NHS SCOTLAND

SPAH
SCOTTISH PAEDIATRIC AND ADULT HAEMOGLOBINOPATHIES NETWORK

Scottish Paediatric & Adult Haemoglobinopathy Network

Adult Guideline – Stroke and other CNS complications in sickling disorders

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

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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.

1. Stroke

Contact the Haematologist immediately if a stroke is suspected in a patient with SCD

- Acute ischaemic and haemorrhagic events are usually related to pre-existing cerebral vasculopathy but can occur in otherwise well patients. Limited evidence suggests that TCD velocities are not predictive of stroke risk in adults**.**
- Ischaemic stroke may occur at all ages, but is most common in children. Haemorrhagic stroke is more common in adults.
- Precipitating factors: dehydration, fever, acute anaemia
- May be silent and only detected on neuropsychological assessment - if cognitive impairment is suspected, consider referral to local neuropsychology services for formal assessment
- Can present with:
    - Limb weakness
    - Paraesthesia
    - Fits
    - Acute confusion/altered level of consciousness
    - Dysphasia/dysarthria
    - Headache

Special investigations

- Urgent CT within one hour of presentation to confirm diagnosis and look for haemorrhage but a negative scan at an early stage does not exclude brain infarction
- CT perfusion scan if presents within 3-4 hours of onset
- MR angiography/Contrast enhanced CT angiography

Acute Management

In general – standard neurological measures with acute exchange transfusion in most cases

- Admit, rehydrate immediately, consider analgesia and antibiotics as clinically indicated
- Arrange immediate neurological assessment/scans
- Routine bloods (Including blood group (ABO, RhD and Kell) and urgent cross match (sickle negative blood)
- If scans are delayed, and there is a strong clinical suspicion of stroke, commence exchange transfusion whilst awaiting scans
- Haematology specialist review re exchange transfusion to achieve Hb S < 20%
- If delay in arranging exchange and Hb<80g/l, then urgent top-up to HB 100g/l.
- Aim for Hb <110g/dl, HCT<0.34
- Avoid/stop aspirin, NSAIDs and LMWH until haemorrhage excluded
- Neurological observations
- Neurological review
- There is limited data on the role of thrombolysis in adults with ischaemic stroke and co-morbidities such as AF in SCD. The sickle standards suggest that adults with SCD may benefit from both thrombolysis and acute red cell exchange. Thrombolysis is not routinely recommended due to an increased intracerebral bleeding risk and should be considered on a case by case basis by a multidisciplinary team.

Long term management

- Regular exchange transfusion programme (every 4-6 weeks) to maintain HbS level below 30%
- Hydroxycarbamide should be considered for prevention of recurrent stroke where transfusion is not possible or acceptable
- Sibling allogenic bone marrow transplantation could be considered in select cases and would need discussion at the National SPAH clincal case discussion.
- MRA may help to determine the duration of the transfusion regimen. The risk of recurrent neurological events is greatest in those with abnormal cerebral vasculature:
    - No occlusion, no neurological deficit: monitor without further transfusion
    - Occlusion of vessels and/or neurological deficit: regular transfusion for at least 36 months
- For TIA consider lifelong anti-platelet therapy if there is no contraindication
- Neurology review

2. Subarachnoid haemorrhage (SAH)/Haemorrhagic stroke

- Occurs at all ages, but median age of onset is 22 years
- Often multiple aneurysms

Management and investigation

- CT brain plus angiography with contrast
- +/- LP
- Exchange transfuse as for stroke; refer to neurosurgeons; neurological observations
- Avoid/stop aspirin/NSAIDs and LMWH

3. Seizures

- Common after stroke, SAH or meningitis
- May be caused by large dose of pethidine (still administered at some centres)

Investigations

- Urgent CT or MRI to exclude vascular event
- EEG
- Consider MR angiography
- Infection screen including blood cultures +/- LP
- Consider toxicology screen for pethidine if indicated

Management (in consultation with neurology):

Immediate:

- Stop pethidine / opioids
- Anticonvulsants
- Neurological observations

Definitive:

- If no abnormality on EEG, or no recurrence, no long term intervention is necessary, except to avoid pethidine
- If EEG abnormal, but CT/MRI and MRI angiogram normal; long term anticonvulsants
- If infarction on scanning, or vessel stenosis/occlusion on angiogram, exchange transfuse and consider long term transfusion programme
- Neurological opinion

4. Headaches

The first episode of acute severe headache or a significant change in type of headache should be evaluated as an emergency and the diagnoses of intracranial haemorrhage, bacterial meningitis or venous sinus thrombosis considered
Investigations:

CT or MRI
Lumbar puncture (if no contraindication)

Chronic headache is common in SCD.

Causes

- Migraine
- Benign intracranial hypertension
- Sleep apnoea
- Tension

Patients with persistent chronic headache should be referred to a neurology clinic.

5. Stroke prevention

There is currently no evidence for primary stroke prevention in adults. In children there is clear evidence that the presence of a raised Trans-cranial Doppler blood flow is associated with increased stroke risk. For children who have been identified as having abnormal Transcranial Doppler scans and who have been commenced on long term blood transfusion regimes, there is no clear evidence of how long stroke prevention therapy should be continued.

On transition to the adult service, these children should be continued on transfusion therapy and discontinuation of transfusion considered on an individual cases by case basis.

The TWiTCH trial has shown that for high-risk children with sickle cell anaemia and abnormal TCD velocities, after four years of transfusions and without severe MRA vasculopathy, hydroxycarbamide therapy can substitute for chronic transfusions to maintain TCD velocities and help prevent primary stroke.

Silent infarcts

Silent strokes may have effects on IQ and cognitive performance, including memory. In patients with subtle neuro-cognitive defects, investigation with MRI/MRA scans and neuropsychological testing may be appropriate.

The SIT Trial (Controlled Trial of Transfusions for Silent Cerebral Infarcts in Sickle Cell Anemia) showed a reduction in recurrent silent cerebral infarct and overt stroke in children in the transfusion vs the observational arm. There is no consensus on the use of chronic transfusion programmes in children or adults with silent cerebral infarction.

Acknowledgement

Guy’s and St.Thomas’ NHS Trust: Sickle cell disease adult guidelines.

West London HCC Clinical Guideline: Guidelines for the management of sickle cell disease in adults