Current and future management of diabetic renal failure

(or, how we see your patients)

Why are we interested?

- Number of patients
- Morbidity
- mortality

Contribution to “new starts” on renal replacement therapy (RRT) (UK, 2003)

- Diabetes as primary renal disease:
  22% < 65, 15% > 65
- Co-existent diabetes:
  5% < 65, 10% > 65
- OVERALL 26% DIABETES

Co-morbidity at start of RRT (UK 2003)

% with disease	Non-diabetics	Diabetics
cardiovascular	23	32
cerebrovascular	11	17
Peripheral vasc	11	28
COPD	8	6
malignancy	13	4
Liver disease	2	2

Unrecorded but significant…

- Blindness
- Memory loss
- Depression
- History of poor adherence
- Limitations of access to health care

Mortality

- Greater in diabetic patients at all age groups and all time periods
- One-year survival 83% < 65, 72% > 65
  RR 1.65 v. non-diabetics ($p<0.0001$)

  (UK 2003, 90 day exclusion applied)
- Five-year survival 30% (EDTA, SRR)

Morbidity of diabetic patients on RRT – bed stay in Western Infirmary Renal Unit

- Prevalence in RRT population 12%
- Admissions > 10 nights 16%
- Bed nights occupied 22%
  (29% of <65s, 20% post-rehab)

Peripheral vascular disease leading to amputation

- Medicare data 1991-4
  (*Eggers et al. Kidney Int 2000 56 1524)*

  Diabetes + renal failure = 10 x diabetes

  2/3 die within 2 yrs of amputation

- Newer VA data
  (*Young et al. Diabetes Care 2006 495)*
  diabetic nephropathy = 3 x diabetes
  diabetes + renal failure = 4 x diabetes

Clinical consequences of delay in amputation

- Malnourished, wasted, immobile patient
- Oedema (albumin 20g/l)
- Pressure necrosis
- C difficile
- MRSA
- Opiate toxicity

Prevention is better than cure (or failure to cure)

- Is the management of diabetic nephropathy the same as that of
  a) other vascular complications of diabetes?
  b) other renal diseases?

eGFR, CKD

- Stage 3 CKD = eGFR 30-59ml/min
- Stage 4 = 15-29
- Stage 5 = <15

Cardiovascular interventions

- Aspirin
- Antihypertensives
- Blockers of Renin-angiotensin system
- Statins

Blood pressure control

- Excellent evidence at all stages
- Targets keep falling

Renin-angiotensin system blockade

- Reduces proteinuria
- Delays progression of nephropathy, BUT
- Difficult to sustain in severe renal impairment (hyperkalaemia)
- Note effect of pre-existing hyporeninaemic hypoaldosteronism

ACE inhibition in stage 4 CKD

N Engl J Med 2006 354 131-140 & 189-191

Benazepril is safe (Hou et al)

"Their conclusions may come as news to the many clinicians who avoid or abandon the use…in stage 4 chronic kidney disease" (Hebert, Editorial)

Statins – and cholesterol?

- Easy till renal failure…
- Is cholesterol a risk factor in dialysis patients?
- Eg atorvastatin in type II diabetes –
  CARDS study in favour, BUT
- no overall benefit in haemodialysis patients
  (*Wanner et al N Engl J Med 2005 353 238-248)*

CKD Stage IV

- Anaemia
- Renal osteodystrophy
- Vascular calcification

Causes of anaemia in renal failure

- Erythropoietin deficiency
- Reduced red cell life span (2/3 normal)
- Everything else eg iron deficiency

- Treated with erythropoietin or analogues

Calcium/phosphate metabolism

- Alfacalcidol?
- Phosphate binders…
  often prescribed, rarely taken

  calcium-based or sevelamer

Sevelamer (Renagel)

- Less calcification
- Lower cholesterol
- Lower glucose?
- Much more expensive
- No more palatable

When to start RRT

- Early start? Lead time bias in studies
- Symptoms (earlier in diabetic patients)
- Biochemistry
- Option of conservative management

Dialysis

- Haemodialysis (2/3 in UK)
- Peritoneal dialysis –
  may be nocturnal automated peritoneal dialysis, with glucose-based dialysate by night and icodextrin in situ by day

Transplantation

- Kidney
- Kidney-pancreas

- Both apply only to fitter patients

Immunosuppressive drug therapy

- Effects on blood pressure
- Effects on lipids
- Effects on glucose tolerance

Islets and stem cells

- Five-Year Follow-Up after Clinical Islet Transplantation *(Ryan et al. Diabetes 2005 54 2060-2069)*
- Islet Transplantation as a Treatment for Diabetes – A Work in Progress *(Robertson. N Engl J Med 2004 350 694-705)*
- No Stem Cell is an Islet (Yet) *(Stainier. N Engl J Med 2006 354 521-523)*

Hope for the future

- Finnish registry data of Type I diabetes *(JAMA 2005 294 1782-1787)*
- Risk of nephropathy falling
- Survival improving