Haematology Department

Hydroxycarbamide for Sickle Cell Disorders

Information for patient, parents and carers

Introduction

This leaflet aims to provide you with general information about medication used in children / young people with sickle cell disorders.

If you are ever worried about your child then please contact your sickle cell team or take your child to accident and emergency.

What is hydroxycarbamide?

Hydroxycarbamide, also known as hydroxyurea or hydrox, is a medicine that is used in sickle cell disease to try to reduce sickling of the red blood cells. It can be used in both adults and children and has been used in people with sickle cell disease for over 20 years.

How does hydroxycarbamide work?

Hydroxycarbamide mainly works to reduce the amount of sickle haemoglobin in the blood and increase a protective haemoglobin called HbF.

HbF is the same haemoglobin that is in us all at birth and this haemoglobin is the reason babies with sickle get no sickle problems until they are older.

The HbF not only dilutes out the sickle haemoglobin but actively protects it from sickling and causing damage.

Hydroxycarbamide also reduces inflammation and blood clotting which are also part of the tissue damage that occurs in sickle.

Why has hydroxycarbamide been recommended for me / my child?

It is recommended that children / young people with sickle cell should be on hydroxycarbamide, as the evidence is now overwhelming that it saves lives by:

- reducing deaths from sickle complications,
- reducing pain,
- reducing hospital admissions,
- reducing the need for blood transfusions,
- reducing stroke,
- reducing time off school,
- improving general wellbeing,
- reducing long term complications of sickle cell disease.

There have been national guidelines in the USA since 2014, and the UK since 2018, which recommends that all children with HbSS or HbS/β° types of sickle cell should be commenced on hydroxycarbamide from 9 months of age.

Other types of sickle cell HbSC, HbSD can be considered for hydroxycarbamide, your sickle cell team will be happy to discuss this with you.

How is hydroxycarbamide taken?

Hydroxycarbamide comes as either a liquid or tablet that is taken once a day. The amount that you/r child is given depends upon your / their weight on how well you / they respond to it. Some individuals need a low dose to give them benefit, others need a higher dose. The dose you/your child is started on will be low, and this will be gradually increased by your sickle cell team over a number of months, with careful monitoring of blood tests to ensure it is tolerated well.

You/your child will need to take hydroxycarbamide once a day every day. If you forget to take / give the medicine one day do not take / give them a double dose the next day.

What are the benefits of hydoxycarbamide?

Hydroxycarbamide should reduce the frequency and severity of sickle cell crisis. It should also reduce the long term complications of sickle cell disease. By reducing the frequency of sickle cell crisis and long term complications this can lead to a better quality of life for you/r child and an increased life expectancy. In our experience, the improvement of children and young people being on hydroxycarbamide has been transformational, many have now forgotten what sickle pain feels like.

What are the common side effects of hydroxycarbamide?

Hydroxycarbamide is usually well tolerated and it is very unusual to have to stop it because of a serious side effect.

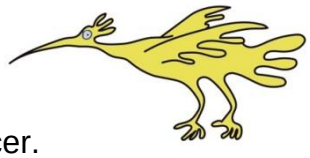
Hydroxycarbamide can reduce some of the healthy blood cells that help fight infection and form blood clots (white blood cells and platelets). Some reduction in these cells is beneficial.

If these cells are reduced too much it could cause an increased risk of infection or bleeding. Sometimes hydroxycarbamide can cause the haemoglobin to fall, making them more anaemic.

This is the reason that regular blood tests need to be taken to make sure the dose is the correct dose. The dose will have to be adjusted depending on the response in the blood tests.

Other very rare side effects include headaches, hair loss or hair thinning, darkening of the skin and nausea.

All these side effects are temporary and will improve once the hydroxycarbamide is temporaily stopped.



Is hydroxycarbamide safe for me/my child?

In the past, there was some concern that hydroxycarbamide may cause cancer. Hydroxycarbamide has now been used in individuals with sickle cell disease for over 25 years, and in large national studies there has been shown to be no increased risk of developing cancer in those individuals taking hydroxycarbamide.

Will hydroxycarbamide affect my/my child's fertility?

There is no clear evidence in females or males that hydroxycarbamide affects fertility.

In boys it may reduce sperm production but evidence for this is unclear and no large studies have been done to prove that hydroxycarbamide affects sperm production.

However we do know that sickle cell disease itself can cause reduced sperm production. Sperm counts can also be reduced by other medicines such as paracetamol.

In girls, hydroxycarbamide does not affect fertility, but women should not become pregnant while they or their partner is taking hydroxycarbamide, as research suggests that fetal abnormalities may occur.

