World’ Kidney Day - March 09th 2023

Launched at the initiative of the International Society of Nephrology, World Kidney Day comes at the right time to raise awareness among the general public of the importance of kidney disease, silent conditions whose late diagnosis multiplies the consequences. It often happens that many of them are not detected until they approach the terminal stage and, in this case, recourse to dialysis or a transplant is made compulsory. Our current lifestyles, unbalanced diet, sedentary lifestyle, are aggravating factors and the increase in the number of patients suffering from diabetes or arterial hypertension, "mechanically" leads to an increase in cases of renal failure.

**Protecting your kidneys is saving your heart**

Each year a new theme is chosen. In 2011, the theme chosen for the 6th World Kidney Day was to raise awareness of the relationship between kidney disease and heart disease. In 2013, it was about drawing attention to acute kidney failure. In 2016, the choice fell on a very proactive theme: "Taking care of your kidneys is your health tomorrow" In 2020, the watchword was: "Move for your kidneys".

In 2023, the campaign of March 9 is focused on the efforts to be made to maintain good kidney health for all in order to face the unexpected, by supporting the most vulnerable, by developing information and prevention campaigns kidney diseases.

As part of this celebration, the Center for the Development of Best Practice in Health, propose these summaries of Cochrane systematic reviews aiming to inform the patients, medical staff and others stakeholders interested with kidney diseases issues.
Journée Mondiale du Rein – 09 Mars 2023
Lancée à l'initiative de l'International Society of Nephrology, la Journée Mondiale du Rein vient à point nommé pour sensibiliser le grand public à l'importance des maladies rénales, affections silencieuses dont le diagnostic tardif multiplie les conséquences. Il arrive souvent que nombre d'entre elles ne soient dépistées qu'à l'approche du stade terminal et, dans ce cas, le recours à la dialyse ou la greffe est rendu obligatoire. Nos modes de vie actuels, alimentation déséquilibrée, sédentarité, sont des facteurs aggravants et l'augmentation du nombre de patients souffrant de diabète ou d'hypertension artérielle, entraînent "mécaniquement" une augmentation des cas d'insuffisance rénale.

Protéger ses rênes, c'est sauver son cœur
Chaque année, un nouveau thème est choisi. En 2011, la thématique retenue pour la 6e journée Mondiale du Rein avait pour thème la sensibilisation aux relations maladies du rein / maladies du cœur. En 2013, il s'agissait d'attirer l'attention sur les insuffisances rénales aiguës. En 2016, le choix s'était porté sur un thème très volontariste : "Prendre soin de ses reins, c'est garantir sa santé de demain". En 2020, le mot d'ordre était : "Bougez-vous pour vos reins". En 2023, la campagne du 9 mars est concentrée sur les efforts à faire pour maintenir la bonne santé rénale pour tous afin de faire face à l'inattendu, en soutenant les plus vulnérables, en développant des campagnes d'information et de prévention des maladies rénales.
Dans le cadre de cette célébration, le Centre pour le développement des Bonnes pratiques en santé, propose ces résumés de revues systématiques Cochrane visant à informer les patients, le personnel médical et les autres parties prenantes intéressées par les problèmes de maladies rénales.
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1. Non-pharmacological interventions for preventing clotting of extracorporeal circuits during continuous renal replacement therapy

What is the issue?
Acute kidney injury (AKI) is a major problem in people with severe illness. In cases of severe AKI, kidney replacement therapy/dialysis (KRT) using circuits is necessary. Continuous kidney replacement therapy is performed continuously over 24 hours. Clotting of the CKRT circuit can interfere with this treatment. To prevent this, a variety of non-pharmacological (not using medication) interventions have been studied. We aimed to summarise current evidence regarding the efficacy of non-pharmacological interventions for preventing clotting of extracorporeal circuits during CKRT.

What did we do?
We searched for available evidence from the Cochrane Kidney and Transplant Specialised Register up to 25 January 2021. Our review summarised the results of 20 randomised studies involving a total of 1143 people.

What did we find?
We found that the quality of the 20 included studies was low, and the number randomised was small. The majority of the included studies did not report death as an outcome. We found that continuous venovenous haemodialfiltration (CVVHDF), as compared with continuous venovenous haemofiltration (CVVH), may prolong circuit lifespan. In addition, pre-dilution haemofiltration, as compared with post-dilution haemofiltration, a longer catheter placing the tip at the right atrium, as compared with a shorter catheter placing the tip in the superior vena cava, and surface-modified double lumen catheter, as compared with standard double lumen catheter, may extend the circuit lifespan. However, higher blood flow compared to standard blood flow rate might not affect circuit lifespan. Overall, the data was limited and of very low certainty.

Conclusions
We found that the effects of non-pharmacological interventions in people with AKI receiving CKRT remain unclear. There is a need for studies assessing CKRT circuit lifespan as well as other clinically important outcomes.
Implications for practice
Current evidence shows that the following non-pharmacological strategies: CVVHDF, pre-dilution haemofiltration, longer catheter, and surface-modified double-lumen catheter, may extend circuit lifespan during CKRT. On the other hand, a filter with more and shorter hollow fibres may reduce circuit lifespan. Analyses revealed that applying a higher blood flow may not alter circuit life. The available evidence is limited and thus we are unable to draw any solid conclusions in regards to the role and impact of the other non-pharmacological interventions for preventing circuit clotting amongst people receiving CKRT.

