ROYAL COLLEGE of PHYSICIANS of EDINBURGH

Evening Medical Update: Renal Medicine
September 2022

The renal transplant patient in AMU - Dr Caroline Whitworth, Consultant Nephrologist and Medical Director for Acute Services, Royal Infirmary of Edinburgh

Dr Whitworth, any benefit vs risk study on not removing the old kidney during transplant?

No studies that I am aware of. Unless there is an indication to remove native kidneys (ie infection, severe hypertension, massive polycystic kidney) then it is major surgery that adds no benefit. Failed transplants may be removed to create room for further transplant on same side.

Dr Whitworth, which primary conditions, which led to the renal failure in the first place, could recur in a transplanted kidney?

IgA, FSGS, Diabetic nephropathy, MCGN are main ones.

Dr Whitworth, how does prednisolone (steroids) increased risk of GI haemorrhage?

Corticosteroid use is associated with increased risk of gastrointestinal bleeding and perforation, statistically significant for hospitalised patients only. For patients in ambulatory care, the total occurrence of bleeding or perforation was very low, and the increased risk is not statistically significant. In the stomach, high doses of glucocorticoids inhibit prostaglandin biosynthesis, thereby inhibiting the gastric alkaline response and producing severe gastric lesions. However, in man, peptic ulcer disease is not clearly associated with glucocorticoid therapy. Exacerbation of subclinical intestinal infections and perforative lesions have been observed in patients given glucocorticoids.

Dr Whitworth, ss procalcitonin a useful Ix in Tx patients with regards to bacterial infection detection, or is this result skewed in transplant patients?

I have no specific knowledge about this. Have not used it clinically (except in context of covid)

Dr Whitworth, is NODAT reversible?

Yes, with reduction of cessation of steroids, weight loss, and change of diet.

Dr Whitworth, during acute infections do you still continue tacrolimus or withhold?

Usually continue uness severe life threatening infections, in which case decision may be to withhold recognising that graft loss is likely.

Dr Whitworth, as a GP working in the community occasionally we see transplant patients with a short history vomiting who in that case may not be absorbing their immunosuppressant medication. How long can you trial an anti emetic for before you need to think of admission?

Good question, 2-3 days. Have to say that most patients do still seem to manage to absorb tacro even if frequent vomiting, we rarely need to look at IV administration even in patients with vomiting

Dr Whitworth, is there a place for anticoagulant in these patients?

In the peri-operative period yes – we use LMWH but not routinely beyond discharge. No good evidence for aspirin in primary prevention in transplant patients.

Dr Whitworth, can we use fructosamine to diagnose diabetes control or diagnosis of diabetes

Yes

Dr Whitworth, may be silly question, any development about xenotransplantation?

Some developments, but we are still a long way away, I think. Issues are latent viruses, and antigenicity.

Dr Whitworth, we have a patient with a second transplanted kidney. Would the first transplanted kidney be removed? If a transplant fails, does the patient need to stay on immunosuppressive drugs?

First transplant does not always need to be removed – often left and new transplant goes into other side. If a graft fails, and there is a reasonable likelihood of a future subsequent transplant then there is evidence to recommend continuing immunosuppression to reduce risk of increased sensitisation to transplanted HLA antigens which would otherwise increase risk of a positive crossmatch to a future transplant, assuming shared antigens.

An update on renal vasculitis - Dr Neeraj Dhaun, Senior Lecturer in Nephrology, University of Edinburgh and Consultant Nephrologist, Royal Infirmary of Edinburgh

Dr Dhaun, ANCA negative vasculitis - is diagnosis made on histology in these patients? Are there other ix that can increase clinical suspicion of vasculitis if Bx is not possible (eg acutely unwell patient not fit for Bx)

Generally, to make the diagnosis of ANCA-negative vasculitis you need histological evidence of vasculitis. Otherwise, the diagnosis relies on a physician experienced in vasculitis making the diagnosis on clinical grounds. The major differentials being infection and/or cancer.

Dr Dhaun, why give both Rituximab and cyclo together and not alone?

This is a treatment strategy followed by some centres including our own. We find cyclo works faster than rituximab and the combination allows more rapid steroid taper and results in better long-term outcomes.

Dr Dhaun, for the PR3 +ve vasculitis case, is there a reason why she was not pulsed with IV methylpred initially?

There is no evidence that intravenous methylprednisolone adds anything to oral prednsilone. However, there are data that it adds to steroid burden and associated longer-term complications. The trend now is to use lower doses of glucocorticoid [see PEXIVAS study and Dhaun & McAdoo, Kidney Int 2022].

