



The Significance of Non-Drug Correction of Carbohydrate Metabolism Disorders

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Abstract: *Today, one of the main tasks of the healthcare system in many countries of the world is the development and implementation of measures for primary and secondary prevention of the onset and progression of socially significant diseases. In recent decades, the prevalence of carbohydrate metabolism disorders and DM in particular has acquired the character of a pandemic, both in developed and developing countries of the world [1]. According to the latest data, the number of patients with DM in the world over the past 10 years has more than doubled, and by the end of 2015 reached 415 million people [2]. According to the forecasts of the International Diabetes Federation, 642 million people will suffer from diabetes in 2040 [2]. Such a rapid increase in the incidence of diabetes was the reason for the adoption of UN Resolution 61/225 of December 20, 2006 on diabetes mellitus, and in 2011 - the UN Political Declaration addressed to national health systems, calling for the creation of multidisciplinary strategies in the field of prevention and control of non communicable diseases, where special attention is drawn to the problem of diabetes, as one of the leading causes of disability and mortality in the population.*

Keywords: *Non-Pharmacological Treatment, Medical Nutrition Medical Aid, Mediterranean Diet, Exercise in Polygenic Disease, Bariatric Surgery, Polygenic Disease Remission.*

1. INTRODUCTION

Carbohydrate metabolism disorders are a group of metabolic disorders. Normally your enzymes break carbohydrates down into glucose (a type of sugar). If you have one of these disorders, you may not have enough enzymes to break down the carbohydrates. Or the enzymes may not work properly. This causes a harmful amount of sugar to build up in your body. That can lead to health problems, some of which can be serious. Some of the disorders are fatal.



These disorders are inherited. Newborn babies get screened for many of them, using blood tests. If there is a family history of one of these disorders, parents can get genetic testing to see whether they carry the gene. Other genetic tests can tell whether the fetus has the disorder or carries the gene for the disorder. Treatments may include special diets, supplements, and medicines. Some babies may also need additional treatments, if there are complications. For some disorders, there is no cure, but treatments may help with symptoms.

It is appropriate to recall that the prevalence of DM, according to the World Health Organization and the International Diabetes Federation, ranks third after cardiovascular and oncological diseases. The total number of patients with this diagnosis in the world is about 371 million people [8, 3, 4]. The data of statistical reports showed that the prevalence of DM, taking into account its types, varies quite widely and is largely determined by belonging to certain ethnic and age groups. As of 01.01.2018 in the Republic of Uzbekistan. 230,610 patients with DM were registered at the dispensary [1, 3, 4].

There are several typical forms of carbohydrate metabolism disorders: hypoglycemia, hyperglycemia, glycogenosis, hexosypentosemia, aglycogenosis [1]. Hypoglycemia is a condition characterized by a decrease in plasma glucose levels below normal. Hyperglycemia is an increase in the level of sugar in the blood and is a violation of the relationship between its absorption, synthesis and utilization. In endocrinological practice, the main disease associated with impaired carbohydrate metabolism is DM [2]. From the point of view of the modern position, DM can be defined as a group of metabolic diseases characterized by hyperglycemia due to impaired insulin synthesis and/or its biological action [3]. A chronic increase in blood glucose levels leads to damage and dysfunction of various organs and their systems, especially the visual, nervous, urinary and cardiovascular systems.

India has an estimated 77 million people (1 in 11 Indians) formally diagnosed with diabetes, which makes it the second most affected in the world, after China.[59] Furthermore, 700,000 Indians died of diabetes, hyperglycemia, kidney disease or other complications of diabetes in 2020. One in six people (17%) in the world with diabetes is from India.[60] (India's population as calculated in October 2018 was about 17.5% of the global total.[60]) The number is projected to grow by 2045 to become 134 million per the International Diabetes Federation.[59]

In India, type 1 diabetes is rarer than in western countries, and about 90 to 95% of Indians who were diagnosed had type 2 diabetes. Only about one-third of type 2 diabetics in India have a Body Mass Index above 25.[61] A 2004 study suggests that the prevalence of type 2 diabetes in Indians may be due to environmental and lifestyle changes resulting from industrialization and migration to urban environment from rural.[62] These changes also occur earlier in life, which means chronic long-term complications are more common.

