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Are we looking for nephropathy in type 2 diabetes patients actively enough?

Czy wystarczająco aktywnie poszukujemy nefropatii u pacjentów z cukrzycą typu 2?

INTRODUCTION

Diabetes nephropathy is an effect of glomerular capillaries damage due to persistent, increased blood glucose level.

The earliest clinical evidence of nephropathy is the appearance of low but abnormal levels (≥ 30 mg/day or 20 μg/min) of albumin in the urine, referred to as microalbuminuria, and patients with microalbuminuria are referred to as having incipient nephropathy (1).

A higher proportion of individuals with type 2 diabetes are found to have microalbuminuria and overt nephropathy shortly after the diagnosis of their diabetes, because diabetes is actually present for many years before the diagnosis is made and also because the presence of albuminuria may be less specific for the presence of diabetic nephropathy, as shown by biopsy studies. Without specific interventions, 20–40% of type 2 diabetic patients with microalbuminuria progress to overt nephropathy. By 20 years after onset of overt nephropathy about 20% will have progressed to end-stage renal disease (1).

Diabetes nephropathy becomes a more frequent, significant chronic diabetes complication. The percentage of microalbuminuria in type 2 diabetic patients is similar in European (2) and American (3) population: 28 – 29%. The UKPDS showed, that every year 2% of diabetic patients with normoalbuminuria developed microalbuminuria and 2.8% with microalbuminuria developed macroalbuminuria. The risk of serum creatinine level increase over 175 μmol/l (2 mg/dl) or necessary of renal replacement therapies in type 2 diabetes patients with macroalbuminuria was assessed at 2.3% a year. Ten years after diagnosis of type 2 diabetes the risk of microalbuminuria was assessed at 24.9%, macroalbuminuria at 5.3% and renal failure at 0.8% (4).

Actual data suggest that in Poland about 2 million people live with type 2 diabetes. Assuming that 20% of them develop diabetes nephropathy in different stages of the disease, we should assess that about 200 000 of them are in the risk group (5).

The persons with diabetes are the largest group of patients dialyzed because of end-stage renal disease. In Poland we observe the persistent increase of the number of diabetic patients using renal replacement therapies. In 1991 there were 142 (4.68%) diabetic subjects among 3036 dialyzed patients, in 2003 there were 2359 (20.62%) among 11 440, respectively (6).

Albuminuria is an independent risk factor of cardio-vascular complications. The UKPDS authors showed that the chance of 10 years surviving for patients with type 2 diabetes without nephropathy at baseline was 87.1%, in subjects with microalbuminuria - 70.8%, with macroalbuminuria - 65.1%, in patients with elevated serum creatinine or dialysis - 8.5% (4).

According to Polish Diabetes Association (PTD) guidelines in 2005 – 2008 the proper conditions of good diabetological care in the field of prophylaxis and treatment of diabetes nephropathy were:

– good control of glycaemia and blood pressure

– the use of angiotensin convertase inhibitors (ACE-I) or angiotensin II receptor blockers (ARB) as a first-line drugs for hypertension treatment and also for patients with normal blood pressure and microalbuminuria or proteinuria.

– albuminuria test and serum creatinine concentration assessment at least once a year

– maintaining of normal albuminuria level (urine albumin concentration < 20 mg/l) and serum creatinine concentration not exceeding 1 mg/dl (88.4 μmol/l) (7, 8).

THE AIM OF THE STUDY

The aim of the study was to assess the implementation of PTD recommendations concerning prophylaxis and treatment of nephropathy in patients with type 2 diabetes (DM2), who were admitted to the Department of Internal Diseases.

MATERIAL AND METHODS:

We examined 102 patients below 80 years of age with DM2 diagnosed at least 2 years before, who were admitted to the Department of Internal Diseases in Lublin between 23rd March 2006 and 22nd March 2007. Medical history of previous diagnostics and treatment was collected. A urinary tract infection or any known kidney disease, other than diabetes nephropathy, was exclusion criteria. Overall urine analysis was done. Urine albumin concentration was assessed using photometric method on NycoCard Reader II. Serum creatinine concentration was assessed by kinetic method with Konelab 60 camera.

