

DOI: 10.21802/artm.2019.1.9.44

UDC 616-61-02:616.379-008.64:616.12-008.331.1:577.175.532

NEPHROPATHIC CHARACTERISTICS IN PATIENTS WITH DIABETES MELLITUS TYPE 2 AND ESSENTIAL HYPERTENSIVE DISEASE

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Abstract. In diabetes mellitus type 2 combined with essential hypertensive disease, the risk of kidney failure increases by 15-20 times. Diabetic nephropathy is the most common cause of kidney failure - about 34% of all cases. So important is early diagnosis and regular monitoring of renal function in patients with diabetes mellitus type 2 and essential hypertensive disease.

Aim. To study nephropathic characteristics in patients with diabetes mellitus type 2 (DM2) combined with essential hypertensive disease (EHD) on the basis of blood pressure, glucose metabolism and lipid levels.

Materials and methods. 75 patients were examined: 25 patients with essential hypertensive disease degree 1-2, stage II, treatment-compensated (Group I), and 25 patients with subcompensated diabetes mellitus type 2 [glycated hemoglobin (HbA_{1C}) - from 7.0% to 11.0%] (Group II) and 25 patients with subcompensated diabetes mellitus type 2 [glycated hemoglobin (HbA_{1C}) - from 7.0% to 11.0%] combined with essential hypertensive disease (Group III). Among the patients surveyed, there were 40 females and 35 males, the average age was (59.8 ± 5.3) years. The control group consisted of 20 healthy volunteers. Groups surveyed were randomized in age, sex, body mass index, duration of diabetes mellitus type 2 and essential hypertensive disease. Determination of glucose metabolism based on the assessment of glycated hemoglobin (HbA_{1C}), blood lipid profile tests, renal function tests etc were carried out. The decrease in GFR from 89 to 60 mL / min. / 1.73 m² was regarded as mild kidney failure or dysfunction, from 59 to 30 ml / min. / 1.73 m² as moderate and from 29 to 15 ml / min. / 1.73 m² as severe; for 3 months or more with or without the presence of features of nephropathy that meet the definition of chronic kidney disease (CKD).

Results. In patients with DM2 combined with EHD, there is a severe impairment of kidney function with increasing microalbuminuria (MAU) and a decrease in glomerular filtration rate (GFR). Correlations between increased microalbuminuria, reduced GFR, systolic blood pressure (SBP), HbA_{1C}, total cholesterol (TC), triglycerides (TG) and low density lipoprotein (LDL) indicate the multifactorial process of kidney damage in patients with DM2 combined with EHD and a high risk of cardiovascular diseases.

Conclusion. To study nephropathic characteristics in patients with DM2 combined with EHD, it is necessary to constantly monitor MAU, GFR together with blood pressure, HbA_{1C} and blood lipid profile.

Keywords: nephropathy, subcompensated, glycated hemoglobin, glomerular filtration rate, microalbuminuria.

Introduction. Diabetes mellitus type 2 is a multicomponent disease and in most cases, it is accompanied by dyslipidemia, which is a risk factor for cardiovascular disease. Diabetes is now ranked third in the overall morbidity and mortality after cardiovascular disease and cancer. According to the World Health Organization, its estimated prevalence in 2025 will increase to 300 million patients (1, 7, 12). Prevalence of essential hypertensive disease in patients with diabetes mellitus type 2 is 2-3 times higher than in the general population, and increased blood pressure in 70% of patients with diabetes mellitus type 2, significantly increases the risk of cardiovascular complications which worsen the prognosis and quality of life of patients and are the main causes of mortality. The combination of diabetes mellitus type 2 with essential hypertensive disease is accompanied by a significant increase in the risk of complications such as stroke, coronary artery disease (CAD), congestive heart failure, atherosclerosis. However, in the presence of diabetes mellitus type 2 occur the following risk factors for cardiovascular complications such as central obesity, dyslipidemia, microalbuminuria, disturbance of coagulation properties

of blood, signs of systemic inflammation (4-6, 10, 13). In diabetes mellitus type 2 combined with essential hypertensive disease, the risk of kidney failure increases by 15-20 times (2, 3, 8). Diabetic nephropathy - the most common cause of kidney failure – in about 34% of cases (1, 9, 12, 14). So, very important is early diagnosis and regular monitoring of renal function in patients with diabetes mellitus type 2 and essential hypertensive disease.