The pathogenesis or continuum of development of DM is a rather long process and consists of several stages, and timely intervention in the early stages of this process prevents or slows down the rate of development of this multifaceted pathology [60]. According to prospective studies, the early stage of carbohydrate metabolism disorders lasts an average of 5 to 10 years.

The development of hyperglycemia is based on three different mechanisms:

- i) Decrease in insulin-stimulated glucose utilization by peripheral tissues (skeletal muscle, adipose tissue and liver) or IR;
- ii) Increased production of glucose by the liver;



iii) Impaired synthesis and secretion of insulin by pancreatic β -cells Today, the dominant opinion is that the cause of the development of type 2 diabetes is genetically determined insulin resistance (IR), fixed in the course of evolution. The presence of IR ensured the accumulation of energy in the form of fat deposition, and these reserves contributed to the survival of primitive people in conditions of famine. Nowadays, a person began to lead a sedentary lifestyle, greatly increased the amount of fat and refined carbohydrates consumed, which, in conditions of IR preserved in the genetic memory, leads to the accumulation of energy, leading to the development of abdominal obesity.

The DM continuum consists of 4 stages [2]:

- i) IR and compensatory hyperinsulinemia without clinical manifestations of carbohydrate metabolism disorders;
- ii) IGT, which manifests itself in the form of an increase in glucose levels at least 2-3 hours after eating;
- iii) The initial stage of diabetes due to a decrease in basal insulin secretion;
Decompensation of DM as a result of a pronounced decrease in insulin secretion. The conversion of IGT to type 2 DM depends on many factors: the presence of factors (RFs) of cardiovascular disease (CVD) and DM, lifestyle, and social status.
- iv) Conducted prospective studies show that the annual conversion of IGT to type 2 diabetes in different countries ranges from 1.5% to 7.3% [3]. It is known that most chronic non communicable diseases (CNCs), such as CVD, DM, etc. have common risk factors. In general, today more than 200 risk factors are known, which are divided into modifiable and non-modifiable, environmental factors, biological, socio-behavioral factors, etc. [1–4]. The results of prospective studies indicate that the same risk factors can simultaneously contribute to the development of several CNCs. In table. Table 1 shows a causal relationship between 8 major risk factors and CVD, DM, oncological and respiratory diseases [5–7].

Table1. Common risk factors for major non communicable diseases

Risk factors	CVD	SD	OZ	RZ
Smoking	+	+	+	+
Excess alcohol consumption	+	+	+	+
Irrational food	+	+	+	+
Flaw physical activity	+	+	+	+



Obesity	+	+	+	+
Increase in blood pressure above 140/90 mm rt. Art.	+	+	+	
Increased blood glucose > 5.6 mmol/l	+	+	+	
elevated cholesterol level in blood > 5.5 mmol/l	+	+	+	

Risk factors can be combined according to the principle of causation (obesity and impaired carbohydrate metabolism), pathogenetic interaction (for example, metabolic syndrome) and mechanical combination (arterial hypertension and hypercholesterolemia). A number of studies have shown that early disorders of carbohydrate metabolism are not only an intermediate stage in the development of DM, but also an independent risk factor for CVD and other chronic NCDs. There are several groups of biological and behavioral RF disorders, in the presence of which early disorders of carbohydrate metabolism can be detected in patients. Moreover, the probability of detecting early disorders of carbohydrate metabolism in cardiological practice among individuals with CVD risk factors is high. Therefore, the study of screening methods for predicting DM and their application among individuals with cardiovascular risk is a priority in the primary prevention of DM.

In recent years, in connection with the development of the diagnostic basis of the metabolic syndrome (MS), interest in early disorders of carbohydrate metabolism has increased markedly, since prediabetes is one of the main components of MS. According to the Russian population study PRIMA, 40% of patients with MS have early disorders of carbohydrate metabolism.

