Derby Medical Society Meeting Minutes
Wednesday 8th March 2023
Derby Medical School Lecture Theatre

Professor Jonathan van Tam has been unable to speak this season due to illness.

Speaker
Professor Maarten Taal
Professor of Medicine and Honorary Consultant Nephrologist
Centre for Kidney area search and Innovation, University of Nottingham
Department of Renal Medicine, University Hospitals of Derby and Burton

Novel therapies for chronic kidney disease: hope for a better future.

CKD is a silent condition with a global prevalence of 11.1% of adults (844 million)
More prevalent than diabetes.

4 million people are on dialysis worldwide but most in developed countries. There is very little dialysis provision in the south Asian and African nations.

Diabetes is the single most common cause of CKD.

Prevention is better than dialysis.

History of Renal Protective Treatments

Treating blood pressure

Early 1990s - ACE-I found to half the progression of renal function decline.
Early 2000s - ARB found to reduce renal function decline.
There was still an unmet need with 25% of patients still having progressive renal disease in the trials.
There was then no new treatments for the next 15 years and renal medicine was a frustrating place to be.

SGLT2 inhibitors

Sodium glucose transport 2 inhibitors (SGLT2) then found to be beneficial for renal protection

SLGT2 first developed from tree bark and apples (phlorizin) was first found to be effective.

Mechanism of action of SGLT2:

Block SGLT2 in proximal tubule.
Lower HBA1c by +/- 0.5%.

Additional effects:
Weight loss
Natriuresis
Lower blood pressure
Lower intraglomerular pressure
Sympathetic inhibition
Lipolysis – ketone formation
Increase Hb, HCT and EPO

Some mechanisms of action are still being discovered.

Studies on SGLT2 came 10 years after the issues with new diabetes drugs being withdrawn due to cardiovascular side effects. The USA FDA required any new diabetes drug to be trialed with cardiovascular risks studied. Renal end points were reported as a secondary outcome and this showed significant renal benefits.
CVS events risk was reduced.
Renal outcomes were unexpected and reduced renal disease progression by 40%.

SCORED trial looked at CVS outcomes in people with diabetes and established CKD. Despite a short follow up CVS benefits were evident.

CREDENCE randomised controlled trial looked at renal outcomes.
Trial was stopped early as renal benefits were clear and unethical to continue with placebo group.
30% risk reduction with NNT 22.
Cardiovascular outcomes also reduced.
Clear evidence that people with diabetic nephropathy benefitted from SGLT2.

DAPA-CKD trial showed benefit of SGLT2 in people without diabetes but with CKD.
39% relative risk reduction with NNT 19.

What the trials did not answer was if patients without albuminuria would benefit from SGLT2.
EMPA-KIDNEY trial looked at this and we're still recruiting when the CoVid pandemic started.
This trial was also stopped early due to benefits.
Trial confirmed that renal benefits whether or not albuminuria was present.

Meta analysis

All SGLT2 trials in adults, n>500, duration over 6 months were reviewed.
All clinical contexts – Type 2 DM, HF, CKD were included.

Renal, cardiovascular and safety outcomes we reviewed.

Other trials have shown benefits of SGLT2 on heart failure.
SGLT2 have benefits for all types of CKD.
They reduce risk of AKI by 23%.

Adverse effects of SGLT2
Ketoacidosis (absolute risk is low - 0.3%)
Lower limb amputation (found in canagliflozin trial only). Use caution when used in people with high risk feet/legs
Urinary tract infection
Genital fungal infections.

Who to treat with SGLT2

Type 2 diabetes.
Heart failure
CKD

Who should not have SGLT2

Type 1 diabetes
Renal transplant
Pregnant or breastfeeding
Children
On immunosuppressant

On mineralocorticoid inhibitors
Liver disease
Bilateral renal artery stenosis
Polycystic kidney disease
GFR < 25

Monitoring
No GFR monitoring needed
Genital hygiene advice
Sick day guidance

Other new treatment - Finerenone
Currently being considered by NICE
Non-steroidal mineralocorticoid inhibitor

The Future

There is still a residual unmet need.
New combinations for SGLT2 and finerenone or endothelin antagonists being developed
New anti-inflammatory and anti-fibtrotic drugs
Stem cell therapy
New goals aim for regression of CKD, not just slowing progression