

This Weeks Question:

The Preferred Diuretic in Diabetic Nephropathy

Which diuretic should be preferred in diabetic nephropathy with edema and normal creatinine values or with compromised renal function and creatinine levels around 2-3 mg/dL?

1. Furosemide
2. Chlorthiazide
3. Bumetanide
4. Hydrochlorthiazide
5. 1 & 3

Diabetic nephropathy, with its associated hypertension, is a fluid expansion/sodium retention state, although the reasons may differ between type 1 and type 2 diabetes. In type 1 diabetes, hypertension and fluid retention are almost entirely due to glomerular and tubular damage, thus they become manifest with increasing albuminuria.^[1] In type 2 diabetes, hypertension is present in over 25% of patients at diagnosis and is a part of the metabolic syndrome of insulin resistance. The resulting hyperinsulinemia has secondary effects on the renal tubule, leading to salt and water retention and sympathetic nervous system activation.^[2]

Other factors that may lead to edema are peripheral neuropathy, hypoalbuminemia secondary to nephrosis, local vascular factors such as venous insufficiency, and possible drug-induced effects -- for example, dihydropyridine calcium channel blocking agents. Thus there are several potential causes, and it is important to exclude them because, of course, not all will reflect sodium/fluid overload and thus be responsive to diuretics.

Assuming that the edema is due to nephropathy and not nephrosis and is associated with hypertension, then treatment is an important part of blood pressure control and consequent nephroprotection. ***In these circumstances, a loop diuretic such as furosemide or bumetanide is required, because low-dose thiazides are often not potent enough and higher doses can have unwanted metabolic effects on glycemia and lipidemia.***^[3] The early studies of Parving and others^[4] of blood pressure treatment in type 1 diabetic nephropathy used furosemide as a key component of the treatment regimen. In the RENAAL (Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan) study of losartan in type 2 diabetic nephropathy,^[5] around 58% of patients were on a diuretic at the outset and 84% at the end (mean follow-up, 3.4 years). These patients had a mean baseline serum creatinine of 1.9 mg/dL. In the IDNT (Irbesartan Diabetic Nephropathy Trial) of irbesartan vs amlodipine vs conventional antihypertensive therapy in type 2 nephropathy,^[6] investigators have reported that split doses of loop diuretics were particularly effective (unpublished but discussed at investigator meetings). The synergistic effect of diuretics and drugs that block the renin-angiotensin system makes them an integral part of most modern antihypertensive regimens in diabetic nephropathy. It is worth mentioning, however, that dietary salt restriction will also augment the hypotensive action of this combination.

References

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