The results were compared in the groups: patients treated in primary care departments (PCD, n = 64) and patients treated in diabetological ambulatory (DA, n = 38). To detect significant differences between groups we used $\chi 2$ test for qualitative characteristics, U test Mann-Whitney test for quantitative. The level of significance was $p < 0.05$.

RESULTS

The mean time of DM2 duration was 10 ± 6 years and it was significantly longer in patients treated in DA (12 ± 6 years vs. 9 ± 6 years; $p \approx 0.007$).

We found that examinations recommended for the renal function assessment were performed in the studied population not often enough. Also blood pressure measurements were often neglected. Eighty four subjects (82%) reported that they had blood pressure measurement during each visit, 6 (6%) – that they had blood pressure measurement once every 3 months on average, 2 (2%) – once every 6 months, and 10 (10%), that they had such an examination only occasionally or never. Blood pressure measurement was more frequently (p 0.04) checked in the DA group (every visit: 95% vs. 75%, once every 3 months: 3% vs. 8%, once every 6 months: 0% vs. 3%, occasionally or never: 3% vs. 14%).

According to the case history, during the year prior to the admission to the hospital, urine analysis was performed in 82 subjects (80%). Forty two (66%) of PCD and 23 (61%) of DA patients made this test in the ambulatory conditions, where the treatment of DM2 was performed, respectively: 8 (13%) and 9 (24%) – in another medical department, 14 (22%) and 6 (18%) had not performed that analysis during the previous year. There were no significant differences between the study groups ($p \approx 0.3$). None of the examined patients had urine albumin concentration assessed during the previous year, and only 1 (3%) DA patient had such a test done about 2 years earlier.

Seventy six subjects (75%) reported that they had had urine analysis performed every year or more frequently, 10 (10%) – once every 2 years, 12 (12%) – less than once every 2 years, 4 (4%), that they had never performed such a test. The differences were not statistically significant ($p \approx 0.3$).

According to the case history during the year prior to the admission to hospital, serum creatinine concentration was assessed in 52 (51%) of subjects. Fourteen (22%) PCD and 20 (53%) DA patients had made his test in the ambulatory conditions, where the treatment of DM2 was performed, respectively: 10 (16%) and 8 (21%) – in another medical department, 40 (63%) and 10 (26%) had not had such a test performed during the previous year. The differences were statistically significant ($p \approx 0.001$).

Thirty five subjects (34%) reported they had creatinine level assessed every year or more frequently, 12 (12%) – once every 2 years, 17 (17%) – less than once every 2 years, 38 (37%), that they had never performed such a test. Creatinine level was assessed significantly more frequently ($p \approx 0.0002$) in DA patients (once a year or more frequently: 55% vs. 22%, once every 2 years: 16% vs. 9%, less than once every 2 years: 16% vs. 17%, never: 13% vs. 52%).

According to the interview 8 subjects (8%) had been consulted by a nephrologist prior the admission to the hospital: 2 (3%) PCD and 6 (16%) DA ($p \approx 0.02$).

HbA1c level < 6.1% was found in 15 subjects (15%), between 6.1% and 7% - in 28 (28%), between 7.1% and 8% - in 20 (20%) and > 8% - in 38 (38%). The mean HbA1c level was assessed at 7.82 ± 1.84%. There were no differences in the degree of metabolic control ($p \approx 0.2$) and mean HbA1c level (PCD: 7.82 ± 1.84%, DA: 8.08 ± 1.64%, $p \approx 0,1$) between study groups.

We found no significant differences in the prevalence of hypertension in the groups (PCD: 58 (91%) vs. DA: 36 (95%); $p \approx 0.4$). RR < 130/80 mm Hg on admission to hospital was found in 10 (10%) patients: 7 (11%) from PCD and 3 (8%) from DA ($p \approx 0.6$).

