Renal and Transplant Medicine Symposium

RJ Molyneux
ST7 Nephrology, York Teaching Hospitals, York, UK

The Renal and Transplant Medicine Symposium was held on 10 October 2013 at the Royal College of Physicians of Edinburgh

DECLARATIONS OF INTERESTS No conflicts of interest declared.

Correspondence to ***RJ Molyneux***

e-mail ***rebekah.molyneux@nhs.net***

INTRODUCTION

This symposium attracted nephrologists, intensivists, general practitioners and other members of the multidisciplinary team from around the world, and was streamed live to nine countries. It aimed to address some of the challenges in managing patients with chronic kidney disease (CKD), including cardiovascular disease, anaemia, the transition period from adolescent to adult nephrology care and some of the issues around transplantation.

SESSION ONE: CHRONIC KIDNEY DISEASE OR CARDIO-KIDNEY DISEASE

Chronic kidney disease is common, but is it as common as the epidemiologists would have us believe? Professor Meguid El Nahas (Professor of Nephrology, Sheffield Kidney Institute) explained that the predicted prevalence of CKD is based on epidemiological studies which only look at single creatinine readings, not a series as recommended by the Kidney Disease Outcomes Quality Initiative (KDOQI).[1] Using epidemiological data only, up to 50% of the world's population is predicted to be at risk of developing CKD; however people over the age of 60 commonly have an estimated glomerular filtration rate (eGFR) of about 30%. This does not predict who will develop End Stage Renal Disease (ESRD). He discussed how a better predictor would be the presence of cardiovascular risk factors and proteinuria. Those with a low eGFR but without any cardiovascular risk factors or albuminuria do not have a reduced life expectancy.[2] Further development of models for cardiovascular risk in CKD patients is required to accurately predict the future disease burden.

Dr David Wheeler (Reader in Nephrology and Honorary Consultant Nephrologist, UCL Medical School and President of the Renal Association) provided an overview on managing advancing CKD. Only 19.9% of those with CKD 4 progress to end stage kidney disease; the majority of patients with CKD 1–4 will die from another cause. Managing cardiovascular risk factors such as obesity, diabetes, hypertension and proteinuria all help to reduce the risk of renal progression, however aspirin should be used with caution in patients with advancing CKD, due to increased bleeding risk.

Dr Bryan Conway (MRC Clinician Scientist, University of Edinburgh) discussed the specific risk factors associated with diabetic patients who develop nephropathy. The incidence is small, with only 0.1% of diabetics reaching end stage renal disease (ESRD). Diabetic nephropathy develops most commonly in patients with poor glycaemic control, a high salt diet, hypertension and obesity. However this is not always the case; there is some evidence that DNA repair is impaired in those who develop diabetic nephropathy,[3] which is associated with an increased risk of parental cardiovascular disease.

SESSION 2: URINALYSIS – BLOOD IS THICKER THAN WATER

Dr Jonathan Barrett (Consultant Nephrologist, Leicester General Hospital) reviewed how urine has been used over the centuries and continues to be used to assess disease. Pregnant women have used it to predict pregnancy for thousands of years, while ants are attracted to the urine of diabetics. Urine can be every colour of the rainbow and in the presence of ethylene glycol overdose may also be fluorescent.

Albuminuria is commonly used as a predictor of renal disease progression and is recommended in all patients with an estimated GFR <60 ml/min. He suggests that there should be a biomarker in urine which detects changes in renal function. New areas of interest, which may reveal new biomarkers, are exosomes shed from podocytes membranes. Podocyte injury is involved in both the initiation and progression of renal disease. These may give a greater insight into cellular function within the kidney and lead to an early indicator of kidney damage.

Professor Iain MacDougall (Professor of Clinical Nephrology, King's College Hospital, London) introduced three H's in his talk on new therapies for renal anaemia: hematide, hypoxia-inducible factor (HIF) stabilisers and hepcidin, as possible future targets for stimulating erythropoeisis. Hematide mimics erythropoietin (EPO) in regulating red cell production. A synthetic peptide was recently developed which showed a dose dependent increase in haemoglobin, however it had to be withdrawn due to hypersensitivity reactions.[4] Professor MacDougall

also discussed HIF stabilisers, which would regulate EPO production to avoid variability in levels. However, there is some debate over how safe it is to have high haemoglobin levels and increased activation of substances such as vascular endothelial growth factor (VEGF). However populations with high levels of haemoglobin e.g. those living at high altitudes, do not seem to suffer detrimental effects from the use of HIF.[5] hepcidin regulates metabolism and is a key mediator of iron restriction in anaemia. If the actions of hepcidin were blocked then the supply of iron to the bone marrow could be increased. Speigelmers are chemically synthesised non-immunologic alternatives to antibodies; a Speigelmer is being developed to neutralise the effects of high levels of hepcidin and is currently in pre-clinical phase trials.[6]

SESSION THREE: DIFFICULT CLINICAL SCENARIOS IN NEPHROLOGY

Dr Rachel Hilton (Consultant Nephrologist, Guy's & St Thomas' Hospital, London) considered the causes of kidney disease in patients with HIV. These patients are at increased risk of AKI, and CKD is the fourth most common cause of death. Risk factors are the same as for the general population but patients of African ancestry are at particularly high risk. HIV-associated nephropathy (HIVAN) usually presents with very advanced disease and highly active antiretroviral therapy (HAART) has led to a more favourable outcome. The risk of patients reaching ESRD had been reduced by 40% with the advent of HAART and patients on dialysis now have a similar life expectancy to other patients with ESRD. Bearing this in mind, with careful monitoring of immunosuppressive regimens and prophylaxis against opportunistic infection, transplantation is also becoming an option for patients with HIV.[7]