Dr Dhaun, do ANCA levels always fall with response to treatment? Isn't ANCA levels told to not always correlate with disease activity?

This varies depending on the individual patient.

Dr Dhaun, comments on Cyclophosphamide treatment by generalists as emergency when patients present critically unwell and not able to transfer to specialist units?

This should be discussed with someone experienced in prescribing and delivering cyclophosphamide. Often steroids can stabilise the patient and allow transfer. However, to deliver IV cyclo you will need a pharmacy that can make it up. Also, critically unwell patients will need other important causes like infection ruled out first. I have rarely given cyclo in the first 24h as an emergency.

Dr Dhaun, is risk of PE DVT increased in these patient group ?

Yes, significantly, and most commonly during active inflammation. The co-existence of a DVT/PE and its treatment needs to be weighed against the risks of anticoagulation especially in those with pulmonary haemorrhage.

Dr Dhaun, whats the approach for the persistent low positive ANCA titres patients despite treatment?

The relevance of these varies between patients but treatment should not be guided by ANCA titre alone.

Dr Dhaun, if clinical history and ANCA serology very convincing of PR3 or MPO vasculitis, is a renal biopsy necessary? Would it change management?

It depends on the situation and level of biopsy-associated risk. If safe, and in younger patients I will biopsy before treatment as it gives an insight of what kidney function trajectory might be and guide duration/intensity of treatment. In the very elderly, we may forego kidney biopsy.

Dr Dhaun, similar to previous Qs: is biopsy always necessary prior to starting treatment?

Not always and it may not be practical for example in those presenting with pulmonary haemorrhage.

Dr Dhaun, great talk. Sorry if I missed this but do you ever use IVIG for induction, especially if worry of active infection?

I do not use IVIg.

Dr Dhaun, what skin manifestation to look out for for Vasculitis? And are they enough to go on a chase of vasculitis based on them?

This may be a better Q for a dermatologist but ischaemic and embolic manifestations should prompt consideration of vasculitis (small and medium vessel) or other conditions such as cryoglobulinaemia.

Dr Dhaun, when do you introduce Avacopan?

Currently, not licensed so watch this space!

Dr Dhaun, thanks Bean. Are there any other indications to avoid steroids beyond advanced age and significant psych history (esp depression & bipolar)?

These are the main ones but also in those with significant osteopenia/osteoporosis or wit previous significant steroid exposure.

Dr Dhaun, in patients with lung involvement, does initiation of steroids int he acute setting affect sensitivity of bronchoscopy?

No, and this is also true of kidney biopsy. Obviously, if you wait weeks then the relevant findings may have disappeared. I would not withhold treatment if the diagnosis is secure whilst waiting for an investigation.

Chronic kidney health - Dr Jane Goddard, Consultant Nephrologist, Royal Infirmary of Edinburgh

Dr Goddard, your view in role of combined ACEI & ARB nn patient with proteinuria. thank you

It definitely works as we used to do this but MRHA guidance is now very strongly not to combine because of the risk of hyperkalaemia and AKI.

Dr Goddard, Good GP consult or lifestyle gurus in the community?

Like Joe Wicks? I think he has been very effective for some people but we need this to be more prevalent – make the good way the easy way and the 'cool' way. Essentially we need lifestyle Gurus in School! – We set the patterns that will stay with us for life very early on – this is the preventative stage.

Dr Goddard, any guidance for intervention autoinflamamtory disease patients earlier intervention thresholds?

Not sure what this one means – sorry. To intervene on inflammatory renal disease earlier means earlier diagnosis which requires a high index of suspicion.

Dr Goddard, what do you think about Spironolactone /amiloride / eplerenone and the newer agents?

Answered this one on the night – mostly encountered in the context of cardiac failure patients with CKD or cardio renal balance – the heart comes first and we deal with the renal consequences

Dr Goddard, I would point out that Dapa has very little glycaemic effect when eGFR is <45 and esp < 30, we tend to use it more for CKD / HF not diabetes

Fully agree but was pointing out the anomaly with current GFR thresholds – if you are diabetic you can have this down to a GFR of 15 so it is safe to give at this level of renal function but the SMC approval for heart failure is 20 and CKD (non diabetic) 25 purely because these were the cut off thresholds in the studies. Dapa is on formulary locally for CKD, diabetic or not, down to a GFR of 15.

Dr Goddard, with the evidence of reduced CV risk with use of the 'poly-pill', could this become standard practice to aid preservation of kidney health?

Along the lines of statin, ACE inhibitor combo? If it improves concordance yes but this is mitigation and prevention by going hard at lifestyle early is by far the better option.