In those who are sexually active, an effective form of contraception should be used to avoid pregnancy. You can ask your general practitioner (GP), practice nurse or the sickle cell team for further advice.

If someone is taking hydroxycarbamide, they should stop taking it at least three months before trying to conceive. This will reduce the risk to the baby. Stopping hydroxycarbamide must be discussed this with the sickle cell team first as an alternative treatment may be necessary.

What follow up will I/my child need?

If you/r child is on hydroxycarbamide you / they will have regular visits to the clinic to check that you / they are not experiencing any side effects and to establish if the hydroxycarbamide is reducing the amount and severity of crisis. You/r child will also have regular blood tests to make sure that the bone marrow has not been affected. When you/r child starts hydroxycarbamide or if the dose is changed you / they will have a blood test 2 weeks later. If all is okay, another blood test will be done 2 weeks after that. If you/r child's blood test remains okay they will have the blood test done every 4-6 weeks.

If you/r child's blood test shows a reduction in their haemoglobin, white blood cells or platelets the hydroxycarbamide may be reduced or stopped until they return to normal. The hydroxycarbamide can be started again and occasionally restarted at a lower dose than previously given.

Is there any research into hydroxycarbamide in children with sickle cell?

There have been 3 large studies published between 2010 and 2013 that really prove that Hydroxycarbamide should be used in almost all patients from a young age. These studies are so important they will be highlighted each in turn:

<u>Steinberg 2010</u>

299 adults with sickle cell disease and 17.5 years follow up.

Patients on Hydroxycarbamide benefited with:

- 43% overall reduction in death
- Less stroke, less kidney disease, less liver failure

This study also looked at theoretical concerns about Hydroxycarbamide that it can cause cancer or can be damaging if taken by parents having a baby. No increased cancer was seen. No abnormalities in babies was seen in mums or dads taking hydroxycarbamide.

No serious side effects seen.

Limitations - No children were in the study and it wasn't a formal clinical trial. It was a long term detailed observation of the outcome in a large number of adults.

<u>Baby HUG Trial</u>

This is a large American trial of using hydroxycarbamide in all children with sickle cell disease from about 1 year of age.

193 children aged 9-18 months.

Hydroxycarbamide gave benefits of:

- 52% fewer crisis
- Fewer acute chest syndromes
- Fewer hospital admissions
- Fewer transfusions

No serious side effects seen.

This is the first major trial in young children. The limitations of this trial are that it only had short follow up.

Lopes 2013

Total 1760 children.

The most severe 267 were put on Hydroxycarbamide.

1493 were given standard treatment.

7 year follow up.

Death rate in Hydroxycarbamide patients 1 in 267 (0.037%).

Death rate in standard treatment patients who were clinically less severe was 82 children (5.5%).

It would have been expected that more deaths would have been seen in the most severe patients. The study concluded that Hydroxycarbamide could be said to have prevented more than 90% of deaths from sickle cell disease in childhood.

One child was diagnosed with cancer, and on further investigation they were in the standard treatment group, ie not on hydroxycarbamide treatment. No child on Hydroxycarbamide got cancer.

How long will my child be on hydroxycarbamide for?

Hydroxycarbamide can be given for a long period of time.

The Baby Hug trial has reviewed patients treated with hydroxycarbamide continuously since infancy, for a minimum of 15 years, and found that the effects of the drug persist without major toxicity. Growth is normal, and pubertal development timely.

Will Hydroxycarbamide cure my child of sickle cell disease?

Hydroxycarbamide is not a cure for sickle cell disease. It is an effective treatment for preventing or reducing sickling crisis and its effect will only last as long as the person is taking it.

Further information

The leaflet **Sickle Cell Disease – Taking Hydroxycarbamide** is available for more information once you/r child starts taking hydroxycarbamide.

https://www.sicklecellsociety.org/hydroxyurea-treatment-transforming-lives-children-sickle-cell-disease-liverpool-area/

If you have any questions or want any further information please contact your sickle cell team on 0151 252 5070.

Useful websites

www.alderhey.co.uk
www.sicklecellsociety.co.uk

This leaflet only gives general information. You must always discuss the individual treatment of your child with the appropriate member of staff. Do not rely on this leaflet alone for information about your child's treatment.

This information can be made available in other languages and formats if requested.

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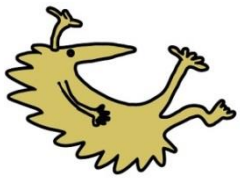

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