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Chapter 6

Pain Management in Patients with Impaired Kidney Function

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Abstract

Huge numbers of patients referred to pain service have kidney function impairment to some extent. Pain physicians face puzzling cases and may find themselves struggling and divided between the decisions of providing adequate pain reliever, at the same time avoiding further damage to kidneys, and excessive accumulation of medications and their metabolites, also negative interactions with patient's other medications. In this chapter, we will reason about the prevalence of pain in patients with renal impairment, pharmacodynamics and pharmacokinetics of pain medications in this group, optimization of pain control, preferred choice of drugs according to the level of kidney damage, and feasibility of alternative pain management techniques.

Keywords: impaired kidney function (IKF), chronic kidney disease (CKD), acute pain, chronic pain

1. Introduction

Across all subspecialties, pain is the most encountered problem. It is particularly difficult to deal with in patients with organ dysfunction such as acute or chronic kidney failure, due to the fact that most medications depend on kidneys for clearance. Moreover, pharmacokinetics becomes almost unpredictable due to fluctuations in kidney function depending on patient factors such as volume status, other medication actions, or enzyme build of certain individual.

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2. Epidemiology

The prevalence of pain in patients with chronic kidney disease (CKD) has been shown in many epidemiologic studies, and all of them unanimously demonstrate that pain is more common in CKD patients than the general population.

Murtagh et al., in a cross-sectional survey of symptoms prevalence in stage 5 chronic kidney disease managed without dialysis, found that pain was present in 53% (42–63%) of total 66 patients with a mean age of 82 ± 6.6 years [1].

Davison et al. have analyzed publications from 1992 to 2009 and concluded that 58% of CKD patients are suffering from pain, 49% of those patients rated their pain as moderate to severe [2].

As quality of life is greatly diminished by any kind of pain, it has been studied in CKD patients as part of symptom burden, for example [3], older patients found musculoskeletal symptoms, including pain in bones/joints (69% of 283 CKD Stage 1–5 patients), are more disturbing and bothersome, while younger patients found that reduced concentration is more intrusive. Perlman et al. also demonstrated that the presence of pain was associated with lower quality-of-life scores in a multicenter cross-sectional analysis of 634 patients with CKD [4].

Additionally, in prospective cohort study of 205 Canadian hemodialysis (HD) patients, 50% of them reported pain which was related to those who was on longer HD therapy, 52.5 months with pain versus 37.7 months for those without pain.

The etiology of pain was multiple in 18.4% of patients with pain, among which musculoskeletal was the most frequent (50.5%); same study found that almost one third of all patients with pain were not on any painkillers, and authors concluded that pain management was ineffective in 74.8 of patients [5].

Pain in CKD patients is an important factor, which immensely affects quality of life. Weisbord et al. showed clear correlation between symptom excess and severity with diminished quality of life. If they had considered pain-related symptoms such as muscle cramps, headache, and chest pain in pain group, the prevalence would have increased to 50–85% [6].

Moreover, CKD patients with pain tend to decide to withdraw from HD more often; as shown by Davison and Jhangri, they also were more depressed and suffered sleep disturbances [7].

3. Definition and staging of chronic kidney disease

It is very important to identify the degree of IKF and the nature of CKD and on what stage it is, because these factors will guide the management of pain and to some extent predict pain medication pharmacokinetics.

Definition for CKD must have the following criteria:

1. Kidney damage for 3 months or more, represented by structural or functional abnormalities of the kidney, with or without decreased GFR and manifested by following:
   a. Pathological abnormalities
   b. Markers of kidney damage, such as abnormalities in the composition of the blood or urine, or abnormalities in imaging tests
2. GFR less than 60 mL/min/1.73 m^2 for more than 3 months with or without kidney damage [8]

Evaluation of kidney function is more dependent on GFR or the presence of other markers of kidney damage rather than a single serum creatinine reading.

Stages of CKD according to GFR are described in **Table 1**.

Stages	GFR (mL/min/1.73 m^2)	Terms/uremic symptoms
Stage 1	90 or more	Normal function/asymptomatic
Stage 2	60–89	Mild/asymptomatic
Stage 3	30–59	Moderate/mild symptoms
Stage 4	15–29	Severe/mild to moderate symptoms
Stage 5	15 or less	End-stage renal disease/moderate to severe symptoms, may require dialysis

Table 1. Stages of chronic kidney disease according to glomerular filtration rate [8].