ACE-I or ARB were taken by 67 (66%) patients. Thirty four (34%) of them had not received such a drug, including 1 (1%), who had not received it because of contraindications. One patient couldn't report what drugs he had been administering. He was excluded from the study. The patient with contraindications was also excluded from group. Out of 88 subjects with hypertension known before admission to the hospital, 64 (73%) received hypotensive treatment. DA patients received hypotensive drugs more frequently: 79% vs. 60% ($p \approx 0.043$) in the whole cohort, 85% vs. 69% ($p \approx 0.07$) among subjects with hypertension.

Among the examined subjects: 6 of them (6%) had diagnosed diabetes nephropathy before the admission to the hospital, in other 47 patients (46%), increased urine albumin concentration was determined ($\geq$ 20 mg/l), what may suggest that they also had such a complication. The prevalence of diabetes nephropathy (including its suspicion) didn't differ significantly in the examined groups (PCD: known - 2 (3%), suspicion - 31 (48%) vs. DA: known - 4 (11%), suspicion - 16 (42%); $p \approx 0.3$).

The presence of protein in the overall urine analysis was found in 34 (33%) patients: 18 (29%) of the PCD and 16 (42%) of the DA ($p \approx 0.2$). Urine analysis was not performed in one PCD patient.

Normal urine albumin concentration was found in 49 (48%) subjects: 31 (48%) in PCD and 18 (47%) in DA group ($p \approx 0.9$). Mikroalbuminuria (urine albumin concentration $\geq$ 20 mg/l and < 200 mg/l) was found in 48 (47%) subjects: 29 (48%) and 19 (51%) respectively. Makroalbuminuria (urine albumin concentration $\geq$ 200 mg/l) was found in 5 (5%) subjects: 4 (6%) and 1 (3%) respectively. There were no significant differences in urine albumin level between study groups ($p \approx 0.7$).

Serum creatinine concentration < 1 mg/dl was determined in 69 (68%) examined subjects: 48 (75%) in the PCD group and 21 (55%) in the DA group ($p \approx 0.04$).

Creatinine clearence $\geq$ 90 ml/min/1.73 m^2 was estimated in 56 (55%) examined subjects, $\geq$ 60 and < 90 ml/min/1,73 m^2 – in 27 (26%), $\geq$ 30 and < 60 ml/min/1,73 m^2 – in 17 (17%), < 30 ml/min/1,73 m^2 – in 2 (2%). There were no significant differences in creatinine clearence level between study groups ($p \approx 0.9$).

