Chairman's Workshop Report

Should anaemia in subtypes of CRF patients be managed differently?

C. van Ypersele de Strihou

Cliniques Universitaires St. Luc, Brussels, Belgium

Workshop Participants: M. Broyer, France; C. Fresco, Italy; J. D. Harnett, Canada; K. A. Kirsch, Germany; R. Nosadini, Italy; F. Schaefer, Germany; G. R. Serjeant, Jamaica; P. E. Stevens, UK; Y. Vanrenterghem, Belgium; D. Verbeelen, Belgium; P. J. Watkins, UK

Abstract In patients with cardiovascular disease, partial correction of anaemia with epoetin improves quality of life and exercise capacity, and reduces left ventricular hypertrophy. The currently recommended haemoglobin in these patients is 11–12 g/dl. The optimal haemoglobin in patients with diabetes mellitus does not differ from that in non-diabetic patients; however, haemoglobin should be increased slowly. There is no difference in the recommended haemoglobin between children and adults. However, epoetin sensitivity is lower in children who, therefore, typically need the same absolute dose of epoetin as adults. Epoetin treatment may delay the progression of chronic renal failure (CRF) in paediatric patients. Elderly patients obtain similar benefits from epoetin as younger adults; moreover, there are no differences in the doses of epoetin required or the optimal haemoglobin. There are very few data available on the effects of epoetin in patients with CRF and chronic obstructive pulmonary disease. At present, a haemoglobin of 11 g/dl seems appropriate. In sickle-cell anaemia patients with CRF, a high haemoglobin could precipitate painful crises; consequently, the recommended haemoglobin is the pre-CRF concentration of 6–9 g/dl. There is no convincing evidence of any effect of previous epoetin treatment on the long-term outcome of renal transplantation. In patients with a failing or failed transplant, the required dose of epoetin may be higher than in pre-transplantation patients. In such cases, transplant nephrectomy might be considered.

Key words: anaemia; diabetes; elderly patients; epoetin; ischaemic heart disease; renal transplantation

Introduction

Epoetin has been used to treat the anaemia of chronic renal failure (CRF) for more than a decade, and much experience has been gained in its use. Attention is now turning towards optimizing treatment in various subgroups of patients with CRF, divided according to either age or concomitant disease. This workshop considered how epoetin might be used most effectively in:

- patients with cardiovascular disease;
- patients with type 1 or type 2 diabetes mellitus;
- children;
- the elderly;
- patients with chronic obstructive pulmonary disease (COPD);
- patients with sickle-cell disease; and
- patients receiving renal transplants.

This article presents the recommendations that were made for each category based on the available evidence.

Cardiovascular disease

Dialysis patients are 3.5 times more likely to die than their age-matched counterparts in the general population. Most of these premature deaths are due to cardiovascular disease [1]. At the onset of renal replacement therapy, symptomatic coronary artery disease, cardiac failure and left ventricular hypertrophy (LVH) are present in 21, 31 and 74% of patients, respectively [2].

LVH is known to be associated with arrhythmias, chronic heart failure and ischaemic heart disease, the major causes of death in dialysis patients. In a prospective echocardiographic study by Foley et al., anaemia was clearly established as an independent risk factor for the development of LVH, heart failure and mortality [3]. In this study, there was no independent association between anaemia and the development of ischaemic heart disease while patients were on dialysis. However, given the role of anaemia in promoting LVH, and the fact that LVH is strongly associated with the de novo development of ischaemic heart disease, this finding may be a reflection of the small size of the group rather than the absence of any effect.

It has been shown that epoetin therapy can reduce...
the increased LV diastolic dimensions and the elevated cardiac output that are characteristic of the anaemic uraemic state [4]. Increasing haemoglobin to 11–12 g/dl has a beneficial effect on LVH within 6–12 months, though the heart does not return completely to normal [5–9]. No prospective study has yet been carried out to determine whether this reduction in LVH translates into a reduction in mortality.