4. Pain in patients with CKD

4.1. Acute pain in patients with CKD

The cause for acute pain is mainly acute injury such as surgery, procedures, and childbirth. It can be caused by acute inflammation or ischemia as well, for example, acute abdomen, colic, and ischemic heart diseases. Treatment should be directed to reduce the pain as soon as possible with multiple modalities; at the same time, the primary cause should be addressed.

Blocking the pain along different parts of pain pathway allows reducing the required doses and diminishing side effects. This approach has been defined as multimodal analgesia.

Multimodal analgesia can be achieved by combining systemic paracetamol, NSAID, opioids, and local anesthetics according to patient's condition. All these medications may require dose adjustment, and locoregional anesthesia may raise a concern of hematoma formation due to reduced platelet activity and anticoagulant use in patients receiving hemodialysis [9].

Choice and dosage of medications depend on the condition of the kidneys; here the staging can roughly guide physicians to correct regimen.

For example, in stages 1 and 2, kidney function is preserved well enough to excrete the medications and their metabolites. But still, kidney function tests should be frequently done so not to miss any deterioration due to trauma, dehydration, and surgical stress during perioperative period. In young patients who are not taking other nephrotoxic medications and in stage 1, acetaminophen plus short course of NSAIDs could be used. NSAIDs should not be used in stage 2 with GFR 60–89 mL/min/1.73 m^2. Locoregional anesthesia must be used when applicable, especially for postoperative pain and trauma patients. In cases of moderate to severe pain, opioids should be added including tramadol, with or without gabapentinoids (Gabapentin or Pregabalin) to supplement for neuropathic pain, especially in trauma [9].

In stages 3 and 4, kidney function significantly reduced (GFR between 15 and 59 mL/min/1.73 m^2) which mandate all the pain medications to be dose adjusted and NSAIDs to be avoided. Acetaminophen should be used in regular doses for mild pain, reduced dose tramadol may be added, and for stronger pain, opioid such as fentanyl or hydromorphone may be useful. Morphine and codeine are not recommended. Regional anesthesia proves to be a valuable modality to avoid opioids and their undesired properties, especially in this stage, but should be avoided in individuals with impaired platelet function and/or coagulation. Reduced doses of gabapentinoids are considered in neuropathic pain, and caution should be taken when patients receive concomitant opioids. A decrease in around 50% of the dose for each 50% decline in GFR or CCr and an increase in the time interval between the doses are recommended [9, 10].

Acute pain management in end-stage renal disease (ESRD) patients follows the same abovementioned principles; in addition to it, more than half of them may already have been experiencing chronic pain as well. Moreover, these patients are usually malnourished and have many other multiple concomitant diseases. If they are already undergoing dialysis, sudden drop in serum concentration of pain medications and exacerbation of pain is expected. Acetaminophen may be used in regular doses of 4 g/day, but general condition of patient and other organ system diseases may require dose reduction. NSAIDs should be avoided in ESRD; even if nephrotoxicity is not of a concern, they cause gastrointestinal damage, electrolyte disturbances, and hypertension. Cyclo-oxygenase-2 inhibitors are also considered unsafe as they contribute to already existent multiple risk factors for myocardial ischemia in this group of patients [11].

Morphine, codeine, and meperidine produce active metabolites, in which clearance depends on kidney function. In ESRD patients, the accumulation of active metabolites of opioids produces excessive somnolence, as well as more dangerous complications such as respiratory depression, seizures, myoclonus, and exacerbation of acidosis. Safe alternative to these long-acting opioids are fentanyl, alfentanil, and adjusted dose of hydromorphone [12]. These can be best given as PCA in acute pain cases if strong opioids are required.

4.2. Chronic pain in CKD patients

Chronic pain is defined by Treede et al. as pain that persists past normal healing time [13] and hence lacks the acute warning function of physiological nociception [14]. It may be due to prolonged tissue injury with persistent activation of nociceptors or other undefined mechanisms [15].

Recommendations of the WHO for cancer pain and its three-step approach can be tailored to manage pharmacologic treatment of chronic pain in CKD patients [2, 15, 16]. In patients with mild pain, acetaminophen may suffice, and if NSAIDs are required, care should be taken to avoid other medications which worsen the hemodynamics (compounds that affect the renin-angiotensin-aldosterone system). NSAIDs should be avoided in patients with impaired cardiac output or with dehydration.

