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Role of Pharmacist Management and Novel Therapies of Diabetic Nephropathic Patients

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Diabetic nephropathy is kidney disease that develops as a result of diabetes mellitus (DM). DM, also called simply diabetes. This disease damages many organs, including the eyes, nerves, blood vessels, heart, and kidneys. Diabetes is the most common cause of kidney failure and accounts for over one-third of all patients who are on dialysis. Diabetic nephropathy (DN) is typically defined by macro albuminuria—that is, a urinary albumin excretion of more than 300 mg in a 24-hour collection—or macro albuminuria and abnormal renal function as represented by an abnormality in serum creatinine, calculated creatinine clearance, or glomerular filtration rate (GFR). Clinically, diabetic nephropathy is characterized by a progressive increase in proteinuria and decline in GFR, hypertension, and a high risk of cardiovascular morbidity and mortality. Nephropathy means kidney disease or damage. Diabetic nephropathy is damage to your kidneys caused by diabetes. In severe cases it can lead to kidney failure. But not everyone with diabetes has kidney damage .The kidneys have many tiny blood vessels that filter waste from your blood. High blood sugar from diabetes can destroy these blood vessels. Over time, the kidney isn't able to do its job as well. Later it may stop working completely. This is called kidney failure. Certain things make you more likely to get diabetic nephropathy. If you also have high blood pressure or high cholesterol, or if you smoke, your risk is higher. There are no symptoms in the early stages. So it's important to have regular urine tests to find kidney damage early. Sometimes early kidney damage can be reversed. The first sign of kidney damage is a small amount of protein in the urine, which is found by a simple urine test. As damage to the kidneys gets worse, your blood pressure rises. Your cholesterol and triglyceride levels rise too. As your kidneys are less able to do their job, you may notice swelling in your body, at first in your feet and legs. Community pharmacist can take to increase their involvement and contribution to public health at a local level in collaboration with other public health. During this role shift, the competency of community pharmacists is in higher demand than ever before. In view of availability of numerous new medicines and drug delivery systems, community pharmacists are challenged to ensure that patients get maximum benefit from their medicines. It is essential that discovery of new drug, new therapeutics effect of relatively older drugs, clinical trials, toxicological studies etc. are all carried out involving community pharmacy at different phases.

Keyword: Diabetic Nephropathic, Pharmacist Management, Nephropathic Patients

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INTRODUCTION: It has been predicted that worldwide the prevalence of diabetes in adults would increase to 5.4% by the year 2025 from the prevalence rate of 4.0% in 1995. Consequently the number of adults with diabetes in the world would rise from 135

million in 1995 to 300 million in the year 2025. It is expected that much of this increase in prevalence rate will occur in developing countries. While a 42% increase is expected in developed countries, a 170% increase is expected in the developing countries. In the latter, most of the diabetic patients are in the age range of 45–64 years, while in developed countries most of them are ≥65 years. Therefore diabetic patients in developing countries are even more vulnerable to develop the micro- vascular complications of diabetes including diabetic nephropathy. Diabetic nephropathy is the leading cause of chronic renal disease and a major cause of cardiovascular mortality. Diabetic nephropathy has been categorized into stages: microalbuminuria and macroalbuminuria. The cut-off values of micro- and macroalbuminuria are arbitrary and their values have been questioned. Subjects in the upper-normal range of albuminuria seem to be at high risk of progression to micro- or macroalbuminuria and they also had a higher blood pressure than normoalbuminuric subjects in the lower normoalbuminuria range. Diabetic nephropathy screening is made by measuring albumin in spot urine. If abnormal, it should be confirmed in two out three samples collected in a three to six-months interval. Additionally, it is recommended that glomerular filtration rate be routinely estimated for appropriate screening of nephropathy, because some patients present a decreased glomerular filtration rate when urine albumin values are in the normal range. The two main risk factors for diabetic nephropathy are hyperglycemia and arterial hypertension, but the genetic susceptibility in both type 1 and type 2 diabetes is of great importance. Other risk factors are smoking, dyslipidemia, proteinuria, glomerular hyperfiltration and dietary factors. Nephropathy is pathologically characterized in individuals with type 1 diabetes by thickening of glomerular and tubular basal membranes, with progressive mesangial expansion (diffuse or nodular) leading to progressive reduction of glomerular filtration surface. Concurrent interstitial morphological alterations and hyalinization of afferent and efferent glomerular arterioles also occur. Podocytes abnormalities also appear to be involved in the glomerulosclerosis process. In patients with type 2 diabetes, renal lesions are heterogeneous and more complex than in individuals with type 1 diabetes. Treatment of diabetic nephropathy is based on a multiple risk factor approach, and the goal is retarding the development or progression of the disease and to decrease the subject's increased risk of cardiovascular disease. Achieving the best metabolic control, treating hypertension (<130/80 mmHg) and dyslipidemia (LDL cholesterol <100 mg/dl), using drugs that block the renin-angiotensin-aldosterone system, are effective strategies for preventing the development of microalbuminuria, delaying the progression to more advanced stages of nephropathy and reducing cardiovascular mortality in patients with diabetes. Diabetes can affect many parts of the body, including the kidneys. In healthy kidneys, many tiny blood vessels filter waste products from your body. The blood vessels have holes that are big enough to allow tiny waste products to pass through into the urine but are still small enough to keep useful products (such as protein and red blood cells) in the blood. High levels of sugar in the blood can damage these vessels if diabetes is not controlled. This can cause kidney disease, which is also called nephropathy (say: nef-rah-puh-thee). If the damage is bad enough, your kidneys could stop working.

