

Guideline for the Management of Acute Chest Syndrome in Children with Sickle Cell Disease

STSTN Clinical Guidelines Group

Definition

Acute chest syndrome (ACS) is defined as an acute illness characterized by fever and/or respiratory symptoms, accompanied by a new pulmonary infiltrate on chest X-ray in a child with sickle cell disease (SCD).

Clinical Features

Some of the following symptoms and signs are typically present:

Symptoms

- Chest and more generalised pain, which may be absent particularly in younger children.
- Cough, which may be productive.
- Breathlessness.
- Wheezing.
- Fever/rigors.

Signs

- Fever
- Tachypnoea.
- Tachycardia.
- Wheeze, crackles
- Bronchial breathing.
- Cyanosis.

Initial Assessment

History and examination should identify the above features. It is important to identify severely ill or deteriorating patients who may require admission to HDU or PICU and discuss with one of the Sickle Cell Centres to arrange early transfer (see below for contact details). Deteriorating patients may need STRS retrieval.

Investigations

These should include:

- Chest x-ray: in patients with any of the following features: temperature $>38.5^{\circ}\text{C}$, chest pain, cough, tachypnoea, chest signs, drowsiness, hypoxia.
- Full blood count, reticulocyte count, urea and electrolytes, LFTs, C-reactive protein.
- Group & save and antibody screen.
- Blood cultures, sputum culture if productive cough.
- Combined nose and throat swab (respiratory viruses screen)
- Pulse oximetry in air

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- Venous blood gas

Management

All patients with ACS should be admitted to hospital.

Monitoring

The following should be measured and recorded 4 hourly in the PEWS ward charts temperature, pulse, blood pressure, oxygen saturation (in air), pain score, respiratory rate, level of consciousness.

Hypertension (defined by age/sex/weight centile charts) should be treated.

FBC, reticulocytes and electrolytes should be repeated daily until patient improves.

Oxygen

All patients should be given oxygen to maintain their oxygen saturations at 99-100%. Some patients may be known to have low steady-state oxygen saturations (of <95%), but in the presence of acute chest syndrome, the aim should be to keep their oxygen saturation levels near to 100%.

Physiotherapy

Physiotherapy may be helpful in the presence of a productive cough. Incentive spirometry may help prevent children with acute pain developing acute chest syndrome, and should be used in any child with SCD and back or chest pain.

Intravenous Fluids

In general, all patients with ACS should receive intravenous fluids at the following maintenance rates, which may need to be modified according to fluid loss and fever:

- 1 - 3 years 100 ml/kg/24hr
- 4 - 6 years 90 ml/kg/24hr
- 7-14 years 70 ml/kg/24hr
- 15 -18 years 60 ml/kg/24hr

If patients are considered to be dehydrated and require higher rates of iv fluid replacement this must be reviewed within 12 hours and reduced once patients are adequately hydrated, to reduce the risk of fluid overload which can complicate ACS and lead to clinical deterioration. Close attention should be paid to monitoring and maintaining fluid balance. If a patient is generally well apart from lung consolidation on chest X-ray and is able to drink adequately, intravenous fluids may not be necessary.

Antibiotics

Studies show that infections are identified in about 30% cases, with chlamydia and mycoplasma being most common (in the USA). All patients should receive clarithromycin orally and cefuroxime iv. If the patient is unable to take oral treatment, erythromycin iv should replace clarithromycin. Culture results may suggest different antibiotics. If clinical deterioration occurs despite these antibiotics, then cefuroxime should be replaced with piperacillin and Piperacillin with tazobactam (Tazocin) and Gentamicin, and clarithromycin or erythromycin continued.

Penicillin Allergy: If the patient has a genuine allergy to penicillin, give meropenem and gentamicin instead of Piperacillin with tazobactam and gentamicin.

Drug Doses:

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Cefuroxime 20 mg/kg (max 750 mgs) every 8 hours

Clarithromycin (oral):

- body weight under 8 kg: 7.5 mg/kg twice daily
- body weight 8-11kg: 62.5 mg twice daily
- body weight 12-19 kg: 125 mg twice daily
- body weight 20-29 kg: 187.5 mg twice daily
- body weight 30-40 kg: 250 mg twice daily
- Children 12-18 years: 250 mg twice daily

Or

Erythromycin (intravenous): 12.5 mg/kg (max 1g) every 6 hours or

Clarithromycin IV (but not licensed for under 12 years).

