Anaemia due to Kidney Complications in Tuberous Sclerosis Complex

Introduction

If you've ever been told that you or your child are 'anaemic' what does that actually mean? What symptoms of anaemia should you be aware of if you or someone you care for has tuberous sclerosis complex (TSC)? And are you receiving the right treatments at the right time? There are a number of common causes of anaemia in the general population, which are mentioned here, however, this fact sheet concentrates on anaemia in TSC due to kidney problems.

What is anaemia, and what causes it?

Being anaemic means you've got less than the normal number of red blood cells, or less than the normal quantity of a protein called haemoglobin in your blood. So the oxygen-carrying capacity of your blood is decreased. The common symptoms of anaemia include loss of energy and shortness of breath. If you're anaemic, you may feel tired, appear pale, develop unpleasant sensations of an irregular heartbeat, and find it difficult to complete everyday tasks. Children with chronic anaemia are prone to infections and learning problems.

The common causes of anaemia in the general population include iron deficiency (e.g. due to diet or blood loss), long-standing infections and bone marrow dysfunction. People with TSC are not immune from any of these. However, in TSC there are some additional specific causes to look out for, namely, rectal polyps (a type of TSC-related tumour) or - more importantly, kidney failure. Anaemia is always secondary to some other disorder. It affects 5-10% of people with TSC.

How does anaemia relate to TSC?

Polycystic kidney disease is a condition that affects 1 in 100 people with TSC. It can impair blood production, resulting in anaemia, and may also lead to kidney failure. Renal AMLs (angiomyolipomas) are another type of TSC-related kidney problem. They are benign growths containing fat, blood vessels and muscle-like cells, and usually don't cause any symptoms. However, sometimes AMLs may bleed and this can lead to anaemia. Each of these problems can occur in people with TSC at any age from childhood to adulthood.

The diagnosis of anaemia may be the first sign of kidney and blood pressure-related problems in people with TSC. Anaemia may also aggravate the symptoms of chronic renal failure. These can include tiredness, mood fluctuations, disturbed sleep patterns and impaired sexual function. Therefore, early diagnosis of anaemia, proper treatment and regular monitoring of TSC patients may prevent or reduce its potential long-term effects.

When should I get checked for kidney problems in TSC?

Kidney failure itself occurs in 1% of people with TSC, usually due to polycystic kidney disease. Symptoms may include swelling of the legs, a need to pass urine at night, shortness of breath, poor appetite, itching of the skin, or (in children), weight loss or poor growth. However, all these symptoms can occur for other reasons. Most people with a TSC-related kidney disorder have no symptoms at all.

Because of this, it is a good idea for those with TSC to get screened for any possible kidney problems by getting regular blood pressure and urine tests, kidney ultrasounds (every 1 to 3 years), and blood tests to check kidney function. If you are persistently unwell for no apparent reason, remind your doctor that you have TSC, and ask about getting monitored for kidney problems. **(Please see the TSA Fact Sheet 24 on kidney screening for more information.)**

How is anaemia diagnosed?

Your doctor can detect anaemia by a simple blood test, followed by other investigations to determine the cause. The test involves measuring the content of the haemoglobin protein in the blood. Haemoglobin produces the blood's red colour and contains iron. It is responsible for transporting oxygen around the body. The normal haemoglobin range in the blood is 14-16 grams per decilitre (g/dl) for men and 12-15g/dl for women. These levels are reduced in anaemic patients, sometimes as low as 4g/dl. If you already suffer from anaemia it is vital to keep track of your haemoglobin level, so that any problems can be dealt with early.

Why treat anaemia early?

Recent studies now indicate that symptoms of anaemia actually occur much earlier in the course of kidney disease than previously realised. Experts point out that delayed diagnosis and treatment of anaemia associated with chronic kidney disease might increase the risk of cardiovascular complications, such as coronary artery disease, left ventricular disorders and cardiac failure, which can be life threatening.

What treatments are available?

In the past, blood transfusions were the only successful treatment for anaemia due to kidney failure, once iron and vitamin deficiencies had also been treated. However, the disadvantages of blood transfusion limit its value. These problems include: variable haemoglobin levels, the risk of infection and the formation of antibodies, which could complicate any later kidney transplant. New technology has now allowed researchers to identify a natural human substance produced by the kidneys, called erythropoietin, and to create an artificial version of this to treat anaemia. This medical treatment is called recombinant erythropoietin - or EPO.

How does EPO work?

By making natural erythropoietin, your kidneys stimulate the production of red blood cells in your bone marrow. Less erythropoietin is made in someone with kidney problems, so the bone marrow makes fewer blood cells. Anaemia then occurs, so that person becomes weak and tired.

EPO initially became available in 1989 as a replacement for natural erythropoietin. It is made by using the genetic code for human erythropoietin. This is then placed in special cells to produce EPO in large amounts. So EPO looks and acts very much like the natural erythropoietin in your body. That is important, because some anaemia patients often have to take EPO for many years.

How do I take EPO?

EPO is taken by injection, usually 1 to 3 times each week depending upon the type of drug prescribed and the medical instruction given. Most patients or carers learn how to inject EPO, so it can be taken at home. It is available either in ready-to-inject, pre-filled syringes, or in vials containing ready-to-inject liquid, or a powder needing water to be added before injection.

Who can take EPO?

EPO can be prescribed for pre-dialysis patients (those with chronic kidney failure), for patients on haemodialysis and peritoneal dialysis; and for those with a failing kidney transplant. New evidence suggests that EPO is also useful for some patients with low haemoglobin levels.

What should I be asking my doctor?

Unfortunately, EPO is not always prescribed early enough for patients who could benefit from it. New studies show that symptoms of anaemia are actually present at the very early stages of kidney disease among the general population. Kidney disease is often at an advanced stage by the time patients are referred for treatment. In fact, upon referral, haemoglobin levels are often already below the recommended levels, yet only a minority of people have received EPO by that time.

The National Kidney Foundation (NKF) recommends that if you are offered blood transfusions to treat your anaemia at any time, then you should always ask about erythropoietic agents like EPO instead. You should also ask about getting a referral to a specialist. If you have a problem in getting EPO, the NKF states they will do their best to help (see contact details at the end of this Fact Sheet). GPs and carers are now urged to improve the diagnosis and referral of anaemia patients so that they receive appropriate treatment early.

Are there any side-effects?

Most patients have no ill effects from taking EPO. Studies show all erythropoietic agents are effective and relatively safe in raising blood haemoglobin

levels. To limit the risk of increased blood pressure, which appears in 1 in 5 people, anyone taking EPO should also control salt and fluid intake. Very rarely, high blood pressure has caused a fit but careful monitoring should prevent this. Some patients have experienced flu-like effects shortly after injection and others have reported rashes. However, these effects are not serious and usually decrease with time. Very occasionally, EPO can make anaemia worse by causing anti-bodies to the EPO receptors. This is called PRCA or Pure Red Cell Aplasia. As with any other aspect of treatment, if you feel unwell you should tell your doctor immediately.

For more information: UK National Kidney Foundation: *6 Stanley Street, Worksop, S81 7HX Tel: 01909-487795; Fax: 01909-481723; Helpline: 0845-601-0209; email: nkf@kidney.org.uk.*

Corinne Swainger
Medical Writer
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Further information on TS and the work of the TSA can be obtained from: Diane Sanson, Head of Administration,
P.O. Box 12979, Barnt Green, Birmingham, B45 5AN.
Tel/Fax: 0121 445 6970
Email: diane.sanson@tuberous-sclerosis.org
Web: www.tuberous-sclerosis.org

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