NHS SCOTLAND

SPAH
SCOTTISH PAEDIATRIC AND ADULT HAEMOGLOBINOPATHIES NETWORK

Paediatric guideline

Management of Priapism in Sickle Cell disease

NOTE
This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined based on 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.

Priapism is defined as a sustained painful erection and is one of the vaso-occlusive complications of sickle cell anaemia. The prevalence of severe priapism in sickle cell is unknown but a survey in young males suggested that 89% will experience priapism by 20 years of age and 25% of children with sickle cell disease related priapism are pre-pubertal.

Priapism can be acute/fulminant or stuttering:

ACUTE / FULMINANT PRIAPISM:

- severe pain
- duration >4 hours
- penis fully erect
- high risk of cavernosal fibrosis and impotence
- urgent intervention indicated

STUTTERING PRIAPISM:

- recurrent
- pain of variable intensity
- lasting 30 minutes to < 3hours
- penis may not be fully erect
- risk of subsequent fulminant attack

The optimal management of priapism is still a subject of debate. This guideline is based on a recent review of the literature.

Aims of Treatment

- achieve rapid relief from pain and discomfort
- preserve potency
- prevent recurrence

Outcome is dependent on the pubertal status of the patient and length of time to detumescence. Poor long-term outcome in terms of impotence is associated with post-pubertal males and a long duration of erection. Interventional procedures are most effective in the first 6 hours and relatively ineffective after 24-48 hours.

Hence **PRIAPISM IS A UROLOGICAL EMERGENCY** requiring rapid assessment and treatment to prevent irreversible ischaemic penile injury, corporal fibrosis and impotence.

Patient Education

Male sickle cell patients and their families should be educated about priapism early after diagnosis or transfer to the service and written information should be given. Specific enquiry should be made about this symptom at follow-up. They should be instructed to present to hospital immediately if an episode of priapism does not resolve within 1 hour.

History and examination

- duration of episode
- pain severity (usually very painful)
- medications including alcohol and recreational drugs, analgesia
- prior episodes
- crisis pain elsewhere
- abdomen – masses, spleen, bladder, external genitalia
- full set of observations including SaO_2

Investigations

- full blood count
- urea and electrolytes and creatinine
- group and save with extended red cell phenotype

General Principles of Early Management

- attempt to urinate (consider catheter if unsuccessful and a full bladder is present)
- try a warm bath
- gentle exercise e.g. climbing stairs
- hydration
- analgesia

Management Plan for Acute/Fulminant Priapism

1 If the episode has not resolved by 4 hours, then from onset the initial treatment of choice is aspiration and irrigation which should be performed with 4-6 hours of onset. Therefore, **urgent involvement of paediatric surgeons/urology is needed, and this should not be delayed while initial supportive measures are carried out.**

2 Initial supportive management in hospital should include:
- careful assessment of individual fluid status and administration of appropriate intravenous hydration with close monitoring of fluid balance.
- nil by mouth
- analgesia – (morphine is usually needed)
- sedation may be useful in some cases – take care with concomitant opiate use
- oxygen if needed to maintain SaO_2>94%
- if there is likely to be a delay in accessing definitive management with aspiration/irrigation then oral etilifrene or pseudoephidrene can be considered. Obtaining this should not delay definitive management.

3 If there is no detumescence after 1-2 hours of in-hospital management (4 hours from onset) then aspiration and lavage should be performed and by itself is successful in 30% of cases. GA is likely to be required in paediatric patients.

4 If detumescence does not occur with aspiration, then injection of sympathomimetic agents with or without irrigation can be performed. The agent of choice is phenylephrine but alternatives are epinephrine or etilefrine which can be instilled intracavernosally at the end of the procedure. Table 1.

5 Aspiration and irrigation are reported to be effective in more than 85% of cases. Failure is usually associated with prolonged episodes of priapism >24 hours. Second line management consists of exchange transfusion and/or formal surgical shunting operations such as Winter's cavernosal shunt performed under general anaesthesia.

Role of transfusion

Acute exchange transfusion has been associated with an increased incidence of neurological events. Top-up transfusion should only be considered if otherwise indicated by the clinical picture and initial surgical intervention should not be delayed for transfusion However, a review of 10 adult patients with recurrent major priapism unresponsive to medical therapies who underwent automated exchange transfusions reported no neurological complications.

6 Exchange transfusion could be considered if timely aspiration/irrigation is not available or if this procedure is unsuccessful and in preparation for a shunt procedure if aspiration is successful then the patient should be observed for a few hours and then, if well, discharged home.

7 If the patient has had previous episodes of priapism, then medium to long term prophylaxis should be discussed (see stuttering priapism below).

