Experience of Phototherapy Application in Treatment of Osteoarthritis in Patients with Diabetes Mellitus

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***Abstract* — To evaluate the effectiveness of Korobov's apparatus for the complex treatment of patients with diabetes mellitus, complicated by musculoskeletal disorders. The study was performed on 60 patients, mean age 57.51±1.13 years with combined course of DM and OA. All patients were divided into 2 groups: 1st group - 29 patients, who received standard therapy for OA and DM and 2nd group - 31 patients, who received treatment by the Photon Matrix "Barva-Flex" in addition to standard therapy. A positive dynamics was observed in both groups of patients after the course of treatment was done. There was a decrease of pain in the joints, an increase of motion range, marked improvement of the functional state of the joints and decreased stiffness. A positive dynamic of biochemical parameters of blood serum was noted in both groups, but better resuls were achieved in patients that received phototherapy. The use of photon matrices in the complex treatment of patients with DM and muskuloskeletal disorders has led to significant improvement of the functional state of joints, decrease of pain intensity and lowering of inflammatory markers in blood. Phototherapy is a safe and effective method of treatment because of its good tolerability, absence of side effects and a positive impact on the course of diabetes.**

Keywords— phototherapy; osteoarthritis; diabetes mellitus.

I. INTRODUCTION

The disorders of the musculoskeletal system take an important place among the chronic complications of diabetes mellitus (DM). Their prevalence varies from 24 to 60% according to various sources [1]. Taking into consideration the fact that the largest group of patients with diabetes are those of working age, an additional disorder of the musculoskeletal system further complicates the course of the disease, reduces performance, accelerates disability, worsens the psychological state and socio-economic status, and thus, lowers the quality of life [2].

The common lesions of the musculoskeletal system in patients with DM include osteoarthrosis of the knee joints, shoulder periarthritis ("diabetic shoulder"), osteoarthropathy and osteoporosis. Diabetic osteoarthropathy is a compound syndrome of specific degenerative changes in bones, joints and periarticular tissues, which affects mainly lower limbs, and is also known as Sharko's foot / joint [3-4]. The development and progress of these complications in diabetes depends on the degree of metabolic disorders, which in turn is associated with the severity and duration of the disease. The complications are more common for patients with moderate to severe diabetes, above 50 years old and with a duration of disease more than 5 years [1-5].

The mechanism of the formation of bone and muscular complications in diabetes is associated with the inhibition of bone matrix synthesis and its mineralization due to insulin deficiency. At the same time, glucose toxicity enhances bone resorption by osteoblasts. In addition, due to the decrease of calcium absorption because of the lack of active metabolites of vitamin D, a negative balance of inorganic elements develops in the body, which further accelerates bone resorption [6].

It should be noted that patients with diabetes have common underlying processes, leading to osteoarthrosis (OA), such as: a change in the remodeling of bone tissue, leading to the disturbance of the structure of the subchondral bone in the early stages of the disease, and later to its thickening (Bone Atrophy), synovial inflammation (Synovial Inflammation), along with an increase of release of proinflammatory mediators and an increase in the catabolism of the articular cartilage matrix (Cartilage Catabolism). Sinovitis activates sensory nerve fibers, an thus causes pain and neurogenic inflammation [7]. A chronic inflammatory disease develops, in which the imbalance of cytokines (interleukin (IL) 1, 6, 17, and tumor necrosis factor-α (TNF-α) play an important role). The proinflammatory IL-1 influences plasminogen, and promotes its transformation to active plasmin, which, in turn, converts inactive pro-metal proteases into an active form, enhancing the degradation of the extracellular matrix. The catalytic action of IL-1 manifests by its ability to stimulate the production of nitric oxide (NO) by chondrocytes and synoviocytes. The release of NO causes damage to the extracellular matrix, mainly by reducing the concentration of IL-1 receptor antagonist, activation of IL-1 itself and induction of chondrocyte apoptosis. IL-1β enhances calcium excretion, activates osteoblasts, which leads to the decrease of the intensity of

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bone formation. The decrease of osteocalcin concentration contributes to the destruction of the subchondral bone. Also, the hyperexpression of the enzyme cyclooxygenase-2, which induces the synthesis of prostaglandins, is involved into the development of inflammation. Chronic inflammation leads to the activation of bone resorption caused by RANK/RANKL system, which provides the development, activity and survival of osteoclasts. IL-1β, TNF-α and RANKL increase Nfκβ activity in target cells, which causes exacerbation of inflammation and/or bone destruction [8-11].