For moderate pain, weak opioid tramadol may be added, but codeine and dihydrocodeine should not be prescribed. Tramadol dose is adjusted according to CKD stage, given in regular doses for stages 1 and 2, but is reduced by 50% in advanced stages of CKD.

Severe pain requires the use of strong opioids, preferably those without active metabolites such as methadone, fentanyl, and oxycodone. Although, oxycodone is mainly metabolized in the liver, around 20% is eliminated by kidneys. For that reason, it may be wise to reduce the dose according to CKD stage; in mild renal failure, up to 50% of normal dose should be given, and in advanced stages, 25% of normal dose and increase in dosing interval should be done. In patients with consistent pain, fentanyl patch can be a good option [15, 16].

In all steps of WHO ladder, adjuvant medications should be added and tailored to a particular type of pain. If patient is experiencing neuropathic pain, antidepressants and anticonvulsants should be added to pain regimen. Musculoskeletal pain may have spastic component; thus muscle relaxants are beneficial. Bisphosphonates are considered adjuvant for bone pain due to malignancy. There is at least one meta-analysis to support the effect of omega-3 polyunsaturated fatty acids as an effective adjunct for joint pain (rheumatoid arthritis, inflammatory bowel disease) [17].

Pharmacologic treatment of chronic neuropathic pain for adults should be done in a stepwise approach. The first line is tricyclic antidepressants (TCAs), followed by selective serotonin norepinephrine reuptake inhibitors (SSNRIs). Gabapentinoids are next to use.

Topical lidocaine should be considered alone or in combination with one the first-line therapies for localized peripheral neuropathic pain.

Opioid analgesics or tramadol could be used alone or in combination with one of the first-line therapies.

In painful diabetic peripheral neuropathy, gabapentinoids are recommended.

5. Medications used for pain and their pharmacologic properties in CKD patients

5.1. Acetaminophen

Acetaminophen, chemical name N-acetyl-p-aminophenol, is used as a first-line medication for mild and moderate pain. It is very well absorbed from the gastrointestinal tract, mainly in the small intestine, via passive transport, and its serum concentration peaks around 2 hours.

Any factors suppressing gastric emptying will slow paracetamol absorption, because negligible amount is absorbed in the stomach. It readily crosses the blood-brain barrier, and most antipyretic and analgesic actions are executed in the central nervous system.

Mechanism of action on receptors is not entirely made clear, but it has proposed actions on serotonergic pathways, potentiation of cannabinoid receptors, and inhibition of cyclooxygenase−3 and central prostaglandin production. Recent studies have questioned its biological activity regarding cyclooxygenase inhibition in peripheral tissues, and at least two recent studies experimentally proved that paracetamol possessed peripheral cyclooxygenase-2 inhibition [18–20].

Acetaminophen has been regarded as pain medication with very favorable side effect profile, when used within therapeutic range doses. But recently, some authors started to question its safety, especially possible association with kidney damage. In this study [21], CKD patients who were regularly taking acetaminophen were more likely to progress to ESRD, especially with increasing exposure. In another population-based, case-control study in Sweden, 926 patients were newly diagnosed with renal failure and acetaminophen was regularly consumed by 25% of them and only 12% of controls, and authors have concluded that the regular use of paracetamol increased the risk of CKD by 2.5 times from any cause [22]. Roberts et al. conducted systematic review of observational studies looking at acetaminophen's side effects, and they found increased relative rate of mortality from 0.95 to 1.63 and for cardiovascular adverse events risk ratio of all events increased from 1.19 to 1.68 and also that gastrointestinal adverse events or bleeds were found to increase from 1.11 to 1.49; moreover, kidney damage odds ratio increased more than 30% [23]. Another notable paper published on acetaminophen's cardiovascular side effect could only demonstrate small association with major cardiovascular events and short-term use of acetaminophen (odds ratio 1.21, 95% confidence interval 1.04–1.42) [24].

Acetaminophen's well-known hepatotoxicity occurs when the liver's glucuronide and sulfate stores are used up, forcing it to enter minor pathway, which is oxidation by CYP 450 enzymes and formation of N-acetyl-*p*-benzoquinone imine (NAPQI). This metabolite is harmless in the presence of glutathione but causes hepatotoxicity in patients with limited glutathione reserves.

