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The role of pharmacy technicians in the care of patients on dialysis

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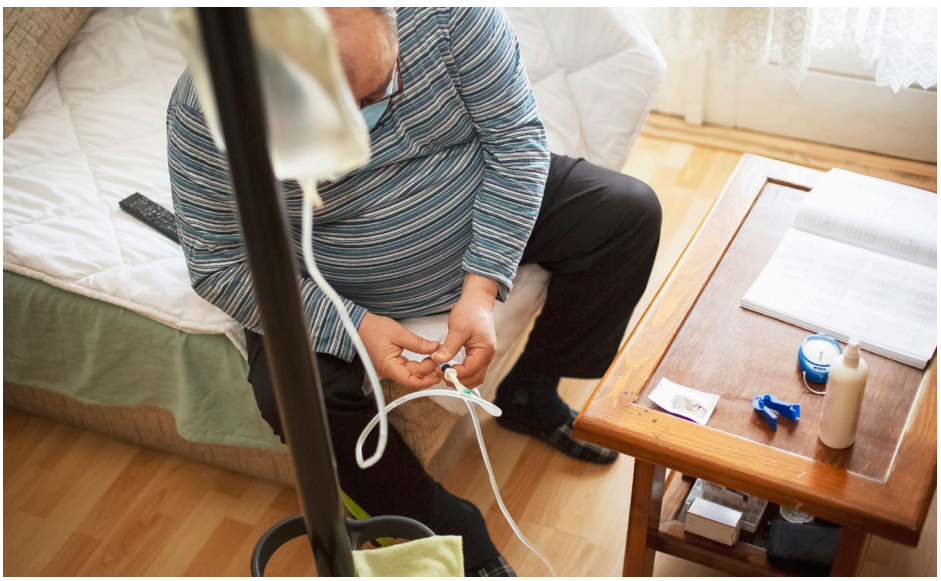

Learning objectives

After successful completion of this continuing education program, pharmacy technicians will:

1. Explain the different modes of dialysis: hemodialysis, home hemodialysis and peritoneal dialysis.
2. Describe common medications used by dialysis patients with a focus on anemia and bone disease management.
3. Identify medications that require dose adjustments during dialysis.
4. Discuss the role of the pharmacy technician in the care of a patient on dialysis

Introduction

Chronic kidney disease (CKD) is a global public health burden with a mean prevalence of 13.4%, and within Canada, it is estimated that at least 4 million people have the disease.[1]

Hypertension, diabetes and the growing elderly population are driving factors for the increase in numbers of people developing CKD.[1] Unfortunately, CKD is associated with adverse clinical outcomes, including end-stage kidney disease (ESKD), cardiovascular disease and increased mortality.[2-5]

There are five stages of kidney disease. To determine what stage of kidney disease a person may have, serum creatinine is measured in a blood test, and along with gender and age is

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used to calculate an estimated glomerular filtration rate (eGFR). The eGFR measures how much blood the kidneys filter each minute, recorded as millilitres per minute/average body surface area (mL/min/1.73m^2). The eGFR declines as kidney function declines. The five stages of CKD refer to how well the kidneys are working. In the early stages (Stages 1–3), the kidneys are still able to filter waste out of blood. In the later stages (Stage 4), the kidneys must work harder to filter blood and by later stages (Stage 5), they may stop working altogether. The goal of treatment at each stage of CKD is to take steps to slow down the damage to the kidneys and keep the kidneys working as long as possible.

As a part of kidney disease staging, urine is also tested to detect if there is any protein (albuminuria). If the kidneys are damaged, protein can "leak" out of the kidneys into urine. Having protein in the urine is called "albuminuria" or "proteinuria." There are 3 stages of albuminuria, with the first stage being normal or slightly higher amounts of protein in the urine while stage 3 is severely increased amounts of protein in the urine. Therefore, overall staging of kidney disease evaluates both the eGFR and amount of protein in the urine.

End-stage kidney disease (ESKD) usually occurs when kidney function is less than 15% of typical kidney function or an eGFR 15mL/min/1.73m^2.[6] When ESKD is reached the decision to start dialysis, transplantation or supportive care is made.

Choosing a Dialysis Modality

A kidney transplant is a surgical procedure to place a healthy kidney from a live or deceased donor into a person whose kidneys no longer function properly. Although a kidney transplant is often the treatment of choice for ESKD with a better mortality benefit and, especially when compared with a lifetime on dialysis, it is not always feasible and thus other modalities need to be considered.

