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Importance Of Daily Monitoring Of Blood Pressure In Diabetic Nephropathy In Patients With Diabetes Mellitus Type 2 With Arterial Hypertension

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Abstract: The paper studies the peculiarities of vascular wall elasticity disorders and microcirculatory disorders in patients with AH and types 2 DM with different degrees of severity of DN. Elastic properties, structural and functional state of the heart, functional state of the kidneys in correlation with the indices of DMBP, EchoKG, BFS in the patients with AH and DM 2 type DN were assessed. The importance of early study of macro- and microhemodynamic parameters in this category of patients is shown, as DN is associated with the maximum risk of cardiovascular complications. In the survey, we studied blood pressure indicators according to the daily monitoring data (DMBP) in patients with diabetes mellitus type 2, depending on the severity of DN. Thus, the DMBP method allows timely detection of labile forms of AH in patients with type 2 diabetes, especially in the initial stages of kidney damage. It is expedient to include DMBP in the algorithm of examination of patients with diabetes mellitus type 2 with beginning nephropathy, for the earliest possible detection of AH and prevention of vascular complications progression.

Keywords: diabetes mellitus, diabetic nephropathy, microalbuminuria, daily monitoring, ball filtering speed, lipid spectrum, glycemic profile,

Introduction

Diabetes mellitus (DM) is one of the most critical and complex problems of modern medicine, which is caused by its widespread, clinical polymorphism and severity of complications [1, 12]. With the increase in the life expectancy of diabetic patients, a new problem has arisen related to vascular complications of DM [2,4,13].

One of the most dangerous vascular complications is diabetic nephropathy (DN). The cunning of this complication is that developing quite slowly; diabetic kidney damage remains unnoticed for a long time because at the initial stages of DN runs asymptomatically [2, 4, 19].

Kidney damage leads to the activation of the renin-angiotensin-aldosterone system (RAAS) and, as a consequence, the development of arterial hypertension (AH). Among patients with diabetes mellitus 2, the frequency of AH exceeds the general population and reaches 10-30% [5, 11,18]. The appearance of AH in patients with diabetes mellitus two may indicate the development of diabetes mellitus; an increase in the frequency of hypertension is observed as the severity of renal damage increases, mainly at the proteinuria (PU) stage [2, 3, 6, 14]. On the other hand, the development of AH itself is a factor contributing to the progression of renal damage [9, 15, 16]. There is evidence that blood pressure (BP) in diabetes mellitus two may increase even before the development of obvious DN, at the stage of microalbuminuria (MAU) and also in normal excretion of albumin with urine (NAU) [2, 3, 8, 10]. Insufficient study and inconsistency of data on early changes in blood pressure and their relationship to renal conditions in patients with diabetes mellitus 2 make the problem relevant at the present stage [14, 17, 20].

The purpose of our study was to study the blood pressure values according to the daily monitoring data (DMBP) in patients with diabetes mellitus 2, depending on the severity of the DM.

MATERIALS AND METHODS

The research included 100 patients from 38 to 65 years of age, of whom 56 were men and 44 were women, with an average age of 62.9 ±5.3 years. The 1st group - the main group (n=60) was represented by the patients of stage II-III AH and type 2 diabetes mellitus (36 men, 24 women, mean age - 61.9 ± 6.2 years). Of these, 20

people were a group of patients with AH and DM without diabetic nephropathy, 20 people were patients with AH and typed 2 diabetic nephropathies, and 20 people were patients with stage II diabetic nephropathy. 2nd group - control (n=40) included patients with arterial hypertension (20 men, 20 women, mean age - 59.7 ± 5.9 years). Patients underwent a physical examination, electrocardiography by standard method. Evaluation of daily blood pressure monitoring (DMBP), echoCG study (Echocardiographic study) was carried out. Besides, biochemical blood tests were carried out to determine the level of glucose on an empty stomach, glycated hemoglobin (HbAlc), total cholesterol (THC), triglycerides (TG), low-density lipoprotein cholesterol (LDL cholesterol), high-density lipoproteins (HDL lipoproteins) with the calculation of atherogenicity index (AI) and kidney function.

