Principles in the management of chronic kidney disease

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Abstract

Chronic kidney disease (CKD) is the term used to describe renal disease or impairment which has persisted for three months. This paper presents a brief overview of CKD, including classification, epidemiology, aetiology, clinical presentation, investigations and a discussion regarding the principles of management. The aims of management include: preservation of remaining renal function, avoiding further injury, correction of electrolyte disturbances, anaemia and fluid imbalance and also maintenance of good nutrition, bone health and growth. Some children will progress to end-stage disease and there is a brief discussion of renal replacement therapy. Prognosis depends largely on the cause of CKD. Where children should be followed-up is dictated primarily by their renal function and the likely clinical course.

Keywords acute kidney injury; anaemia; bone and mineral disorder; CKD; hypertension; renal replacement therapy

Introduction

Chronic kidney disease (CKD) is the term used to describe a renal injury with or without a decline in renal function that is present for at least three months. Estimates of incidence and prevalence are inexact as the early stages can be asymptomatic and so the condition may go unrecognized.

Definition

CKD results from irreversible damage to the renal parenchyma. Such damage needs to be bilateral as there can be significant compensation if only one kidney is affected. As renal function declines there is a rise in the serum creatinine and a lowering of the glomerular filtration rate (GFR). The current definition of CKD is that of either proven renal injury or a GFR of less than 90 ml/min/1.73 m^2 that persists for three months or more. CKD is associated with considerable morbidity and an increased risk of mortality.

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Classification (Table 1)

The currently used classification for CKD was published by the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (NKF-KDOQI) in 2002. It describes five stages of disease which are defined by the patient's GFR. These guidelines are applicable to both adults and children over two years of age.

Calculation of the GFR

The modified Schwartz formula is often used for estimation of the GFR, where GFR (ml/min/1.73 m^2) = $k \times$ height (cm)/serum creatinine (μmol/l). We use a k value of 40 but there is quite a lot of variation across the nephrology centres in the UK. Serum creatinine reflects total body creatinine and so is influenced by muscle mass. Children with low muscle mass, for example infants or those with poor nutrition or a neuromuscular disorder, will have a lower creatinine and so their calculated GFR will be an overestimate of actual kidney function. As serum levels increase in advanced CKD, creatinine is secreted into the tubules and diffuses into the gastrointestinal tract. A calculated GFR in this scenario will therefore overestimate the true filtration rate. When a more accurate assessment of GFR is required, the gold standard test is by measurement of serum and urinary inulin clearance following intravenous administration. Alternative substances used include iohexol and Cr EDTA, which similarly to creatinine and inulin are filtered at the glomerulus but not reabsorbed by the tubules.

Epidemiology

There are no accurate statistics on either the prevalence or incidence of CKD in childhood. The early stages are relatively asymptomatic and so many children elude diagnosis until stages 3, 4 or 5. In some cases this can be into early adulthood. A significant proportion (approximately 25%) of children will require renal replacement therapy (RRT) to be commenced following their first contact with a nephrologist. There is good data regarding children less than 16 years of age who are receiving RRT in the United Kingdom from the UK Renal Registry. This annually collects data from the 13 specialist Paediatric Nephrology centres. The most recent statistics for 2010 showed a prevalence rate of 59.3 per million age related population (pmarp), which has risen steadily over the past fifteen years. Incidence has also increased and was 8.1 pmarp in 2010. A similar incidence is reported in Australia and New Zealand (9–10 pmarp) with a higher incidence of 15 pmarp in the USA.

Aetiology

Congenital abnormalities of the kidneys and/or urinary tract (CAKUT) such as renal dysplasia/hypoplasia and obstructive uropathy are responsible for approximately 50% of cases of CKD in the paediatric population. The next commonest causes are renal cystic diseases and nephrotic syndromes, followed by nephronophthisis and the glomerulonephritides.

Pathophysiology

Regardless of the cause of the deterioration in renal function, progression towards end-stage disease follows a common

Classification of CKD

Stage	GFR (ml/min/1.73 m^2)	Description of GFR	Features
1	>90	Normal	Renal parenchymal disease or proteinuria
2	60–90	Mildly lowered	Usually asymptomatic
3	30–60	Moderately lowered	Anaemia and biochemical abnormalities are seen
4	15–30	Severely lowered	Increasing severity of symptoms
5	<15	'Renal failure'	Renal replacement therapy is indicated

Table 1

pathway which results in fibrosis of the interstitium with accompanying tubular atrophy of the kidney. A detailed review of this process is beyond the scope of this review. Essentially, the altered haemodynamics of the kidney, together with on-going hypoxia and inflammation, leads to cellular dysfunction and fibrogenesis.

Presentation

As discussed, many of the children with CKD will present in the neonatal period. The majority of these will have been diagnosed antenatally during ultrasound scanning of the fetus. Children with CKD can also present acutely with urinary tract infection, polyuria and polydipsia or as an acute decompensation of their renal function, precipitated by an ordinarily self-limiting illness. Alternatively, children can present more insidiously with features relating to the complications of CKD. These include: poor nutrition, with resultant failure to thrive, anaemia, and the CKD-mineral and bone disorder (CKD-MBD), previously called renal osteodystrophy. Some will be found to have hypertension or proteinuria on urinary dipstick testing during an incidental examination. Finally, practitioners should be alert to those children with a family history of renal pathology (autosomal dominant polycystic kidney disease, Alport syndrome, tuberous sclerosis and cystinosis).

Investigation (Table 2)

Newly-presenting patients will undergo investigation to determine the cause of their CKD. Additional investigations will be led by the most likely cause of the CKD, as suggested by the clinical presentation and examination findings, including the presence of any dysmorphic features. An increasing number of conditions can now be confirmed through genetic testing. A renal biopsy may be indicated if the aetiology is not clear.

Management

In addition to the specific therapies for the underlying disease e.g. immunosuppression for vasculitis, mercaptamine for cystinosis, the main focus of the management of CKD is to prevent or slow disease progression and to avoid further insult to the kidneys. The other aims include correction of electrolyte abnormalities and treatment of anaemia and CKD-MBD. Every effort should be made to maintain normal growth, development and quality of life.

Prevention of progression of CKD

Reduction of proteinuria: it is noteworthy that the serum creatinine does not rise until renal function has decreased to 50% of normal for that individual. In general, as renal function worsens, more protein will be filtered at the glomerulus and will appear in the urine. This is because glomerular hypertrophy (and raised intraglomerular pressure) occurs in response to a decrease in the number of functioning glomeruli. Increasing proteinuria is treated with an ACE-inhibitor or ARB, which lowers the filtration pressure by dilating the glomerular afferent arteriole. Response to therapy must be carefully monitored as ACE-inhibitors can cause hyperkalaemia, worsening of renal function, marked

Investigation of the child presenting with CKD

Blood test	Urine test	Imaging
FBC	Urine dipstick	Renal ultrasound scan
Ferritin	Urinary microscopy, culture and sensitivity	
Urea and electrolytes	Urinary protein (or albumin): creatinine ratio	
Bicarbonate		
Parathyroid hormone		
Vitamin D		
Consider:	**Consider:**	**Consider:**
Complement C3, C4, ANA, ANCA	Urine oxalate excretion	DMSA
and GBM antibodies	Retinol binding protein	Micturating cystogram
White cell cystine	Beta 2 microglobulin	

Table 2