In addition, it has been shown that correcting anaemia with epoetin improves exercise capacity and quality of life in CRF patients, including those with cardiovascular disease [10].

A prospective analysis of data from the Lombardy Registry [11] provides encouraging evidence for a beneficial effect of epoetin on both general and cardiovascular mortality. The results showed a statistically significant progressive reduction in the relative risk of mortality up to the highest haematocrit, with or without adjustment for co-morbid conditions.

In patients with pre-existing cardiovascular disease, it is possible that the beneficial effects of epoetin on the cardiovascular system might be offset by adverse effects. For example, approximately one-third of patients treated with epoetin experience a significant increase in mean arterial blood pressure, although the mechanism of this pressor response remains controversial [12–15]. Other potential adverse effects on the cardiovascular system include increased blood viscosity and an increased tendency towards thrombosis in polytetrafluoroethylene grafts.

The optimum haemoglobin for patients with existing cardiac disease has not yet been established. However, the linear relationship seen between the occurrence of congestive heart failure and haemoglobin as it declines to <14 g/dl [16] suggests that there may be no ‘threshold’ haemoglobin for cardiac protection.

It is possible that normalization of haemoglobin might provide the greatest benefits to CRF patients. The risks and benefits of normalizing the haematocrit in patients with cardiac disease who were undergoing haemodialysis were examined in the Normal Hematocrit Cardiac Trial [17]. A total of 1233 haemodialysis patients with clinically evident congestive heart failure or ischaemic heart disease were included in the trial. Patients were randomized to one of two groups: a normal haematocrit group (n=618), in which patients received doses of epoetin sufficient to achieve and maintain a haematocrit of 42±3%, and a low haematocrit group (n=615), in which patients received doses of epoetin sufficient to maintain a haematocrit of 30±3%. The primary end point was time to death or a first non-fatal myocardial infarction.

The study was stopped prematurely after an interim analysis at 29 months showed 183 deaths and 19 first non-fatal myocardial infarctions in patients randomized to the normal haematocrit group vs 150 deaths and 14 first non-fatal myocardial infarctions in those randomized to the low haematocrit group (risk ratio normal vs low haematocrit: 1.3; 95% repeated confidence interval: 0.9–1.9). Although the difference in event-free survival between the two groups did not reach the pre-specified statistical stopping boundary, the study was halted because of safety concerns and because it was considered that an attempt to prove benefit for the higher haematocrit group would be futile. See C. Jacobs, this volume, for a discussion of the results, as well as a recent commentary [18], which discusses limitations and criticisms of the Normal Hematocrit Cardiac Trial.

Preliminary results from two recently completed trials, conducted in Canada and Scandinavia, indicated that normalization of haemoglobin did not have adverse cardiovascular effects. However, publication of the full results is needed before any conclusions can be drawn on the benefits of normalizing haematocrit in patients with cardiovascular disease.

Further studies are also needed to determine the effects of epoetin treatment and haemoglobin on prognosis in different subgroups of patients with ischaemic heart disease. For example, it would be interesting to investigate possible differences between symptomatic and asymptomatic patients, or among different angiographic and functional categories.

In the meantime, it seems prudent to recommend that patients with ischaemic heart disease continue to be treated to a haemoglobin of 11–12 g/dl, as recommended by the National Kidney Foundation–Dialysis Outcomes Quality Initiative (NKF–DOQITM) [19].

Diabetes mellitus

Diabetes mellitus is the most common cause of end-stage renal disease (ESRD). Overall, 16% of new patients commencing renal replacement therapy in Europe have diabetic nephropathy. Two-thirds of these patients have type 2 diabetes. Elderly patients account for a large proportion of new cases: between 1985 and 1995, there was a 10- to 20-fold increase in the subgroup of diabetic patients ≥65 years of age [20,21]. Compared with type 1 diabetes, renal damage in type 2 diabetes is associated with heterogeneous patterns of renal structural lesions [22,23]. Whatever the method of renal replacement therapy, survival rates for diabetic patients are lower than for non-diabetic patients; most deaths are due to cardiovascular disease. LVH is more prevalent in diabetic compared with non-diabetic patients with ESRD, and it is possible that the beneficial effects of epoetin on LVH could be particularly relevant for diabetic patients [24].

