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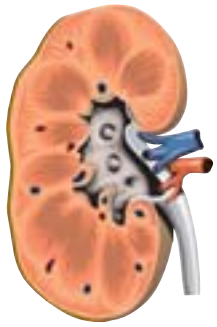
Anaemia in Moderate Chronic Renal failure

Commoner than you think



Anaemia is recognised as a major feature of severe chronic renal failure (CRF), defined as glomerular filtration rate (GFR) < 30mls/min. Recent USA and Australian population data has shown that anaemia is common even with only moderate degrees of CRF, i.e. where GFR < 60mls/min (see Table 1). Considering the linear drop in GFR with age, an estimated 2 million Australians have moderate or severe CRF.

Table 1. Prevalence of anaemia in moderate and severe CRF

GFR (mls/min)	% patients with Hb < 130g/L	% patients with Hb < 110g/L
> 50	9	2
35-50	24	10
25-35	40	18
<25	59	34

Why does it happen?

The kidney normally rapidly produces large quantities of the hormone erythropoietin (EPO) in response to a fall in blood oxygen content, stimulating the compensatory production of marrow erythroblasts within hours.

Relative deficiency of EPO synthesis is the major cause of anaemia in most forms of CRF (see Figure 1). Polycystic kidney disease is a notable exception, where Hb levels may be well-preserved or high, even on dialysis.

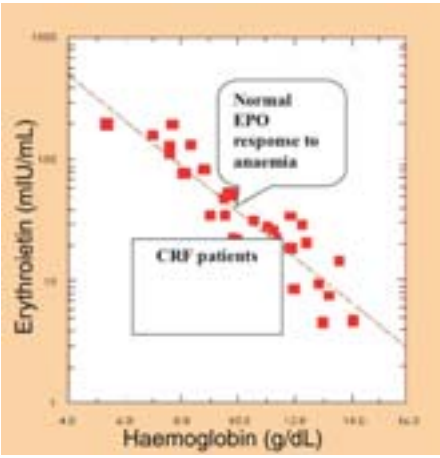


Fig. 1 EPO response to anaemia in normal subjects and CRF patients

Additional causes of anaemia are often present in CRF, including: relative iron deficiency from GI losses (especially with aspirin or NSAID use); shortened RBC survival from uraemia; intercurrent sepsis or inflammation; ACE inhibitor/ARB medication (which further suppress EPO production); or severe hyperparathyroidism.

EPO Therapy in CRF

Since the mid-1980s, recombinant DNA technology has permitted EPO therapy of the anaemia of CRF, albeit at an average annual cost of $4000 per-patient. Hb response usually takes 6-8 weeks and can deplete iron stores.

Controlled trials have shown significant improvements in LVH, cognition, quality of life, and hospitalisation, with variable effect of mortality. However, rapid rises in haemoglobin have been associated with hypertension, convulsions or vascular access thrombosis.

PBS guidelines restrict prescription to transfusion-requiring patients with Hb < 100g/L and GFR < 60mls/min, where therapy is initiated by a nephrologist.

At RPH, 92% of dialysis and 43% of pre-dialysis patients receive EPO, to a total cost of 10% of the hospital drug budget, reimbursed by the Commonwealth via the S100 Scheme.

Two formulations are available in Australia, one with a three-fold longer half-life needing less frequent injection, but the same rate of response. Antibodies to the natural shorter-acting preparation of EPO have recently been described, occurring only once per 1000 patient-years of subcutaneous injection, and associated with the onset of pure red cell aplasia. For medico-legal reasons, despite uncertain causality, this has prompted the widespread transfer of most patients to either intravenous administration (appropriate for haemodialysis patients) of the short-acting product, or subcutaneous administration (appropriate for pre-dialysis or PD patients) of the longer-acting product.

Optimum management

Given the enormous cost implications, and potential for complications, EPO therapy is best given according to strict protocols with close monitoring, especially after initiation.

Active intravenous iron supplementation is routinely practised, using the well-tolerated polymaltose preparation, to a target ferritin of 300-800ug/L or transferrin saturation of 20-50% in haemodyalisis patients. This strategy can significantly reduce (or even avoid) EPO dose requirements.

Take-home Messages

- Anaemia from EPO deficiency is frequent when GFR < 60mls/min (moderate CRF)
- Unexplained anaemia in the elderly may be due to unrecognised CRF.
- Exacerbating factors are often present (relative iron deficiency, inflammation, ACEi/ARB drugs, hyperparathyroidism).
- Recombinant EPO provides effective treatment - two formulations are available in Australia, but can only be initiated by a nephrologist where Hb is < 100g/L
- Pure red cell aplasia is a recently-described rare side-effect of subcutaneous EPO therapy
- Optimum EPO therapy requires close monitoring and active iron supplementation

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Further reading

For basic notes on Chronic and Endstage Renal Failure, see: www.rph.wa.gov.au/nephrol under /Teaching/Tutorial

CARI Guidelines at <www.kidney.org.au/cari>

Footnote. Kidney Health Australia (formerly the Australian Kidney Foundation) has initiated a nation-wide education project, Kidney Check Australia Taskforce (KCAT), to reduce endstage renal disease through earlier detection and management of mild chronic renal failure. The key elements are investigation of high risk groups, initiation of appropriate therapy and timely referral. The opinions expressed in the above article are those of the author and not necessarily endorsed by KCAT.