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CORRECTION OF CLINICAL AND BIOCHEMICAL PARAMETERS USING BEE POLLEN IN PATIENTS WITH DIABETES

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Abstract. We have studied the effect of course taking bee pollen (BP) in patients with insulin-independent diabetes mellitus (IIDM). We have proven the efficacy and safety of BP in treatment of secondary manifestations of insulin-independent diabetes, a positive effect on some important links of pathogenesis of IIDM development (oxidant and antioxidant systems, lipid metabolism).

Key words: diabetes mellitus, bee pollen, oxidant and antioxidant systems.

Резюме. Вивчено вплив курсового прийому пилку квіткового (ПК) у хворих на інсулін-незалежний цукровий діабет (ІНЦД). Доведена ефективність і безпечність ПК в лікуванні вторинних проявів інсулін-незалежного цукрового діабету, позитивний вплив на окремі важливі ланки патогенезу розвитку ІНЦД (оксидантну, антиоксидантну системи, ліпідний обмін).

Ключові слова: цукровий діабет, пилок квітковий, оксидантна, антиоксидантна системи.

Introduction. Diabetes mellitus (DM) is a chronic endocrine-metabolic disease caused by a relative deficiency of insulin due to the combined effect of different endogenous (genetic) and exogenous factors that lead to the disorders in all types of metabolism, to a damage of vessels, nerves, different organs and tissues. A specific everpresent manifestation of the disease is a disorder in carbohydrate metabolism with progressive increase of blood glucose and its excretion with urine.

The incidence is higher among the elderly. According to the forecast of US experts in case of an increase in life expectancy to 80 years the number of diabetic patients in the USA will be more than 17% of the population. Ukraine's population is also steadily aging. Gerontologists believe that in 25 years, almost every 3rd citizen of the country will be over 60 years old. Considering the socio-economic and ecological situation in Ukraine, the likelihood of unexpected growth of diabetes, especially of type 2, is very high. The highest incidence rate is observed among obese people. For instance, in moderately obese people the incidence of diabetes increased by 4 times, in those with sharply pronounced obesity by 30 times. Thus, obesity and advanced age are among the main risk factors that cause a predisposition to diabetes [1, P.269-270; 2, p.111; 3, p.15-25].

The increase of morbidity, serious consequences of disability, especially among the working-age population contingent, high mortality made diabetes one of the three diseases that are the most common causes of morbidity and mortality among people (atherosclerosis, cancer, diabetes actually). The World Health Organization states that diabetes leads to increased mortality by 2-3 times and reduces life expectancy by 10-30% [4, p.22-32].

Fighting diabetes is attributed to medical and social problems. This disease is a heavy burden for health care, with 80% of the costs for examination and treatment of diabetes accounts for patients with complications. Therefore, many countries developed special national programs on diabetes.

Bee pollen (BP), according to the research, as an antioxidant, lipotropic agent, hepatoprotector, hastraprotector and immunomodulator can be used in primary and secondary prevention of secondary manifestations of diabetes [5, p. 10-15; 6, p. 8-12; 7, 191].

Objective: to study the effect of BP on clinical laboratory and organ functional and morphological manifestations of diabetes.

Materials and methods: The study involved 50 patients with insulin-independent diabetes mellitus (IIDM) with concomitant chronic cholecystitis, among them - 40% of men and 60% of women aged 44 to 76 years. Disease duration since diagnosing IIDM was from 4 to 15 years. 20% of patients suffered from a mild form of the disease, the rest of them had moderately severe form (WHO classification of 1985). Compensation of carbohydrate metabolism was found in 26% of patients subcompensation in 64%, decompensation in 10% of patients. All the patients, regardless of their age were diagnosed with coronary heart disease (CHD), of whom 60% of patients with exertional angina of functional class (FC) I (10%), FC II (28%), FC III (32%). The rest of the patients suffered from atherosclerosis of the aorta and coronary arteries as well as from atherosclerotic cardiosclerosis.