To date, the effects of epoetin on peripheral vascular disease and microangiopathic complications associated with diabetes have not been systematically assessed. The possible benefits of an improved oxygen supply to target areas require further study.

Several case reports indicate that anaemia may develop in diabetic patients prior to renal failure (i.e. in patients with normal serum creatinine). It may therefore be helpful to identify and treat anaemia in such patients [25,26].

The workshop panel concluded that, currently, there is no reason to recommend a different target haemoglobin for diabetic and non-diabetic patients; a haemo-
globin of 11–12 g/dl is therefore also appropriate for diabetic patients.

Nevertheless, attention must be paid to the rate at which the haemoglobin is increased in diabetic patients. These patients are particularly at risk of adverse effects related to rapid expansion of the red cell mass and the impact of such expansion on blood volume and viscosity. Furthermore, glycosylation of epoetin can modify the epoetin clearance rate. The degree of metabolic control in diabetic patients can therefore modify viscosity through its influence on osmolarity (changes in blood glucose) and on haemoglobin (changes in epoetin metabolism in body tissues) [24,27,28].

Increases in peripheral vascular resistance and blood pressure, worsening of hypertension, vascular access clotting and even seizures have been observed more frequently in diabetic dialysis patients when haemoglobin was increased too rapidly. A sudden increase in haemoglobin could also be particularly harmful to diabetic patients with microangiopathy, leading to further deterioration of circulation in the microvessels.

While it is difficult to define what constitutes a ‘slow’ increase in haemoglobin, a suggested strategy is: (i) a cautious dosage of epoetin (initial dose of 2000 IU three times weekly, followed by increments of 2000 IU at monthly intervals); and (ii) careful adjustments of heparinization during dialysis [24,27,28].

The haemoglobin should be measured at least once a week to determine the initial response. If haemoglobin increases by >1.3 g/dl (haematocrit >4%) over a 2 week period, the epoetin dose should be reduced. Once the target haemoglobin has been reached, the weekly dosage should be reduced and the haemoglobin monitored at regular intervals.

Paediatric patients

Renal anaemia in children can be corrected successfully using epoetin, with a dose-dependent increase in haemoglobin (Figure 1) [29,30]. As in adults, epoetin treatment in children markedly reduces the need for blood transfusions, improves exercise tolerance and regresses LVH [31].

Clinical experience in paediatric patients shows that, with adequate iron supplementation, the subcutaneous (s.c.) and intravenous (i.v.) routes of epoetin administration are equally efficacious. Today, epoetin is usually administered once weekly s.c. in children on peritoneal dialysis and three times weekly i.v. in haemodialysed children.

Children require absolute epoetin doses that are similar to those of adults [30,32]. Thus, in relation to their body weight, the required doses in children are higher than in adults. Interestingly, the rise in haemoglobin is related to absolute dose and not to weight-normalized dose (Figure 2).

Most paediatric patients report a subjective increase in appetite after initiation of epoetin treatment [29,33–38], although no consistent changes have been found in either dietary intake of calories and proteins or overall nutritional state in this patient group [29,33–39]. Weight gain was observed in four trials studying the effects of epoetin in children [33,35,40,41], yet no weight gain was seen in a further four trials [36,38,42,43].

A growth-promoting effect has been reported during the correction of anaemic states of non-uraemic origin [44]. It has been hypothesized that epoetin treatment could improve growth, which is often retarded in children with renal failure. An increase in growth velocity was observed by Rees et al. in three prepubertal, but not in three pubertal, haemodialysis patients [42]. In addition, Scharer et al. found an increase in height standard deviation score in two of six prepubertal pre-dialysis patients [41]. However, the majority of studies, including two large multicentre trials [33,43], have found no effect of epoetin on growth in terms of height. For example, Schuefer et al. [43] showed that epoetin did not affect height growth or bone maturat-
Fig. 2. Dose dependence of the effect of epoetin in children. The increase in haemoglobin is related to the absolute dose of epoetin, not to the weight-normalized dose.