When diagnosing MS, TSH is necessary, since 60% of those with IGT have fasting glycemia within the normal range [8]. British scientists claim that only 39% of patients suffering from hypertension have normal glucose tolerance, while 10% have NGN, and 22% have IGT [9, 10, 41, 42]. An analysis of the literature suggests that individuals with risk factors such as: low physical activity (LFA), abdominal obesity (AO), with a hereditary burden of diabetes (first-degree relatives suffering from diabetes), dyslipidemia (hyperTH, low HDL cholesterol), Hypertension, fatty liver, people with manifestations of atherosclerosis (IHD, stroke, intermittent claudication), repeated skin infections, unexplained fatigue - have a high risk of developing diabetes. The social significance is supported by significant economic costs for many countries of the world. Thus, the economic damage from diabetes mellitus (DM) amounted to 376 billion US dollars in 2010 and will amount to 490 billion US dollars in 2030 [36, 44, 45]. The magnitude of the economic costs associated with the treatment of such patients requires the search for new solutions. It is now generally recognized that



diseases of the endocrine system (diabetes mellitus and its late complications, diseases of the hypothalamic-pituitary system, thyroid gland, adrenal glands and gonads) represent an acute medical and social problem that is among the priorities of national health systems in almost all countries of the world, and are protected by the regulations of the World Health Organization (WHO) [8, 10, 40, 43].

Rehabilitation in the health care of the Republic of Uzbekistan, as well as other countries of the world, is a long-term state policy aimed at the optimal restoration of people's livelihoods. The Law "On the Fundamentals of Protecting the Health of Citizens in the Republic of Uzbekistan" interprets medical rehabilitation as a set of medical and psychological measures aimed at full or partial restoration of impaired and (or) compensation for lost functions of the affected organ or body system, maintaining body functions in the process of completing an acutely developed pathological process or exacerbation of a chronic pathological process in the body, as well as prevention, early diagnosis and correction of possible dysfunctions of damaged organs or body systems, prevention and reduction of the degree of possible disability, improvement of the quality of life, preservation of the patient's working capacity and his social integration into society. Tasks that puts a rehabilitation direction, significantly expands the scope of the traditional therapeutic approach, combines preventive and curative-restorative medicine with the activities of social security agencies. Medical rehabilitation is an incomparably broader concept than treatment in general and restorative treatment in particular (the so-called post-treatment). Rehabilitation in health care covers the entire period from the provision of first aid to the highest possible level of restoration of a person's social and professional functions [8, 14, 46, 47]. In the process of rehabilitation, the doctor turns to those resources of the body that were not affected by the disease. The issues of rehabilitation of patients and disabled people suffering from endocrine diseases have been dealt with since the late 80s, and by now quite a lot of experience has been accumulated [3–5, 10, 14, 37, 38, 48, 49]. The most important factor in the rehabilitation of patients with diabetes is the restoration of disturbed glycemic control, maintaining the level of glycemia as can be closer to the normal level of values, depending on the personal characteristics of patients (duration of diabetes, age or life expectancy, the presence of complications or concomitant diseases and the risk of hypoglycemia) [8, 22, 31, 50]. The main directions of rehabilitation measures include: optimization of eating behavior (including diet therapy); development of an individual regimen of physical activity (with the help of exercise therapy); appointment or correction of ongoing hypoglycemic therapy; patient education in chronic disease management, self-control; achievement of normal values of indicators of metabolic control; correction of disorders of the blood coagulation system; blood pressure monitoring; correction of excess body weight; psychological support and motivation; providing the patient with auxiliary means for administering insulin (syringe pen, insulin pump) and self-monitoring (glucometer, test strips for monitoring glycemia and glucosuria, kenonuria); rational employment [9, 17, 19, 30, 51]. According to international recommendations, it is advisable to recommend a combined program of diet therapy and physical training to patients with prediabetes. The diet should be based on several principles, namely: □ the correct distribution of portions of food taken during the day. □ increase in the intake of proteins, including vegetable ones. □ reduction of food calories to 1500 kcal/day, □ reduction of carbohydrate intake (increase in fiber intake to 30 g/day, limiting the intake of liquid mono



and disaccharides. □ limiting fat intake to 30-35% of the total caloric intake. The most important in the development of DM 2 type have malnutrition and a sedentary lifestyle.^{16,17,52,53} As shown in the European evidence-based guideline for the prevention of type 2 diabetes,¹⁸ randomized trials demonstrate that lifestyle modification consisting only of reducing body weight and increasing physical activity, prevents or slows the progression of glucose disorders in individuals with IGT. Therefore, individuals at high risk of type 2 diabetes and with existing IGT should be advised of the need for lifestyle modification and assistance in its implementation.