Results and discussion:

40% of patients had signs of fatty liver with minor, sometimes moderately impaired liver function. In 58% of cases there were symptoms of visceral and peripheral neuropathies, particularly in the form of impaired gastric and intestinal motility and diabetic neuropathic gallbladder.

All patients were examined for a complex of biochemical parameters (including blood glucose levels, blood cholesterol and triglycerides, liver function tests), blood count, immunogram, ionogram, the state of lipid peroxidation (LPO) and glutathione system, electrocardiography, ultrasound examination of the abdomen, in case of clinical manifestations of the cardiac lesion they underwent echocardiography.

The patients were administered a standard dietotherapy (1800 kcal / day). Hypoglycemic therapy suggested maninil intake in doses corresponding to glycemia. In addition, the patients were treated with necessary pathogenetic therapy (nitropreparations, antirhythmic and anti-anxiety drugs).

BP was administered to 30 patients against the background of basic therapy at a dose of 250 mg / kg of body weight twice a day in the form of an aqueous suspension in 100 ml of warm boiled water 20-30 minutes before meals. The course of treatment lasted 21-28 days.

The control group consisted of 20 patients with IIDM suffering from coronary heart disease who were representative by age, gender and clinical features, fatty liver disease, visceral, and peripheral neuropathy. The patients in the control group only received the basic therapy.

In order to avoid possible negative effect of BP like a significant

increase in blood glucose levels in diabetic patients, we studied the glycemia level in 20 patients two hours after taking a daily dose of pollen at one time before the beginning of the course of treatment. We found out that even a double dose of therapeutic BP does not cause a significant increase of glycemia compared with its level on an empty stomach. One hour after the intake of BP blood glucose rate grew by 5.6% from the baseline, and after 2 hours it reduced to a level of only 3.74% higher than the initial one. In the study of two-hour glycemia on an empty stomach we found: by the end of the first hour glucose rise by 3.3% above the initial level with a decrease by the end of the second hour by 5% below the baseline.

Against the background of a standard breakfast glycemic curve was qualitatively and quantitatively different. Therefore, the use of BP in diabetic patients is safe and does not require increasing doses of hypoglycaemic drugs (Fig.).

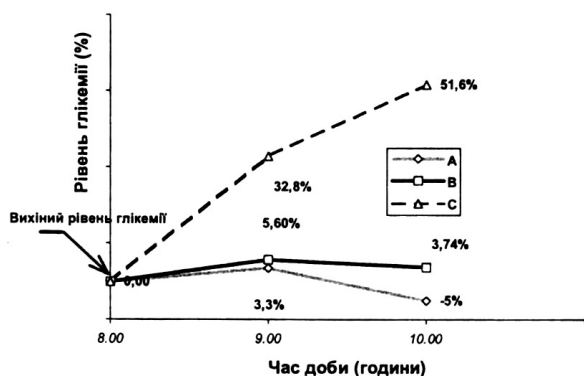


Fig. Effect of one time intake of double BP dose on the level glycemia (duration of observation was 2 hours):

- A - fasting glucose levels for 2 hours of observation;
- B - glucose level after BP intake (at 8.00 am);
- C - blood glucose level during two hours after having a standard breakfast in IIDM patients in a state of a very good compensation

All the patients felt less thirst in the course of taking BP (the amount of fluids decreased by 40%) with a corresponding decrease in urine output. They had a feeling of satisfaction with meal and it eliminated the need for its frequent taking (and therefore helped reduce the volume and calorie content of daily meals). 80% of patients experienced a significantly decreased or disappeared feeling of heaviness in the right upper quadrant within two weeks. Patients with coronary artery disease felt a reduction in the frequency of attacks of heart pain and heart palpitations during exercise 5-6 days earlier than patients in the control group. We could observe the weakening effects of paresthesia and seizures in the muscles of the lower extremities, a pronounced shift of paresthesia upper border as early as on the second week of the course of treatment in 60% of patients, while patients in the control group needed vitamins and lipoic acid to achieve this result.