SIGNS AND SYMPTOMS OF DIABETIC NEPHROPATHY

Diabetes can affect many parts of the body, including the kidneys. In healthy kidneys, many tiny blood vessels filter waste products from your body. The blood vessels have holes that are big enough to allow tiny waste products to pass through into the urine but are still small enough to keep useful products (such as protein and red blood cells) in the blood. High levels of sugar in the blood can damage these vessels if diabetes is not controlled. This can cause kidney disease, which is also called nephropathy (say: nef-rah-puh-thee). If the damage is bad enough, your kidneys could stop working. Early signs and symptoms of kidney disease in patients with diabetes are typically unusual. However, a vast array of signs and symptoms listed below may manifest when kidney disease has progressed:[4]

- Albumin or protein in the urine
- High blood pressure
- Ankle and leg swelling, leg cramps
- Going to the bathroom more often at night
- High levels of blood urea nitrogen (BUN) and serum creatinine
- Less need for insulin or antidiabetic medications
- Morning sickness, nausea, and vomiting
- Weakness, paleness, and anemia
- Itching

The differential diagnosis of diabetic nephropathy is vast, but includes the following in a patient with known diabetes mellitus:

- Primary or secondary glomerular disease
- Nephrosclerosis
- Renovascular hypertension
- Renal artery stenosis
- Renal vein thrombosis
- Multiple myeloma
- Cholesterol embolization
- Chronic obstruction
- Interstitial nephritis
- Amyloidosis

Approximately 25% to 40% of patients with DM 1 ultimately develop diabetic nephropathy (DN), which progresses through about five predictable stages.

1. **Stage 1** (very early diabetes)—Increased demand upon the kidneys is indicated by an above-normal glomerular filtration rate (GFR).
2. **Stage 2** (developing diabetes)—The GFR remains elevated or has returned to normal, but glomerular damage has progressed to significant microalbuminuria (small but above-normal level of the protein albumin in the urine). Patients in stage 2 excrete more than 30 mg of albumin in the urine over a 24-hour period. Significant microalbuminuria will progress to end-stage renal disease (ESRD). Therefore, all diabetes patients should be screened for microalbuminuria on a routine (yearly) basis.
3. **Stage 3** (overt, or dipstick-positive diabetes)—Glomerular damage has progressed to clinical albuminuria. The urine is "dipstick positive," containing more than 300 mg of albumin in a 24-hour period. Hypertension (high blood pressure) typically develops during stage 3.
4. **Stage 4** (late-stage diabetes)—Glomerular damage continues, with increasing amounts of protein albumin in the urine. The kidneys' filtering ability has begun to decline steadily, and blood urea nitrogen (BUN) and creatinine (Cr) has begun to increase. The glomerular filtration rate (GFR) decreases about 10% annually. Almost all patients have hypertension at stage 4.
5. **Stage 5** (end-stage renal disease, ESRD)—GFR has fallen to approximately 10 milliliters per minute (<10 mL/min) and renal replacement therapy (i.e., hemodialysis, peritoneal dialysis, kidney transplantation) is needed.