Procedure for Aspiration and Irrigation

- aspiration can be performed under sedation/general anaesthesia depending on the age of the patient
- if not under GA, then using an aseptic technique infiltrate 0.5ml 1% Lignocaine under the skin on the lateral aspect of the penis
- insert a 23-gauge needle or butterfly into the corpus cavernosum with a lateral approach (10 or 2 o'clock position) taking care to avoid the dorsal vein (superior aspect) and the urethra (inferior aspect). Attach a 3 way tap and aspirate into a dry 10ml syringe: 3–5-mL aliquots should be aspirated until bright red (oxygenated) blood is seen (not exceeding 10% of the circulating blood volume; 7.5 mL/kg in children aged ≥1 year). The corpora should then be flushed with warmed 0.9% saline. The procedure is unilateral as there is a connection between the two corpora

- if aspiration and irrigation do not achieve detumescence, sympathomimetic intracorporal injection should be performed with cardiovascular monitoring: pulse, BP and pulse oximetry should be monitored at 15-minute intervals until >30 minutes post-procedure. Side-effects are rare but include headache, dizziness, hypertension, reflex bradycardia, tachycardia, arrhythmias. Injections must stop when detumescence is achieved

- **if phenylephrine is being used**: attach another 10ml syringe containing 200mg/ml solution of phenylephrine and instill in aliquots as per Table 1

- **if epinephrine is being used**: then attach another 10ml syringe containing a 1:1 000 000 solution of epinephrine to the 3 way tap and irrigate with this solution (see table 1 for volume). If needed additional blood can be aspirated until detumescence occurs

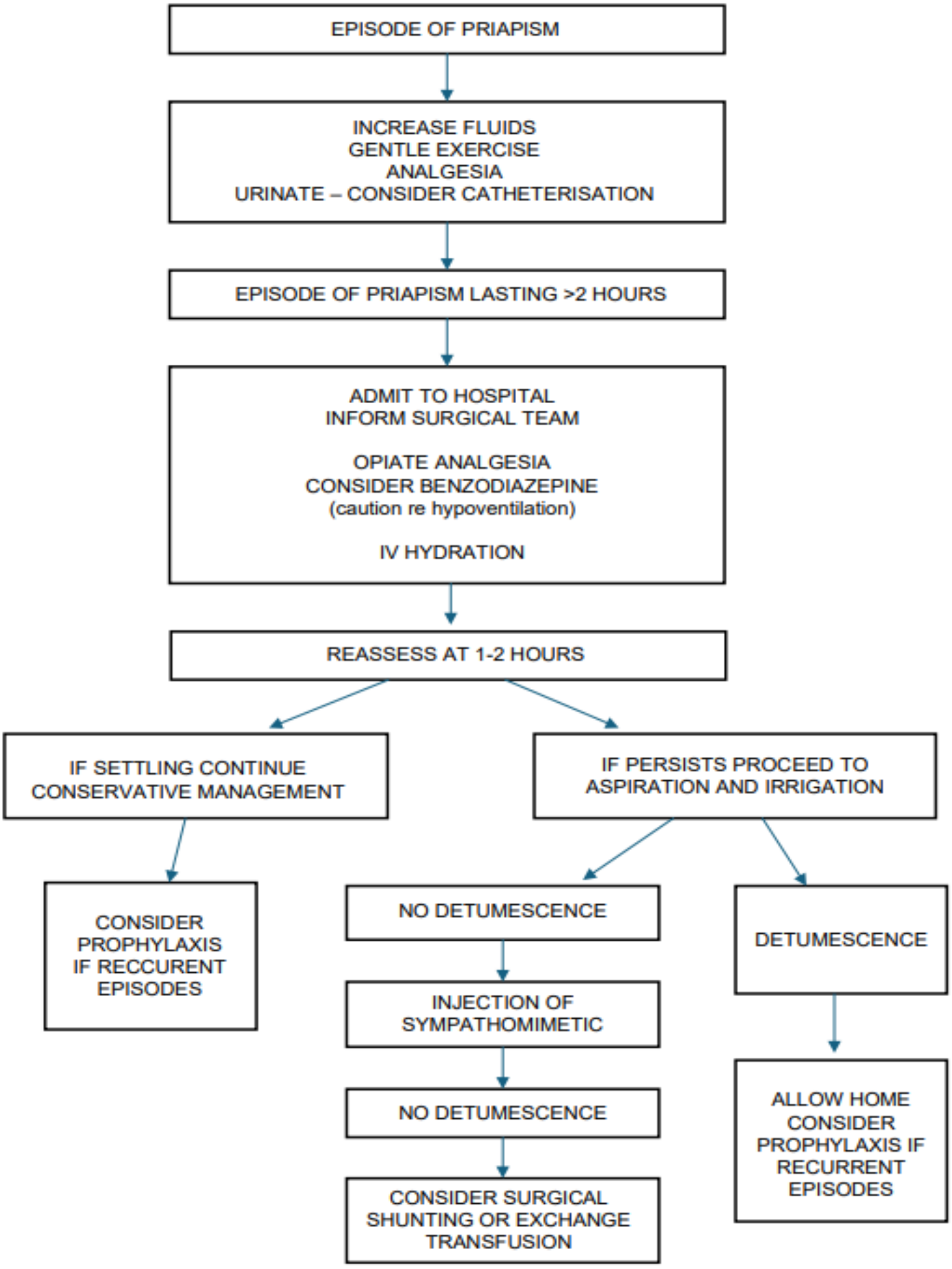
- **if etilefrine is being used**: then attach a 10ml syringe containing 0.9% sodium chloride to the 3 way tap and irrigate. Additional blood can be aspirated until detumescence occurs. 5mg (0.5ml) of undiluted etilefrine can be instilled into the corpora via the 3 way tap at the end of the procedure (*NB* irrigation is not always required prior to etilefrine instillation)

