Children's Cancer and Leukaemia Group
the EXPERTS in CHILDHOOD CANCER

Veno-occlusive disease (VOD) in children and young people

An information guide for patients, parents and carers

The purpose of this guide is to help you understand more about veno-occlusive disease (VOD) in children and young people with cancer.

Information in this guide should be used to support professional advice specific to your/your child's diagnosis. If you have any questions, it is important to ask your medical team.

What is Veno-occlusive disease (VOD)?

Veno-occlusive disease (VOD) is a serious complication sometimes caused by chemotherapy. It is most often seen during stem cell transplant (SCT). Veno-occlusive disease is not another illness, but a complication that affects the liver.

Veno-occlusive disease is also called sinusoidal obstruction syndrome (SOS).

VOD can range from mild to severe. It occurs in approximately 10-30% of children/young people who have received total body irradiation (TBI), busulphan or high-dose melphalan as part of their conditioning treatment before a stem cell transplant.

VOD is usually a temporary problem, but it can cause long-term issues, and is sometimes life-threatening. Your SCT team will discuss this in more detail with you.

In VOD the chemotherapy damages cells in the liver, so the veins within the liver become obstructed (occluded) by dead or damaged cells. This causes the blood flow from the liver to back up.

The protein-rich fluid content of the blood leaks out into the peritoneal cavity (the space between the membranes which separate the organs from the wall of the tummy). Body weight and the size of the tummy increases as the fluid collects in this space.

As the tummy gets bigger, it becomes uncomfortable and pain relief medicine may be needed.

The role of the liver and the impact of VOD

The liver is a large organ in the right upper part of the abdomen. You can't usually feel it as it is under your ribs. It is made up of two lobes, each consisting of 50,000 to 100,000 liver cells, called lobules.

Beyond each row of lobules is a tiny blood vessel, called a sinusoid. Blood flows through the sinusoids, bringing nutrients to be stored in the liver cells, and collecting products that need to be removed from the body.

The lining of the sinusoids is made up of cells, called endothelial cells. It is these cells that become damaged and stop the liver from working properly, causing VOD.

The liver helps the body in many ways:

Digestion – helps to break down carbohydrates, proteins, vitamins, minerals and fats gained from food.

Detoxifies – helps to break down drugs so they can be used by the body, and removes some drugs from the body once their job is done.

Breaking down of red blood cells – red blood cells live for around 120 days and when they die, the liver helps to break them down.

Production of blood products – produces vital blood products, including factors essential for stopping you from bleeding (clotting). If the cells of the liver are damaged, it may not produce these blood products as quickly or as well as it needs to. You/your child will probably need lots of blood and platelet transfusions.

Risk factors for VOD

We know that some young people/children are more likely than others to develop VOD. If you/your child falls into any of the categories listed below it does not mean that you will get VOD, but you may be more likely to.

Before the transplant, the SCT team will discuss your/your child's care in more detail and will explain why this happens. Some of the circumstances which may trigger VOD include:

- children with osteopetrosis
- children with thalassaemia
- children with adrenoleukodystrophy (ALD)
- children with macrophage activating syndromes (MAS), for example haemophagocytic lymphohistiocytosis (HLH), Griscelli syndrome (GS)
- evidence of previous liver damage (including prior abdominal radiotherapy)
- previous treatment with certain anti-cancer drugs
- infection before or during the conditioning phase of SCT
- long-term treatment drugs that may harm the liver
- unrelated donor transplants
- second stem cell transplant
- the use of busulphan, high-dose melphalan, and/or total body irradiation in the conditioning regimen

Signs and symptoms

Sudden weight gain

This may take place over a few days or, in extreme cases, hours. It is due to fluid collecting in the abdomen rather than staying in the blood system. The fluid has collected in the wrong place, so it cannot be passed by the kidneys.

Abdominal (tummy) swelling

As the liver swells, fluid is squeezed out of the liver and collects in the abdomen (tummy). This is called ascites. This fluid contains a lot of protein which encourages more fluid to collect in the abdomen. As a result, the abdomen gets bigger and it may be uncomfortable or difficult to breathe, especially when lying down.

Abnormal blood clotting

If this happens, more frequent platelet transfusions may be needed as platelets do not live as long in patients who have VOD. Plasma or other clotting factors, e.g. cryoprecipitate or vitamin K, may also be needed.

Pain

As the VOD causes the liver to get larger, it presses on the capsule around it and this can be painful. Pain may be felt in the upper right hand part of the tummy.

Abnormal bilirubin

When VOD makes the liver unable to break down dead red blood cells, bilirubin (a yellowish pigment found in a fluid made by the liver, called bile) cannot be removed from the body effectively. Blood tests (liver function tests – LFTs) will show the liver is not working as hard as it should be. If the level of bilirubin in the blood becomes very high, the skin and whites of the eyes may look yellow. This is called jaundice. It may also cause dry and itchy skin.

Feeling or being sick (nausea and vomiting)

Nausea and vomiting may happen for many reasons with VOD such as pain, ascites or an enlarged liver pressing on the stomach.