Progression through these five stages is rather predictable because the onset of DM 1 can be identified, and most patients are free from age-related medical problems.

Causes

The exact cause of diabetic nephropathy is unknown, but it is believed that uncontrolled high blood sugar leads to the development of kidney damage, especially when high blood pressure is also present. In some cases, your genes or family history may also play a role. Not all persons with diabetes develop this condition.

Each kidney is made of hundreds of thousands of filtering units called nephrons. Each nephron has a

cluster of tiny blood vessels called a glomerulus. Together these structures help remove waste from the body. Too much blood sugar can damage these structures, causing them to thicken and become scarred. Slowly, over time, more and more blood vessels are destroyed. The kidney structures begin to leak and protein (albumin) begins to pass into the urine.

Persons with diabetes who have the following risk factors are more likely to develop this condition:

- African American, Hispanic, or American Indian origin
- Family history of kidney disease or high blood pressure
- Poor control of blood pressure
- Poor control of blood sugars
- Type 1 diabetes before age 20
- Smoking

Diabetic nephropathy generally goes along with other diabetes complications including high blood pressure, retinopathy, and blood vessel changes.

Prognosis

Nephropathy is a major cause of sickness and death in persons with diabetes. It is the leading cause of long-term kidney failure and end-stage kidney disease in the United States, and often leads to the need for dialysis or kidney transplantation.The condition slowly continues to get worse once large amounts of protein begin to appear in the urine or levels of creatinine in the blood begin to rise.Complications due to chronic kidney failure are more likely to occur earlier, and get worse more rapidly, when it is caused by diabetes than other causes. Even after dialysis or transplantation, persons with diabetes tend to do worse than those without diabetes.

Exams and Tests

The main sign of diabetic nephropathy is persistent protein in the urine. (Protein may appear in the urine for 5 to 10 years before other symptoms develop.) If your doctor thinks you might have this condition, a microalbuminuria test will be done. A positive test often means you have at least some damage to the kidney from diabetes. Damage at this stage may be reversible. The test results can be high for other reasons, so it needs to be repeated for confirmation.High blood pressure often goes along with diabetic nephropathy. You may have high blood pressure that develops rapidly or is difficult to control.

Laboratory tests that may be done include:

- BUN
- Serum creatinine

The levels of these tests will increase as kidney damage gets worse. Other laboratory tests that may be done include:

- 24-hour urine protein
- Blood levels of phosphorus, calcium, bicarbonate, PTH, and potassium
- Hemoglobin
- Hematocrit
- Protein electrophoresis - urine

A kidney biopsy confirms the diagnosis. However, your doctor can diagnose the condition without a biopsy if you meet the following three conditions:

- Persistent protein in the urine
- Diabetic retinopathy
- No other kidney or renal tract disease

A biopsy may be done, however, if there is any doubt in the diagnosis.

Mortality/Morbidity

Diabetic nephropathy accounts for significant morbidity and mortality. The fraction of patients with IDDM who develop renal failure seems to have declined over the past several decades. However, 20-40% still have this complication. On the other hand, only 10-20% of patients with NIDDM develop uremia due to diabetes. Their nearly equal contribution to the

total number of patients with diabetes who develop kidney failure results from the higher prevalence of NIDDM (5- to 10-fold).

Race

The severity and incidence of diabetic nephropathy are especially great in blacks (the frequency being 3- to 6-fold higher than it is in whites), Mexican Americans, and Pima Indians with type 2 diabetes. The relatively high frequency of the condition in these genetically disparate populations suggests that socioeconomic factors, such as diet, poor control of hyperglycemia, hypertension, and obesity, have a primary role in the development of diabetic nephropathy. It also indicates that familial clustering may be occurring in these populations.

By age 20 years, as many as half of all Pima Indians with diabetes have developed diabetic nephropathy, with 15% of these individuals having progressed to ESRD.

Sex

Diabetic nephropathy affects males and females.

Age

Diabetic nephropathy rarely develops before 10 years' duration of IDDM. The peak incidence (3%/y) is usually found in persons who have had diabetes for 10-20 years

PATHOPHYSIOLOGY

The key change in diabetic glomerulopathy is augmentation of extracellular material.

