Intestinal Failure and Chronic Kidney Disease

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Chronic kidney disease (CKD) may occur in patients with intestinal failure (IF) and may be due to underlying disease, dehydration, renal stones and/or medication. In patients with a jejunostomy it can result from dehydration due to high stomal losses of water and sodium. In patients with a retained colon, it may be due to oxalate precipitation within the kidney. Some studies report that CKD relates to the length of bowel remaining, older age, longer duration of parenteral support (PS); however, a large UK study demonstrated that, although renal impairment is common when home parenteral nutrition (HPN) is begun, after the first year the decline in estimated glomerular filtration rate (GFR) is similar to the general population. Close monitoring of renal function is important due to the risk of acute kidney injury (AKI) from volume losses, as recurrent or prolonged episodes of AKI may lead to progressive loss of kidney function. If CKD occurs it may result in protein breakdown (partly due to metabolic acidosis). Maintenance of volume status and effective circulating volume is the cornerstone of preventing and managing kidney disease in patients with IF.

Key points

1. CKD is not uncommon in patients with IF but with proactive management that includes close monitoring and patient education to optimise volume status, the risk of progression of CKD can be reduced.
2. Patients with a high output stoma (generally over 1.5 L/24 hour due to a small bowel stoma or fistula may become hypovolaemic and chronically dehydrated, resulting in impaired renal function. Prolonged or recurrent episodes of dehydration are associated with a risk of a progressive decline in kidney function.
3. Serum urea, creatinine, estimated GFR, sodium, potassium, calcium, magnesium, chloride, bicarbonate and phosphate should be measured. A urine dip test for pH, proteinuria/haematuria should be completed and a urine albumin creatine ratio (ACR) sent for those with evidence of proteinuria. A mid-stream urine (MSU) should be sent for microscopy and culture.
4. Estimated GFR will overestimate kidney function in patients who have reduced muscle mass (e.g. malnourished, elderly and amputees). A cystatin C measurement may play a role.
5. Specific investigations may include a plain abdominal radiograph, renal ultrasound, 24-hour oxalate collection (and citrate) and a random urine sodium concentration.
6. Treatment for hypovolaemia (e.g. in patients with a high output stoma [HOS]) is with giving intravenous fluid (containing more than 100 mmol/L Na) (e.g. 0.9% sodium chloride).
7. Generally, patients who develop an AKI secondary to hypovolaemia will not require renal replacement therapy (haemodialysis or continuous veno-venous haemofiltration). Indeed, renal replacement therapies can worsen the situation if more fluid is removed.
8. Patients with a jejunostomy may develop urate (non-radio-opaque) renal stones. These are typically treated with urine alkalisation (e.g. with potassium citrate) and increased rehydration solutions.
9. Patients with a jejuno-colonic anastomoses have a 25% chance of developing calcium oxalate renal stones (radio-opaque) either as discrete stones or more rarely as diffuse nephrocalcinosis. All such patients should be given advice on a low fat (high carbohydrate), low oxalate diet and management should aim to avoid dehydration.
10. Both urate and oxalate stones may present with renal colic, pyelonephritis, or reduced renal function with hydronephrosis (obstructive uropathy).
11. Abdominal pathology (e.g. fibrosis or neoplasia) may cause obstruction of the renal tract and present as AKI or CKD.
12. Care should be given to prescribing drugs that are known to affect renal blood flow such as angiotensin converting enzyme (ACE) inhibitors/angiotensin receptor blockers, calcineurin inhibitors (CNIs) (e.g. tacrolimus) or non-steroid anti-inflammatory inhibitors (NSAIDs).
13. Recurrent episodes of sepsis with associated acute tubular necrosis can lead to CKD.
14. Vitamin D deficiency is highly prevalent in CKD and IF. In Stages 4 and 5 of CKD there is impaired conversion of vitamin D in the kidney to 1 alpha-hydroxycholecalciferol.
15. In addition to sodium, potassium, phosphate and calcium, micronutrients (e.g. vitamins A, D, E) and trace elements (e.g. zinc, copper, selenium and manganese) need careful consideration as CKD progresses.
16. Intradialytic PN (IDPN) can be administered at the same time as haemodialysis; however, this is not without complications, there are limitations to the amount of nutrition that can be administered (usually less than 1000 kcal per haemodialysis session), and the evidence base is limited.