The level of physical activity can be assessed using simple questionnaires and pedometers. The program "10000 steps" daily helps to reduce the main metabolic indicators, including glycemia up to 25%. Persons without clinical manifestations of atherosclerosis are recommended any type of physical activity of their choice, including sports; physical activation is also possible in everyday life, for example, walking up the stairs instead of using the elevator. The most accessible form of aerobic exercise is vigorous walking. Patients with prediabetes should be prescribed exercise for 30–60 minutes, 5 days a week, until a heart rate is reached, usually determined by a pulse rate equal to 65–70% of the maximum for this age. The maximum value of heart rate can be calculated by the formula: 220age in years. For patients with coronary artery disease, the exercise regimen is selected individually, taking into account the results of the stress test [19, 54].

In table.2 presents the main recommendations for lifestyle changes (diet and physical activity) in individuals with early disorders of carbohydrate metabolism.

Table2. Non-drug therapy for persons with early disorders of carbohydrate metabolism

Diet (recommended by ADA)	Recommended (servings, g / per day)	Not recommended
Bread, cereals and other starchy products	6-11 servings	Fats, oils, sweets, including refined carbohydrates
Vegetables	3-5 servings	Sweet carbonated, alcoholic drinks
Fruit	2-4 servings	
Skimmed milk	2-3 servings	
Meat substitutes	100–170 g	
Physical activity	Physical exercise 30-60 minutes 5 days a week (start with 5-10 minutes a day) Physical activities may	physical intensity exercise without taking into account age, weight body, objective somatic data state, non-



	include: walks around the block using the stairs instead of the elevator, gardening, dancing, bowling, cycling, swimming.	preliminary physical training. fatigue is pronounced, passing within 5–10 minutes or pronounced for a long time. BP and pulse exceeding the recommended limits with a recovery period after (5–10. min.)
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One of the main problems in the implementation of the lifestyle change program is the unsatisfactory adherence of patients to the regular implementation of these recommendations. The design of lifestyle change programs should be based on an understanding of the important role of participants in accepting and participating in already implemented programs. Implementation of the programs is still a challenge as the required methodology is at an early stage of development, not fully understood and rarely applied. In addition, we need to expand theoretical knowledge, using data from experience gained and analysis of implementation research in real life. The establishment of a school for such patients is recommended. Along with this, the support of family members is essential. Obviously, in the near future, a team of specialists, together with psychologists, should develop various lifestyle change programs, since standard recommendations do not always give the desired success.

The main tasks of medical rehabilitation of patients with diabetes mellitus, which can be attributed to priority, are: optimal speed, effective achievement and long-term maintenance of individual indicators of glycemic control (HbA1c) with maximum safety for the patient; maintaining good health; prevention of development of acute metabolic complications; prevention of development of late complications; improving the quality of life. The main principles of medical rehabilitation of patients with diabetes mellitus: timeliness of care (the earliest possible start and comprehensive implementation of all types of rehabilitation therapy with the involvement of specialists in various fields (up to lawyers, sociologists, etc.); specialization of medical care; differentiation of medical methods and means in depending on the characteristics of the disease; staging of assistance with the obligatory solution of the goals and objectives of the current stage; continuity of treatment and recovery methods based on their effectiveness; complexity, i.e. the optimal combination of methods and means of therapy that ensure the maximum rate and effectiveness of rehabilitation; correctability (controllability) of therapeutic effects by means of operational control of effectiveness; continuity of the rehabilitation process; optimal recovery of deficient body functions in each specific case; individualized nature of all rehabilitation measures; the development of rehabilitation in a team of patients; the presence of a system of legal framework for the provision of rehabilitation assistance to members of society: state and public type of management of the rehabilitation system in the country; legal status of persons subject to rehabilitation; universal accessibility of the necessary stages, methods and means of rehabilitation. A special place in the provision of medical care to patients with diabetes mellitus is occupied by non-drug therapy. To date, extensive clinical and experimental



experience has been accumulated in the use of technologies for the medical rehabilitation of patients with diabetes mellitus [2, 11, 12, 17, 19–21, 27, 28, 39, 55].