The earliest morphologic abnormality in diabetic nephropathy is the thickening of the glomerular basement membrane (GBM) and expansion of the mesangium due to accumulation of extracellular matrix. The image below is a simple schema for the pathogenesis of diabetic nephropathy.

PATHOGENESIS OF DIABETIC NEPHROPATHY.

Light microscopy findings show an increase in the solid spaces of the tuft, most frequently observed as coarse branching of solid (positive periodic-acid Schiff reaction) material (diffuse diabetic glomerulopathy). Large acellular accumulations also may be observed within these areas. These are circular on section and are known as the Kimmelstiel-Wilson lesions/nodules.

The glomeruli and kidneys are typically normal or increased in size initially, thus distinguishing diabetic nephropathy from most other forms of chronic renal insufficiency, wherein renal size is reduced (except renal amyloidosis and polycystic kidney disease).

Immunofluorescence microscopy may reveal deposition of immunoglobulin G along the GBM in a linear pattern, but this is not immunopathogenetic or diagnostic. Immune deposits are not observed. The renal vasculature typically displays evidence of atherosclerosis, usually due to concomitant hyperlipidemia and hypertensive arteriosclerosis.

Electron microscopy provides a more detailed definition of the structures involved. In advanced disease, the mesangial regions occupy a large proportion of the tuft, with prominent matrix content. Further, the basement membrane in the capillary walls (ie, the peripheral basement membrane) is thicker than normal.

The severity of diabetic glomerulopathy is estimated by the thickness of the peripheral basement membrane and mesangium and matrix expressed as a fraction of appropriate spaces (eg, volume fraction of mesangium/glomerulus, matrix/mesangium, or matrix/glomerulus).

Three major histologic changes occur in the glomeruli of persons with diabetic nephropathy. First, mesangial expansion is directly induced by hyperglycemia, perhaps via increased matrix production or

glycosylation of matrix proteins. Second, GBM thickening occurs. Third, glomerular sclerosis is caused by intraglomerular hypertension (induced by renal vasodilatation or from ischemic injury induced by hyaline narrowing of the vessels supplying the glomeruli). These different histologic patterns appear to have similar prognostic significance.

The exact cause of diabetic nephropathy is unknown, but various postulated mechanisms are hyperglycemia (causing hyperfiltration and renal injury), advanced glycosylation products, and activation of cytokines.

Hyperglycemia increases the expression of transforming growth factor-beta (TGF-beta) in the glomeruli and of matrix proteins specifically stimulated by this cytokine. TGF-beta may contribute to the cellular hypertrophy and enhanced collagen synthesis observed in persons with diabetic nephropathy.[1]

Hyperglycemia also may activate protein kinase C, which may contribute to renal disease and other vascular complications of diabetes.

In addition to the renal hemodynamic alterations, patients with overt diabetic nephropathy (dipstick-positive proteinuria and decreasing GFR) generally develop systemic hypertension. Hypertension is an adverse factor in all progressive renal diseases and seems especially so in diabetic nephropathy. The deleterious effects of hypertension are likely directed at the vasculature and microvasculature.

Familial or perhaps even genetic factors also play a role. Certain ethnic groups, particularly African Americans, persons of Hispanic origin, and American Indians, may be particularly disposed to renal disease as a complication of diabetes.

Some evidence has accrued for a polymorphism in the gene for angiotensin-converting enzyme (ACE) in either predisposing to nephropathy or accelerating its course. However, definitive genetic markers have yet to be identified.

The two main risk factors for DN are hyperglycemia and arterial hypertension. However, DN develops in only about 40% of patients, even in the presence of hyperglycemia and elevated BP for long periods of time. This observation raised the concept that DN will develop only in a susceptible subset of patients Furthermore, family studies have confirmed a genetic contribution for the development of DN in both type 1 and type 2 DM Once DN is present, progression factors may act, favoring evolution to more advanced stages. There is evidence that some factors involved in the development of proteinuria are also common to the loss of GFR, but others are unique to each one of them

Hyperglycemia

Hyperglycemia is a significant risk factor for the development of microalbuminuria, both in type 1 and in type 2 DM A reduction of 1% in HbA1c is associated with a 37% decrease in microvascular endpoints In the presence of micro- and macroalbuminuria the role of metabolic control is less defined, even though some studies showed a deleterious effect of high glucose levels on GFR Moreover, it was demonstrated that pancreas transplantation reversed renal damage in type 1 DM patients with mild to advanced DN lesions Recently a large trial also reinforced the importance of intensive treatment of DM to decrease the microvascular complications .