- after withdrawal of the needle firm pressure should be applied for at least 5 minutes to prevent haematoma formation (the most common complication of the procedure)

Table adapted from Donaldson et al 2014**

Drug	Available preparations	Concentration	Age and aliquot	Further doses
Phenylephrine	10 mg/mL (1%)	0.1 mL + 4.9 mL 0.9% saline (200 µg/mL)	≥11 yrs: 0.5 mL	≤10 doses at 5–10 min (max 1 mg)
Epinephrine (adrenaline)	1 in 10,000 (100 µg/mL)	1 mL + 99 mL 0.9% saline (1 in 1 000 000 or 1 µg/mL)	≥11 yrs: 15 mL, 3–11 yrs: 10 mL, <2 yrs: 2.5–5 mL	≤4 doses at 10 min intervals
	1 in 1000 (1 mg/mL)	1 mL + 1000mL 0.9% saline (1 in 1 000 000 or 1 µg/mL)		
Etilefrine	10 mg/mL (1%)	Undiluted	0–18 yrs[a]: 0.5 mL	≤2 doses at 10 min

Suggested sympathomimetic preparations for intracorporal injection (ICI). This is an unlicensed indication and route of administration. When available phenylephrine should be used in boys aged ≥11 years; epinephrine should be used in boys ≤10 years. There are no reliable data on ICI ≤2 years: we recommend using a reduced dose of epinephrine.


EPISODE OF PRIAPISM
INCREASE FLUIDS
GENTLE EXERCISE
ANALGESIA
URINATE – CONSIDER CATHETERISATION
EPISODE OF PRIAPISM LASTING >2 HOURS
ADMIT TO HOSPITAL
INFORM SURGICAL TEAM
OPIATE ANALGESIA
CONSIDER BENZODIAZEPINE
(caution re hypoventilation)
IV HYDRATION
REASSESS AT 1-2 HOURS
IF SETTLING CONTINUE CONSERVATIVE MANAGEMENT
IF PERSISTS PROCEED TO ASPIRATION AND IRRIGATION
CONSIDER PROPHYLAXIS IF RECCURENT EPISODES
NO DETUMESCENCE
DETUMESCENCE
INJECTION OF SYMPATHOMIMETIC
NO DETUMESCENCE
ALLOW HOME
CONSIDER PROPHYLAXIS IF RECURRENT EPISODES
CONSIDER SURGICAL SHUNTING OR EXCHANGE TRANSFUSION

Management of Stuttering Priapism

1. Initial treatment out of hospital should consist of:
   - empty bladder before bed
   - increased fluid intake
   - oral analgesia
   - gentle exercise
   - attempts to urinate soon after onset

2. If the episode lasts more than 2 hours, then the patient should be advised to attend hospital at once and acute priapism protocol should be followed.

3. Prophylaxis should be discussed with the patient and parents. Options are:
   - Exchange Transfusion Programme
   - oral Etilefrine (an α- agonist)
   - Hydroxycarbamide

An **exchange transfusion programme** has the disadvantages of potential iron overload, alloimmunisation, difficulties with venous access and repeated hospital visits but has the advantages of reducing other sickle related morbidity during the period of transfusion.

Etilefrine is a direct acting alpha-adrenergic agonist. In normal physiological circumstances adrenergic impulses keep the penis flaccid in the absence of sexual stimulation.

Etilefrine has advantages over other alpha agonists such as epinephrine and phenylephrine in that it is rapidly absorbed orally and has a short half-life (150 minutes) and it may have a lower risk of systemic hypertension. A recent Cochrane review found a lack of quality evidence for any pharmacological intervention in part due to small numbers and there is only limited experience in children. Systemic hypertension has not been seen in paediatric patients reported in the literature but should be assessed regularly on treatment.

Etilefrine is given in a dose of 0.5mg/kg daily. This can be given as one dose of 0.5mg/kg in the evening for patients with nocturnal priapism or 0.25mg/kg twice daily in other patients. It will not reduce other sickle cell related symptoms.

Hydroxycarbamide has been shown to be effective in reducing sickle related complications in children. There are case reports documenting its efficacy in treatment of recurrent priapism, but this outcome was not studied in the large-scale trials reported to date.

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