic insulin doses. Because poor glycemic control is considered a cause of periodontitis, the increase induced by exercise theoretically also improves the periodontal status. Other findings indicate that exercise can induce elevated levels of anti-inflammatory cytokines, for example, IL-10 and IL-6 and cytokine inhibitors (such as IL-1 antagonist receptors, TNF- $\alpha$  receptors). In other words, regular exercise can cause anti-inflammatory mechanisms (Schulze and Busse, 2009; Venkatasamy *et al*, 2013).

Persistent systemic immune deficits also reduce local immune responses. According to many studies, TNF- $\alpha$  is recognized as a pro-inflammatory cytokine. TNF- $\alpha$  is produced and secreted from adipocytes and plays a major role in mediating the occurrence of the immune response. TNF- $\alpha$  is also an important mediator in insulin resistance. Therefore, all factors that reduce TNF- $\alpha$  levels have the effect of increasing the immune response. IL-6 is involved in TNF- $\alpha$  level regulation. IL-6 has an inhibitory effect on TNF- $\alpha$  production. IL-6 promotes the anti-inflammatory environment by inducing IL-10 production and also inhibits TNF- $\alpha$  production which induces insulin resistance. IL-6 also increases lipid turnover, stimulates lipolysis and fat oxidation (Venkatasamy *et al*, 2013).

Adipose tissue increases TNF- $\alpha$  production, which contributes to insulin resistance. TNF- $\alpha$  and IL-1 stimulate IL-6 production. Regular exercise increases anti-inflammatory cytokine secretion. Exercise also decreases inflammation by improving endothelial function. Exercise reduces peripheral inflammatory markers from endothelial dysfunction such as soluble intra-cellular and vascular adhesion molecules, granulocyte-macrophage colony-stimulating factors. Exercise also provides the availability of nitric oxide which improves endothelial function (Venkatasamy *et al*, 2013). With the decrease in proinflammatory cytokines, increased blood flow in the periodontal decreased levels of bone damage, periodontal tissue repair so that the periodontal status in patients who exercise regularly becomes good (Schulze and Busse, 2009).

## CONCLUSION

The management of hyperglycemia in diabetes mellitus by exercise can produce upregulation of antioxidant defense mechanisms in various tissues, including periodontal tissue. Regular exercise can induce an increase in anti-inflammatory cytokine levels, resulting in an anti-inflammatory mechanism. Thus, periodontal also increases blood flow, decreases the level of bone

damage, repairs periodontal tissue so that periodontal status in patients who exercise regularly becomes good.

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