All mentioned above suggests that proinflammatory cytokines demonstrate various pathophysiological effects on cartilage catabolism and subchondral bone. Therefore, cytokines can be the target for therapeutic strategy in patients with such disorders.

At the present stage, the main goal of diabetes treatment is to ensure the quality of life of the patient. This can be achieved by the fullest compensation of metabolic processes: normalization of glycemia, lipid, protein, and mineral metabolism. The effective measures to prevent chronic complications and to ensure glycemic control in diabetes include diet, drug therapy and physical exercise [12]. The benefits of regular exercise for the prevention and slowing down of musculoskeletal complications are well known, but the commitment of patients to training remains low due to the relative intolerance to physical exercise and premature muscle fatigue [13].

Therefore, the complex approach to treatment should be taken, aimed at improving the neurological status, tissue microcirculation and reducing the inflammatory response. Such approach is able to accelerate the treatment time, reduce the frequency of relapses and provide effective prevention.

Photobiomodulatory therapy, also known as phototherapy, is an alternative, non-invasive and painless method, with has proven efficiency in reducing articular and neuropathic pain [14-17]. Presented as low-level laser therapy (LLLT) and/or LED therapy (LEDT), it uses the non-ionizing light sources (lasers, LEDs, and broadband lights; visible to infrared spectrum).The light interacts with chromophore, which results in photoinduced reactions in various tissues of the body [18].

The accumulated data indicate that phototherapy can be used effectively for patients with musculoskeletal complications against the background of diabetes, as it promotes regeneration of skin, ligaments, bones, tendons as well as cartilage tissue, improves metabolic processes and rheological properties of blood [19-21].

The possible mechanism of therapeutic action of phototherapy for people with diabetes is to stimulate cellular molecules and atoms without significant increase of tissue temperature. Photochemical reactions change the permeability of the cell membrane, increase the accumulation of RNA messengers and stimulate cell proliferation. The light, which is emitted during the LLLT reacts with cytochrome C oxidase - a mitochondrial respiratory enzyme, that stimulates the production of adenosinetriphosphate (ATP) and at the same time reduces the levels of active forms of oxygen [22].

The increased metabolic activity in phototherapy is associated with the stimulation of electron transport and increased mitochondrial ATP production. Accumulation of ATP, in turn, increases the energy supply for cells' metabolic needs. Acceleration of cell proliferation is associated with stimulation of the oxidative metabolic pathway and an increase of total cellular metabolism [23]. Neovascularization of connective tissue, increased blood flow by vasodilation and increased levels of nitric oxide characterize the angiotrophic effect of phototherapy, which is especially important for patients with diabetes mellitus with peripheral vascular lesions [24]. The mechanism of anti-inflammatory effect, as well as wound healing properties, is the following: reduction of the levels of prostaglandin-2 and cyclooxygenase-2, stimulation of fibroblasts, acceleration of collagen synthesis and growth factors release in damaged tissues [25]. Other mechanisms, such as increase of the nociceptive threshold, enhance of the synthesis of endorphin and increase of opioid receptors sensitivity explain the analgesic effect of phototherapy [26].

The technical parameters that determine the therapeutic effect of phototherapy include output power, wavelength, power density, and dose range. Low-Level Laser Therapy (LLLT) is characterized by power range from 0.001 to 0.1 W, wavelength from 300 to 10 600 nm, frequency from 0 to 5000 Hz, intensity from 0.01 to 100 W/cm^2 and power density from 0.01 to 100 J/cm. Along with LLLT, LEDs can be used. A combined type of phototherapy provides higher surface fineness and even distribution of lower power energy. The duration of phototherapy, according to numerous clinical studies, can range from 4 to 50 minutes per session, up to two times a day, 15 to 90 days [27].

Currently, there are no recommendations for a standard phototheapy procedure for the treatment of musculoskeletal disorders in patients with diabetes. Therefore, we developed and offered a method for the treatment of diabetic osteoarthropathies and osteoarthrosis in this category of patients with the use of flexible "Barva-Flex" photomatrix [28-29], which influences the affected joints with blue and infra-red light together with magnetic radiation for 30 minutes. The base version of the matrix contains 24 LEDs, which are distributed equidistant in 4 rows (6 LEDs in each row). Special matrixes have 3x8 LEDs (to be applied on extended areas) and 2x12 (to be applied on the spine and paravertebral zones). During the procedure, the light is absorbed by body tissues, in which it spreads according to the laws of nonlinear optics due to heterogeneity of tissues.

The study was designed to evaluate the effectiveness of Korobov's apparatus for the complex treatment of patients with diabetes mellitus, complicated by musculoskeletal disorders.