Explanations

1. The incidence of renal impairment in adults with a short bowel (60% having HPS) has been reported as 28%, and the median duration from the diagnosis of a short bowel to the development of renal impairment was 12 months. However, more reassuringly, in the largest UK study to date (357 HPN dependent patients with median follow-up of 4.7 years), >40% of patients had renal impairment at baseline, with 15.4% fulfilling the criteria for CKD. Mean estimated GFR decreased significantly during the first year after initiation of HPN from 93.32 ml/min/1.73 m^2 to 86.30 ml/min/1.73 m^2 at the first year of follow-up (P = 0.002), with sequential stabilisation of renal function. Increased age at HPN initiation and renal impairment at baseline were associated with decreased estimated GFR. By the end of follow-up, 6.7% patients developed renal calculi and 26.1% fulfilled the criteria for CKD. Notably, only 2 of 357 (0.6%) of patients required dialysis by the end of the study follow-up, with one patient undergoing a renal transplant. These findings should reassure patients and clinicians that close monitoring of renal function can lead to good outcomes.
2. A high output stoma results initially in postural hypotension and a low random urinary sodium concentration (<20 mmol/L). With prolonged/worsening hypovolaemia, renal blood flow reduces leading to a pre-renal AKI with reduced urine output and raised in serum creatinine and urea. Electrolyte abnormalities such as hypokalaemia are common due to excess intestinal losses and the presence of hypernatraemia indicate free water deficiency and cellular dehydration – a poor prognostic sign.
3. Serum tests: renal profile should include serum sodium, potassium, creatinine, phosphate, adjusted calcium, magnesium, parathormone (PTH) and bicarbonate levels. Additionally, the measurement of chloride is needed to calculate the anion gap. Magnesium is often low in patients with a HOS. However, in the context of chronic kidney disease (CKD), magnesium replacement and maintenance requirements are typically lower than expected due to reduced renal clearance. Similarly, potassium, calcium, and phosphate requirements in PS formulations are often reduced in CKD. In bespoke compounded PS infusions, the chloride-to-acetate ratio can be adjusted to manage acid–base balance in patients with CKD. Acetate, supplied as either sodium or potassium acetate (as opposed to sodium or potassium chloride), is metabolised to bicarbonate primarily by skeletal muscle and liver cells. This can help to mitigate metabolic acidosis. Ketonuria may be present if the patient is catabolic or malnourished.

   Urine should be tested with dipstick urinalysis to assess for evidence of a urinary infection in unwell patients. The presence of isolated haematuria on dipstick should trigger investigations to rule out urological malignancy or (rarely) concomitant glomerulonephritis (such as IgA nephropathy). The presence of proteinuria on dipstick, in the absence of features consistent with a urinary tract infection, should trigger the sending of a urine ACR. The presence of proteinuria increases the likelihood of progressive CKD and can indicate the need for further investigations/specialist treatment. A low level of citrate is a risk factor for calcium stone formation as citrate is a natural inhibitor of crystallisation.
4. Formal GFR measurement in these patients with inulin clearance or isotope GFR measurement may be necessary to accurately measure kidney function. Cystatin C has a low molecular weight and is excreted by the kidneys. As GFR declines, the blood levels of cystatin C rise. It may be a more precise test of GFR than serum creatinine.
5. Imaging investigations: a plain film abdominal radiograph can be used to see radio-opaque stones, though in many centres this has been superseded with a computerised tomography (CT) of the kidneys, ureters and bladder (KUB) scan. In cases of unexplained reduced kidney function an ultrasound renal tract is useful to ensure there is no obstruction causing renal impairment.

6/7. Care must be exercised in treating these patients as fluid commonly needs to be given rather than restricted as is the case in most other cases of CKD. It is a rare scenario that there is an indication for acute renal replacement therapy (e.g. for symptomatic uraemia), in most cases there will be no requirement to remove fluid with mechanical ultrafiltration – indeed often it is appropriate to give fluid during dialysis to help restore circulating volume and aid renal recovery.