Aim. To study nephropathic characteristics in patients with diabetes mellitus type 2 and essential hypertensive disease on the background of blood pressure, glucose metabolism and blood lipid levels.

Materials and methods. The study involved 75 patients made up of 25 patients with essential hypertensive disease, degree 1-2, stage II, treatment-compensated (Group I), 25 patients with subcompensated diabetes mellitus type 2 [glycated hemoglobin (HbA_{1C}) - from 7.0% to 11.0%] (Group II) and 25 patients with subcompensated diabetes mellitus type 2 [glycated hemoglobin (HbA_{1C}) - from 7.0% to 11.0%] and essential hypertensive disease (Group III). Among the patients studied, there were 40 females and 35 males, the average

age was (59.8 ± 5.3) years. The control group consisted of 20 healthy volunteers. Groups surveyed were randomized in age, sex, body mass index, duration of diabetes mellitus type 2 and essential hypertensive disease. Verification of diagnoses was carried out under orders of the MOH Ukraine № 384 dated 24.05.2012 and № 1118 of 21.12.2012 respectively and with consultative conclusions of cardiologists and endocrinologists.

In all patients, general clinical examinations were performed; systolic blood pressure (SBP) and diastolic blood pressure (DBP) were monitored. Features of glucose metabolism were assessed by levels of fasting glucose, postprandial glucose method and measurement of HbA_{1c}; blood lipid levels - by total cholesterol (TC), triglycerides (TG), low density lipoprotein (LDL) and high density lipoprotein (HDL). The level of microalbuminuria (MAU) was determined using rapid test strips (PentaPhan, «LaChem»). Glomerular filtration rate (GFR) was calculated using the formula MDRD (Modification of Diet in Renal Disease). The decrease in GFR from 89 to 60 mL / min. / 1.73 m² was regarded as mild kidney failure or dysfunction, from 59 to 30 ml / min. / 1.73 m² as moderate and from 29 to 15 ml / min. / 1.73 m² as severe; for 3 months or more with or without the presence of features of nephropathy that meet the definition of chronic kidney disease (CKD) (1, 12).

Clinical and laboratory tests were carried out in accordance with the recommendations of manufacturers

of diagnostic test systems using modern laboratory technologies and under ethical principles of the Helsinki Declaration.

Statistical analyses of the results of research were carried out by a computer program Microsoft Excel using the methods of variation statistics, Student t-test series and such computer program as "Statistica 7.0 for Windows". Evaluation of statistical significance/difference was determined by the method of χ^2 . For clarification of the correlations between a pair of individual indices, a correlation analysis was performed with calculation of Pearson's correlation coefficient (r) and probability of error (p).

Results and discussion. Analyses of the results of the study revealed that changes in the kidney were observed in patients of all groups surveyed and by the results of laboratory tests, these changes were more pronounced in Group III patients (subcompensated diabetes mellitus type 2 combined with essential hypertensive disease). In particular, MAU was observed in 20.0 % of Group I patients, in 52.0% of Group II patients and in 72.0% of Group III patients. The average level of albumin excretion in urine (MAU) in Group III patients was greater when compared with healthy volunteers by 87.54% (p <0.05), in Group I patients by 66.09% (p <0.05) and in Group II patients by 31.04% (p <0.05) (Table 1).