Arterial Hypertension

Arterial hypertension is a main risk factor for the development of DN and probably the best known relevant factor related to its progression. Analysis of UKPDS showed that every 10 mmHg reduction in systolic BP is associated with a 13% reduction in the risk of microvascular complications, with the smallest risk among those patients with systolic BP <120 mm Hg .

Smoking

Smoking is a risk factor for DN and might contribute to its progression. Although some studies did not confirm these observations it is strongly recommended to quit smoking in any phase of DN, also aiming to reduce the associated cardiovascular and cancer risk.

Dyslipidemia

In type 2 DM, elevated serum cholesterol is a risk factor for the development of DN . In type 1 DM patients increased serum triglycerides, total and LDL-cholesterol were associated with micro- and macroalbuminuria. High serum cholesterol also seems to be a risk factor for GFR loss in macroalbuminuric type 1 diabetic subjects

Proteinuria

Proteinuria itself could lead to progression of DN. Proteinuria >2 g/24 h is associated with a greater risk of ESRD. Increased leakage of albumin may induce glomerular damage probably through activation of inflammatory cascades. This would be a reason to target decreased urinary albumin excretion in DN treatment.

Glomerular hyper filtration

Elevated GFR values are present in about one third of type 2 DM patients and theoretically it could cause DN due to glomerular damage. Studies led to controversial findings regarding its role as a risk factor for the development of DN Type 2 DM patients with a single-kidney more often present increased UAE levels On the other hand, type 1 DM patients with only one kidney do not have a more aggressive disease Glomerular hyperfiltration probably plays a small role, if any, in the development of DN.

Dietary factors

Increased dietary protein intake seems to be associated with the presence of higher UAE values, at least in patients with type 1 DM. In patients with type 2 DM this association has not been documented. The source of proteins in the diet also seems to be related to the presence of DN. A higher intake of fish protein is related to a lower risk of microalbuminuria in type 1 DM patients. The mechanisms involved in these findings are unknown but probably related to hemodynamic factors.

Regarding the dietary lipid content, an association has been observed between the higher intake of saturated fat and the presence of microalbuminuria in patients with type 1 DM. In patients with type 2 DM, very recently, it was observed that the presence of microalbuminuria was associated with the lower content of polyunsaturated fatty acids, especially those of vegetal origin In a study performed with patients with type 1 and type 2 DM, followed for 6 years, it was also demonstrated that those who evolved with regression of the DN presented a higher intake of polyunsaturated fatty acids and a lower intake of saturated fatty acids

Genetic risk factors

The exact genetic model underlying DN susceptibility is uncertain, but theoretically few genes with a major contribution and some with minor interaction with the environment could cause DN. Unfortunately, no gene with a major effect had been identified so far. The knowledge of which gene(s) predisposes to DN will allow the identification of patients at high risk for this complication, and adoption of preventive measures.

In genetic studies the clear definition of the phenotype, DN, is very important. DN could be defined by different parameters: for instance, the presence of microalbuminuria, macroalbuminuria, ESRD or decreased GFR. Some genes probably are involved in the development of proteinuria, others with decline in GFR and some will be involved in both situations. Therefore, a more comprehensive definition of DN used in the genetic studies is important to make the results more comparable.

A familial aggregation of DN has been demonstrated in studies of sibling-pairs parent-offspring pairs or studies of extended families. One practical application of the studies with diabetic siblings is that the chance of having DN increases 2-3 times if the subject's sibling has DN when compared to the subject who has

a normoalbuminuric sibling, either in type 1 or type 2 diabetes

Recent advances in technology make easier to look for regions in whole genome linked to different DN phenotypes. This approach identified regions and putative genes not previously known to be associated with DN and it could raise new candidate genes. Moreover, new targets for drug development may come into sight, since some of the genes found are novel and have not been previously implicated in the pathogenesis of DN.

