kidney news

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Introduction

Diabetes mellitus and diabetic nephropathy.

Recent research is now being published, that supports our previous suspicions. It is nearly ten years since data was first published revealing the benefits of ACE inhibitors and improved diabetic control on renal tissue in type I diabetes mellitus patients.
There is probably some differences in the nephropathy physiology of both type I and type II diabetes. The histopathology is similar. The clinical picture is similar, except – perhaps – the severity of macrovascular changes in type II diabetes mellitus seen, especially in groups such as in the Polynesian population. The survival of the type II diabetes mellitus patients with established diabetic nephropathy is also poor.

Type I diabetes mellitus patients with established diabetic nephropathy (more than micro-albuminuria) progress to end-stage renal failure in 7 to 10 years, and longer with better control of HbA_{1c}, and BP and use of ACE inhibitors.

The question remained over the benefits of ACE inhibitor therapy and diabetes control in type II diabetes mellitus patients. It is pleasing to see that evidence supporting the management of diabetes mellitus types I ***and II*** similarly, for both diabetes control and ACE inhibitors is now available.

With the recent evidence of therapies delaying the progression of established nephropathy in type II diabetes mellitus patients we can hope the two to four year period from diagnosis to ESRF will be also prolonged.

We do not know if good diabetic control in ESRF patients will benefit their survival and/or reduce the macrovascular complications. Similarly we do not know which group will gain greater benefit attaining good glucose and blood pressure control aggressively - type I or type II diabetes mellitus. Such studies may never be undertaken.

We must go with what we have now. Clearly good glucose control by keeping the HbA_{1c} in the optimal range (monitoring HbA_{1c} every three months should be adequate) and blood pressure control are even more important goals to strive for.

ACE inhibitors and cough.

One of the more common ACE inhibitor side-effects is dry-cough. Various reports put the incidence of cough at between 5 and 39%. Not always does this side-effect lead to discontinuation of the ACE inhibitor, fortunately. On enough occasions, however, therapy is ceased and the benefits of the ACE inhibitor lost.

Therapies to either treat the cough, or angiotensin II receptor blockers have since been tried.

The cough seems to be related to a genetic predisposition, and a particular genotype is associated with the ACE-induced cough. Short of gene analysis, how to identify these high-risk people is not yet available. Meanwhile anti-cough remedies such as cromoglycate, baclofen, theophylline, or NSAIDs – even oral iron! - will continue to be used.

A second option is the application for and approval of an A-II receptor blocker.

Angiotensin II receptor blockers.

These agents have quickly replaced ACE inhibitors where a cough side effect has occurred, rather than the additional of cough-therapies. The pharmaceutical companies have been quick to show the renal benefits of ACE inhibition are similarly seen with the A-II receptor blockers – leaving very few patients suffering with the ACE inhibitor cough.

But which is better “renally” - ACE or A-II blockade?

WHAT'S IN HERE THIS TIME?

ACE and A-II in combination.

Some South Auckland diabetes mellitus ***type II*** patients took part in a multi-centre, multi-national study recently published. The trial studied the A-II receptor blocker irbesartan. Blood pressure control, mortality and diabetic nephropathy (the time taken for the serum creatinine to double) were some of the end-points.

Mortality reduced in the treated arm. Blood pressure control was similar in the irbesartan and placebo arms of the study.

From the renal failure progression aspect, irbesartan was effective in prolonging the time taken for the serum creatinine to double, and hence delaying the time to end-stage renal failure.

So what? This is further support to the theories, and further evidence that A-II receptor blockers, along with ACE inhibitors are renal friendly. They provide protection to the renal tissue over and above that seen with just improved blood pressure control. Irbestartan lowered the number of patients whose diabetic nephropathy progressed.

Clearly, in impaired renal function, stimulation of the reno-angiotensin system is not a good thing; and blockade of either the receptor or enzymatic pathway is a good thing.

In a subsequent analysis of this irbesartan in hypertensive and diabetic patients study, the results equated to:
The need to treat with irbesartan
15 patients
with **hypertension** and **type II diabetes mellitus**
for **three years**
to save
one patient from **worsening renal function/end-stage kidney failure or death**.

So where from here for diabetes mellitus patients?

1. Type I and type II diabetes patients should optimise glucose control at all times.
2. Patients with microalbuminuria, or established nephropathy (with macroalbuminuria, with or without impaired renal function) should definitely be considered for an ACE or an A-II blocker (nothing new here).
3. Of interest, some early evidence suggests that we are not using enough ACE inhibition. We should be using much higher doses of ACE inhibition (eg. quinapril 40mg/day) even in the presence of renal dysfunction, and gain further renal protection than lower doses of ACE inhibitors.
4. And of more interest, the ***combination*** of a high dose of an ACE inhibitor with an A-II receptor blocker is more reno-protective than either agent alone.

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Investigation of urinary calculi
Investigation of proteinuria and haematuria
Investigation and management of impaired renal function.
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