The most important therapeutic factor in the rehabilitation of diabetic patients is drinking balneotherapy. Mineral waters containing carbon dioxide, hydrogen sulfide, bicarbonate, sulfate, sodium, magnesium, calcium, chlorine ions have a positive effect on the carbohydrate metabolism of patients with diabetes mellitus: the early phase of insulin secretion increases significantly, alimentary hyperglycemia decreases by 10-15%, glucosuria increases, the influence of certain enzymes that promote the penetration of glucose into tissues, antioxidant defense enzymes - catalase and superoxide dismutase are activated. At the same time, the processes of tissue metabolism of carbohydrates improve: the formation of adenosine triphosphoric acid (ATP) increases, the breakdown of which releases a large amount of energy [23, 26, 56]. Bicarbonate and sulfate waters reduce the content of ketone bodies in the blood, increase alkaline reserves and thereby eliminate the accumulation of underoxidized products in the body. The use of mineral water inside reduces the content of cholesterol, total fats, beta-lipoproteins, free fatty acids, triglycerides, increases the level of phospholipids involved in the transport of fats [24, 25, 57]. A characteristic feature of the effect of mineral water on the liver is a decrease in the severity and prevalence of necrobiotic processes in it. Drinking treatment improves the metabolism of trace elements. Waters containing copper and zinc ions have a direct effect on the activity of the insular apparatus and the activity of enzyme systems that break down insulin, and also have an immunomodulatory effect [9]. External balneotherapy has a positive effect in the treatment of diabetes. The effect of hydrogen sulfide and dry carbon dioxide baths is well known. Hydrogen sulfide baths normalize the state of the autonomic nervous system, activate tissue respiration, enhance microcirculation in tissues, stimulate regeneration of peripheral nerves and tissue repair, improve lipid and carbohydrate metabolism, the functional state of the myocardium, lower blood pressure, improve local immunity [1, 7, 9, 58]. Carbon dioxide baths increase the utilization of oxygen by tissues, increase the activity of metabolic processes, increase the tone of the parasympathetic division of the autonomic nervous system, normalize electrolyte balance, improve myocardial contractility, reduce the tone of bronchial muscles and intestinal muscles, reduce hypercholesterolemia, and improve protein and carbohydrate metabolism [16]. Due to the complex effect, balneotherapy has an impact on various links in the pathogenesis of diabetes mellitus. The tasks of physiotherapeutic methods of treating patients with diabetes mellitus are the correction of neurohumoral dysregulation of the endocrine system, the enhancement of the excretory function of the pancreas, the correction of carbohydrate and fat metabolism, and the relief of astheno-neurotic state [13, 15, 18, 59]. The optimal coverage of physiotherapeutic treatment for endocrine pathology is 70% [2]. However, the effectiveness of the influence of aerodynamic and sodium chloride baths in the treatment of diabetic polyneuropathy, especially in combination with physiotherapeutic factors, has not been studied enough. At the same time, the creation of effective, affordable and inexpensive technologies is an important task of medical rehabilitation in diabetes mellitus. Physiotherapeutic methods at the sanatorium stage of rehabilitation are used in the treatment of type 2 diabetes as part of complex therapy. Physiotherapy does not have a direct hypoglycemic effect, mainly physiotherapeutic methods are used to treat complications of diabetes mellitus, as well as concomitant diseases. An indispensable condition for the



appointment of physiotherapeutic procedures is stable compensation of metabolic disorders, the absence of ketoacidosis and hypoglycemic conditions. At the same time, both general contraindications to physiotherapy and the peculiarities of the reaction of patients with diabetes mellitus to certain methods of physical influence, in particular, the increased sensitivity of their skin to thermal procedures, to high-density electric current, are taken into account. In recent studies, it has been proven that long-term disorders of the endocrine system in some cases can cause the irreversibility of the pathological process and cause individual "affective" responses of the body. Leading clinical scientists noted that the psychosocial deterioration associated with incomplete remission of endocrine disease suggests the need to develop and apply innovative approaches to treatment with the introduction into clinical practice of the concept of rehabilitation, which is already recognized in other areas of medicine (for example, internal medicine, neurology, traumatology), cardiology, pulmonology, rheumatology and a number of others). In accordance with the purpose of a particular stage of rehabilitation, a multidisciplinary medical team develops and approves individual programs (based on standard schemes).