The workshop concluded that the optimal haemoglobin in children and in adults should be the same (11–12 g/dl). However, children typically will need the same absolute dose of epoetin as adults.

**Elderly patients**

Treatment of anaemia in elderly patients with CRF is more complex than in younger patients, due to the high prevalence of anaemia in this age group and the multiplicity of possible causes (Table 1). In the UK, ~20% of elderly women and 14% of men presenting to their general practitioner are anaemic [46]. As anaemia in elderly CRF patients is often multifactorial, it is important to characterize the anaemia by examining red blood cell volume, reticulocyte counts and the appearance of the peripheral blood film.

Iron deficiency is encountered frequently in the elderly patient [47], and is usually due to blood loss, especially from the gastrointestinal tract. An inadequate dietary supply of iron, as well as impaired absorption associated with gastric surgery, atrophic gastritis and intestinal malabsorption, may exacerbate the increased iron requirements related to blood loss.

Vitamin B₁₂ deficiency is also common in the elderly. This deficiency often results from an inability to separate vitamin B₁₂ from the R proteins in food, which is due to a lack of hydrochloric acid or pancreatic enzymes [47]. In ~10% of elderly patients with vitamin B₁₂ deficiency, classical haematological, laboratory or clinical manifestations may be absent. All elderly CRF patients should therefore be screened for vitamin B₁₂ deficiency.

Folate deficiency may also be present, as a result of malnutrition, excessive folate utilization, increased loss or malabsorption of folate by the body, or drugs affecting folate metabolism. Red blood cell folate
Table 1. Red blood cell abnormalities in anaemia and associated underlying causes.

<table>
<thead>
<tr>
<th>RBC abnormality</th>
<th>Associated causes</th>
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<tbody>
<tr>
<td>Target cells</td>
<td>Liver disease, iron deficiency, haemoglobinopathies</td>
</tr>
<tr>
<td>Spherocytes</td>
<td>Hereditary spherocytosis, autoimmune haemolytic anaemia, microangiopathic anaemias, mechanical haemolysis</td>
</tr>
<tr>
<td>Fragmented cells</td>
<td>Microangiopathic anaemias, mechanical haemolysis, DIC</td>
</tr>
<tr>
<td>Elliptocytes</td>
<td>Iron deficiency, thalassaemia, hereditary elliptocytosis</td>
</tr>
<tr>
<td>Tear drop cells</td>
<td>Myelofibrosis, marrow infiltration</td>
</tr>
<tr>
<td>Nucleated RBCs</td>
<td>Severe anaemia (except bone marrow aplasia)</td>
</tr>
<tr>
<td>Rouleaux</td>
<td>Myeloma, hyperglobulinaemia</td>
</tr>
<tr>
<td>RBC agglutination</td>
<td>Cold agglutination</td>
</tr>
<tr>
<td>Acanthocytes</td>
<td>Liver disease, hypothyroidism, post-splenectomy</td>
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<tr>
<td>Polychromasia</td>
<td>Reticulocytosis</td>
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<tr>
<td>Parasitosis</td>
<td>Malaria, bartonellosis, babesiosis</td>
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<tr>
<td>Blister cells</td>
<td>Oxidant damage (e.g. G-6-PD deficiency)</td>
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<tr>
<td>Burr cells</td>
<td>Renal failure</td>
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<tr>
<td>Basophilic stippling</td>
<td>Sideroblastic anaemia, thalassaemia, heavy-metal poisoning</td>
</tr>
<tr>
<td>Howell–Jolly bodies</td>
<td>Asplenism, megaloblastosis</td>
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should be interpreted carefully because it may be misleadingly low in patients with vitamin B	extsubscript{12} deficiency and misleadingly high in patients with reticulocytosis or a recent blood transfusion.