Implications for research
Recent clinical practice guidelines did not address the use of non-pharmacological interventions for maintaining circuit patency (KDIGO Acute Kidney Injury Work Group 2012). Current evidence is limited and thus further high-quality RCTs are needed to provide a more comprehensive assessment before anyone particular non-pharmacological intervention is to be recommended for clinical practice. Our review illustrates that any research into non-pharmacological methods should be prospective, randomised, adequately powered, and transparently reported. Furthermore, future studies should not only consider circuit lifespan as an outcome measure but also other patient-important outcomes including death. We remain cautious as to the appropriateness of a cross-over study design for future studies in this field due to systematic differences between the two periods of the cross-over studies are highly likely, which may lead to a higher risk of bias; a potentially higher rate of drop-outs/losses to follow-up after the first period is also likely due to high death rates in the critically ill patients in the ICU settings.


2. Interventions for preventing and treating kidney disease in IgA vasculitis

What is the issue?
IgA vasculitis (IgAV), previously known as Henoch-Schönlein Purpura, causes inflammation of small blood vessels in children and rarely in adults. Symptoms and signs include a skin rash of small red spots and larger bruises, particularly on the bottom and legs, tummy pain, pain and swelling of joints, and occasionally bleeding from the gut. About a third of children have kidney involvement with blood and protein found in the urine on testing. In most children, kidney involvement is mild (small amounts of blood and protein in the urine only), and it resolves completely, but a few children have persistent kidney disease that may progress to kidney failure.

What did we do?
We looked at information from 20 randomised controlled trials (RCT), which included 1963 participants. Eleven studies included children with IgAV with mild or no kidney involvement. Five studies compared prednisone tablets given for 14 to 28 days with placebo tablets or no treatment, five studies compared medications that reduce blood clotting, and one study compared montelukast (a medication usually used in children with asthma) with a placebo. Nine studies included children with moderate or severe kidney involvement. Five studies compared different medications which suppress the immune system (cyclophosphamide, mycophenolate mofetil, tacrolimus, cyclosporin, leflunomide, azathioprine). One study compared plasma exchange (where the patient's plasma is removed and replaced with normal plasma) and cyclophosphamide and methylprednisolone with cyclophosphamide and methylprednisolone alone. The last study compared fosinopril, which reduces the amount of protein in the urine, with no treatment.

What did we find?
We wanted to see whether the tested treatments prevented or treated persistent kidney disease at six to 12 months after the onset of IgAV. We found no definite benefits of prednisone or other treatments in preventing more serious kidney involvement in children with none or mild kidney involvement at study entry. We did not find any studies which evaluated prednisone in children presenting with IgAV and severe kidney involvement, although it is recommended for such children in treatment guidelines. In children with severe kidney involvement, we found no benefit of any medication that suppresses the immune system or of plasma exchange in treating kidney involvement in IgAV. As in other kidney diseases, we found that the ACE inhibitor, fosinopril, reduced the number of children with protein in the urine.
Conclusions
There are few data from RCTs examining interventions to prevent or treat kidney disease in people with IgAV. We found no evidence that giving prednisone at the onset of IgAV reduces the risk of serious kidney disease subsequently. We found no evidence that some agents are more effective than others in treating kidney involvement when it occurs. However, the numbers of people studied were too small to exclude a benefit of treatment, so further studies are required. No serious side effects were reported.


3. Antiplatelet agents for chronic kidney disease

What is the issue?
People with chronic kidney disease (CKD) have an increased risk of heart disease that can block the blood supply to the heart or brain causing a heart attack or stroke. Drugs that prevent blood clots from forming (antiplatelet agents) can prevent deaths caused by clots in arteries in the general adult population. However, there may be fewer benefits for people who have CKD, because blood clots in arteries is a less common cause of death or reason to be admitted to hospital compared with heart failure or sudden death in these people. People with CKD also have an increased tendency for bleeding due to changes in how the blood clots. Antiplatelet agents may therefore be more hazardous when CKD is present.

What did we do?
This updated review evaluated the benefits and harms of antiplatelet agents to prevent cardiovascular disease and death, and the impact on dialysis vascular access (fistula or graft) function in people who have CKD. We identified 90 studies comparing antiplatelet agents with placebo or no treatment and 29 studies directly comparing one antiplatelet agent with another.

What did we find?
Antiplatelet agents probably prevent heart attacks, but do not clearly reduce death or
stroke. Treatment with these agents may increase the risk of major and minor bleeding. Clotting of dialysis access was prevented with antiplatelet agents.

Conclusions

The benefits of antiplatelet agents for people with CKD is probably limited to the prevention of a heart attack. The treatment does not appear to prevent stroke or death and probably incurs excess serious bleeding that may require hospital admission or transfusion.


4. Altered dietary salt intake for preventing diabetic kidney disease and its progression

What is the issue?