Association studies of candidate genes have been performed aiming to identify polymorphic variants associated with DN or with different degrees of renal disease. Often, genes that play a role in the expression of proteins that are related to the modulation of cytokines, proteins involved in the glycid and lipid metabolism, in the formation of extracellular matrix, in blood pressure homeostasis, and in insulin sensitivity, have been considered candidates for the development of DN. However, the studies have not been successful in identifying genes that consistently show an association with DN. Replication studies has demonstrated conflicting results. The evaluation of 360 thousand polymorphisms in patients with type 1 DM, with and without DN, showed a total of 13 polymorphisms located at 4 loci in two independent cohorts of subjects strongly associated with the presence of DN. Some of these polymorphisms are located in genes highly expressed in the kidney with DN, and its development over time

Another approach that has been used to investigate the genetics of DN involves the study of microRNAs role on this process. These are non-encoding short RNAs that induce post-transcriptional protein modifications. Little is known about these molecules and their role in DN. In a study, microRNA mirR-192 expression was increased in the glomeruli of rodents with DM . Their induction by TGF-β in mesangial cells caused increased collagen synthesis and suggests that this type of molecule may be implicated in the development of DN, opening up a new prospect of research in elucidating the pathogenesis of this DM complication. The replication of this finding and this type of approach must be better explored in studied conducted in human beings.

As previously stated, Brazilians of African descent have more aggressive renal disease than people of European ancestry This could be due to several reasons, such as the presence of different risk factors, different access to medical attention, and socioeconomic differences. However, none of the assessed known risk factors were different between African and Europeans make unclear an explanation for the different rates of DN between black and white subjects. Unfortunately, data on socioeconomic status were unavailable. An alternative explanation for this observation, but hard to prove, would be a different genetic susceptibility.

DIABETIC NEPHROPATHY TREATMENT

People with diabetes often focus on keeping their blood sugar levels in the right ranges. And while it is important to control blood sugar, it turns out that controlling blood pressure is at least as important. That's because high blood sugar and high blood pressure work in concert to damage the blood vessels and organ systems. (See "Treatment of diabetic nephropathy".)

For these reasons, the most important things you can do to stall kidney disease and protect against other diabetes complications are to:

- Make healthy lifestyle choices
- Keep your blood sugar as close to normal as possible (see 'Manage blood sugar levels' below).
- Keep your blood pressure below 130/80, if possible (see 'Manage high blood pressure' below).

Lifestyle changes — changing your lifestyle can have a big impact on the health of your kidneys. The following measures are recommended for everyone, but are especially important if you have diabetic nephropathy:

- Limit the amount of salt you eat (see "Patient information: Low sodium diet")
- If you smoke, quit smoking (see "Patient information: Quitting smoking")
- Lose weight if you are overweight (see "Patient information: Diet and health" and "Patient information: Exercise" and "Patient information: Weight loss treatments")

Manage blood sugar levels — keeping blood sugars close to normal can help prevent the long-term complications of diabetes mellitus. For most people, a target for fasting blood glucose and for blood glucose levels before each meal is 80 to 120 mg/dL(4.4 to 6.6 mmol/L); however, these targets may need to be individualized. (See "Patient information: Self-blood glucose monitoring in diabetes mellitus".)

A blood test called A1C is also used to monitor blood sugar levels; the result provides an average of blood sugar levels over the last one to three months. An A1C of 7 percent or less is usually recommended; this corresponds to an average blood glucose of 150 mg/dL (8.3 mmol/L) (table 1). Even small decreases in the A1C lower the risk of diabetes-related complications to some degree.

Manage high blood pressure — many people with diabetes have hypertension (high blood pressure). Although high blood pressure causes few symptoms, it has two negative effects: it stresses the cardiovascular system and speeds the development of diabetic complications of the kidney and eye. A healthcare provider can diagnose high blood pressure by measuring blood pressure on a regular basis. (See "Patient information: High blood pressure in adults".)

The treatment of high blood pressure varies. If you have mild hypertension, your healthcare provider may recommend weight loss, exercise, decreasing the amount of salt in the diet, quitting smoking, and decreasing alcohol intake. These measures can sometimes reduce blood pressure to normal. (See "Patient information: High blood pressure, diet, and weight".)

If these measures are not effective or your blood pressure needs to be lowered quickly, your provider will likely recommend one of several high blood pressure medications. Your provider can discuss the pros and cons of each medication and the goals of treatment. (See "Patient information: High blood pressure treatment in adults".)