The exact mechanisms for acetaminophen's renal toxicity have not been identified, whereas experimental research proposed that kidneys must be saturated and push acetaminophen via CYP 450 pathway for tubular damage to occur. Diminished glutathione reserve also exacerbated kidney toxicity [25]. Another possible mechanism is the formation of arylating intermediates by p-aminophenol, which is formed by deacetylation of acetaminophen [26]. Clinical manifestation of kidney injury appears as acute tubular necrosis, with corresponding urinary changes, such as granular casts, maybe with hematuria or pyuria, urine sodium increase, and azotemia as well [27]. Toxicity is exacerbated by factors such as fall in glutathione levels (any cachectic state, alcoholism) or induction of CYP 450 enzymes.

In normal conditions, plasma half-life of acetaminophen is 1.5–2.5 hours, large portion of which is metabolized and excreted in urine as sulfate and glucuronide conjugates, and

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minor pathway comprising less than 5% produces mercapturic and cysteine conjugates. Approximately 4% is excreted as unchanged drug. All of these processes will vary with age and dose administered. Urine flow rate is the main factor determining the clearance of acetaminophen by kidneys, but glucuronide and sulfate conjugates are not dependent of urine flow, most of the time surpassing glomerular filtration rate [28]. In CKD patients, it has been proved that glucuronide and sulfate metabolites are significantly accumulated, for example, in moderate stage of CKD, they have half-life around 21.8–30.5 hours as opposed to 3 hours in a normal person [29]. In ESRD patients undergoing dialysis, acetaminophen is removed by hemodialysis, but not by peritoneal dialysis.

Nonetheless, acetaminophen is still a preferred drug for mild to moderate pain, and no dose reductions are mandatory.

5.2. NSAIDs

NSAIDs as a group are highly unfavorable for any patient with kidney damage; nevertheless, many epidemiologic researchers have identified them as popular analgesics among CKD patients.

NSAIDs can be classified according to their chemical structure. They are divided into propionic acid derivatives (ibuprofen, ketoprofen, fenoprofen, naproxen), fenamates (diclofenac, ketorolac, tolmetin), enolic acid derivatives (meloxicam, piroxicam, nabumetone), and acetic acid derivatives (indomethacin, etodolac, sulindac). All these group medications inhibit the formation of prostaglandins in the peripheral tissues and, centrally, from arachidonic acid [30], hence exhibiting to different degrees analgesic, antipyretic, and anti-inflammatory effects. The action is achieved by blocking the cyclooxygenase (COX), which has two isoforms. COX-1 produces the group of prostaglandins which are necessary to maintain various physiological processes such as kidney function, maintenance of the gastrointestinal mucosa, and platelet aggregation. Yet, COX-2 is an inducible enzyme, production of which is prompted by inflammatory mediators (lipopolysaccharides, cytokines, and growth factors) by upregulating the expression of the enzyme up to 20-fold following the insult. Despite the fact that COX-2 is regarded as an inducible enzyme of inflammation process, the recent findings show that it plays an important role in normal physiology as well. It was found as an integral part of developing kidneys and brain, being a necessary enzyme for maturation and function. COX-2 maintains water electrolyte balance, contributes to arterial pressure regulation, and is mainly expressed in the thick ascending loop of Henle, macula densa of the nephron. The same enzyme is thought to play an important role in various tumor developments; especially it is overexpressed in intestinal adenomas, supporting many epidemiologic studies on the role of NSAIDs for colorectal cancer risk reduction.

Some authors believe that classification of NSAIDs should be according to their COX-2-to-COX-1 ratio, to better reflect their side effect profile [31], but along with inconsistent laboratory data, epidemiologic studies also show discrepancies in side effect profile of many NSAIDs. Instead, tabulating them according to half-life is of much clinical importance, which lets us to schedule medicine around the clock and avoid long-acting representatives in certain

patients, including CKD patients. If the use of NSAIDs is required in CKD patients, preference should be given to those with short to medium half-life, such as ibuprofen, diclofenac, ketoprofen, and indomethacin, which have half-life less than 6 hours. Long-acting NSAIDs as naproxen, phenylbutazone, piroxicam, sulindac, diflunisal, and meloxicam (with half-life more than 10 hours) should be avoided.

Most of the NSAIDs have good bioavailability from the gastrointestinal tract, and their hepatic clearance is low. They also have almost equivalent efficacy, and most studies have demonstrated even comparable efficacy between nonspecific NSAIDs (nsNSAIDs) and coxibs [32]. Detailed pharmacokinetics of each NSAID is beyond the scope of this chapter; instead we will review their comparable side effect profile and application in CKD patients.