8. Urate stones are radiolucent and are not usually visible on a plain abdominal radiograph. Uric acid stones form in acidic concentrated urine, typically in patients with a small bowel stoma (jejunostomy or ileostomy). As with any stone, they can present with renal colic, obstruction or acute pyelonephritis. Treatment and prevention of uric acid stones involves appropriate oral (or intravenous) rehydration and urine alkalinisation therapy (often with potassium citrate, though sometimes sodium bicarbonate) to dissolve existing stones and prevent recurrence. The aim of treatment is to raise the urine pH above 6.5.
9. The causes of enteric hyperoxaluria include bile salt malabsorption, fat malabsorption, increased dietary oxalate, reduced calcium intake and treatment with high-dose phosphate supplements. Treatment of enteric hyperoxaluria currently requires restriction of dietary oxalate and 'oxalate binder' therapy, plus citrate supplementation if hypocitraturic. Calcium intake must not be restricted as this increases the risk of renal stones and a supplement may be helpful. Therapy with oxalate-degrading enzymes and biotherapy with oxalate-degrading bacteria may prove to be effective in the future.
10. Renal stones may present with renal colic if they become lodged in the ureter, with classical waves of loin to groin pain with associated nausea and vomiting. A CT KUB scan is now the standard first-line investigation for renal colic. Treatment of uncomplicated obstructing stones depends on the size and location. Smaller stones may be managed conservatively with supportive therapies to help dissolve the stone and manage pain to help the stone pass. Larger stones may require extracorporeal therapy to break them up or in some cases of complicated obstruction surgical lithotripsy may be required. Renal stones increase the risk of upper urinary tract infection. Infected stones will often require removal and extended periods of antimicrobial therapy to ensure resolution and no recurrence.
11. Obstructing stones may cause an AKI and radiologically there will be hydro-ureter/hydronephrosis visible on ultrasound or CT. The degree of obstruction does not associate well with impairment of kidney function and mild obstruction can result in marked AKI, whilst severe obstruction may sometimes have relatively pre served function. The decision to relieve the obstruction (nephrostomy or stenting) is based on renal function, not the radiological degree of obstruction. If the obstruction is relieved swiftly, then full recovery of renal function is likely. In cases where the obstruction persists then full recovery may not occur, and a degree of CKD may persist. Suspected cases of an in infected obstructing stone should be dealt with urgently with antibiotics and relief of the obstruction.

12. General factors to prevent progression of CKD include good control of blood pressure and diabetes. However, care should be given to prescribing drugs that are known to affect renal blood flow such as ACE inhibitors/angiotensin receptor blockers, CNIs (e.g. tacrolimus) or NSAIDs. These medications impair the kidneys' ability to autoregulate blood flow at times of hypovolaemia. If these medications are required, then the patient must be counselled that should stoma output increase or they become unwell for any reason to pause temporally these medications while seeking an urgent medical review with a test of renal function.

    Patients who have a small bowel transplant are at a high risk of developing CKD due to their immunosuppressive drugs – particularly CNIs. Monitoring levels of CNIs is an important part of the long-term care of these patients and either acutely and chronically raised CNI levels can lead to acute and chronic kidney impairment.
13. As with any condition that leads to an AKI (e.g. hypovolaemia/sepsis), recurrent episodes of severe AKI, with acute tubular necrosis can lead to the establishment of CKD. AKI is a risk factor for both future episodes of AKI and for future CKD. Efforts should therefore be made to prevent AKI in patients with IF by preventing hypovolaemia/infection, but when they do occur, swift action to reverse hypovolaemia with appropriate oral (with or without potassium) or intravenous volume repletion, and sepsis must be rapidly treated with appropriate antibiotic therapy. These measures will aid renal recovery and help prevent development of CKD.
14. In CKD stage 4-5 with an estimated GFR <30 ml/min/1.73m^2 there will be impaired renal conversion of vitamin D. Alfacalcidol is used in end-stage CKD to manage secondary hyperparathyroidism, with its use guided by serum PTH levels. An increase in PTH is a normal adaptive response in the earlier stages of CKD, often exceeding three times the upper limit of normal. However, if PTH levels continue to rise progressively alfacalcidol may be initiated. The dose should then be titrated based on repeated PTH measurements, along with regular monitoring of serum adjusted calcium and phosphate.
15. In the later stages of CKD iron and zinc deficiency are common, whilst elevated levels of selenium, copper and manganese are prevalent due to reduce renal clearance. In patients requiring dialysis, there is risk of both deficiency and toxicity of micronutrients. Notably, deficiencies of water-soluble vitamins, copper, zinc and selenium are seen, however micronutrient levels must be interpreted with caution in the presence of an elevated CRP. PS formulations usually require bespoke micronutrient dosing in these patients.

    Vitamin A toxicity is a significant risk for patients with CKD (including those receiving dialysis), especially those receiving PN or enteral nutrition, because reduced kidney function impairs vitamin A metabolism and excretion, leading to accumulation in the body. This can result in hypercalcaemia, which may be caused by vitamin A's effect on bone. To prevent toxicity, caution is necessary when prescribing vitamin A for patients with CKD and IF even at doses considered normal for patients on HPS. Vitamin A levels should be measured at least every 6 months.
16. High blood glucose, fluid overload and electrolyte disturbances pre and post dialysis sessions are potential complications following the administration of IDPN. Additionally, there is uncertainty regarding the extent to which PS is retained versus removed during dialysis. For long-term patients, objective monitoring of weight gain over a defined period remains the most reliable indicator of nutritional benefit. The use of IDPN should be guided by locally agreed protocols with appropriate monitoring in place. Notably, there remains considerable debate regarding the indications for IDPN and its perceived clinical benefits.

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Suggested reading

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