Dialysis does some of the work of the kidneys. This includes removing extra fluids and waste products from the blood, restoring electrolyte levels, and helping control blood pressure. Dialysis options include peritoneal dialysis and hemodialysis. Peritoneal dialysis is done at home while hemodialysis can be done either at a dialysis centre or at home.[7]

In peritoneal dialysis (PD), a permanent catheter is placed into the abdomen by a surgeon and it is used to fill the peritoneal cavity with dialysis solution called dialysate.[7] This solution remains in the patient's peritoneal cavity for a few hours.[7] Dialysis occurs as wastes and excess water from the blood flow through the filter-like peritoneal membrane.[7]After a period of time (or 'dwell') an exchange step takes place where the fluid full of wastes from the peritoneal cavity is drained and the peritoneal cavity is then filled with a fresh solution or dialysate.[7] There are two main types of PD: continuous ambulatory PD (CAPD) and automated PD (APD). CAPD is usually carried out during the daytime and the process of filling and draining the peritoneal cavity is done manually about four or five times in a 24-hour period. With APD, a machine performs the cycling of the dialysis solution in the body, usually at night when the patient sleeps.[7]

In hemodialysis (HD), the patient's blood is passed through an external filter on a dialysis machine which filters wastes and extra water from the blood and then the 'clean' blood is returned to the patient.[7] Conventional HD is performed three times per week for four hours each time, usually at a dialysis centre (but can also be performed at home). Nocturnal hemodialysis can be performed either at home or in a dialysis centre during the night. If performed at a centre, the typical session lasts seven hours and is performed three times per week. If dialysis is completed at home, the session lasts approximately seven hours and is performed on average five times per week with some patients performing dialysis at home seven days per week.[7]

Finally, some people choose not to do dialysis or have a transplant. In these situations, supportive care is provided to help manage some of the symptoms of end stage kidney disease. Without either dialysis or a transplant, kidney failure progresses, eventually leading to death. Death can occur quickly or take months or years.

Management of Potential Complications in Patients on Dialysis

Dialysis cannot replace all functions of the kidney and thus patients will require medicines which either mimic other processes of the kidney or treat complications of kidney dysfunction. For example, dialysis will only partially control blood pressure, as there is a build up of uremic toxins and water which can worsen blood pressure control. Dialysis cannot remove all the phosphate that builds up from the intake of foods like dairy and meat. Moreover, the kidneys produce and excrete hormones such as erythropoietin (EPO), which is required to produce new red blood cells, or erythropoiesis. Therefore, dialysis patients are commonly prescribed a number of medications such as antihypertensives, phosphate binders and erythropoiesis-stimulating agents (ESAs). Finally, because many medications are cleared by the kidneys, medications should always be assessed for the most appropriate dosing in patients on dialysis. This review focuses on the management of anemia and bone disease in CKD.

Anemia of CKD

Anemia is defined as a reduction in one or more of the major red blood cell measurements: hemoglobin (Hb) concentration, hematocrit or red blood cell count. The World Health Organization defines anemia as a hemoglobin level < 130 g/L in men and postmenopausal women, and < 120 g/L in premenopausal women.[8] While anemia in patients with CKD can result from multiple mechanisms (iron, folate or vitamin B12 deficiency, gastrointestinal (GI) bleeding, severe hyperparathyroidism, systemic inflammation, and shortened red blood cell survival), decreased erythropoietin synthesis in the kidney is the most important and specific cause of anemia in patients with CKD, as the kidneys produce 90% of erythropoietin.[8]

Anemia of CKD is treated with erythropoietin-stimulating agents (ESAs), such as darbepoetin and erythropoietin (epoetin). The Canadian Society of Nephrology now recommends the initiation of ESA treatment when the Hb level is 90–100 g/L, and states that an acceptable range for Hb level is 95–115 g/L, with a target of 100–110 g/L.[8,9]

Iron supplementation may also be administered to ensure adequate iron stores for erythropoiesis, to correct iron deficiency and, in patients receiving ESA treatment, to prevent iron deficiency from developing.

Oral iron is typically prescribed to provide approximately 100-200mg of elemental iron daily (e.g., ferrous fumarate 300mg twice daily; each pill provides 100mg elemental iron).[10] Although ferrous fumarate is commonly available and inexpensive, other oral

iron preparations such as ferrous gluconate, ferrous sulfate, heme iron polypeptide or iron polysaccharide may also be used; however, there is no significant evidence to suggest that these oral iron formulations are more effective or associated with fewer side effects than ferrous fumarate. Furthermore, some of these agents are more costly. Oral iron supplementation commonly causes constipation, as well as nausea and vomiting. It can also cause staining of the teeth and dark tarry stools. Iron is best absorbed when taken on an empty stomach with water. To avoid drug-drug interactions, it is recommended to take in the evening and separated by at least two hours from other medications such as calcium carbonate and levothyroxine.

