

CHAPTER 8

Haematological, osteological and metabolic complications

CHAPTER 8.1 Diagnosis and treatment of anaemia

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Background

- Definition of post-transplant anaemia (PTA): Haemoglobin concentration below the age norm after kidney transplantation (KTx).
- The prevalence of PTA is high, especially within the first year after KTx (1 month after KTx: 80–87%, 1 year: 20–48% and > 3 years: 35–57%). Females and younger children are more often affected.
- The target haemoglobin is the normal value for age and sex (Table 1).
- The aetiology of PTA is varied (see causes [below]).
- PTA is a risk factor for cardiovascular morbidity and is negatively associated with graft function, graft and patient survival and quality of life.

Causes

Reduced production of haemoglobin/erythrocytes

- Underlying disease affecting the bone marrow (e.g. cystinosis, oxalosis)
- Iron, vitamin B12 or folic acid deficiency (e.g. due to reduced dietary intake (vegans), impaired absorption or intestinal losses)
- Medications that are toxic to bone marrow: anti-infectives (e.g. valgancyclovir, cotrimoxazole), inhibitors of the renin-angiotensin-aldosterone system, immunosuppressants (antibodies such as ATG, basiliximab) and maintenance immunosuppressants (MMF, everolimus, tacrolimus, azathioprine), analgesics (metamizole).

Table 1 Age- and sex-specific reference values for haemoglobin and haematocrit in childhood

Age	Haemoglobin (g/dL)	Haematocrit (%)
1 year	10.7–13.1	33–40
2–6 years	10.8–14.3	34–41
7–12 years	11.3–14.9	37–43
13–18 years female	12.0–16.0	36–44
13–18 years male	14.0–18.0	39–47

Reference: www.laborlexikon.de/Lexikon/Tabellen/17-Blutbild_Kinder.htm

- Viral infections (parvovirus B19, human herpesvirus 6 (HHV6), cytomegalovirus (CMV), Epstein-Barr virus (EBV), hepatitis viruses, HIV)
- Acute/chronic inflammation (infection, rejection)
- Post-transplant lymphoproliferative disease (PTLD)
- Graft dysfunction (primary non-function or chronic graft failure, e.g. due to acute/chronic rejection)
- Chronic kidney disease (reduced synthesis of erythropoietin, metabolic acidosis, secondary hyperparathyroidism)

Increased loss/turnover

- Repeated blood sampling, surgery, interventions (biopsy)
- Female patients: Dysmenorrhoea, hypermenorrhoea
- Chronic intestinal bleeding (gastric or intestinal ulcers, e.g. due to glucocorticoids)
- Haemolysis (e.g. drug-induced haemolytic uraemic syndrome (cyclosporin A, tacrolimus))
- Hepatosplenomegaly (e.g. in autosomal recessive polycystic kidney disease)

Clinical symptoms

- (Mucus) skin pallor
- Tiredness, fatigue, reduced stamina
- Tachycardia, low blood pressure
- Melana
- Icterus
- Hepatosplenomegaly

Diagnostics

Medical history

- Underlying disease
- Medications (immunosuppressants, anti-infectives, analgesics, ACE inhibitors, sartans)
- Diet (e.g. vegetarianism, veganism)

Laboratory values

- Blood count with MCV, MCH, reticulocytes, Ret-Hb
- Iron, ferritin, transferrin, transferrin saturation, folate, vitamin B12
- Blood gas analysis
- Creatinine (GFR), urea, uric acid
- LDH, haptoglobin, bilirubin
- Parathyroid hormone, 25-OH vitamin D
- Virology: Parvovirus B19, HHV6, CMV, EBV (IgG, IgM, DNA), polyomavirus (BK and JC virus), hepatitis B and C serology, HIV
- Haemocult

Diagnostic imaging

- Sonography of the abdomen (kidney transplant, liver and spleen size, ascites, intra-abdominal lymph nodes, bowel wall thickening) and neck (cervical lymph nodes, parathyroid glands)
- Oesophagogastroscopy and colonoscopy if necessary (to rule out intestinal bleeding)
- Bone marrow aspiration (if necessary)

Table 2 Drug therapy for post-transplant anaemia

Medication	Dosage¹
Oral iron supplementation (e.g. Ferro sanol®, Ferrum Hausmann®)	2–6 mg/kg b.w. per day in 2–3 doses (at least 1 hour before or after intake of immunosuppressants)
Intravenous iron supplementation	
Sodium ferrogluconate	1–1.5 mg/kg b.w. in 50 mL 0.9% NaCl over 60 min i.v.
Iron sucrose	1–2 mg/kg b.w. in 25 mL 0.9% NaCl over 60 min i.v.
Iron carbomaltose	2–8 mg/kg b.w. in 20 mL 0.9% NaCl over 15 min i.v.
Erythropoiesis-stimulating agents	
Epoetin alpha	Initially: 100–300 IU/kg b.w. per week s.c. (in 1–3 doses) Long-term: 100 IU/kg b.w. per week s.c. (in one dose)
Darbepoietin alpha	0.45 ug/kg b.w. per week s.c. or 0.75 µg/kg b.w. every 2 weeks s.c. (in one dose)
Methoxy-polyethylenglycol-epoetin beta	1.5–3 µg/kg b.w. every 4 weeks s.c. or i.v.
Supplementation with vitamins	
Folic acid	5–10 mg/day p.o.
Vitamin B12	0.5–1 mg/week (in one dose) p.o.

Abbreviations: b.w., body weight; i.v., intravenous; p.o., per os; s.c., by subcutaneous injections

¹ Caution: higher doses may be required in case of non-response.

Treatment

Treatment depends on the underlying cause and degree of anaemia.

- Identification and, if necessary, modification of immunosuppressive or other potentially bone marrow toxic drugs
- Treatment of viral infections
- Correction of metabolic acidosis and vitamin D replacement in renal hyperparathyroidism
- Oral replacement for iron or vitamin B12/folic acid deficiency (i.v. for non-responders or severe deficiency [Table 2])
- Subcutaneous or intravenous administration of erythropoietin/analogues (dose and frequency according to response (haemoglobin). Younger patients often require higher doses per kg body weight. Dose adjustment during therapy is recommended.

References

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- 3 Krischock LA et al. *Pediatr Nephrol* (2016) 31:325–333
- 4 Galutira PJ and Del Rio D (2012) *Pediatr Nephrol* 27:1079–1085