Feeling tired (lethargy)

All of the symptoms of VOD are likely to make you/your child feel tired and generally unwell.

How is it diagnosed?

Your SCT team will be familiar with the signs and symptoms of VOD. Various tests may be done to make an accurate diagnosis. Some of the symptoms may be signs of other problems, such as graft versus host disease or infection. But, it is only in VOD that there is unexplained weight gain and fluid retention.

To confirm a diagnosis of VOD an ultrasound scan is done. This uses a probe that is run over the skin to give a picture of what is happening in the liver. It shouldn't hurt but may be uncomfortable if your/your child's abdomen is already painful. Sometimes a liver biopsy is needed to confirm the diagnosis. Your SCT team will discuss which is the best option with you.

Treatment of VOD

Monitoring of busulphan levels

Your doctor will decide if busulphan levels should be monitored. This is done by taking blood samples at different intervals after the first dose. The samples show how the liver is processing the chemotherapy and help doctors decide if changes to further doses are needed.

Prophylaxis (preventative treatment)

Where there is a high-risk of VOD, prophylactic or preventative treatment is considered. An oral medicine called ursodeoxycholic acid or an intravenous (IV) medicine, called defibrotide, may be given from the start of the chemotherapy conditioning.

Defibrotide (medication)

Defibrotide is used for the prevention of VOD in children and young people undergoing SCT who are considered to be at high-risk of developing the disease, or as treatment of suspected or established VOD.

Defibrotide is usually given as an intravenous infusion, (over 2 hours, four times a day, directly into a vein). In severe cases of VOD, or poorly responding cases, the dose may be increased.

Defibrotide works in a number of ways; antithrombotic (prevents clotting), anti-inflammatory (reduces swelling) and anti-ischaemic (reduces the restriction of blood flow). Defibrotide can help to protect the liver from the effects of chemotherapy on the endothelial cells.

The management of medicines

All the therapies required to support a child or young person through transplant have an impact on the liver, including IV feeding (TPN - total parenteral nutrition), pain relief, antibiotics or blood products.

The SCT team will plan your/your child's care on a daily basis to consider how to best manage your medication. Your/your child's care will be discussed with you but remember you can always ask questions if you are finding something difficult to understand.

Supportive care

The management of fluid retention and ascites are an essential part of the treatment of VOD. The aim is to reduce the amount of fluid that has collected in the abdomen and elsewhere within the body.

This is achieved by giving diuretics (drug treatment) to encourage the passing of urine, and restricting the amount of oral fluids allowed within a day.

Restricting the amount you are allowed to drink within a day can be very distressing if you are thirsty. Small drinks or ice lollies/cubes can sometimes relieve the distress.

To monitor the effects of this treatment regular blood tests will be done. The accurate monitoring of fluid input and output is essential, as well as weighing you/your child and measuring the tummy once or twice a day. In severe cases of VOD, fluid retention and a swollen abdomen can have an effect on kidney function. Sometimes support is needed from the renal team (kidney specialists).

When the abdomen gets bigger, it sometimes causes difficulties with breathing. This can mean that you/your child may need to be cared for in a high-dependency or intensive care unit. Your SCT team will discuss this with you should it be required.

VOD can be very uncomfortable and painful. Pillows and loose clothing may help. Your/your child's skin may also become dry and itchy. Continue to bath every day and use emollients (moisturisers) to stop your/your child's skin itching. Drug treatments with antihistamines may also help to relieve itching.

i USEFUL ORGANISATIONS

Children's Cancer and Leukaemia Group (CCLG) publishes a variety of free resources to order or download
www.cclg.org.uk

Young Lives vs Cancer offers practical support to children and young people with cancer and to their families
www.younglivesvscancer.org.uk

Macmillan Cancer Support offers support and advice to those affected by cancer.
www.macmillan.org.uk

If you have any questions or if there is anything you don't understand please talk to your SCT team.

Scan to order or download this factsheet or any other CCLG publications FREE of charge.

With thanks to Julie Guest and Craig Baillie, Stem Cell Transplant Nurse speclialists, who reviewed this factsheet on behalf of the National Paediatric Stem Cell Transplant Nurses Group, in conjunction with the CCLG Information Advisory Group, comprising parents, survivors and multi-professional experts in the field of children's cancer.

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Children's Cancer and Leukaemia Group (CCLG) is a leading national charity and expert voice for all childhood cancers.

Each week in the UK and Ireland, more than 30 children are diagnosed with cancer. Our network of dedicated professional members work together in treatment, care and research to help shape a future where all children with cancer survive and live happy, healthy and independent lives.

We fund and support innovative world-class research and collaborate, both nationally and internationally, to drive forward improvements in childhood cancer. Our award-winning information resources help lessen the anxiety, stress and loneliness commonly felt by families, giving support throughout the cancer journey.

Our work is funded by donations. If you would like to help, text 'CCLG' to 70085 to donate £3. You may be charged for one text message at your network's standard or charity rate. CCLG (registered charity numbers 1182637 and SC049948) will receive 100% of your donation.

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