Treatment of anaemia in elderly patients with CRF is therefore likely to include supplements necessary for normal erythropoiesis (e.g. iron, vitamin B	extsubscript{12}, folate), followed by epoetin therapy. Blood transfusion should be limited to patients with acute blood loss and patients with chronic anaemia that cannot be corrected by other means.

The suggestion that, even in the absence of complicating factors, the elderly patient might not respond as well to epoetin therapy as the younger patient [48] appears to be unfounded. No significant differences between induction and maintenance doses of epoetin, or in haemoglobin increment with duration of treatment, have been observed in elderly vs younger haemodialysis patients.

A study by Goodnough et al. found that the endogenous erythropoietin response to blood-loss anaemia was similar in elderly and younger patients [49]. Age had no influence on response to endogenous or exogenous erythropoietin. While maintenance dosages for epoetin are similar in elderly and younger patients, it should be borne in mind that the response to epoetin must be monitored closely in any patient with complicated anaemia as dosage requirements may be greater.

Compared with younger patients, the elderly CRF patient with uncomplicated anaemia will obtain a similar benefit from epoetin therapy in terms of haemoglobin response [50] and improvement in quality in life [51]. Moreno et al. [51] found no relationship between age and improvement in quality-of-life scores in patients receiving epoetin (Figure 4). Based on these results, the authors concluded that the use of epoetin in elderly patients is fully justified.

There is no evidence that the optimal haemoglobin need be any lower in elderly than in younger patients. At present, a haemoglobin of 11–12 g/dl is recommended.

**Chronic obstructive pulmonary disease**

In patients with CRF, erythropoietin concentrations are reduced due to impaired erythropoietin secretion. In contrast, polycythaemia has been reported in some patients with COPD, apparently as a result of enhanced erythropoietin secretion in response to hypoxia. However, not all findings in COPD patients show an unequivocal trend towards increased erythropoietin concentrations [52].

These divergent findings can be understood partly in terms of the multiple mechanisms that allow the body to adapt to chronic hypoxia [53], including oxygen-sensing devices, i.e. (i) the carotid bodies, which sense the oxygen concentration in the blood; (ii) the Liljestrand–Euler mechanism in the lung, which redistributes blood flow to optimize oxygen uptake, and (iii) the erythropoietin-secreting mechanism in the kidneys, which eventually enhances oxygen transport.
within the vascular system; and to other mechanisms, i.e. (i) endothelial mechanisms, which induce the formation of vascular endothelial growth factor (VEGF); and (ii) intracellular mechanisms, which optimize metabolic pathways to increase the energy yield [54].

COPD patients sometimes develop high haematocrits (>55%) as a result of both the continuous hypoxic drive outlined above and a relative lowering of the plasma volume. Due to increased blood viscosity, convective transport within vessels >1 mm in diameter is impaired, although oxygen delivery in the capillaries remains unaffected. In this situation, according to the literature, a haematocrit of 37–47% (haemoglobin of 12–15 g/dl) allows optimal oxygen transport as well as optimal oxygen delivery within the capillaries [55]. Plugging is prevented as long as the perfusion pressure remains sufficiently high and the white blood cell count remains within the normal range.

In contrast, in CRF patients, it has been suggested that low haemoglobin concentrations do not impair oxygen delivery at the capillary level as long as sufficient oxygen is transported. Oxygen transport is enhanced through hypoxic vasodilatation [56]. The interrelationship between the oxygen-transporting and the volume-regulating mechanisms in CRF requires further investigation.

The effect of epoetin on peripheral tissues must still be investigated. It is possible that epoetin-induced vasoconstriction only increases blood pressure and reduces tissue perfusion. Alternatively, the volume capacity of the total vascular system may be reduced, so that there is a beneficial increase in the filling pressure of the heart.