RESULTS AND DISCUSSION

According to our data, the average DMBP SAD and PAD values were significantly higher in the group of AH and DM type 2 patients in comparison with AH and DM type 2 patients without DM type 2 at comparable figures of "office" AD (153.1±13.2 vs. 150.6±13.3 mm Hg. and 85.6±9.4 vs. 81.7±12.9 mm Hg., respectively) (Table 3.3.1.). HSC at night in patients with AH without type 2 diabetes was significantly lower in comparison with patients with AH and type 2 diabetes (62.6±12.4 vs. 69.6±8.3 U/min., respectively, $p < 0.05$) in the absence of positive differences between the average office hourly rate in groups during physical examination. In addition, both the time index (TI) of DAD and TIAD were increased during the day in both the main and control groups in comparison with normal values. However, the first group of TI ADS was significantly higher in comparison with the group of patients with "isolated" AH (60.9±14.2 vs. 60.5±18.7%, respectively, at $p < 0.05$).

It was revealed that VSAD during a day and a day time were significantly higher in patients with AH in combination with DM of type 2 in comparison with

patients with "isolated" AH (18,1±5,1 and 15,7±3,8 and 16,5±5,7 vs. 14,5±4,4 mm Hg respectively).

It has been established that SARS is higher among the patients of the main group in comparison with patients with AH without DM 2 type (36,2±19,1 vs. 28,8±20,5 mm Hg. of st./h, respectively, $p<0,05$). In the group of AH and type 2 DM patients in comparison with the group of AH patients without type 2 DM patients, patients with SIAD and SI DAD less than 10% (non-dipper and night-peaker) prevailed - 75,3 vs. 53,8% and 65,3 vs. 30,3%, respectively.

Table 3.3.1: Daily blood pressure monitoring indicators for patients included in the research.

Indicators	Group 1 (main) AG and type 2 SD2	Group 2 (control) AG
DBP average, mm.m.p.	155,4±14,2	152,6±12,3*
DBP average, mm.m.p.	86,8±8,4	81,7±12,6 *
HR average, oud/min	76,7±9,8	70,4±10,7 *
HBP average, mm.m.p.	65,1±14,1	60,6±6,9*
DBP day, mm.m.p.	152,1±20,2	150,2±15,4*
DBP day, mm.m.p.	88,4±9,6	81,8±12,1 *
HR day, oud/min	75,2±10,6	73,3±11,5
HBP day, mm.m.p.	60,1±14,8	59,7±11,7
DBP night, mm.m.p.	150,8±19,0	149,9±21,9
DBP night, mm.m.p.	80,3±12,2	75,8±10,2
HR night, oud/min	69,2±8,9	62,6±10,9*
HBP night, mm.m.p.	64,5±14,8	65,3±13,4
IT DBP day, %	62,5±19,4	60,5±18,7*
IT DBP day, %	50,7±20,0	47,8±23,7

IT DBP day, %	63,1±29,9	59,9±27,6
IT DBP day, %	54,4±33,8	54,2±24,1
IT DBP night, %	62,6±27,9	62,6±20,8
IT DBP night, %	47,4±27,0	43,2±25,0
BDBP day, mm.m.p.	18,1±5,1	16,1±4,0*
BDBP day, mm.m.p.	12,8±4,1	10,8±2,6
BDBP day, mm.m.p.	16,7±5,7	14,5±4,4*
BDBP day, mm.m.p.	13,2±5,3	13,2±3,0
BDBP night., mm.m.p.	15,3±7,6	15,6±3,8
BDBP night., mm.m.p.	11,2±4,8	9,6±2,4
MLR DBP, mm.m.p.	58,1±14,7	51,4±13,2
MLR DBP, mm.m.p.	36,8±15,2	33,2±14,6
MLS DBP, mm.m.p./ч	35,2±19,1	28,2±21,2*
MLS DBP, mm.m.p./ч	35,7±22,3	32,2±15,2
DI DBP <10%, %	75,5	55,3*
DI DBP 10-20%, %	14,4	28,3*
DI DBP <10%, %	63,7	30,5*
DI DBP 10-20%, %	27,9	52,9*