Table 1

Clinical and laboratory indices in patients with diabetes mellitus type 2 and essential hypertensive disease, M±m

Indices	Healthy volunteers, n=20	Group I patients, n=25	Group II patients, n=25	Group III patients, n=25
Fasting glucose (mmol/L)	4.26 ± 0.18	4.69 ± 0.25•	8.33 ± 0.36*•	9.27 ± 0.56*
HbA _{1c} (%)	4.62 ± 0.25	4.78 ± 0.30•	7.74 ± 0.38*•	8.83 ± 0.40*
SBP (mmHg)	122.4 ± 4.3	143.5 ± 5.9	132.2 ± 5.0*•	148.8 ± 7.1*
DBP (mmHg)	77.5 ± 4.6	88.4 ± 5.6	82.5 ± 5.2•	92.7 ± 6.3
Microalbuminuria (mg/L)	7.9 ± 1.2	14.52 ± 1.03*•	22.72 ± 1.90*•	29.40 ± 2.16*
Proteinuria (g/L)	-	-	0.28 ± 0.02	0.55 ± 0.04
GFR (ml/min/1.73m ²)	108.7 ± 5.8	94.1 ± 5.3*•	78.4 ± 4.7*	67.7 ± 3.5*
Urea (mmol/L)	5.53 ± 0.37	6.64 ± 0.46•	7.78 ± 0.52*•	9.15 ± 0.60*
Creatinine (mmol/L)	80.4 ± 5.6	107.3 ± 6.2*•	130.4 ± 7.5*	146.8 ± 8.2*
Total cholesterol (mmol/L)	4.42 ± 0.22	5.52 ± 0.27*•	6.19 ± 0.31*•	6.89 ± 0.35*
HDL (mmol/L)	1.65 ± 0.13	1.35 ± 0.12*•	1.22 ± 0.10*	1.13 ± 0.08*
LDL (mmol/L)	2.13 ± 0.15	2.68 ± 0.20*•	3.15 ± 0.23*	3.59 ± 0.25*
Triglycerides (mmol/L)	1.38 ± 0.10	1.82 ± 0.15*•	2.20 ± 0.18*	2.47 ± 0.21*

Notes: n - the number of patients in a group; * - Probability of error in comparison with healthy group, p <0.05; • - the correlation coefficient in comparison with Group III, p <0.05

Microalbuminuria level of 50 mg / ml was observed in Group I patients - 4.0% of cases, in Group II patients - 32.0% of cases and in Group III patients - 48.0% of cases (p <0.05). It is known that the presence of MAU above 50 mg / ml per day significantly increases the risk of cardiovascular complications (11, 12). In addition, 16.0% of Group II patients and 28.0% of Group III patients revealed slightly significant proteinuria - up to 0.66 g / l.

Most reduced GFR was in Group III patients (67.7 ± 4.8) ml/min, which was lower when compared with healthy at 37.72% (p <0.05), in Group I patients – by

28.06% (p <0.05) and in Group II patients – by 48.00% (p <0.05).

In diabetes mellitus type 2 patients combined with essential hypertensive disease (Group III), the correlation coefficient between indices of systolic blood pressure, SBP and MAU was - (r = +0.38; p <0.05), between SBP and GFR - (r = -0.45; p <0.05).

The HbA_{1c} level as an indicator of the course of diabetes in Group III patients was (8.83 ± 0.40)%, and exceeded the figure for the healthy by 47.68% (p <0.05), in Group I – by 45.87% (p <0.05) and in Group II - by 12.34% (p <0.05), indicating a more pronounced disturbance of glucose metabolism in subcompensated diabetes

mellitus type 2 combined with essential hypertensive disease. In Group III patients, we found correlation coefficient between HbA_{1c} and SBP - ($r = +0.56$; $p < 0.05$), between HbA_{1c} and MAU - ($r = +0.68$; $p < 0.05$) and between HbA_{1c} and GFR - ($r = -0.63$; $p < 0.05$), indicating a relationship between nephropathy and glucose metabolism in subcompensated diabetes mellitus type 2 combined with essential hypertensive disease.

