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Renal disease in patients with sickle cell disease (SCD)

Adapted from Guy's and St Thomas' sickle guidelines and West London HCC Clinical Guidelines

NOTE
This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

Chronic kidney disease is one of the most frequent complications in sickle cell disease. End stage renal disease is unusual though its incidence is rising with increasing longevity in SCD. Renal dysfunction can present in multiple ways.

Sickle nephropathy typically presents with microalbuminuria. Routine assessment by urine dip and protein: creatinine ratio (PCR) estimation are central to the monitoring of the development of renal disease in this population. Albumin: creatinine ratio (ACR) is more sensitive, but not necessary. Non-sickle related cause of renal impairment (e.g. lupus, chronic viral infection, glomerulonephritides, myeloma) should also be considered in all cases.

Microscopic haematuria is common in SCD. Macroscopic haematuria may be due to urinary infection or papillary necrosis. Passing of necrosed renal papillae may cause renal colic and ureteric blockage. Haematuria can also occur in patients with sickle cell trait. Patients with renal medullary carcinoma may also present with haematuria, sometimes with additional back or abdominal pain and weight loss. This rare and aggressive cancer is virtually restricted to those with the sickle gene, particularly sickle cell trait, sickle cell/haemoglobin C disease and occasionally sickle cell anaemia. It has usually metastasised at the time of presentation and has a very poor prognosis with a median survival of less than one year from diagnosis.

Nocturia and enuresis are common in part due to obligatory high fluid intake, coupled with reduced urinary concentrating capacity. All children and adults should be directly questioned about the presence of enuresis as many patients do not realise this is SCD related and will not volunteer the information. Patients may also have an incomplete form of distal renal tubular acidosis leading to acidosis and hyperkalaemia this can usually be corrected with dietary potassium restriction and oral bicarbonate however this should be discussed with a nephrologist if persistent.

Urinary tract infection is not uncommon in SCD, in both sexes. It should be vigorously investigated and treated to prevent serious renal pathology. Haematuria, secondary to papillary necrosis, can precipitate UTI, but other factors must be excluded.

Creatinine levels are often low in people with sickle cell anaemia and sickle cell/β0 thalassaemia due to hyperfiltration and increased proximal tubular excretion, resulting in a high estimated glomerular filtration rate (eGFR). Increased rate of change of creatinine may, therefore indicate declining renal function before the value moves out of the normal range.

Monitoring for kidney disease in Sickle Cell Disease

At annual review

- Blood pressure measurement (plus at each routine appointment)
- Urine dipstick
- FBC
- Urea & Electrolytes
- Review eGFR trend
- Urine protein: creatinine ratio (PCR)

Management of abnormal findings

1. Haematuria:

Renal ultrasound
MSU
Urine Cytology
If painful, consider CT-KUB
Refer to Urology

2. Proteinuria:

- Dipstick negative and PCR< 50 - Repeat 6 monthly
- Dipstick positive - Send for protein: creatinine ratio (PCR) and MSU
- PCR >50 (on at least 2 occasions) - Investigate by: Glucose, ANA, ANCA, complement, Immunoglobulins and electrophoresis, serum free light chain ratio
- 24-hour urine collection to quantitate

If abnormal consider renal ultrasound scan and starting Ace Inhibitor and refer to renal clinic for further investigation

3. Falling eGFR and/or rising creatinine:

- Anyone with an eGFR which is declining by >5 ml/min/year or an absolute value <60 ml/min should be identified and discussed with a nephrologist

Check:

- Urine for protein: creatinine ratio
- Urinary culture
- Urinary microscopy for casts
- ANA, Complement, Immunoglobulins and Electrophoresis
- Chronic viral serology (HIV, hepatitis B and C)
- Renal tract Ultrasound
- Predictors for chronic renal impairment include increasingly severe anaemia, hypertension, proteinuria, and microscopic haematuria.

Treatment for sickle nephropathy, manifest by proteinuria

- First line ACEi, e.g. Ramipril 2.5mg titrating up to 10mg. Alert GP for them to monitor and escalate if necessary, (check U&E 1-2 weeks post starting ACEi- a fall in GFR of 10-20% is common and tolerated if stabilises)
- Start medication at a lower dose if GFR<45ml/min/1.73ml
- If ACEi not tolerated, consider angiotension receptor blocker (ARB) e.g. Losartan
- Consider hydroxycarbamide (see below)
- Avoid/stop NSAIDs and other nephrotoxic drugs
- Optimise BP control

Hydroxycarbamide in patients with sickle nephropathy

Data are currently lacking to demonstrate a clear improvement in renal function in patients with sickle nephropathy. However, it is to be expected that hydroxycarbamide would have a beneficial effect through the inhibition of ongoing renal vaso-occlusive episodes. Hydroxycarbamide is therefore to be considered in all patients with sickle nephropathy (urine PCR > 50 mg/mmol) unless contraindicated.

Similarly, red cell exchange could be predicted to be beneficial. There is no current evidence to support it for this indication alone.

Hypertension

- If no proteinuria consider treatment if BP >140/90 mmHg and aim for a target of <140/90 mmHg
  Overview | Hypertension in adults: diagnosis and management | Guidance | NICE

- If proteinuria is present, treat if BP > 130/80 mmHg, and aim for a target of <130/80 mmHg
  Recommendations | Chronic kidney disease: assessment and management | Guidance | NICE

End stage renal disease (ESRD) and transplantation

This is managed by the nephrologists and should include early discussion of renal replacement therapy options including transplant and dialysis. Patients with renal failure associated anaemia can be considered for erythropoietin therapy as in the non-sickle population. Patients with SCD on dialysis may require much higher than the average dose when erythropoietin is used to correct anaemia. This should be done in discussion with the haematologists and nephrologist.

Transplantation has better outcomes than dialysis for patients with sickle cell disease, although long term graft and patient survival is lower for this patient group than the national average. If transplantation is possible, consideration should be given to commencing a red cell exchange programme as soon as listed, to maximize their fitness for surgery, NB aim for Haemoglobin S less than 30%. An exchange programme should be commenced after the procedure and should be maintained for the lifetime of the graft as this has been shown to improve graft survival. There is no evidence base to guide the choice of HbS % target. An empiric target of 30% is suggested. The lack of ethnically matched donors can increase waiting times in the absence of a living/unrelated donor.

The management of renal transplantation in patients with sickle cell disease, particularly in relation to perioperatively and also management of immunosuppression can be different, and when a patient is listed, it is recommended that discussion is facilitated with nephrologists and haematologists at a centre with sickle renal transplantation expertise.

References

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