If the goals of iron supplementation are not met with a one- to three-month course of oral iron, it may be appropriate to consider IV iron supplementation.[8,9] Several IV iron preparations are available in Canada, including iron sucrose, iron gluconate and ferric derisomaltose. All IV iron preparations carry a risk for immediate reactions, which may include hypotension, dizziness and nausea. These reactions are usually short-lived and caused by too large a dose given during too short a time.

Electrolyte, Mineral and Bone Abnormalities in CKD

Electrolyte abnormalities, such as hyperkalemia, are present in 3%–11% of patients with CKD.[11] Initial treatment strategies usually involve dietary restrictions and, sometimes, medications. For example, patients with hyperkalemia should follow a low-potassium diet and in more severe cases a potassium binder (i.e. sodium polystyrene, patiromer, sodium zirconium cyclosilicate) is recommended.[12,13]

Mineral and bone disorders are also common. CKD-associated mineral bone disorders significantly increase morbidity and mortality in this patient population.[12,13] In fact, hyperphosphatemia and hyperparathyroidism have been associated with vascular calcification, which can lead to increased risk of cardiovascular events such as myocardial infarctions and stroke.[12,13] However, use of calcium-based phosphate binders and excessive vitamin D therapy may also contribute to vascular calcification.[12,13]

The principal goal of the treatment of CKD-associated bone and mineral disorders is to reduce phosphate levels to normal.[12,14] Initial treatment restricts dietary phosphorus intake when phosphate or parathyroid hormone (PTH) levels begin to rise. Different classes of phosphate binders can also be used to accomplish this goal. Calcium-based formulations for management of CKD-associated hyperphosphatemia (e.g., calcium carbonate) are the most widely used class of phosphate binders. However, calcium-based phosphate binders can induce hypercalcemia, which can also cause vascular calcification. They also commonly cause GI disturbances such as constipation.

Non-calcium-based phosphate binders such as sevelamer hydrochloride, lanthanum carbonate and sucroferric oxyhydroxide are also used. These non-calcium-based binders are more expensive and can also cause GI side effects such as nausea, vomiting, constipation and/or diarrhea.[12,13] Furthermore, it is important to note some drug-drug interactions with these agents, including fluoroquinolones and levothyroxine similar to calcium. These drugs should be dosed separately from the phosphate binders. See Table 1 for a comparison of phosphate binders.

In addition to phosphate binders, active vitamin D supplements and calcimimetics are used to manage elevated PTH levels. Since the kidney cannot produce activated vitamin D, agents such as calcitriol or alfacalcidol are required to raise the serum calcium concentration sufficiently to suppress PTH secretion. Patients can also be given a calcimimetic (i.e., cinacalcet), which act to increase the sensitivity of the calcium-sensing receptor to extracellular calcium and therefore decreases parathyroid hormone. Calcimimetics are costly and can also cause

GI disturbances (nausea and vomiting) and in some cases, severe hypocalcemia.[12,13]

Drug Dosing

Healthcare workers looking after patients with CKD should be aware of the pharmacokinetic changes in patients requiring dialysis. The most common pharmacokinetic alteration in patients with CKD is the reduced excretion of medications that are primarily eliminated by the kidneys. Reduced clearance of medications can lead to accumulation and increased risk for drug toxicity. Furthermore, certain properties of medications will determine how much will be cleared through dialysis and dose adjustment may be required to ensure that the medication remains effective. Dose adjustment also minimizes the risk for drug toxicity if the drug accumulates systemically due to poor clearance from dialysis.

Common medications that require dose reduction include some antibiotics (e.g., amoxicillin, ciprofloxacin), direct oral anticoagulants (e.g., apixaban), gabapentin, pregabalin, oral hypoglycemic agents, insulin, chemotherapeutic agents and opiates, among others.[15,16] Many references are available to aid pharmacists in adjusting doses in patients with CKD. For instance, the latest Canadian Diabetes Guidelines include a figure (Figure 2) which shows hypoglycemic agents and appropriate dosage adjustments for patients with CKD (https://guidelines.diabetes.ca/docs/cpg/Ch13-Pharmacologic-Glycemic-Management-of-Type-2-Diabetes-in-Adults.pdf).[17] In general, use of medications with more risk than benefit should be minimized because patients with CKD are at high risk of adverse medication events.[18-20]