Dr Chris Laing (Clinical Lead Acute Kidney Injury/Renal Patients, UCL Centre for Nephropathy, Royal Free Hospital, London) gave an overview of water and sodium metabolism and presented some clinical approaches to hyponatremia. Hyponatraemia is common in inpatients and is an important cause of increased length of hospital stay. The rate of change of sodium and the underlying cause determines the individual approach to management of hypo and hypernatraemia. Serum and urine osmolalities and urinary sodium are helpful in determining the cause, while tolvaptan may be used to treating resistant hyponatremia in patients with SIADH, heart failure and cirrhosis.[8]

Professor Neil Turner (Professor of Nephrology, University of Edinburgh and Royal Infirmary of Edinburgh) discussed the sometimes very challenging transition from paediatric to adult nephrology care. Thought-provoking cases were presented which raised questions about the natural developmental stages that children go through on their way to learning how to live with their condition. Some guidance was provided on how to make this process as smooth as possible: ensure all paediatric patients attend a transition clinic; simplify the drugs prescribed; use technology to engage with patients; don't provide them with excuses and address their anxieties. The latter may be normal teenage concerns about exams and boyfriends/girlfriends, or may be about having blood tests or seeing older patients looking ill.

SESSION FOUR: NEW HORIZONS IN TRANSPLANT MEDICINE

Professor J Andrew Bradley (Professor of Transplantation, Addenbrooke's Hospital) reviewed the advances that have been made in expanding the donor pool. This has largely been due to an increase in organs from donors after cardiac death (DCD), which seem to do as well as kidneys from donors after brain death (DBD), even though there is an increase in delayed graft function. Living donation numbers have also doubled, with an increasing number of altruistic donors. The advances in pre-conditioning have led to a rise in ABO-incompatible transplants. When a living kidney donor and recipient are incompatible with each other, the paired matching scheme may match them with another pair in a similar position, which further increases the likelihood of patients receiving a transplant. However, due to the advancing age of donors and more marginal kidneys being accepted, the expanding pool has come at a cost to quality.

Professor Anthony Warrens (Dean for Education, Barts and the London School of Medicine and Dentistry and Professor of Renal and Transplantation Medicine) reviewed the issues around the use of calcineurin inhibitors, and argued that it is not their nephrotoxicity that should restrict our use of them, but rather their vasculotoxic effects. When we review patients who have died with a functioning graft, a more logical argument for reducing calcineurin exposure would be if vascular events had led to premature deaths.

Immunosuppression following transplantation can lead to an increased risk of infection, and particularly in renal transplant patients, a risk of significant BK virus, cytomegalovirus (CMV) and varicella zoster virus (VZV) infections. Dr Nicholas Torpey (Consultant Nephrologist, Addenbrooke's Hospital, Cambridge) discussed a screening programme for BK virus in transplant patients. With 82% of the population having latent infection during childhood, reactivation of the virus has caused significant morbidity in transplanted patients. Biopsies at regular intervals revealed an increased incidence in BK viraemia and as a result of the screening programme no grafts were lost due to BK

virus infection. This type of programme relies on an efficient and easily accessible biopsy and pathology service, which is not available everywhere.

TAKE-HOME MESSAGE

Chronic kidney disease is the largest single problem facing nephrology services in the UK, and yet its diagnosis and prognosis remain difficult to predict. It impacts heavily both on long-term disease burden and acute illness, and its management encompasses diverse aspects of clinical practice across traditional specialty boundaries. It was evident from the symposium that new avenues are open for the development of novel diagnostic tools and therapeutic agents, but it can be unclear how best to integrate these into everyday practice. The scope of transplantation continues to broaden, bringing with it new challenges but also new possibilities for patients.

REFERENCES

1 McCullough K, Sharma P, Ali T et al. Measuring the population burden of chronic kidney disease: a systematic literature review of the estimated prevalence of impaired kidney function. *Nephrol Dial Transplant* 2012; 27:1812–21. http://dx.doi.org/10.1093/ndt/gfr547

2 Gansevoort RT, Correa-Rotter R, Hemmelgarn BR et al. Chronic kidney disease and cardiovascular risk: epidemiology, mechanisms, and prevention. *Lancet* 2013; 382:339–52. http://dx.doi.org/10.1016/S0140-6736(13)60595-4

3 Kottgen A, Pattaro C, Boger CA et al. New loci associated with kidney function and chronic kidney disease. *Nature Gen* 2010; 42:376–84. http://dx.doi.org/10.1038/ng.568

4 Macdougall IC, Fishbane S, Duliege AM. Peginesatide for anemia in chronic kidney disease. *N Engl J Med* 2013; 368:1553–4. http://dx.doi.org/10.1056/NEJMoa1203166

5 Smith TG, Robbins PA, Ratcliffe PJ. The human side of hypoxia-inducible factor. *Br J Haematol* 2008; 141:325–34. http://dx.doi.org/10.1111/j.1365-2141.2008.07029.x

6 Schwoebel F, van Eijk LT, Zboralski D et al. The effects of the anti-hepcidin Spiegelmer NOX-H94 on inflammation-induced anemia in cynomolgus monkeys. *Blood* 2013; 121:2311–5. http://dx.doi.org/10.1182/blood-2012-09-456756

7 Stock PG, Barin B, Murphy B et al. Outcomes of kidney transplantation in HIV-infected recipients. *New Engl J Med* 2010; 363:2004–14. http://dx.doi.org/10.1056/NEJMoa1001197

8 Schrier RW, Gross P, Gheorghiade M et al. Tolvaptan, a selective oral vasopressin V2-receptor antagonist, for hyponatremia. *New Engl J Med* 2006; 355:2099–112. http://dx.doi.org/10.1056/NEJMoa065181