A blood pressure reading below 130/80 is the recommended goal for most people with diabetic nephropathy.

Blood pressure medications — Most people with diabetic nephropathy need at least one medication to lower their blood pressure. Several medications can be used for this purpose, but a medication known as an angiotensin converting enzyme inhibitor (abbreviated ACE inhibitor) or a related drug known as an angiotensin receptor blocker (ARB) are used most commonly. ACE inhibitors are generally used first because they have been available longer than ARBs.

ACE inhibitors and ARBs are particularly useful for people with diabetic nephropathy because they decrease the amount of protein in the urine and can prevent or slow the progression of diabetes-related kidney disease. In fact, the kidney benefits of ACE inhibitors and ARBs are so robust that healthcare providers sometimes prescribe them for people with diabetic nephropathy who have normal blood pressure.

Still, despite their kidney-protecting abilities, ACE inhibitors and ARBs do have their downsides. For instance, ACE inhibitors cause a persistent dry cough in 5 to 20 percent of the people who take them. Some people get used to the cough; others find it so disruptive that they cannot continue taking an ACE inhibitor. For them, ARBs are often a good alternative, because ARBs are less likely to cause a cough.

In rare cases, you can have more serious side effects with ACE inhibitors and ARBs. These include a decrease in kidney function or a condition called hyperkalemia, in which too much potassium accumulates in the blood. To monitor for these and other side effects, healthcare providers sometimes run blood tests soon after starting these drugs. In some people, the medications will need to be stopped.

More information on the risks and side effects of ACE inhibitors and ARBs is available (see "Major side effects of angiotensin converting enzyme inhibitors and angiotensin II receptor blockers").

Monitor for signs of change — after beginning treatment and lifestyle changes to stall kidney disease, you will need to have repeat urine and blood tests to determine if urine protein levels have improved. If the urine protein levels have not improved or your kidney function has worsened, your healthcare provider may need to adjust your medications or recommend other strategies to protect your kidneys.

PREGNANCY AND DIABETIC NEPHROPATHY

If you have diabetes and are interested in getting pregnant, it is important to talk with your healthcare provider well in advance, especially if you have diabetic nephropathy. Diabetes and its attendant problems can increase the risk of complications in pregnancy, especially in women with decreased kidney function. However, many women with mild diabetic nephropathy have normal pregnancies and healthy babies. To ensure the best outcome with a pregnancy, the most important thing you can do is to keep your blood sugar and blood pressure under tight control. However, women who are pregnant or attempting to get pregnant should not take ACE inhibitors or ARBs, as these drugs can cause birth defects. Instead, other medications (such as calcium channel blockers) are used during pregnancy to keep the blood pressure in check.

Prevention

All persons with diabetes should have a yearly checkup with their doctor to have their blood and urine tested for signs of possible kidney problems. Persons with kidney disease should avoid contrast dyes that contain iodine, if possible. These dyes are removed through the kidneys and can worsen kidney function. Certain imaging tests use these types of dyes. If they must be used, fluids should be given through a vein for several hours before the test. This allows for rapid removal of the dyes from the body. Commonly used nonsteroidal anti-inflammatory drugs (NSAIDs), including ibuprofen, naproxen, and prescription COX-2 inhibitors such as celecoxib (Celebrex), may injure the weakened kidney. You should always talk to your health care provider before using any drugs

CONCLUSION

Developing countries such as India with its large burden of diabetes and vulnerability to the chronic complications including diabetic nephropathy, obviously must evolve strategies for primary prevention of diabetes and also for prevention of its secondary complications. Early screening and appropriate therapeutic intervention are the first steps towards achieving this goal. Diabetic nephropathy is a chronic complication of DM with a growing incidence. Therefore it is essential to have a better understanding of it, especially in relation to prevention and aggressive management to avoid progression to ESRD. Besides, its direct association with cardiovascular complications makes it imperative to perform intensive, early management of the risk factors. The study of DN has evolved a lot as regards its pathophysiology, stages of renal involvement and, especially, the therapeutic instruments available. Early detection of DN, the multifactorial approach targeting the main risk factors (hyperglycemia, hypertension, dyslipidemia and smoking), and the use of renoprotective agents such as the drugs that act on the renin-angiotensin-aldosterone system, may delay

progression of kidney disease in DM, besides reducing cardiovascular mortality.

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