



Caring together

European Dialysis and Transplant
Nurses Association / European Renal
Care Association

Nurses Pocket Guide ... to managing anaemia in transplant patients



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Preface

Anaemia in kidney transplant recipients

Anaemia is relatively common in kidney transplant recipients. Therefore, regular screening for anaemia and careful evaluation of the multiple factors that may contribute to it are recommended following transplantation.

In order to assess the frequency of post-transplantation anaemia and the working guidelines for its diagnosis and treatment, a questionnaire was sent to 123 renal centres in 13 countries (1). Results from the 39 centres (32%) that responded indicate a wide variance in the percentage of patients with anaemia by unit and the methods used to both screen and treat, for example:

- i) 16% (range 2-60%) of transplant recipients were anaemic according to the European Best Practice Guidelines (2), with Hb < 11 g/dl

- ii) Working protocols varied with respect to:
 - laboratory tests used to assess anaemia,
 - the person responsible for monitoring
 - the person who treats the anaemia,
 - the Hb threshold for treatment, and the treatment itself

Standard guidelines for the monitoring and treatment of anaemia should be applied to kidney transplantation, with specific consideration of the role of the immunosuppressive regime and other factors unique to transplant patients. This leaflet, along with the material on the EDTNA/ERCA website, is designed to increase nurses' awareness of anaemia in these patients, to help understanding of the common causes of anaemia in them and thereby enable and encourage nurses to address the issue.

***An EDTNA/ERCA
Anaemia and Transplantation Interest Group
Research Project***

Introduction

Anaemia is common in patients with Established Renal Failure (ERF).

For patients having dialysis and now more commonly for those approaching ERF, treatment with Erythropoiesis Stimulating Agents (ESA) is often prescribed. For the majority of these patients kidney transplantation is the treatment of choice. A well-functioning graft can be expected to restore normal haemoglobin.

However, it is known that anaemia can be a problem post-transplantation, and it is apparent that this is a neglected group (1,3-5). It is recommended that treatment guidelines for the management of anaemia in the general CKD population be followed in the transplant population, until such time as specific guidelines are developed.

When a patient with a kidney transplant has anaemia, treatment will depend on the cause. The following pages look at the factors which may be considered in order to provide a differential diagnosis.

Anaemia in the immediate and early post-operative period

Anaemia in the immediate and early post-operative period following kidney transplantation can be caused by:

- Loss of blood during the operation.
- Haematuria (lose of blood in the urine) during the first days after surgery.
- Drawing of blood for blood tests.
- Acute gastrointestinal bleeding due to the operative stress.
- Acute Tubular Necrosis. The majority of transplanted renal grafts do not function optimally at first because of **acute tubular necrosis** (ATN) or **delayed graft function**, a common situation after deceased donor transplantation that usually recovers spontaneously after 2 to 4 weeks. Renal dysfunction or diminished function of the renal allograft is the most important risk factor for developing anaemia after kidney transplantation. Because of reduced kidney function uraemic toxins are present in patients' blood, which additionally reduce erythropoiesis, shorten life expectancy of red blood cells and cause transferrin loss with urine (it incorporates absorbed iron in plasma). Erythropoietin and iron deficiency may develop during the period of graft dysfunction. Renewal of erythropoietin secretion will occur when the graft starts to function (4).
- Treatment with **Aspirin** that is started soon after transplantation to prevent thrombosis in the vascular anastomoses. If the recipient is bleeding we should consider stopping this medication for a short period.
- Haemolytic Anaemia associated with minor blood group A, group B, group O incompatibility (6).

Anaemia later in the post kidney transplantation period

Anaemia later in the post kidney transplantation period may be related to reduced renal function or may be medication-related (7,8). The following drugs should be considered as a potential cause:

- **Azathioprine** is an antimetabolite immunosuppressive agent. It has been in use since 1960 to prevent rejection, but not as a treatment when rejection occurs. It prevents proliferation of T and B lymphocytes and inhibits the production of antibodies and cytotoxic cells. Its main side effects are bone marrow suppression and hepatotoxicity. Dose reduction usually causes the side effects to disappear gradually. Because of its side effects, in many centres, Azathioprine has now been replaced.
- **Mycophenolate mofetil (MMF)** is a more selective anti-metabolite, which is more effective than Azathioprine in preventing rejection. **MMF** is myelo-suppressive, its side effects therefore include: anaemia, leucopaenia, gastrointestinal disorders (diarrhoea, vomiting, oesophagitis, gastritis and gastrointestinal bleeding). These side effects disappear after cessation of treatment. Very rarely Pure Red Cell Aplasia can occur.
- **Rapamune** is an antimetabolite that prevents the proliferation of T cells and rejection. Its side effect is bone marrow suppression (especially leucopenia).
- **ACE Inhibitors:** inhibition of the Angiotensin Converting Enzyme reduces blood levels of Angiotensin, thereby causing a reduction in blood pressure, blood volume and sodium. ACE inhibitors are very effective and reduce blood pressure even when Renin levels are normal. Their side effects include bone marrow suppression causing neutropaenia, whose presenting symptoms may be throat pain and fever. ACEI inhibits endogenous erythropoietin production, inhibits angiotensin 11 mediated stimulation of red blood cell precursors and the generation of an erythropoiesis-inhibiting protein.
- **ARBs:** Angiotensin Receptor Blockers. Blocking the angiotensin receptors prevents the secretion of rennin thereby reducing blood pressure. Their side effects are the same as those of ACE inhibitors.

Other causes of Anaemia

In addition to renal function and drug regime, there are other factors to consider:

Iron Deficiency

Iron deficiency is a major cause of anaemia in post transplanted patients and should always be corrected. The prevalence of iron deficiency may be greater in the early transplantation period because of operative blood loss and increased iron utilization with the onset of erythropoiesis after successful transplantation. Transplanted patients should have sufficient iron to allow a Hb concentration of > 11g/dl. Blood samples should be taken to ensure that the ferritin 200-500mg/L, Transferrin Saturation 30-40%, Hypochromic Red Cell < 2.5%, Reticulocyte Hb – 35pg/cell. If these results show that the patient has iron deficiency, treatment with supplementary iron is recommended. The optimal iron dose is 25-150mg/week (2,9-11).

Vitamin B12 and Folic Acid deficiency

Vitamin B12 and red cell folate levels should be checked as part of the haematinic screen in patients with anaemia. Patients with these deficiencies often have an increased mean cell volume (MCV) if red cell indices are checked but this can also be a reflection of immunosuppressive therapy. If the patient has either of these deficiencies, vitamin supplementation should be considered (2,9,11).

Acute Rejection

Early acute rejection is reported to cause a sharp decrease in erythropoietin production and hence anaemia. An additional mechanism for the development of anaemia during rejection is thrombotic microangiopathy, which may develop during episodes of severe vascular rejection (12).

Inflammatory States

The inhibitory effect of inflammatory cytokines on the erythropoietin receptor is still unknown. Macrophages produce interleukin 6 during inflammation. It seems that interleukin 6 causes hepatocytes to produce hepcidin. Hepcidin blocks both iron release from the macrophages and intestinal iron absorption. C reactive protein (CRP) should be evaluated as graft rejection may be a source of inflammation and thus cause anaemia (10,11,13).

Infection

Infection has the same effect on erythropoiesis as inflammation and should be treated appropriately. Anaemia may be a feature of cytomegalovirus infection. Parvovirus B19 infection may cause Pure Red Cell Aplasia (12).

Hyperparathyroidism

As the transplanted graft fails, patients will require treatment to prevent renal bone disease. Parathyroid Hormone levels should be checked because this increases as anaemia develops (15).