Second line for deteriorating patients

Piperacillin with tazobactam (Tazocin): 90 mg/kg iv every 6 hours Max 4.5 gram

Gentamicin: 7 mg/kg iv once per day (maximum 350 mgs), trough level prior to the third dose.

Meropenem:

- By intravenous infusion
- Child 1 month–12 years
- Body-weight under 50 kg 40 mg/kg every 8 hours
- Body-weight over 50 kg dose as for child 12–18 years
- Child 12–18 years 2 g every 8 hours

Antivirals

Consideration should be given to including antivirals, such as oseltamivir, if the child is admitted during an outbreak of seasonal or pandemic influenza, or Influenza is identified from the combined nose and throat swab (respiratory viruses screen):

Oseltamivir (oral for 5 days):

Child 1-2 months 2.5mg/kg twice daily

Child 3 month-11 months 3mg/kg twice daily

Then body Weight

- body weight 10-15 kg: 30 mg twice daily
- body weight 15-23 kg: 45 mg twice daily
- body weight 23-40 kg: 60 mg twice daily
- body weight >40 kg: 75 mg twice daily

Child 13-17years: 75 mg twice daily

Bronchodilators

Regular, nebulised salbutamol should be used if there is wheezing, a history of airways hyper-reactivity, clinical benefit following a trial of nebulisers, or progressive deterioration.

Analgesia

Pain should be treated according to local guidelines.

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Hydroxycarbamide (hydroxyurea)

Some patients may be taking hydroxycarbamide on admission because of previous problems with frequent pain or ACS. This should be continued at the prescribed dose unless there is concern that the patient has bone marrow suppression, suggested by neutrophils $<2.0 \times 10^9/l$, reticulocytes $<100 \times 10^9/l$, platelets $<100 \times 10^9/l$, in which case it should be stopped.

Deteriorating Patients

Patients with ACS can deteriorate rapidly and require close monitoring. Up to 10% may need ventilatory support. Deterioration is suggested by:

- decreasing level of consciousness (please note the PEWS score does not record this).
- decreasing oxygen saturations (measured by pulse oximetry) in air.
- increasing oxygen requirements to maintain 100% oxygen saturations, or failure of oxygen to correct saturations.
- increasing tachypnoea.
- increasing pain.
- increasing shadowing on chest x-ray.
- falling haemoglobin, increasing white cell count.

Management of the Deteriorating Patient

The patient should be discussed with a Consultant Paediatric Haematologist or Paediatrician. HDU/PICU should be alerted that a deteriorating ACS patient is on the ward, and they should arrange to review the child ASAP. The following options should be considered:

- Fluid balance - assess for possibility of fluid overload.
- Opiate analgesia – assess for possibility of opioid toxicity.
- Simple top-up blood transfusion; this may be particularly useful if used early and when the Hb is <70 g/l (and nearly always if the Hb <50 g/l). This should only be arranged following discussion with a consultant and should aim to increase the Hb to 100-110 g/l, haematocrit <0.35 . This threshold should not be exceeded due to the risk of hyper viscosity and complications.
- Dexamethasone 0.3 mg/kg IV every 12 hours for a total of 4 doses; this may be helpful in rapidly deteriorating patients who seem likely to need ventilation. The steroids must not be stopped suddenly, but should be reduced gradually to avoid rebound pain (switch to oral prednisolone).
- Exchange transfusion: this is indicated in rapidly deteriorating patients, particularly with extensive chest x-ray shadowing and low oxygen saturations which do not correct with inhaled oxygen. It may also be necessary in deteriorating patients with higher starting Hb (>90 g/l, such as those with HbSC disease), in whom it is not possible to perform a simple top-up transfusion. This will usually be performed on HDU/PICU, and should follow guidelines
- Mechanical ventilatory support: this will occur on HDU/PICU. Non-invasive support may be an early option in stable patients, to preventing further deterioration, however, invasive ventilation is indicated for severe respiratory distress, low oxygen saturations not corrected by inhaled oxygen, exhaustion etc. Patients requiring this will always also require exchange transfusion. Inhaled nitric oxide may be

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appropriate depending on ventilatory requirements, and is potentially of specific benefit in ACS.