Note: ACAD - variability of ACD, ACD - variability of ACD, ACD - variability of ACD, ACD - value of morning ACD lift, ACD - the value of morning ACD lift, * - reliability of differences in groups at $p<0.05$

When assessing the daily BP monitoring parameters in the patients with AH and DiD type 2, it should be noted that the heart rate during the day in the patients with stage II DN was significantly higher than in the patients with stage I DN (82.6 ±7.7 Üz/min vs. 76.4±9.6 Üz/min, respectively), as well as ADS during the night, IV ADS and ADS during the day (153.4±21.3 vs. 149.5±24.1 mm Hg.The results of the

analysis of the results of the tests were as follows: 70.4±25 vs. 66.1±31.4 %; 45.7±20.0 vs. 35.1±20.1 %, respectively, at p<0.05) (Table 3.3.2.). In addition, it was revealed that the VUP ADS and DAD, VUP ADS were significantly higher in the group with DN I stage (56.5±17.8 vs. 48.5±14.5 mm Hg. In the case of the MDIs with DN II stage (31.9±13 vs. 25.7±7.7 mm Hg/h), the MDI in the group with DN II stage (31.9±13 vs. 25.7±7.7 mm Hg/h).

In the group of patients with AB and type 2 diabetes mellitus with DN II stage II in comparison with the group of patients with AB and type 2 diabetes mellitus without DN and with stage I diabetes mellitus, patients with SI diabetes mellitus and diabetes mellitus less than 10% prevailed (non-dipper and night-peaker) - 48,5 vs24,9vs 26,8% and 53,9 vs 8,4 vs. 9,6% respectively (p<0,05).

Table 2. Daily BP monitoring indicators in the group of AH and type 2 diabetes patients without DN, in the group with DN I and II stages included in the research.

Indicators	Patients with AH and type 2 DM without DN	Patients with AH and type 2 DM from DN I Stage	Patients with AH and type 2 DM from DN II Stage
DBP average, mm.m.p.	150± 11,7	152±13,9	154,2±16,8
DBP average, mm.m.p.	85,3±8,1	87,1±17	89,9±17,1
HR average, oud/min	75,7±6,9	74,3±10	
HBP average, mm.m.p.	61,3±15,3	60,4±15,2	61,5±13,9
DBP day, mm.m.p.	152,3±20,8	154±25,8	157,4±15,9
DBP day, mm.m.p.	86,2±5,8	86,1±6,1	87,4±6,5

HR day, oud/min	79,3±5,5	76,4±9,6	82,6±7,7*
HBP day, mm.m.p	60,7±10,9	60,3±15,4	61,8±13,7
DBP night, мм. рт.ст	144,3±18,9	149,5±24,1	153,4±21,3**
DBP night, mm.m.p	80±12,7	80±11,6	79,2±8,4
HR night, oud/min	72,6±6,5	70,5±10,1	72,8±12,1
HBP night, mm.m.p.	66,6±13,9	60,1±14,6	60,7±14,8
IT DBP day, %	65,9±23,6	66,1±31,4	70,4±25*
IT DBP day, %	34,5±18,8	35,1±20,1	45,7±20,0* *
IT DBP day, %	58±19,1	59,1±34,1	77,4±23,5* *
IT DBP day, %	39,5±17,1	43,2±19,8	50,8±25,7* *
IT DBP night, %	66,2±24,8	65,8±32,4	70,4±27
IT DBP night, %	33,6±26	32,1±27,6	50,6±18,0**
VDBP day, mm.m.p	16,5±3,9	17,9±6,8	17,2±3,5
VDBP day, mm.m.p.	12,3±4,04	14,9±7,5	15,3±5,2
VDBP day, mm.m.p	17,7±3,2	18,8±7,4	18,1±3,5
VDBP day, mm.m.p.	14,6±5,6	14,7±7,4	15,6±4,6
VDBP night, mm.m.p.	13,3±3,2	14,1±6,4	12,9±2,5
VDBP night, mm.m.p.	9±3,4	11,6±6,2	11,2±3,1
MLR DBP, mm.m.p.	54±11,7	56,5±17,8	48,5±14,5**
MLR DBP, mm.m.p.	43,7±19,5	46,9±23,2	29,6±13,7**
MLS DBP, mm.m.p./ч	34,3±20,2	36,2±19,1	28,8±20,5**
MLS DBP, mm.m.p./ч	15±7,2	25,7±7,7	31,9±13**
DI DBP<10%, %	24,9	26,8	48,5**
DI DBP<10%, %	8,4	9,6	53,9**