All NSAIDs possess to some extent of gastrointestinal, renal, and cardiovascular toxicities and fluid retention or aggravation of hypertension. Gastrointestinal toxicity is exacerbated by various additional risk factors such as preexisting *Helicobacter pylori* infection, advanced age, and the concomitant use of corticosteroids or aspirin. Coxibs are the least harmful to the gastrointestinal tract as compared to other nonselective NSAIDs, which increase the risk by 2–4 times [33]. The most hepatotoxic representatives are nimesulide, sulindac, and diclofenac [34].

The recent meta-analysis found that cardiovascular complications were significantly increased by both coxibs (rate ratio (RR) 1.37) and diclofenac (RR 1.41); the same analysis found ibuprofen increased coronary events significantly (RR 2.22), but naproxen was not found to contribute to major vascular events (RR 0.93). Heart failure risk was approximately increase by twofold by all representatives [33].

All NSAIDs, including coxibs, adversely affect kidney physiology, which is expected considering the important role that prostaglandins play in regulation of renal perfusion and filtration. These effects manifest as hypertension, fluid retention, and in severe cases acute kidney failure [30]. Exacerbating factors are preexisting kidney dysfunction and dehydration. But it is not clear if the chronic use of NSAIDs leads to CKD or worsens its course. Several recent epidemiologic studies tried to elucidate this matter. In one meta-analysis [35], authors have concluded that regular-dose NSAIDs were not found to exacerbate the advancement of CKD (OD = 0.96), but CKD accelerated with increased-dose NSAID use (OD = 1.26). And authors have concluded that it was acceptable to use NSAIDs in moderate to severe CKD, but doses must be tailored to minimal and effective at the same time.

In general, NSAIDs should be used in the short term and avoided in elderly, and precautions for gastric protection should be undertaken.

Despite well-known side effects and warnings, most of the CKD patients continue frequent consumption of NSAIDs, because these medications are easily available over the counter.

5.3. Opioids

The extent of opioid use among CKD patients is not well established. In recent review, it was reported to range around 18–36% [36].

As mentioned above, the use of opioids is highly undesirable in CKD patients, but in practice physicians are obliged to, due to the severity and poor pain control with non-opioid medications.

Morphine as a prototype opioid should be avoided as much as possible; it produces active metabolites which depend on kidney functions for clearance. The liver converts morphine to morphine-3-glucoronide approximately 55%, morphine-6-glucoronide 10%, and normorphine 4%.

In CKD patients accumulation of metabolites produces delayed suppression of respiratory drive; at the same time, other bothersome side effects such as pruritus can be challenging to manage. Morphine removed with hemodialysis up to 47%, but its metabolite, morphine-6-glucoronide, is fat-soluble and retained even after dialysis. It might be the cause of rebound phenomenon observed after dialysis.

Starting dose of morphine depends on glomerular filtration rate and should be around quarter to half of normal doses if it is 10–50 mL/min range and must be avoided at all if GFR is less than 10 mL/min.

Codeine is extensively metabolized to codeine-6-glucuronide (70%), to morphine by CYP2D6 enzymes (15%), and only 10–15% to norcodeine. About 5–15% of codeine is excreted by kidneys unchanged. Furthermore, morphine itself undergoes transformation to active metabolites as described above. All this makes codeine unsuitable for CKD patients; thus, no dosing regimen can be recommended at all.

Tramadol is known for its other, non-opioid properties, namely, inhibition of serotonin reuptake, which increases serotonin concentration in the synaptic cleft and low abuse potential. Tramadol produces active metabolites by O-demethylation (M1), which is more potent than tramadol itself and less active N,O-didesmethyltramadol (M5). These metabolites then undergo glucuronidation and are excreted by kidneys, 60% of initial dose as metabolites, and 30% unchanged. In CKD patients tramadol and its metabolites accumulate significantly, increasing the risk for respiratory depression and seizures, as well as serotonin syndrome. Recommended dose for tramadol in CKD patients with CrCl less than 30 mL/min is maximum of 100 mg twice daily and only 50 mg twice daily for stage 5 patients who are usually on dialysis [15].

Hydromorphone is considered relatively a better opioid option in CKD patients, despite the fact that it also produces active metabolite, hydromorphone-3-glucuronide, with seizure-inducing properties. This metabolite is removed via hemodialysis up to 40% [37]. Its analgesic properties are better than morphine, and some authors reported improvement of side effect profile, especially cognitive abilities after switching from morphine to hydromorphone [38]. Nevertheless, doses in CKD patients should be reduced, and dialysis patients should keep in mind that dialysis does not remove metabolites fully.