Accordingly, the study showed an orientation towards atherogenic lipid spectrum in the blood of patients. In particular, in Group III patients total cholesterol increased by (6.89 ± 0.35) mmol / L ($p < 0.05$) when compared with healthy volunteers and exceeded that of Group I patients by 19.88% ($p < 0.05$) and that of Group II patients by 10.16% ($p < 0.05$). TG in Group III patients was (2.47 ± 0.21) mmol / L ($p < 0.05$) when compared with healthy volunteers and exceeded that of Group I by 26.32% ($p < 0.05$) and Group II by 10.93% ($p < 0.05$). LDL in Group III patients was (3.59 ± 0.25) mmol / L ($p < 0.05$) when compared with healthy and exceeded that of Group I by 25.35% ($p < 0.05$) and Group II by 12.26% ($p < 0.05$). Antiatherogenic HDL was reduced in Group III and was (1.13 ± 0.08) mmol / L ($p < 0.05$) when compared with healthy and was lower than that of Group I by 16.30% ($p < 0.05$) and Group II by 7.38% ($p < 0.05$). More pronounced dyslipidemia in Group III patients may be an associated additional risk factor in the defect of vascular wall.

As a result of studying the correlation relationships between HbA_{1c} levels and lipid profile indices, the following correlations were found: between HbA_{1c} levels and total cholesterol exists a direct correlation of medium strength ($r = +0.48$; $p < 0.05$); between HbA_{1c} levels and triglycerides - ($r = +0.45$; $p < 0.05$); between HbA_{1c} level and LDL - ($r = +0.41$; $p < 0.05$) and between HbA_{1c} levels and HDL levels was the presence of inverse correlation of medium strength ($r = -0.58$; $p < 0.05$), indicating the influence of decompensation of diabetes mellitus type 2 on the severity of dyslipidemia.

The correlation coefficient (r) between SBP and TC - ($r = +0.41$; $p < 0.05$), between SBP and MAU - ($r = +0.32$; $p < 0.05$), between SBP and GFR - ($r = -0.35$; $p < 0.05$); between LDL and SBP - ($r = +0.49$; $p < 0.05$), between LDL and MAU - ($r = +0.41$; $p < 0.05$), between LDL and GFR - ($r = -0.38$; $p < 0.05$); between TG and SBP - ($r = +0.52$; $p < 0.05$), between TG and MAU - ($r = +0.45$; $p < 0.05$), between TG and GFR - ($r = -0.40$; $p < 0.05$), indicating the influence of lipid metabolism not only on the clinical course of diabetes mellitus type 2 and essential hypertensive disease, but also on renal function.

Conclusions:

1. In patients with diabetes mellitus type 2 and essential hypertensive disease, there is a severe impairment of kidney function with increased MAU and decreased GFR.

2. Identified correlations between increased MAU, SBP, HbA_{1c}, lipid profile indices and decreased GFR indicate the multifactorial process of nephropathy in patients with diabetes mellitus type 2 and essential hypertensive disease, and a higher risk of cardiovascular disease.

3. In order to determine renal function state in patients with diabetes mellitus type 2 and essential

hypertensive disease, it is necessary to constantly monitor MAU, GFR, along with SBP, HbA_{1c} and blood lipid profile.

Prospects for further research. Further scientific research is advisable to be carried out in search of effective treatment regimens to prevent nephropathy in patients with diabetes mellitus type 2 and essential hypertensive disease.

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УДК 616-61-02:616.379-008.64:616.12-008.331.1:577.175.532

ПОКАЗНИКИ УРАЖЕННЯ НИРОК У ХВОРИХ НА ЦУКРОВИЙ ДІАБЕТ 2-ГО ТИПУ У ПОЄДНАННІ З ЕСЕНЦІАЛЬНОЮ АРТЕРІАЛЬНОЮ ГІПЕРТЕНЗІЄЮ

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Резюме. Актуальність проблеми. При цукровому діабеті (ЦД) 2 типу у поєднанні з артеріальною гіпертензією (АГ) ризик розвитку ниркової недостатності збільшується в 15-20 разів; діабетична нефропатія є найбільш частою причиною ниркової недостатності – біля 34% усіх випадків. Тому важливо є рання діагностика та постійний моніторинг функції нирок у хворих на ЦД 2 типу та АГ.

Мета дослідження. Вивчення показників ураження нирок у хворих на ЦД 2 типу у поєднанні з есенціальною АГ у взаємозв'язку з показниками артеріального тиску, вуглеводного обміну та ліпідного профілю крові.