II. Materials And Methods

A total of 60 patients with diabetes mellitus (28 patients with type 1 DM and 32 patients with type 2 DM) were examined in the endocrinology and rheumatology departments of the Communal Nonprofit Enterprise of the Kharkiv Regional Council "Regional Clinical Hospital". All patients had the subcompensation stage of DM (HbA1c<7.4±0.5%) and the pathology of the musculoskeletal system. The duration of DM ranged from 7 to 25 years, mean age 47.3±0.21 years. All patients were divided into 2 groups: 1st group - 29 patients, who received standard therapy for OA and DM and 2nd group - 31 patients, who received treatment by the Photon Matrix "Barva-Flex" in addition to standard therapy.

Diagnosis of OA was established due to the complaints, anamnesis, results of clinical, laboratory and instrumental studies, according to diagnostic criteria of the American College of Rheumatology (ACR, 1991). Diagnosis of diabetes mellitus was made according to the criteria of the International Diabetes Federation (IDF, 2005).

A complex of clinical, laboratory, biochemical and instrumental methods was used to verify the diagnosis of OA and DM in the examined patients. Biochemical studies included methods for assessing the state of carbohydrate metabolism (fasting plasma glucose test (FPG), glycated hemoglobin (HbA1c), immunoreactive insulin (IRI)), electrolites (ionized calcium, magnesium, phosphorus), the level of serumucoid acid and sialic acid, and the level of C-reactive protein. The study of joints included an objective examination, palpation, a pain estimation in a state of rest and at movements by VAS (visual analog scale). Symptoms of OA were also evaluated by the WOMAC (Western Ontario and McMaster University) index. X-ray examination was performed in all patients. X-ray stages of OA were evaluated according to the classification of J.H. Kellgren and J.S. Lawrens.

Complex examination of patients was performed at a time of admission to the Kharkiv Regional Hospital and was repeated in 4 weeks after beginning of treatment.

Korobov's photon matrices "Barva-Flex" were used for treatment. A distinctive feature of photon matrices is that they have a flexible shape. This allows the matrices to follow the shape of the certain part of the body to which they are applied, which ensures the most efficient transmission of LEDs light and no loss at the boundary air - human skin.

The photon matrix "Barva-Flex" of the optimal spectral composition in conjunction with the magnetic matrix "Barva-Flex / Mag" was installed sequentially on the right and left rear surfaces of the wrist (zone 1), right and left palm (zone 2), the right and left wrist zones (zone 3), the right and left cubital veins (zone 4), the upper surface of the foot (zone 5), the projection of the thymus (zone 6), the liver (zone 7) and the spleen (zone 8) . The duration of procedure is 3-5 minutes for each zone.

Later, the matrices were placed on the projection of pancreas in order to improve the microcirculation of blood and lymph, which provides the inhibition of inflammatory process, decrease of edema and pain; accelerates tissue regeneration; positively influences the regulation of glucose levels. After that, photonic matrices of infrared and blue ranges were applied to the joints for 30 minutes. The course included 10 procedures.

III. Results And Discussion

The main clinical manifestations of OA were: joint pain that appeared after exercise, limitation of a joint mobility, joint crepitation, joint functional disorders (Table 1).

The increased levels of CRP, seromucoid, sialic acids in serum was determined by biochemical studies.

Also, there were changes of electrolite balance, in particular, the levels of calcium and phosphorus. These changes develop due to the disorders of metabolic processes, which affect the state of bone matrix adversely.

TABLE I. Basic Clinical Manifestations Of OA In Examined Patients

Clinical manifestations	***1st group (n=29)***		***2nd group (n=31)***	
	n	**%**	**n**	**%**
Joint pain after exercise	29	100	31	100
"Start" pain	17	58,6	19	61,2
Crepitus in the joint during movement	5	17,2	6	19,35
Morning stiffness in joint	19	65,5	22	70,96
Restrictions range of motion	21	72,4	23	74,19
Dysfunction of joints	17	58,6	20	61,3

If the reabsorption of calcium and phosphorus in the renal tubules is affected (the presence of hypercalciuria and hyperphosphaturia), a negative balance of calcium, phosphorus, and sometimes - magnesium might occur in the body. In addition, there was an increase of CRP level, sialic acids and seromucoid, which is the evidence of the active phase of inflammatory process in the joints.

A positive dynamics was observed in both groups of patients after the course of treatment was done. (Table 2).