Oxycodone has same analgesic potency as morphine but better bioavailability and higher abuse potential. It is converted to inactive noroxycodone (45% of total dose) and active oxymorphone (19%). The latter is more potent than morphine with less pronounced side effects. Around 72%

is excreted via kidneys, of which 8% as oxycodone and the remaining as metabolites. In CKD patients, dose reduction is necessary, if GFR is less than 60 mL/min, the serum concentration of oxycodone reaches 50%; thus, starting dose should be 30% and titrated with lengthening the dosing interval. In stage 5 CKD patients, it is best to be avoided, although it is removed by dialysis.

Methadone was traditionally used in the treatment of opioid addiction but now increasingly prescribed for outpatient chronic pain patients. It has good bioavailability (mean value 75%), although pharmacokinetics greatly varies among individuals due to differences in CYP450 enzyme activity (which depends on genetics or patient's other medications). Eventually it undergoes N-demethylation in the liver by CYP3A4 to inactive metabolite. It has long life, elimination half-life reaching approximately 22 hours. Limited number of studies showed that no significant accumulation in CKD patients occurs, making it a suitable medication for renally impaired population. Therefore no dose adjustments are mandatory, except in cases when the patient is taking other CYP450-altering medications.

Buprenorphine is also extensively metabolized by the liver producing weak analgesic, norbuprenorphine. Thirty percent of both parent drug and metabolite is cleared by kidneys. In CKD patients, it can be used in regular doses in stages 1–4 but in stage 5 used with caution and monitoring. It is dialyzed by both hemo- and peritoneal dialysis.

Fentanyl is considered a safe opioid in CKD patients, and recommended route is transdermal patch (except in ESRD when it is avoided), but dose reduction should be up to 50% in severe to moderate CKD. It is mainly metabolized by oxidation in the liver, producing inactive metabolite, norfentanyl; 75% is excreted within 3 days. It is not dialyzed by either hemo- or peritoneal dialysis.

Alfentanil is similar to fentanyl, can be also used as a transdermal patch, and does not produce active metabolites. It is short and fast acting and also cannot be removed with dialysis. No dose reduction is required in CKD patients in any level.

When prescribing any opioid, all clinicians must follow safety precautions, explaining to patient treatment goals, using lowest dose to reach pain relief, following the patient regularly and frequent questioning of opioid need.

6. Non-pharmacological pain control

Non-pharmacological approach to pain management starts with working on psychological components of the pain. Devine et al. analyzed 191 studies and confirmed significance of psychological and educational care of surgical patients and its role in managing acute postoperative pain. It included providing patients with proper information about procedures and the expected level of pain, instructing them on proper coughing and breathing techniques, and providing emotional support [39].

Transition from acute to chronic pain conditions also involves several psychological factors such as depressive state, somatization, or significant distress [40].

Many kinds of questionnaires and tests were developed to be applied in chronic pain, discussion of which is beyond the scope of this chapter. Generally, psychological management of chronic pain patients should be carried out with the help of certified psychologist or psychiatrist.

Considering the burden of musculoskeletal pain in CKD patients, therapies to reduce muscle tension and myofascial release should be applied, such as bed rest, bracing, traction, manipulation and mobilization, exercise, and heat/cold applications. Acupuncture was proven to be effective in lower back pain and knee pain; therefore, along with mindfulness, meditation and relaxation techniques prove to be safe and applicable to CKD patients too [41].

7. Conclusion

A considerable number of CKD patients experience acute pain at some point of their life, and even bigger portion of this population suffer from chronic pain. It is apparent from epidemiologic studies that pain can be experienced by more than 50% of CKD patients and greatly affects their quality of life. Moreover, poor pain control may lead to exacerbation of other psychological symptoms and contribute to further patient deterioration. If it is relatively clear how to manage acute pain in hospitalized patients, chronic pain remains mostly understudied and not fully understood. WHO stepwise approach to treating cancer pain may be tailored to CKD patients considering disturbances of pharmacodynamics of most medications in renal impairment. When there is a need to prescribe opioids, all precautions for side effects and addiction prevention must be taken. Pain practitioners should actively advocate non-pharmacological pain management techniques in appropriate patients.

Conflict of interest

Nothing to declare.

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