Матеріали та методи дослідження. Було обстежено 75 пацієнтів, серед яких 25 хворих на медикаментозно компенсовану АГ II стадії, 25 хворих на субкомпенсований ЦД 2 типу і 25 хворих на субкомпенсований ЦД 2 типу в поєднанні з АГ. Проведено визначення показників вуглеводного обміну з оцінкою рівня глікованого гемоглобіну (HbA_{1c}), ліпідного профілю крові, функціонального стану нирок.

Результати. Встановлено, що у хворих на ЦД 2 типу за наявності АГ є більш вираженим порушення функціонального стану нирок зі збільшенням мікроальбумінурії (МАУ) і зменшенням швидкості клубочкової фільтрації (ШКФ). Виявлені кореляції між збільшенням мікроальбумінурії і зменшенням ШКФ та величиною систолічного артеріального тиску (АТ), рівнем HbA_{1c}, вмістом холестерину, тригліцеридів, ліпопротеїдів низької щільності, які вказують на багатфакторний процес ураження нирок у хворих на ЦД 2 типу за наявності есенціальної АГ і високий ризик серцево-судинних захворювань.

Висновки. Із метою моніторингу стану нирок у хворих на ЦД 2 типу за наявності АГ необхідно постійно контролювати МАУ і ШКФ разом із оцінкою показників АТ, рівня HbA_{1c}, ліпідного спектру крові.

Ключові слова: нефропатія, субкомпенсований, глікований гемоглобін, швидкість клубочкової фільтрації, мікроальбумінурія.

УДК 616-61-02:616.379-008.64:616.12-008.331.1:577.175.532

ПОКАЗАТЕЛИ ПОРАЖЕННЯ ПОЧЕК У БОЛЬНЫХ САХАРНЫМ ДИАБЕТОМ 2-ГО ТИПА В СОЧЕТАНИИ С ЭСSENЦИАЛЬНОЙ АРТЕРИАЛЬНОЙ ГИПЕРТЕНЗИЕЙ

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Резюме. Актуальность проблемы. При сахарном диабете (СД) 2 типа в сочетании с артериальной гипертензией (АГ) риск развития почечной недостаточности увеличивается в 15-20 раз; диабетическая нефропатия является наиболее частой причиной почечной недостаточности – около 34% всех случаев. Поэтому важным является ранняя диагностика и постоянный мониторинг функции почек у больных СД 2 типа и АГ.

Цель исследования. Изучение показателей поражения почек у больных СД 2 типа при сочетании с эссенциальной АГ во взаимосвязи с показателями артериального давления, углеводного обмена и липидного профиля крови.

Материалы и методы исследования. Было обследовано 75 пациентов, среди которых 25 больных лекарственно компенсированной АГ II стадии, 25 больных субкомпенсированным СД 2 типа и 25 больных субкомпенсированным СД 2 типа в сочетании с АГ. Проведено определение показателей углеводного обмена с оценкой уровня гликированного гемоглобина (HbA_{1c}), липидного профиля крови, функционального состояния почек.

Результаты. Установлено, что у больных СД 2 типа при наличии АГ является более выраженным нарушение функционального состояния почек с увеличением микроальбуминурии (МАУ) и уменьшением скорости клубочковой фильтрации (СКФ). Обнаруженные корреляции между увеличением микроальбуминурии и уменьшением СКФ и величиной систолического артериального давления (АД), уровнем HbA_{1c}, содержанием холестерина, триглицеридов, липопротеидов низкой плотности, которые указывают на многофакторный процесс поражения почек у больных СД 2 типа при наличии эссенциальной АГ и высокий риск сердечно-сосудистых заболеваний.

Выводы. С целью мониторинга состояния почек у больных СД 2 типа при наличии АГ необходимо постоянно контролировать МАУ и СКФ вместе с оценкой показателей АД, уровня HbA_{1c}, липидного спектра крови.

Ключевые слова: нефропатия, субкомпенсированный, гликированный гемоглобин, скорость клубочковой фильтрации, микроальбуминурия.

Стаття надійшла в редакцію 05.11.2018 р.