SHORT COMMUNICATION

Principles of prevention and therapy in diabetic nephropathy

Mojto V, Tison P

*IIIrd Department of Internal Medicine, Derer's University Hospital, Bratislava, Slovakia.***viliam.mojto@fnderera.sk**

Diabetic nephropathy represents the second most common cause of renal failure in Slovak Republic. In 2002, 1993 patients were enrolled in the dialysis program in Slovak Republic, 20.3 % with diabetes mellitus.

Glomerular hyperfiltration and microalbuminuria (albumin excretion rate 20–200 µg/min, accounting for 30–300 mg/24 h) are though to be the most important parameters in diabetic nephropathy classification (Mogensen, 1998).

Recommended evaluation of microalbuminuria include overnight urinary collection or casual sample and determining the albumin/creatinine excretion ratio.

Normal value for albumin/creatinine excretion ratio is 2.5 mg/mmol (Tab. 1).

The main goal of preventive and therapeutic measures is to stop or reduce the progression of diabetic nephropathy in all stages.

We have to achieve three main goals:

1. Normalisation of blood pressure. 2. The best possible metabolic balance. 3. Reduction of protein intake.

Preventive measures are realised via primary, secondary and tertiary prevention.

The aim of primary prevention is to prevent progression from normoalbuminuria to microalbuminuria, i.e. to incipient diabetic nephropathy.

Secondary prevention means to reduce or prevent progression from microalbuminuria to clinical albuminuria (proteinuria) i.e. from incipient to manifest diabetic nephropathy.

Tertiary prevention means to slow down the progression from manifest diabetic nephropathy to end stage renal disease.

Glycemic control

In primary prevention it is important to start an intensive insulin regimen as soon as possible and to improve glucose monitoring in order to achieve normal plasma glucose in the largest portion of patients with type 1. diabetes mellitus.

Secondary prevention. It is possible to achieve the reduction of microvascular complications progression via glycemic control using an intensive insulin therapy.

Tertiary prevention. Strict glycemic control is abandoned. Strict antihypertensive therapy is in forefront.

Antihypertensive treatment

Sodium retention to some degree is a common finding in these patients, and represents a rational indication for the use of diuretics in the therapy.

At the beginning, blood pressure rises approximately about 3-4 mmHg per year. An optimal value for systolic blood pressure should be less than 120 mmHg and for diastolic blood pressure less than 80 mmHg. A normal value for systolic blood pressure should be less than 130 mmHg and for diastolic blood pressure less than 80 mmHg. Blood pressure should not be markedly decreased due to the danger of renal ischaemia.

Primary prevention

Inhibitors of angiotensin converting enzyme (ACE), which are recommended for patients with upper normal blood pressure, BP: 130/80 torr, are drugs of choice. The same is true for patients with type 1. diabetes, normoalbuminuria and normal blood pressure, but with supranormal GF.

Secondary prevention

Long term maintenance of optimal blood pressure in patients with type 1. diabetes and incipient nephropathy (BP<120/80 mmHg), treated with ACE inhibitors, reduces the progression of nephropathy. Multicentric trial IRMA-2 showed an important role of angiotensin II AT1 receptor blocker in secondary prevention of nephropathy in type 2 diabetic patients.

IIIrd Department of Internal Medicine, Derer's University Hospital, Bratislava

Address for correspondence: V. Mojto, MD, PhD, IIIrd Dept of Internal Medicine, Derer's University Hospital, Limbova 5, SK-833 05 Bratislava 37, Slovakia.
Phone: +421.905223868

Tab. 1. Stages of diabetic nephropathy (adapted to Mogensen et al., 1988, 1998).

Stage	GF	Albuminuria	Creatinine	Blood pressure
1. hyperfunction and hyperfiltration	↑	↔↑	↔	↔
2. normal albuminuria	↑↔	↑↔	↔	↔
3. incipient nephropathy	↔	↑*	↔	↑
4. manifest nephropathy	↓	↑↑**	↔	↑
5. renal failure	↓	↑↑**	↑	↑

* microalbuminuria: 20–200 μg/min
* * clinical albuminuria (proteinuria): >200 μg/min
GF glomerular filtration rate

Tertiary prevention

The effect of sartan and ACE inhibitor monotherapy, as well as combination therapy, was evaluated in the clinical study CALM. The highest decrease of both albuminuria and blood pressure was observed in combined ACE inhibitor and angiotensin II AT1 receptor blocker use.

The dosage of angiotensin II AT1 receptor blockers needs not be reduced during the development of renal insuficiency.

High levels of angiotensin II in AT1-receptor blockage stronger stimulate AT2-receptors, leading to local production of bradykinine in interstitial fluid with subsequent stimulation of NO synthesis and accumulation of cyclic guanosin monophosphate. The blood pressure increased by this mechanism contributes to increased elimination of sodium and water. The advantage of angiotensin AT1 receptor blockers is fewer side effects, particularly cough.

Betablockers

Recommended in diabetic patients with manifest coronary heart disease and hyperthyreosis.

Calcium channel blockers

Non-dihydropyridines slightly decrease albuminuria. These drugs belong to second line treatment in diabetic patients.

Diuretics

Tiazid diuretics are reasonable in type 2 diabetes. These drugs have the tendency to worsen glucose tolerance. In renal insufficiency it is necessary to substitute them with loop diuretics.

Low protein diet decreases proteinuria and contributes to preservation of the glomerular filtration decrease. If an incipient or manifest stage of diabetic nephropathy is diagnosed, we recommend to decrease protein intake gradually to 0.6 g/kg of weight/day.

Early *hypolipidemic therapy* is reasonable in prevention of diabetic nephropathy. *Education of patient* with diabetes mellitus represents one of the most important roles in preventive nonpharmacological measures, which should precede any pharmacological treatment. In prevention of complications we highlight a necessary *complex treatment* of diabetic patient, not only plasma glucose and blood pressure control but also weight reduction, particularly actual in type 2 diabetes, as well as other preventive and therapeutic measures.

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