Figure 1. Treatment with ACE-I or ARB before the admission to the hospital

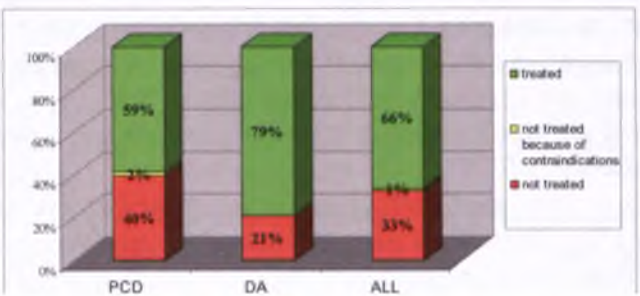


Figure 2. Prevalence of diabetes nephropathy in the examined subjects

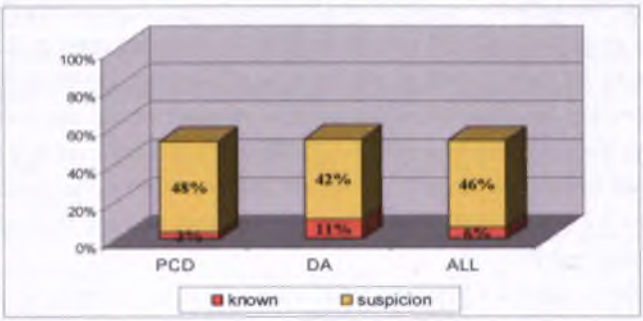


Figure 3. Urine albumin level in the examined subjects

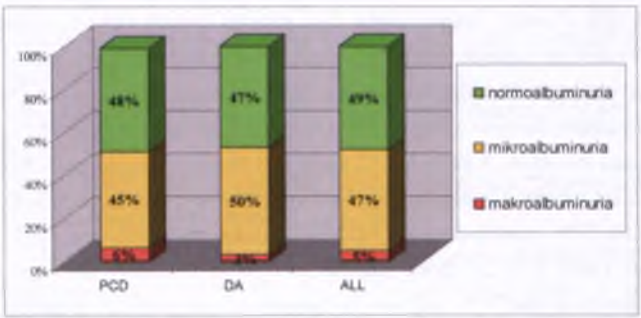
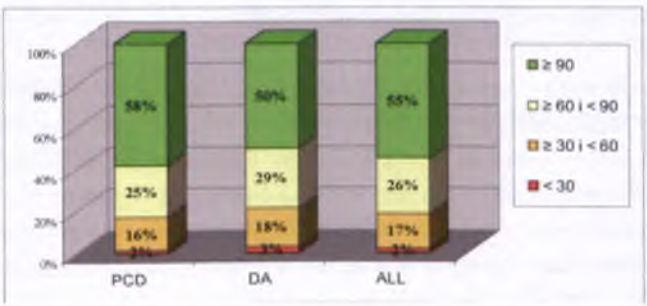


Figure 4. Renal sufficiency in the examined subjects (creatinine clearence in ml/min/1,73 m^2)



DISCUSSION

Poor control of blood glucose concentration and blood pressure appears to be the most important deficiency of the prophylaxis of renal complications in the examined patients. It is not surprising because these were the main reasons of admission to the hospital. However, the unsatisfactory effectiveness especially for hypertensive treatment is common among the diabetic patients. In DINAMIC 2 study blood pressure criteria below 130/80 mm Hg were achieved only in 5% of subjects, although 66% used hypotensive drugs (9). There are also objections to the choice of hypotensive drugs – lack of ACE-I or ARB in treatment, although they are recommended by scientific societies due to their nephroprotective action.

We are concerned about low frequency of diagnostic tests for screening of nephropathy and renal function assessment. The economic factor definitely plays an important role in such a situation. Although at least diabetic ambulatories should work in better compliance to guidelines, especially now, when they have been liberalized (10).

Our study confirms that DM2 patients, being under control of diabetologists, have more frequent screening for chronic diabetes complications than patients treated only in primary care. Similar observations were made for example in the QuED study. On the other hand, the same study demonstrated that more frequent testing itself really does not translate to a better clinical effect. (11). Assessment of renal function is necessary to avoid adverse effects of some drugs used in diabetes (e.g. metformin) and concomitant diseases treatment. Like in QuED study also Nguyen showed more frequent HbA1c and mikroalbuminuria assessment in patients, who were under the specialist care (12). In his study 79% of subjects had HbA1c, 77% - creatinine and 17% urine albumin concentration control.

In France, in 1997, 92% of DM2 patients treated in primary care had serum creatinine concentration assessment and 37% had microalbuminuria test performed during the previous 12 months. These results are significantly better then obtained in our study, but they were still improved after DIABEST programme introduction. A year later, the percentage of subjects, who in the past year had made these tests, were assessed at 95% and 54% respectively (13).

The study performed by McClain in American State - Maine during Diabetes Quality Improvement Project found, that nephropathy screening was performed in 37% of diabetic patients in 1994 and in 50% in 1999 (14).

In the study performed by Czech in 2007 (15) during the previous year, serum creatinine concentration was assessed in 67% of diabetic patients treated in primary care, in 88% under control of county diabetic ambulatories and in 95% treated in provincial diabetes departments, the daily albumin urination in 1,5%, 13% and 29% respectively, which may indicate a higher level of diabetes care in Mazowieckie Voivodship. At that same time it should be noted that frequency of tests for nephropathy screening was also significantly worse than frequency of other periodical tests recommended by diabetes societies.

CONCLUSIONS

Prevention of renal complications in examined patients with diabetes was generally neglected. It is hoped, that popularization of PTD guidelines and adequate valuation of benefit for diabetes care will improve that situation.

