

Nutritional management of anaemia in adult kidney transplant recipients

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GUIDELINES

No recommendations possible based on Level I or II evidence.

SUGGESTIONS FOR CLINICAL CARE

(Suggestions are based on Level III and IV evidence)

There is currently no Level III or IV evidence examining the efficacy of specific dietary interventions in the management of anaemia in kidney transplant recipients. The following suggestions are based on opinion with reference to the evidence relating to the occurrence of anaemia in kidney transplant recipients.

- All adult kidney transplant recipients should be monitored for anaemia.
- Possible dietary causes of anaemia, including iron, folate and vitamin B12 deficiencies, should be investigated.
- A dietitian should be consulted if dietary deficiencies are shown to be contributing to anaemia.
- It is appropriate to use pharmacological doses of nutrients in conjunction with dietary interventions to correct anaemia.

BACKGROUND

Anaemia, defined as a haemoglobin concentration of <11–12 g/dL in women or <12–13 g/dL in men^{1,2} is common in patients with end-stage renal failure. There is a positive correlation between haemoglobin and creatinine clearance in renal transplant patients,^{3,4} probably a function of endogenous erythropoietin production by the graft.⁵ Following successful kidney transplantation, with the rise in endogenous erythropoietin production, haemoglobin levels generally rise and normalize within the first two to 4 months.⁶

However, anaemia may persist after transplantation. The prevalence of anaemia has been found to be as high as 38.6% in long-term kidney transplant recipients (ranging from 6 to 5 months post-transplant), including those patients with normal graft function.^{7–13}

In kidney transplant recipients, anaemia is a significant independent risk factor for cardiovascular death and for all-cause mortality^{14,15} and a positive correlation exists between creatinine clearance and haemoglobin levels.¹⁶

While post-transplant anaemia is associated with treatment with azathioprine, sirolimus and mycophenolate mofetil, as well as angiotensin-converting enzyme inhibitors (ACEi) and angiotensin II receptor antagonists,^{17,18} nutritional factors appear to be potentially important in the aetiology and management of post-transplant anaemia.

There may be a high prevalence of iron deficiency among kidney transplant recipients, in whom anaemia has not been diagnosed.^{14,19–21} Folate and B12 deficiencies may also contribute to anaemia in stable kidney transplant recipients.²²

This review set out to explore and collate the evidence on the safety and efficacy of nutritional interventions in preventing and managing anaemia in kidney transplant recipients, based on the best evidence up to and including September 2006.

SEARCH STRATEGY

Relevant reviews and studies were obtained from the sources below and reference lists of nephrology textbooks, review articles and relevant trials were also used to locate studies. Searches were limited to studies on humans; adult kidney transplant recipients; single organ transplants and to studies published in English. Unpublished studies were not reviewed.

Databases searched: MeSH terms and text words for kidney transplantation were combined with MeSH terms and text words for both anaemia and dietary interventions. Medline – 1966 to week 1, September 2006; Embase – 1980 to week 1, September 2006; the Cochrane Renal Group Specialised Register of Randomised Controlled Trials.

Date of searches: 22 September 2006.

WHAT IS THE EVIDENCE?

There are no published studies of satisfactory quality examining the efficacy of specific dietary interventions in the management of anaemia in kidney transplant recipients.

There is one randomized controlled trial examining the safety of concomitant oral iron supplementation and mycophenolate mofetil (MMF).

Safety of iron supplementation

Mudge *et al.*²³ undertook an open-label, randomized, controlled trial in which new kidney transplant recipients were randomly allocated to either receive iron supplements with a morning dose of MMF; iron supplements given 4 h after MMF; or no iron supplements. Blood samples were taken for estimation of mycophenolic acid (MPA) area under the curve (AUC) at day 5 post-transplant. The primary end-point was the MPA AUC on day 5. Secondary end-points included acute rejection and MMF toxicity in the first 4 weeks post-transplant. Prospective power calculations indicated that a minimum of 13 patients in each group would be required to have a 90% probability of detecting a clinically significant reduction (10 mg/h per L) in MPA AUC for iron-treated patients. Forty patients completed the study and there were no differences in baseline demographic data between the groups. The mean (\pm standard deviation) MPA AUC measurements for the groups receiving no iron ($n = 13$), iron and MMF together ($n = 14$), and iron and MMF spaced apart ($n = 13$) were 34.5 ± 8.7 , 33.7 ± 11.4 , and 32.1 ± 8.1 $\mu\text{g/h per mL}$, respectively ($P = 0.82$). There were no significant differences between the rates of acute rejection, cytopenia, infection, and gastrointestinal intolerance between the groups. The authors conclude that there is no significant effect of oral iron supplements on MMF absorption as determined by measured blood concentrations. Thus, the practice of routinely giving oral iron in such patients seems safe from an immunosuppression drug interaction standpoint.

There is a paucity of published information on the topic of treating post-transplant anaemia and treatment goals but current opinion seems to favour treating persistent anaemia to achieve targets similar to those recommended for patients with chronic kidney disease. To improve accuracy in measuring iron deficiency in this population, % transferrin saturated with iron and % hypochromic red blood cells (currently the best available marker to identify functional iron deficiency) should be assessed. This is in line with the European Best Practice Guidelines.²⁴

SUMMARY OF THE EVIDENCE?

There are currently no studies examining the efficacy of specific dietary interventions in the management of anaemia in kidney transplant recipients.

WHAT DO THE OTHER GUIDELINES SAY?

Kidney Disease Outcomes Quality Initiative: No recommendation.

UK Renal Association: No recommendation.

Canadian Society of Nephrology: No recommendation.

European Best Practice Guidelines:²⁴

Because anaemia is relatively common after kidney transplantation, regular screening and careful evaluation of its causes are recommended. Treatment of anaemia should follow the European best practice guidelines for treatment of anaemia in chronic renal failure.

International Guidelines: No recommendation.

IMPLEMENTATION AND AUDIT

No recommendations.

SUGGESTIONS FOR FUTURE RESEARCH

Well-designed, randomized controlled trials are required examining the safety and efficacy of dietary interventions in the treatment of anaemia and the impact of such measures on long-term health outcomes of kidney transplant recipients.

CONFLICT OF INTEREST

All the above authors have no relevant financial affiliations that would cause a conflict of interest according to the conflict of interest statement set down by CARI.

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