All the patients of the main group noted the improvement in health, efficiency and sense of vitality well before and more than patients in the control group. Patients who used BP even after the first year noted a significant decrease in the frequency of respiratory diseases, especially in autumn and winter, reducing the duration and severity in the event of their occurrence. Half of the patients could reduce the dose of hypoglycaemic drugs by 1/2-2/3 without worsening glycaemia laboratory values and clinical course of IIDM.

According to one of the patients (diabetic doctor with long experience of the disease who was treated with pollen) when taking BP she

felt healthier, more active, quality parameters of her life increased too.

However, in addition to the clinical results, there were positive changes in the findings of laboratory and instrumental studies. For instance, the level of blood glucose after a course of BP declined on average by 22.3% compared with the figures before treatment, allowing some patients to reduce the dose of maninil. The level of blood cholesterol in patients of the main group decreased significantly from $5,77 \pm 0,12$ mmol / l to $4,94 \pm 0,14$ mmol / L ($p < 0.05$), while this value remained virtually unchanged in the patients in the control group. In 50% of patients the blood triglycerides level decreased. All patients showed a clear tendency to increase blood and hemoglobin potassium levels while their previous rates were lowered.

Increased resistance of the body was confirmed by immunogram indicators: the number of T cells increased from 39.52 to 41.33, including active ones from 20.61 to 22.31. The number of B-lymphocytes decreased from 32.40 to 28.31, the index of T-helper / T-suppressor - from 2.06 to 1.86. The level of immunoglobulin G decreased on the average from 160,9h / l to 123.0 g / l. The circulating immune complexes were subjected to BP the most, their number decreased on the average from 17,417.5 units to 13,010.4 units as well as the complement titer, which decreased from 0,056 to 0,038.

Activation of peroxidation processes and reduction of antioxidant systems functional capacity in patients with IIDM were confirmed by our study. All the patients initially showed a significant increase in lipid peroxidation products (diene conjugates, isolated double bonds, ketodiens and conjugated triens) and decreased activity of glutathione system compared to those without diabetes. During the course of treatment with a complex containing BP the level of isolated double bonds decreased from $5,38 \pm 0,38$ E220 / 1 mL of blood to $3,38 \pm 0,30$ E220 / 1 ml, diene conjugates from $2,97 \pm 0,31$ E220 / 1 mL of blood to $2,31 \pm 0,34$ E220 / 1 mL of blood, ketodiens and conjugated triens - from $1,47 \pm 0,145$ E220 / 1 mL of blood to $0,87 \pm 0,045$ E220 / 1 mL of blood. The level of reduced glutathione in patients of the group increased by 40% and the activity of glutathione reductase and glutathione-S-transferase decreased by 25.4% and 24.2% respectively. So, BP enhances the activity of antioxidant (glutathione system in particular) and causes inhibition of LPO, and consequently affecting one of the fundamental pathogenesis of IIDM secondary manifestations.

Improving cardiovascular system in patients was confirmed by positive dynamics of ECG, which manifested itself by fewer signs of myocardial ischemia in 2/3 of patients.

Studying the gallbladder motility by means of dynamic echocholangiography within one hour after administration of a double therapeutic dose of BP showed that 85% of patients had a «diabetic neuropathic gallbladder» (atony, increased size, susceptibility to hypokinesia). BP cholekinetic effect, which was observed in patients without evidence of diabetes, was not found in the patients with this disease or was insignificant and short-lived.

Repeated ultrasound of the gallbladder and liver after the first course of treatment did not show any significant changes in the ultrasound image, however, the patients who received two or three treatments with bee pollen, showed a trend to improve the echostructure, to reduce its size, signs of fatty infiltration, reducing the gallbladder volume, wall thickening, its more active reaction to the introduction of choleretic drugs was noticed as well.