Pharmacy technicians in medication reconciliation for patients on dialysis

Patients on hemodialysis (HD) have the highest pill burden of all chronically ill patient populations, taking on average 12 distinct medications per day.[21-23] Due to the frequent presence of other comorbid chronic conditions (e.g., hypertension, diabetes, cardiovascular disease) that require long-term medication management, patients on HD are at increased risk of adverse events (AE) and mortality related to polypharmacy.[21] In fact, patients on dialysis have an average of 4.5 medication therapy problems (MTPs).[24] In one study of dialysis patients, MTPs were implicated in nearly 50% of hospitalizations.[25] Table 3 lists some common MTPs in dialysis patients. Many of these MTPs can be identified and resolved by providing routinely scheduled medication reconciliation and pharmacy management services. Resolving MTPs in dialysis patients has been shown to reduce prescription medication costs and the frequency and duration of hospitalizations.[26]

Registered pharmacy technicians (RPhTs) can be trained by pharmacists to obtain best possible medication histories (BPMH) and then perform medication reconciliation and complete preparatory work to help pharmacists provide medication management services to patients.[27,28]

The BPMH involves a:

1. Patient (or caregiver) medication interview.
2. Verification of medication information with more than one source as appropriate including:
   - family or caregiver
   - community pharmacists and physicians
   - inspection of medication vials
   - patient medication lists
   - medication profile from other facilities
   - prescription drug claim histories
   - previous patient health records

The BPMH includes drug name, dose, frequency and route of medications a patient is currently taking, even though it may be different from what was actually prescribed. A BPMH is the first step in comprehensive medication management. A medication reconciliation can then be performed to determine MTPs.

TABLE 1 - Summary of Key Characteristics of Phosphate Binders[11-14]

Binder	Daily dose	Advantages	Disadvantages
Calcium carbonate	500—1250 mg	Effective, inexpensive	Potential for increased hypercalcemia – could lead to vascular calcification; GI side effects; pill burden
Lanthanum carbonate	250—3000 mg	Effective; no calcium; lower pill burden	Cost; GI side effects; systemic absorption may be a concern due to potential for accumulation
Sevelamer carbonate	800—7200 mg	Effective; lipid-lowering effect; no calcium	Cost; GI side effects; highest pill burden
Sevelamer hydrochloride	800—7200 mg	Effective; lipid-lowering effect; no calcium	Cost; GI side effects; potential development of metabolic acidosis; highest pill burden
Sucroferric oxyhydroxide	500—3000 mg	Effective; no calcium; does not lead to iron overload; lower pill burden	Cost; discolored feces; GI side effects

TABLE 2 - Potential Medication Therapy Problems in Patients on Dialysis

MTP	Description	Example
Indication	Patient is not receiving medication for a diagnosed medical condition	A patient with hyperparathyroidism is not taking a vitamin D analog (e.g., calcitriol)
Effectiveness	Use of a medication without a valid indication	Patient is taking furosemide when on hemodialysis and not making any urine
Safety	Use of a medication that is dosed too high causing an adverse medication event	Patient taking high-dose gabapentin and is extremely sedated and thus has had many falls
Adherence	Patient is not taking medication according to prescribed dosage schedule due to cost	Inability to pay for medication such as cinacalcet as patient is on provincial drug plan and it is not covered by the plan.
Drug administration	Patient is not taking drug properly.	Patient taking phosphate binder between meals rather than with meals, or is not fully chewing the chewable tablets.

Medication reconciliation performed by a RPhT when a patient returns to an ambulatory dialysis clinic after hospital discharge can facilitate timely identification of MTPs and has the potential to reduce rehospitalizations.[29] Technicians have the knowledge of medication names, drug classes and payment methods thus allowing them to quickly obtain key data from patients and providers, and discharge information to accurately reconcile medications upon a patient's return to the dialysis clinic.[28] The most common MTP in dialysis patients is the dose of a medication being too high.[27] For instance, gabapentin is often dosed too high and patients suffer from adverse events such as drowsiness, dizziness and falls.

In a study conducted in Vancouver, BC, the primary objective was to determine whether a RPhT could conduct interviews with hemodialysis patients (n = 99) or their caregivers to obtain best possible medication histories.[28] The information the RPhT was requested to obtain included the name, dose, and administration schedule of all prescription, nonprescription, and alternative medications. The medication history obtained by interview was then compared with the patient's current medication profile on file to identify any medications that were absent or prescribed in different dosages. All discrepancies were recorded, and those results were recorded. The rate of agreement between the technician and pharmacists for the medication history was recorded. After reviewing a total of 1,334 medication orders, the pharmacist and technician agreed on 99% of all orders.[28] Therefore, having a RPhT perform medication reconciliation with patients on dialysis allows pharmacists extra time to perform other clinical activities, such as management of anemia or metabolic bone disease, and solving other medication-therapy problems.