A further issue to be explored is whether tissue hypoxia in the CRF patient leads to an activation of VEGF without adequate complementary erythropoietin secretion. If this were the case, vascularization of the peripheral tissues would take place and plasma volume would increase to fill the vascular bed adequately. Without an accompanying increase in red cell production, however, haemoglobin would decrease further.

At present, there is no evidence on which to base advice to physicians treating patients who have both CRF and COPD. In the absence of the necessary data, the workshop panel recommended that haemoglobin in such patients be increased to 11 g/dl.

Sickle-cell disease

Sickle-cell disease is characterized by the presence of sickle haemoglobin (HbS). When deoxygenated, HbS tends to polymerize into long chains, reducing the flexibility of red cells and deforming many red blood cells into the characteristic sickled shape. These red blood cells are destroyed prematurely in the circulation, resulting in haemolytic features, such as anaemia, jaundice and gallstone formation. As a result of the anaemia, cardiac output is usually high in patients with sickle-cell disease, even at rest.

Severe damage to the renal vasa rectae system occurs in most patients with sickle-cell anaemia, even in those with the otherwise harmless sickle-cell trait [57]. As a consequence, ability to concentrate urine and to excrete acid loads is impaired. In older patients, there is a tendency to glomerular fibrosis and obsolescence; the result is a rapidly declining glomerular filtration rate and renal impairment, manifested by increasing serum creatinine and declining haemoglobin. Ultimately, ESRD and the need for renal replacement therapy may develop [58].

At present, only a minority of nephrologists have been faced with the problem of how to treat patients with a combination of ESRD and sickle-cell disease. In future, the problem is likely to become more common, as the survival of patients with sickle-cell disease improves, and more patients reach an age at which renal failure develops.

In steady-state sickle-cell disease, haemoglobin is typically between 6 and 9 g/dl. At these levels, most patients have adequate oxygen delivery, and classic symptoms of anaemia are unusual. A high haemoglobin, especially in the absence of a high fetal haemoglobin, has been shown to be a risk factor for painful crises, hip necrosis, proliferative sickle retinopathy and, possibly, acute chest syndrome. These effects are probably a result of increased blood viscosity [59,60]. Painful crises, secondary to the sudden increase in haemoglobin, may also occur following splenectomy for hypersplenism and after successful renal transplantation for renal failure.

Progressive renal impairment is especially common in patients with sickle-cell anaemia who are over 40 years of age. It is characterized by a gradually declining haemoglobin secondary to reduced erythropoietin in the blood [61]. Such patients frequently experience a 'honeymoon period', since the declining haemoglobin protects against painful crises; the patient experiences fewer symptoms until the haemoglobin reaches a value which compromises cardiac function. At this point, which is usually associated with a haemoglobin of 3–5 g/dl, reasonable health can be maintained by top-up blood transfusions every 4–6 weeks, or as determined by patient demand.

Alternatively, administration of epoetin could be used to maintain haemoglobin and eliminate the need for transfusion. However, the determinants of the bone marrow response to epoetin in sickle-cell disease are unknown, and near normal haemoglobin may precipitate painful crises. Moreover, the bone marrow is markedly expanded in sickle-cell disease, and response to epoetin in these patients is variable. In general, doses needed to achieve a given increment in haemoglobin are more than in non-sickle-cell disease patients.

On the basis of the available evidence, the workshop panel suggested that the haemoglobin in these patients should not be increased above the pre-CRF value (typically 6–9 g/dl), in order to avoid painful crises.
Renal transplant patients

Renal transplant patients who could benefit from epoetin therapy can be divided into three main groups: pre-transplantation, early post-transplantation and failing or failed transplant. The effects of previous or concurrent epoetin treatment vary among these groups.

Pre-transplantation

Before the introduction of epoetin, most patients waiting for kidney transplantation had a low haemoglobin. It was suggested that this might be beneficial for early graft function, by protecting the transplanted kidney from reperfusion damage. In contrast, recent in vivo and in vitro data suggest that epoetin has an immunomodulatory function [62–64], in which case epoetin treatment before transplantation might have a beneficial effect on graft survival.