Note: * - reliability of differences between the second and third groups at $p<0.05$, ** - reliability of differences between the first and the third groups at $p<0.05$

When studying the functional state of the kidneys, it was found that the relative density of urine in the morning, which characterises the concentration of the organs, was significantly lower in patients with AH and concomitant type 2 diabetes mellitus with DN, than in the control group (Table 3).

Table 3: Functional state of kidneys in the examined patients.

Indicators	Group 1 (Core) (AH and type 2 DM)	2nd group (control) (AH)
The relative density of urine in the morning portion, c.u.	1014±0,7	1022±0,6*
PU, mg/l	345,1±19,8	272,8±19,4*
Albumin /Creatin, mg/g	33,0±9,3	27,9±11,0*
Albumin /Creatin, %	27,8	16,7
Blood creatinine, micromol/l	99,8±16,7	92±13,4
eBFR(CKD-EPI)	60,5±12,9	68,9±11,6
BFR (CKD-EPI) < 60 ml/min/1,73 м^2, %	44	33,5*

Note: * - differences between groups are reliable at p<0.05

It was revealed that higher values of A/Cr ratio in urine were in the main group in comparison with the control group (33.0 mg/g vs 27.9 mg/g, p<0.05) (Table). When calculating BFR by the formula of CKD-EPI, the percentage of patients with typical values was lower among patients with AH and accompanying type 2 diabetes than among patients with "isolated" AH (44%vs 34%, p<0.05).

At estimation of a condition of a carbohydrate metabolism (tab. 4) statistically significant distinctions between groups on concentration of blood glucose on an empty stomach (8,5 mmol/l in the basic group vs. 5,5 mmol/l in the control group) and on level НЬА1с (7,3 % in group of patients AH and DM 2 of type vs. 5,2 % in the

second group) that is connected with features of design of research are revealed. The analysis of biochemical parameters showed significantly higher values of parameters characterizing lipid metabolism: TCS and its fractions - Blood CS LPLD, CS LPVLD, TG concentrations, and IA among patients with AH and type 2 diabetes in comparison with the control group (Table 4.) and reduction of CS LPHD in both groups of patients under observation.

Table 4: Biochemical indicators of blood in the observed patients.

Indicators	Group I (Core) (AH and type 2 DM)	Group II (control) (AH)
Blood glucose on an empty stomach, mmole/l	8,5±0,7	5,5±0,8*
HbAk, %	7,3±3,2	5,2±2,8*
Total cholesterol, mmole/l	5,6±1,2	5,2±1,1*
Triglycerides, mmole/l	2,36±1,2	2,0±1,1*
CS LPHD, mmole/l	1,3±0,3	1,34±0,3
CS LPLD, mmole/l	3,6±1,1	3,2±1,1*
CS LPVLD, mmole/l	1,2±0,6	0,87±0,7*
Atherogenicity index, c.u.	4,5±1,2	3,65±1,4

Note: * - differences between groups are reliable at $p< 0.05$.