First, there was a decrease of pain in the joints, an increase of motion range, marked improvement of the functional state of the joints and decreased stiffness. It should be noted, that the improvement of the patients' condition was statistically more obvious in the second group. Therefore, the patients' assessment of pain according to VAS has decreased significantly in the second group of patients. In 4 weeks after the start of treatment, the pain in these patients decreased by 43%, while in the 1st group - by 27%. This fact confirms a positive effect of additional phototherapy on the severity of the pain.

TABLE II. The Influence Of Therapy On The Clinical Status Of Patients With Combined Course Of OA And DM

Indicator	**Groups of patients**					
	1st group (n=29)			***2nd group (n=31)***		
	Before treatment	***After 4 weeks***	***Wilcoxon Test (Z, p)***	***Before treatment***	***After 4 weeks***	***Wilcoxon Test (Z, p)***
VAS, rest (mm)	45 [40; 45]	33 [30; 40]	Z=3,2, p=0.001	46 [44; 47]°	26 [24; 27]	Z=3.2, p=0.001
VAS, movements (mm)	60 [55; 65]	38 [30; 40]	Z=3.3, p=0.001	60 [55;65]	34 [32; 36]	Z=3.2, p=0.001
WOMAC, pain (score)	25.5 [25; 28]	22 [20; 25]	Z=3.1, p=0.002	26 [25; 29]	20 [19; 22]	Z=3.1, p=0.001
WOMAC, stiffness (score)	8 [7; 9]	6.5 [6; 7]	Z=3.3, p=0.001	8 [8; 10]	5.5 [5; 6]	Z=3.1, p=0.001
WOMAC, functional limitation (score)	59 [54; 62]	51 [43; 56]	Z=3.3, p=0.001	60 [55;64]°	50 [43;54]°	Z=3.1, p=0.001
WOMAC, total (score)	92.5[89; 99]	79.5 [73; 86]	Z=3.3, p=0.001	94 [101; 110]°	75.5 [79; 107]°	Z=3.1, p=0.001

Note: * Calculated value of statistical criterion
** the level of statistical significance
° - significant difference from group 1.

All patients were exmined after the end of the course of treatment. Also, a biochemical parameters of blood serum (seromucoid, sialic acid and CRP) were assessed, a positive dynamic was noted in both groups, but better resuls were achieved in patients that received phototherapy (Table 3).

TABLE III. INFLAMMATORY ACTIVITY IN PATIENTS WITH A COMBINED COURSE OF OA AND DM BEFORE AND AFTER TREATMENT

Indicator	Groups of patients					
	1st group (n=29)			*2nd group (n=31)*		
	Before treatment	*After 4 weeks*	*Wilcoxon Test (Z, p)*	*Before treatment*	*After 4 weeks*	*Wilcoxon Test (Z, p)*
Sialic acid, mmol/l, M ± m	83.43±0.89	76.64±1.89	Z=3.29, p=0.0009	83.23±0.85	72.31±1.92°	Z=3.18, p=0.001
Seromucoid, Units M ± m	82.32±1.13	62.71±1.26	Z=3.18, p=0.001	83.22±0.97	60.32±1.32	Z=3.075, p=0.0021
CRP, Me , M ± m	17.66±2.43	5.03±1.28	Z=2.67, p=0.007	17.54±2.58	3.55±1.37°	Z=2.93, p=0.0033

Note: * Calculated value of statistical criterion
** the level of statistical significance
° - significant difference from group 1.

While analyzing the electrolite balance before and after treatment, we noted statistically significant changes of all indicators in both groups, namely, an increase of serum phosphorus (by 18% in the first group, by 21% in the second group), an elevation of ionized calcium (by 16% in the first group, by 17% in the second group) and normalization of magnesium level (by 19% in the first group, by 18% in the second group). At the same time, the studied indexes didn't significantly differ between the groups of patients.

Phototherapy was well tolerated. We didn`t note any side effects or allergic reactions. Regarding the degree of compensation of carbohydrate metabolism, all patients remained at a compensated state of diabetes.

Thus, the use of Korobov's photon matrices as the part of the complex treatment of patients with DM and OA is a highly effective, completely safe method that can help to reduce the terms of treatment.

IV. CONCLUSIONS

The use of photon matrices in the complex treatment of patients with DM and muskuloskeletal disorders has led to significant improvement of the functional state of joints, decrease of pain intensity and lowering of inflammatory markers in blood.

The indexes of electrolite balance didn't differ significantly between the studied groups.

Phototherapy is a safe and effective method of treatment because of its good tolerability, absence of side effects and a positive impact on the course of diabetes.

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