In fact, available studies indicate that previous epoetin treatment has no effect on rejection rate or graft survival [65–67]. Furthermore, previous epoetin treatment does not influence the incidence of renal allograft thrombosis, a complication that ultimately leads to graft loss [68].

Results regarding immediate graft function are somewhat equivocal: two studies [65,66] showed no effect, while one showed a significant difference [67]. Linde et al. [65] compared graft function, graft survival and serum creatinine 1 year after transplantation in 26 epoetin-treated patients and 26 untreated controls, and found no differences between the two groups (Figure 5). A similar study by Fernández Lucas et al. [66] found no association between epoetin therapy and dialysis and delayed graft function. Resolution of anaemia after transplantation was similar in the two groups, although the initial pattern of erythropoietin secretion differed slightly between them.

Only one study, by Vasquez and Pollak [67], has reported an increased incidence of delayed graft function in 58 epoetin-treated patients compared with 62 untreated controls (41% vs 18%, \( P < 0.05 \)). Rates of acute rejection, time to first rejection or 1 year graft survival rate did not differ significantly between the two groups. This study has been criticized, however, on the grounds that some patients may have been dehydrated at the time of transplantation, with an attendant variable effect on haemoglobin.

Early post-transplantation

It is interesting to speculate that epoetin might be valuable in the early post-transplantation period. By lowering the need for blood transfusion, it could limit the risk of human lymphocyte antigen sensitization and transmission of infection. Better oxygen delivery to the graft might also lead to an improved outcome.

Only one prospective study has examined the effect of sustained administration of epoetin during the early post-transplantation period [69]. Epoetin- and non-epoetin-treated patients had similar numbers of graft failures and rejection episodes, but epoetin-treated patients had a steeper increase in haemoglobin after transplantation and required fewer blood transfusions. However, it should be noted that the transfusion rate among the controls was unusually high in this study.

Further prospective trials are needed.

Failing/failed renal transplant

The results of studies of a small number of patients with a failing renal transplant [70–74] point to a beneficial effect of the administration of epoetin. It is difficult to determine whether epoetin therapy influences the deterioration of renal function in patients with a failing transplant, but currently there is no cause for concern.

Most patients with failing or failed transplants respond to epoetin, although many require rather high doses. This may be due to concomitant immunosuppressive treatment, in particular with azathioprine, inflammation or infection associated with the failing graft, or the administration of other drugs, such as angiotensin-converting enzyme inhibitors, angiotensin II receptor antagonists or theophylline. In patients with a failed transplant who show resistance to epoetin, transplant nephrectomy may improve response.

Conclusions

The recommendations of the workshop can be summarized as follows.

- The recommended optimum haemoglobin in patients with ischaemic heart disease is 11–12 g/dl.
- The optimal haemoglobin in patients with diabetes mellitus does not differ from that in non-diabetic patients; however, haemoglobin should be increased slowly.
- There is no difference between the optimal haemoglobin recommended for children and for adults. The increase in haemoglobin in children, however,
is related to the absolute dose of epoetin, not to the weight-normalized dose, and children therefore typically need a dose of epoetin similar to adults.

- In elderly patients, haemoglobin should be increased to 11–12 g/dl, as in younger adults.
- There are very few data available on the effects of epoetin in CRF patients with COPD. At present, a haemoglobin of 11 g/dl would seem appropriate.
- In sickle-cell anaemia patients with CRF, an increase in haemoglobin could precipitate painful crises. The recommended haemoglobin is 6–9 g/dl (similar to the pre-CRF value). Response to epoetin is variable and high doses may be required.
- There is no evidence that treatment with epoetin prior to transplantation has any effect on the long-term outcome of renal transplantation.
- In the early post-transplantation period, one study cardiac disease who are receiving hemodialysis and epoetin.

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