In the analysis of the patients under study, statistically significant differences were revealed between the groups of AH patients with the accompanying DM of the 2nd type without DN, with DN of the 1st stage and DN of the 2nd stage: the impact volume (IV), eBFR, were significantly higher in the patients without DN in comparison with the groups of AH and DN 2nd type patients of the 1st stage and with DN of the 2nd stage. (71.1 vs. 72.2 ml vs. 63.0 ml and 77.8 vs. 75.6 vs. 63.0, respectively, $p<0.05$), whereas blood creatinine was significantly higher in the group

of AH patients with DN II st. (98.08 µmol/l vs. 90.2 µmol/l vs. 82.3 µmol/l). Among patients with stage I diabetic nephropathy IMILL was significantly lower in comparison with the group of AH patients without DN and with stage II DN (124 g/m^121 g/m^141 g/m2, at p<0.05). When analyzing the types of remodeling, it should be noted that in the group of patients with DN stage II, there are no patients with normal heart geometry, as well as with concentric remodelling, whereas in the group of patients with DN stage I, eccentric LCF was registered in 23% of cases, and concentric LVH in 4%.

Table 5. - Echocardiographic parameters of the heart, functional state of kidneys of the group of patients with AH and type 2 diabetes without DN, with DN I stage and DN II stage.

Indicators	Patients with AH and DM type 2 without DN	Patients with AH and DM type 2 from DN I stage	Patients with AH and DM type 2 from DN II stage
EF LV, %	61±11,05	61,5±11,05	62,4±9,1
SV, ml	71,1±10,5	72,2±14,4	63,0±14,1**
FDS LV, sm	4,9±0,5	5,2±0,6	4,7±0,5
FSS LV, sm	3,6±1,2	3,4±1,04	3,8±0,5
VCS, sm	0,9±0,2	0,98±0,3	1,0±0,2
BWLV, sm	1,01±0,4	0,9±0,4	1,1±0,9
LVMMI, g/m^2	121±29,6	124±27,9	141,0±45,3**
IVRT, ms	110±19,5	115,6±23,5	103,9±20,7
E/A	0,9±0,5	0,95±0,6	0,9±0,3
DT, ms	228,6±39,7	220,0±51,5	223±37,8
Blood creatinine,	82,3±7,1	90,2±16,7	98,08±6,9**

micromol/l			
eBFR(CKD-EPI)	77,8±11,3	75,6±13,1	63,0±13,5**
BFR(CKD-EPI) < 60 ml/min/1,73 m^2, %	48,8	55,6	78,6**

Note: * - differences between the second and third groups are reliable at $p<0.05$,

**- differences between the first and the third groups are stable at $p<0.05$.

The data obtained by us indicate that the DMBP values in a significant number of patients with diabetes mellitus 2, who do not have PU, differ from average and are associated with the presence of MAU and, possibly, vegetative dysfunction [11]. According to our data and literature, AH diagnosed according to the criteria of DMBP is significantly more frequent in patients with MAU than in patients with NAAA [2]. AH, as an essential risk factor for kidney damage, is present at the early stages of DN, which is consistent with data from other studies [2, 7]. It has been established that diabetes mellitus indexes in diabetes 2 are associated with the excretion of albumin with urine even when the latter is still within the normal range [15]. The increase in the urinary excretion of albumin with urine and the development of MAU is accompanied by the negative dynamics of DMBP parameters. Taking into account the obtained data, the DMBP indicators can be considered as possible predictors of development and progression of DM.

The most important indicator, which can be estimated only with the help of DMBP, is the daily BP profile. It is known that the type of "non-dippers" is more common in essential AH, but to the greatest extent, it is typical for symptomatic hypertension, in particular, renal hypertension.

There are data that the type "non-dippers" is a factor in the progression of nephropathies, as well as a risk factor for the development of AH [10]. Therefore,

patients with diabetes mellitus 2 with this BP profile should be included in the risk group for the formation of DN and cardiovascular disease.

CONCLUSION

Thus, the DMBP method allows timely detection of labile forms of AH in patients with diabetes mellitus 2, especially in the initial stages of kidney damage. It is advisable to include DMBP in the algorithm of examination of patients with diabetes mellitus 2 with nephropathy, for the earliest possible detection of AH and prevention of progression of vascular complications.

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