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SUMMARY:

According to Polish Diabetes Association (PTD), screening for nephropathy for every patient with diabetes mellitus (DM) should be done every year. Angiotensin convertase inhibitors (ACE-I) and angiotensin II receptor blockers (ARB) are the most recommended for diabetes nephropathy prophylaxis and treatment. The aim of the study was assessment of these PTD guidelines realization in the type 2 diabetes patients. Material and methods: One hundred and one (101) patients with DM2 admitted to the Internal Disease Department were included into the study. The case history

about previous diseases, diagnostics and treatment was performed. We assessed urine total protein and albumin concentration, plasma creatinine concentration and calculated creatinine clearance. Results: Fifty (50) out of 64 (78%) patients previously treated in primary health care departments (PCD) said that they had had urine analysis and 24 (37%) subjects stated that they had had plasma creatinine concentration assessment during the previous 12 months. Out of 37 patients previously treated in the diabetological ambulatory (DA), 31 (84%) said that they had had urine analysis and 27 (73%), that they had had creatinine level assessment done respectively. Only 1 patient of DA had ever albuminuria assessed. We found ACE-I and/or ARB treatment in 37 (58%) PCD and in 29 (78%) DA subjects. Six subjects (6%) had diabetes nephropathy recognized before hospitalization. Microalbuminuria was found in 42, macroalbuminuria in 4 subjects. In 8 of them we found creatinine clearance ≥60 and <90 ml/min, in 9 ≥30 and <60 ml/min. Results: Diabetes nephropathy prophylaxis in type 2 patients is often unsatisfactory.

Key words: type 2 diabetes, nephropathy, family medicine practice, diabetological ambulatory

STRESZCZENIE:

Zgodnie z wytycznymi PTD każdy diabetyk powinien raz w roku mieć wykonane badania w kierunku nefropatii. Lekami z wyboru w profilaktyce i leczeniu nefropatii są inhibitory enzymu konwertującego angiotensynę (ACE-I) i blokery receptora angiotensyny II (ARB). Celem pracy była ocena realizacji wymienionych zaleceń u pacjentów z DM2 przed przyjęciem do Kliniki Chorób Wewnętrznych. Materiał i metody: Zbadano 101 osób z DM2 rozpoznaną co najmniej 2 lata wcześniej. Zebrano wywiad odnośnie wcześniejszych schorzeń, diagnostyki i leczenia. U badanych oznaczono stężenie białka i albumin w moczu, kreatyninę krwi, obliczono klirens kreatyniny. Wyniki: Wśród 64 pacjentów poradni lekarza rodzinnego (PLR) 50 (78%) podało, że w ostatnim roku miało wykonaną analizę moczu, a 24 (37%) oznaczoną kreatyninemię. Wśród 37 pacjentów poradni diabetologicznych (PD) 31 (84%) podało odpowiednio, że miało wykonaną analizę moczu, a 27 (73%) oznaczoną kreatyninemię. 4 pacjenci PLR i 1 PD twierdzili, że nigdy nie badano im moczu, odpowiednio u 33 (52%) i 5 (14%) nie oznaczano kreatyninemii. 1 pacjent PD twierdził, że przed 2 laty miał oznaczoną albuminurię, pozostali podali, że takiego badania nigdy nie mieli. ACE-I i/lub ARB przyjmowało 37 badanych z PLR (58%) i 29 z PD (78%). 6 badanych (6%) miało przed hospitalizacją rozpoznaną nefropatię cukrzycową. Wśród pozostałych mikroalbuminurię stwierdzono u 42, a makroalbuminurię u 4 badanych. U 8 z nich stwierdzono klirens kreatyniny ≥60 i <90 ml/min, u 9 ≥30 i <60 ml/min. Wnioski: Profilaktyka nefropatii u pacjentów z DM2 przyjętych do Kliniki często była wcześniej zaniedbywana.

Słowa kluczowe: cukrzyca typu 2, nefropatia, podstawowa opieka zdrowotna, poradnia diabetologiczna