Complications of Acute Chest Syndrome

- Rapid deterioration and death – patients should be monitored closely to allow the timely use of blood transfusions and PICU support.
- Neurological complications – seizures, silent cerebral infarcts, cerebral haemorrhage, strokes and posterior reversible leukoencephalopathy syndrome (PRES) are all common following severe ACS. Neurological complications are associated with hypertension and top-up transfusion increasing the haematocrit to >0.35. If neurological symptoms develop, urgent neurological assessment and CT/MRI should be arranged. Please note the PEWS score does not include neurological assessment.
- Chronic chest syndrome – repeated episodes of acute chest syndrome can result in a chronic, restrictive lung deficit. In general patients should have full pulmonary tests following recovery from an episode of ACS 6-8 weeks later. Oxygen saturations should be recorded when fully recovered in clinic, and it may be appropriate to organise overnight home monitoring of oxygen saturation levels.
- Children who are treated with dexamethasone may develop rebound symptoms such as acute pain if steroids are stopped suddenly. In general the steroids should be stopped gradually with reducing doses of oral prednisolone tailing-off over 5 days.

Discharge from Hospital

Prior to discharge, patients should have:

- Temperature <38°C for 24 hours without IV antibiotics.
- Normal, stable oxygen saturation measurements, as assessed by pulse oximetry, i.e. equivalent to pre-morbid reading.
- Normal respiratory rate.
- If continuing oral antibiotics, instructions to resume prophylactic Penicillin V when finished
- An outpatient appointment arranged with the sickle cell clinic.
- Advice about outstanding immunisations including Pneumovax and Annual Influenza. Check the following immunisations – Hib/MenC, Men ACWY, Men B, PCV13 (up to 5 years of age) PPV (from 2 years of age) and Annual Flu Vaccine.
- Information leaflet about hydroxyurea if severe episode, or more than single episode

Other information

N/A

Related guidelines

Transfusion of patients with Sickle Cell Disease

Incentive spirometry in Sickle Cell Disease

References

- Vichinsky et al (1997). Acute Chest Syndrome in Sickle Cell Disease: Clinical presentation and course. Blood 89, 1787-1792.
- Vichinsky et al (2000). Causes and Outcome of the Acute Chest Syndrome in Sickle Cell Disease. NEJM 342, 1855-1865.

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- Bernini et al (1998). Beneficial Effect of Intravenous Dexamethasone in Children with Mild to Moderately Severe Acute Chest Syndrome Complicating Sickle Cell Disease. Blood 92, 3082-3089
- Johnson CS. The acute chest syndrome. Hematol Oncol Clin North Am. 2005 19(5):857-79.

For more info: The telephone numbers below are available Monday-Friday, 9am-5pm. Outside these hours, please contact your GP or go to your local Emergency Department (A&E).

Guy's and St Thomas' Hospital Consultant Haematologist: Jo Howard / Rachel Kesse-Adu
Telephone: 02071882741 Out of hours – Haematology SpR or on call consultant via switchboard (02071887188)

Evelina London Children's Hospital, Baba Inusa / Maria Pelidis 02071889432 or out of hours Haematology SpR via Switchboard (02071887188)

Kings College Hospital Consultant Haematologist: Moji Awogbade / Sara Stuart-Smith
Telephone: 02032999000 Out of hours – Haematology SpR or on call consultant via switchboard (020 32999 000)

King's College Hospital Paediatric Haematology – Consultant of the week via switchboard 020 3299 9000 Sue Height/ David Rees/ Subarna Chakravorty, Out of hours: Haematology SpR on call via switchboard 020 3299 9000

St George's Hospital Consultant Haematologist: Alison Thomas, Elizabeth Rhodes and Julia Sikorska Telephone: 020 87250885 Out of hours Haematology SpR via Switchboard 0208 6721255

Additional contacts can be found on the STSTN website (www.ststn.co.uk)

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