Other roles of the Pharmacy Technician in the care of patients on dialysis

Although the role in pharmacy technicians in medication reconciliation has shown to help pharmacists and dialysis units to improve the care in their patients, some provinces have pharmacy technicians certified for vaccine administration as well as helping in the procurement of medications and drug navigation, especially medications that are costly and not covered by provincial formularies. Therefore, there are many potential roles pharmacy technicians can play in nephrology clinics to help improve care of these patients.

Conclusion

Patients undergoing dialysis are a medically complex population with a high medication burden and frequent hospitalizations. Comprehensive pharmacy practice presents pharmacy technicians with new opportunities to perform key functions and services like medication reconciliation. Having a technician perform medication reconciliation in patients undergoing dialysis is a useful first step in identification of medication therapy problems by pharmacists and the healthcare team.

***Marisa Battistella** has worked at the University Health Network since 1999 in various positions, including cardiology and internal medicine. In 2002, she completed her Pharm D through Idaho State University. She has worked as a clinical pharmacist specialist in the hemodialysis unit at the UHN since 2002. As an Associate Professor at the Leslie Dan Faculty of Pharmacy and Clinician Scientist in Pharmacy at UHN, Marisa has focused her research in the area of pharmaco-nephrology where she has published several papers and given many presentations on drug therapy in nephrology.*

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QUESTIONS

Find and answer the questions for this CE lesson online at eCortex.ca. Search using all or part of the course title.

1. At which stage of kidney disease are patients often started on dialysis?
a) Stage 1 b) Stage 2
c) Stage 3 d) Stage 4
e) Stage 5

2. Almost 90% of the erythropoietin in the body is produced by the:
a) liver
b) bone marrow
c) kidneys
d) thyroid and parathyroid

3. The main contributing factor to anemia in CKD is:
a) iron deficiency
b) folate deficiency
c) chronic inflammation
d) low levels of erythropoietin

4. In managing CKD bone disease, the first step in treatment is
a) Decrease calcium
b) Start calcimimetic
c) Start calcitriol
d) Decrease phosphorus levels

5.The leading cause(s) of kidney failure is/are:
a) Diabetes b) Infection
c) Hypertension d) A and C

6. A 36-year-old woman with diabetic nephropathy comes to the pharmacy with a new prescription for epoetin. During the interview, the patient says she has had fatigue for the past month. Her laboratory results show a hemoglobin level of 89 g/L and an estimated glomerular filtration rate of 33 mL/min/1.73 m2. Which of the following is the target hemoglobin level for this patient?
a) 78 g/L b) 100-110 g/L
c) 130-140 g/L d) 150-160 g/L

LD is a 70-year-old female patient at your community pharmacy with chronic kidney disease. She arrives today at the pharmacy with new prescriptions for calcitriol, ferrous fumarate and calcium carbonate. She has many questions for you about these new therapies including what they are for, how they will benefit her and what side effects she might experience. She tells you that she has "stage 4 kidney disease" and is thinking about what type of dialysis she might prefer in the future, although she is hoping to be able to arrange a kidney transplant with a family member. You are happy to help answer LD's questions in the pharmacy today.

7. LD informs you that Calcium carbonate is a new prescription and she is not sure why she is using it. You ask the pharmacist to counsel the patient. The indication for LD's calcium carbonate is to:
a) lower phosphate
b) increase calcium
c) bind to the iron
d) increase parathyroid hormone

8. LD returns a week later to tell you that she is experiencing a side effect of the Calcium carbonate. You ask the pharmacist to speak to LD about common side effects of calcium carbonate. A common side effect that LD may experience due to her new medication regimen includes:
a) diarrhea b) headaches
c) constipation d) dizziness

9. The most concerning side effect with oral iron pills is:
a) constipation b) diarrhea
c) dizziness d) hypocalcemia

10. Some medications need to be dose adjusted in dialysis patients as there is concern for accumulation. The most common medication class that needs to be dose adjusted is:
a) blood pressure medications
b) oral iron medications
c) antibiotics
d) phosphate binders

11. A hemodialysis patient comes into the pharmacy and has a question on her new prescription, a phosphate binder, lanthanum. The prescription says to take three times daily with food but the patient would like to know when to take her levothyroxine since she has always taken it in the morning with breakfast. You tell her it is best to take it:
a) at suppertime
b) at lunchtime
c) at breakfast
d) 30 mins before breakfast

12. The most common MTP in patients on dialysis is:
a) Dose too low
b) Dose too high
c) Patient nonadherence to medications
d) Medication not covered by provincial plan

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The role of pharmacy technicians in the care of patients on dialysis

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