A promising area of rehabilitation is a complex rehabilitation impact (rehabilitation therapy), carried out by coordinated activities of various profiles - the so-called interdisciplinary rehabilitation team of specialists [36, 39–43]. The new proposals of N. Sonino, which stem from a number of unresolved issues related to the widespread use of psychosocial deterioration of patients, even those who received adequate treatment - either conservative or surgical [41, 44]. According to the authors of the discussed concept, which is mainly supported by specialists, rehabilitation of patients with various levels of hyperglycemia, as well as complications of diabetes, can be indicated in the following cases: a) slowing down the period of complete recovery of impaired functions after inpatient treatment; b) discrepancy between the endocrine status and the current functioning of the cardiovascular system and the autonomic nervous system; c) decreased physical and social functioning; d) the presence of concomitant (comorbid) diseases, especially those accompanied by any psycho-emotional disorders; e) confirmation of the fact of violation of the quality of life; f) lifestyle and risk behavior problems – reduced compliance; g) newly diagnosed (including reversible) endocrine diseases and disorders as a result of maladaptation after stress. When studying the work of Sonino [et al.], we drew attention to the fact that by now almost all of the above factors have been described in detail, characterized and isolated into separate indicators that can be used as parameters for assessing the clinical status of patients [32, 33, 34]. It seemed important that the attention of researchers is focused on the possibilities of their complex application in order to improve existing or build new clinical programs for the rehabilitation of patients. In our opinion, the use of this approach expands the possibilities for updating, modifying and further improving the already used methods of restorative treatment [3, 35, 40]. It is noteworthy that based on the competent processing of accumulated data in the future, it is possible to create clinical algorithms (simplified schemes) to facilitate the work of doctors (taking into account a specific specialization) It is also likely that the goal of the preventive service should be to educate, support and develop specific individual approaches to care the patient and his family members in order to optimally cope with the difficulties of the recovery process. Thanks to a complex psychosomatic method, the new approach will increase the chances of obtaining a complete, clinically significant remission in



a significant proportion of patients, while demonstrating both clinical efficacy and economic profitability [33, 39–43].

Psychosocial deterioration associated with incomplete clinical remission on the background of an endocrine disease (subject to the normalization of the main laboratory parameters - mainly the level of hormones) requires the development of new methods of treatment and nursing of patients, the introduction into medical practice of the concept of medical prevention, rehabilitation, which, as noted above, has long been recognized and widely used in other areas of healthcare [11, 30, 36]. It should be noted that in recent years the existing system of medical prevention, diagnosis, treatment and rehabilitation has been constantly improved. A good example are scientific publications and manuals, in which which analyzed and summarized the personal results of the restoration activities, and the relevant recommendations were made taking into account the accumulated world theoretical and practical experience [3–6, 8, 17, 31, 43, 45].

Indian Diabetes Prevention Program:

The Indian Diabetes Prevention Program is a three-year randomized control trial that employed LSM and metformin (Met) to prevent type 2 diabetes in subjects with IGT. It concluded that LSM and Met were cost-effective interventions for preventing diabetes among high-risk individuals in India and other developing countries. [63]

National Diabetes Control Program

The National Diabetes Control Program was initiated in 1987 in some districts of Tamil Nadu, Jammu and Kashmir, and Karnataka. Its objectives included : [64]

Identifying high-risk individuals

Introducing health education for the purposes of early intervention

Aiming for early diagnosis and treatment of affected individuals

Reducing morbidity and mortality in high-risk groups

Preventing acute and chronic metabolic, cardiovascular, renal, and ocular complications due to the disease

Rehabilitating people who have been handicapped due to the disease

However, the program was not expanded to other states due to shortage of funds.

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