Since the start of using BP there have not been any allergic reactions due to the intake of pollen in the patients with IIDM. There was one case, when the patient stopped taking pollen because of starting dyspepsia events (nausea, diarrhea), which she associated with the beginning of the BP use. Most of the patients generally tolerated the treatment very well and subsequently expressed a desire to continue receiving BP.

Conclusions.

1. Clinical testing of BP showed that it is a quite effective and safe natural remedy in the treatment and prevention of secondary manifestations of IIDM.
2. BP has a positive effect on some important links of pathogenesis of IIDM (oxidant and antioxidant systems, lipid metabolism, immune system) and improves the quality of life.

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DISORDERS OF RENAL FUNCTION IN IMMATURE RATS WITH INBLIMATE NEPHROPATHY AT LOADING BY 3% SODIUM CHLORIDE SOLUTION UNDER CONDITIONS OF RENAL PROSTAGLANDINS BLOCKADE WITH INDOMETHACIN

НАРУШЕНИЕ ФУНКЦИИ ПОЧЕК В НЕПОЛОВОЗРЕЛЫХ КРЫС ПРИ СУЛЕМОВОЙ НЕФРОПАТИИ С НАГРУЗКОЙ 3% РАСТВОРОМ ХЛОРИДА НАТРИЯ В УСЛОВИЯХ БЛОКАДЫ ПОЧЕЧНЫХ ПРОСТАГЛАДИНОВ ИНДОМЕТАЦИНОМ

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Abstract. Experiments on 40 white non-linear immature male rats evaluated indices of renal function with sublimite nephropathy at loading by 3% sodium chloride solution in volume of 5% of the body weight under conditions of blockade of renal prostaglandins production with indomethacin and had shown inhibition of diuresis, decrease of sign of the syndrome of sodium ions loss.

Key words: sublimite nephropathy, sodium chloride, indomethacin, immature rats.

В опытах на 40 белых нелинейных неполовозрелых (1 месячных) крысах самцах оценка показателей функции почек при сулемовой нефропатии с нагрузкой 3% раствором хлорида натрия в объеме 5% от массы тела в условиях блокады продукции почечных простагландинов индометацином показала снижение диуреза, уменьшение степени синдрома потери ионов натрия с мочой на фоне гипернатриемии. Расстройства клубочково-канальцевого баланса характеризовались потерей положительных корреляционных связей относительной реабсорбции воды с клубочковой фильтрацией, фильтрационной фракцией и абсолютной реабсорбцией ионов натрия.

Известно, что при нагрузке 3% раствором хлорида натрия при сулемовой нефропатии у половозрелых крысах развивается полиурическая форма острой почечной недостаточности, что вызывает максимальную мобилизацию компенсационных возможностей простагландина E2 как вазодиллятора приносящей артериолы почек. Блокада почечных простагландинов индометацином за данных условиях приводит к спазму сосудов почек и развитию олигурии.

Установленные изменения клубочково-канальцевого баланса у половозрелых крысах с сулемовой нефропатией при нагрузке 3% раствором хлорид натрия на фоне введения индометацина ведёт к блокаде продукции почечных простагландинов. Сравнительная оценка клубочково-канальцевого баланса в половозрелых и неполовозрелых крыс с сулемовой нефропатией при нагрузке 3% раствором хлорида натрия в объеме 5% от массы тела в условиях блокады продукции почечных простагландинов индометацином обнаружила более существенные расстройства в половозрелых крыс с сохранением положительной корреляционной связи клубочковой фильтрации с абсолютной реабсорбцией ионов. Увеличенные показатели относительной реабсорбции воды у неполовозрелых крыс в отношении половозрелых животных обусловлен недостаточным уровнем зрелости натрийуретических механизмов у животных младшей возрастной группы.

Ключевые слова: сулемовая нефропатия, нагрузка 3% раствором хлорида натрия, индометацин, неполовозрелые крысы, клубочково-канальцевый баланс, простагландины, гипернатриемия.