Haemoglobinopathy Co-ordinating Centres Advice on COVID-19 for Patients with Diamond Blackfan anaemia

This document is a collaboration between the Haemoglobinopathy Co-ordinating Centres in England, offering guidance to health professionals working with patients with Diamond Blackfan anaemia (DBA). It has been reviewed and agreed by representatives of the Haemoglobinopathy Co-ordinating Centres in England and the Clinical Reference Group for Haemoglobin disorders and DBA(UK).

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Background:
A novel coronavirus named currently SARS-CoV-2 of a zoonotic origin has emerged and the infection called Coronavirus Diseases 2019 (COVID-19) started spreading worldwide. Incubation period: the time from exposure to symptom development is between 2-14 days. Avoiding exposure by adhering to recommended hygiene procedures, isolation of SARS-CoV-2 infected persons and social distancing are the only prevention strategies. There are no approved treatment options and there is no available vaccine. Tocilizumab has been used in China for therapy of severe cases with evidence of response.

Data from China and Italy suggests that children have a milder form of the disease than adults, although we do not understand why this is the case. Only 2 in every 100 diagnosed cases of coronavirus in China have been in children and young people aged <18 years. The Italian experience in Milan and Turin (Prof Nica Capellini and Professor Antonio Piga) is that there has been limited impact in patients with thalassemia, as a model of a transfusion dependent anaemia in a high-risk area. Similarly, the Monza haematology, oncology and BMT paediatric service (Professor Adrianna Balduzzi) has seen limited impact in children with serious haematological disorders. However, the following may indicate a higher risk in DBA:

- approximately a third of patients with DBA are known to have impairment of cellular and/or humoral immunity.
- the experience of bone marrow transplantation and chemotherapy use for malignancies in this population is that patients suffer a greater degree of toxicity and myelosuppression than those receiving identical treatment.
- approximately a third of the patients with DBA are on steroids.
- there is a risk of adrenal insufficiency.
- patients and parents may have concerns/anxiety about undertaking ionising radiation containing radiological investigations because of the increase risk of cancer in DBA.

PROCEDURE

General Guidance
Refer patients to up to date advice on the NHS-E and PHE websites:

- https://www.nhs.uk/conditions/coronavirus-covid-19/
- https://www.gov.uk/government/publications/covid-19-guidance-on-social-distancing-and-for-vulnerable-people/guidance-on-social-distancing-for-everyone-in-the-uk-and-protecting-older-people-and-vulnerable-adults

the British Society of Haematology is hosting the latest updated versions of all the documents produced by the NHP: https://b-s-h.org.uk/about-us/news/covid-19-updates/

All patients with DBA are advised to adopt Social Distancing Measures, which includes being supported to work from home as per the current government guidance, even if the patient is a key worker.

- Adopt remote consultations and postponement of routine monitoring tests and clinical consultations that are not essential.
- Patients to let their specialist teams know if they have symptoms or have to self-isolate or, if they access emergency services or are admitted to hospital.
- Delay steroid trials until resolution of COVID-19 and remain on transfusion programme.
- Delay planned BMT admission unless for MDS/AML or aplastic transformation, in which case assessment of risk:benefit ration needs to be applied.

Shielding in Patients with DBA:
Follow advice on https://www.gov.uk/government/publications/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19/guidance-on-shielding-and-protecting-extremely-vulnerable-persons-from-covid-19

DBA patients require Shielding if:

- on high doses of steroids defined as:
    - children: prednisolone (or equivalent) ≥0.5 mg/kg on alternate days or ≥0.25 mg/kg daily
    - adults: prednisolone (or equivalent) ≥30 mg on alternate days or ≥15 mg per day
- have an associated cellular or humoral immunodeficiency, or due to still being infants or too young to have their immune status assessed.
- have adrenal insufficiency on steroid replacement
- have iron overload defined as
    - T2* <15 ms, previous or current impaired LV function or other cardiac complications due to the iron load or significant congenital heart disease due to DBA,
    - severe hepatic iron overload LIC >15 mg/g DW
    - Please note: the ferritin cannot be used as an assessment tool unlike other transfusion dependent anaemias as it often underrepresents the iron load.
- have had a BMT within 6 months or are still using immunosuppressive drugs

DBA Treatment:
No changes to usual patient treatment are required, but avoid initiating new therapies unless essential.

- **Patients on regular transfusions** to remain on the same regimen. NHSBT are working to maintain the blood supply and will update clinical teams if problems develop. If that were to be the case, there may be a need to lower the transfusion threshold from current recommendation of Hb ≥90 g/L to ≥80 g/L in the first instance. Routine blood tests monitoring for iron overload and for the effects of iron chelation should be continued. For patients on regular transfusions, outpatient review should be co-ordinated to take place at the same time as transfusion. Clinicians should consider if routine MRI

monitoring for iron overload can be postponed. If fever develops, all chelation agents should be stopped unless severe cardiac iron load likely to cause decompensation and patients advised to contact their clinical team.
- **Patients on steroid treatment** should remain on the same steroid regimen.
- **Patients in haematological remission** do not require additional monitoring.

Management of DBA Patients who are Unwell:
All DBA patients need urgent assessment if unwell or have fever to rule out non-COVID-19 causes (e.g. bacterial infections causing sepsis).

Stop all chelation treatment unless there is severe cardiac iron load with risk of decompensation (febrile or acute unwell patients have risk of AKI with both desferrioxamine and deferasirox, risk of severe tubular acidosis with deferasirox, risk of hyperamonaemic encephalopathy with deferasirox and risk of neutropenia in patients on deferiprone).

Red flag symptoms: patients should be encouraged to attend the Emergency Department (A+E) or call 999 if any of the following occur:
- Respiratory distress (new shortness of breath or increased breathlessness compared to baseline particularly at rest or on minimal exertion) +/- chest pain
- Persistent fever $\geq$38° C (lasting for at least one hour).
- Severe headache, confusion or neurological changes.

Management of DBA Patients Fulfilling COVID-19 Criteria:
For a proportion of patients remote supervision will be sufficient:
- systems need to be in place for remote follow-up every 24 hours
- a clear pathway needs to be instituted for patients to seek help

A. All DBA patients positive for SARS-CoV-2 should have a CXR despite lack of lower respiratory symptoms before ascribing them to remote supervision. Patients may need reassurance about the use of ionising radiation.
B. Remote supervision is not appropriate if there are clinical symptoms of lower respiratory tract infection (shortness of breath, hypoxia, tachypnoea) despite the absence of radiological signs on the CXR. Consider an MRI chest in preference to minimise ionising radiation or alternatively a HRCT.
C. Co-pathogens should be evaluated and treated.
D. Assess for possibility of adrenal insufficiency and if known adrenal insufficiency institute hydrocortisone replacement therapy.

There are concerns surrounding NSAIDs in COVID-19 and until these are clarified, the use of paracetamol should be preferred unless there is a contraindication.

References:

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