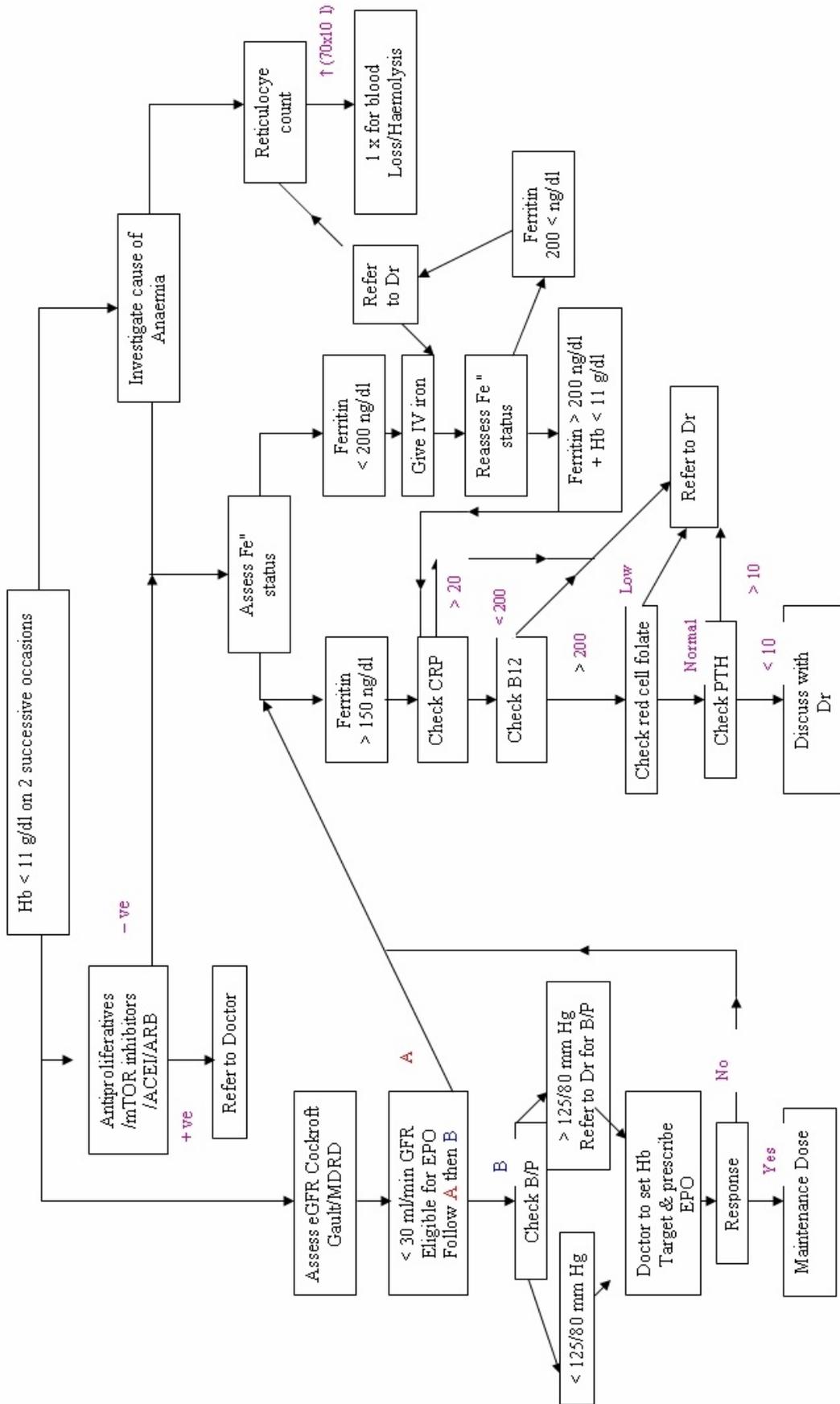
Haemolytic uraemic syndrome (HUS) associated anaemia

HUS is caused by acute Ciclosporin or Tacrolimus toxicity in 4-7% of transplant recipients. It usually develops early after transplantation but may occur later. It affects recipients of deceased donor as well as living donor kidneys. HUS presents clinically with thrombotic angiopathy, Thrombocytopenia, haemolysis, anaemia and acute renal failure, are diagnostic criteria. Close monitoring of laboratory values and clinical status of kidney allograft recipients ensures early detection of HUS and can prevent its consequences, which can/may lead to graft loss. Worsening of anaemia following transplantation will be a warning sign of incipient serious complications following transplantation, which can/should be confirmed with additional investigations, and not be taken lightly. We can make a difference and improve graft survival following transplantation (16-18).

Malignancy

Transplanted patients are at increased risk of developing cancer because of a weakened immune system with the use of immunosuppressive drugs (19). Unexplained anaemia may warrant the screening for potential malignancies, for example the checking of LDH as this is released when cells are destroyed.

Algorithm For Anaemia Management In Transplant Patients



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Information to explain why anaemia occurs in transplant patients:

An anaemia algorithm to help you manage anaemia in your unit

Why Do Transplant Patients Become Anaemic?

How Can You Change Anaemia Management In Your Unit To Help Transplant Patients?

Tools to help educate staff are available on the website:

www.edtnaerca.org/pages/education/publications.php

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