There is strong evidence that we all eat too much salt, which increases our risk of high blood pressure (BP). This is particularly important in people with diabetes as diabetes increases the risk of stroke, heart attack and kidney failure, and also having high BP will further increase these risks. Reducing salt intake could help by reducing BP and thus reducing the risk of heart attacks and of worsening kidney function.

What did we do?

We searched the Cochrane Kidney and Transplant Register of Studies up to 31 March 2022 for randomised controlled trials which compared low and high levels of salt intake in people with diabetes. We calculated the average level of reduction in systolic BP (the "top" level of BP measured) and in diastolic BP (the "bottom" level of BP measured) in diabetics when they received a high salt diet and when they received a low salt diet. We also looked at whether the amount of protein in the urine (a marker of kidney damage) was reduced in diabetics receiving a low salt diet.

What did we find?

We found 13 studies, including 313 people with type 1 or 2 diabetes. We found that reducing salt intake by an average of 5 g/day lowered BP, with systolic BP reduced by 7 mm of mercury (Hg) and diastolic BP reduced by 3 mm Hg. We found that the amount of protein in the urine was reduced in four of the eight studies that reported this outcome.
Only one study reported side effects with low BP when standing up with low salt diets reported in a quarter of the participants.

**Conclusions**

Lowering dietary salt intake to the recommended levels of 5 g/day or less would benefit people with diabetes by lowering BP by similar amounts to a single BP medication.


### 5. Interventions for treating catheter-related bloodstream infections in people receiving maintenance haemodialysis

**What is the issue?**

Patients with kidney failure require kidney replacement therapy (KRT) to sustain life. Among KRT options, haemodialysis (HD) is the primary method of dialysis. Patients receiving HD via an indwelling catheter have a higher risk of developing bloodstream infections. There are several options for treating these bloodstream infections. These include lock solutions (the infusion of high doses of antibiotic inside each of the catheter ports between the dialysis sessions), removal of the catheter followed by a new insertion after initial clinical improvement, exchange of the catheter for a new one by a guidewire (inserted through one of the catheter's ports into the same vein, allowing the preservation of the venous site), and the use of systemic antibiotics (used in isolated or combined with other treatments). Each treatment has its own inherent risks.

**What did we do?**

We searched Cochrane Kidney and Transplant’s Specialised Register up to 21 December 2021 and performed a systematic review of studies investigating treatment options for catheter-related bloodstream infection in patients undergoing HD.

**What did we find?**

We found three studies enrolling 760 participants that compared various treatments for catheter-related bloodstream infections. No studies compared similar treatment strategies or had similar outcomes, and therefore we were unable to combine data in
our meta-analyses. The comparisons included systemic antibiotics with two different lock solutions, systemic antibiotics alone versus systemic antibiotics plus an ethanol lock solution, and systemic antibiotics plus catheter removal versus systemic antibiotics plus catheter exchange. One study reported a higher success rate for clearing infection with systemic antibiotics plus ethanol locking treatment than systemic antibiotics alone. The other studies reported no difference between their two treatment arms. Outcomes such as venous stenosis and/or thrombosis, antibiotic resistance, death, and adverse events were not reported.

**Conclusions**
Further randomised studies to identify the benefits and harms of catheter-related bloodstream infection treatments are needed.


6. **Non-pharmacological interventions for preventing clotting of extracorporeal circuits during continuous renal replacement therapy**

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**Conclusions**
We found that the effects of non-pharmacological interventions in people with AKI receiving CKRT remain unclear. There is a need for studies assessing CKRT circuit lifespan as well as other clinically important outcomes.


7. **Interventions for weight loss in people with chronic kidney disease who are overweight or obese**

**What is the issue?**
People who are overweight or obese with chronic kidney disease (CKD) may experience a faster progression to kidney failure than those who are a healthy weight. Some people with more advanced kidney disease may require treatment such as dialysis or a kidney transplant. Being obese can make these treatments difficult and may increase a person's risk of health complications. There is limited research looking at whether weight loss interventions are safe and beneficial to help people with CKD lose weight, improve their kidney function, and live longer.

What did we do?
We conducted a review of the literature to examine the benefits of weight loss interventions for people with CKD who are overweight or obese.

What did we find?
We identified 17 studies involving 988 overweight or obese adults with CKD looking at whether weight loss interventions improved their health. Studies included adults with CKD stages 1 to 4 or kidney transplant recipients. None of the studies included participants who were undergoing dialysis or supportive care. Weight loss interventions included weight loss diets, physical activity programs, drugs to suppress appetite, and weight loss surgery. The main outcomes we were interested in were death, cardiovascular events, weight loss, body mass index (BMI), waist circumference, protein in the urine (proteinuria), and blood pressure (BP).

After combining the available studies, it's uncertain whether weight loss interventions helped people live longer or prevented cardiovascular events such as heart complications or stroke as none of the included studies measured these outcomes. We found when compared to no weight loss interventions, weight loss interventions may lead to more weight loss. There were little or no differences seen in BMI, waist circumference, proteinuria, or BP. We found that weight loss surgery achieved more weight loss than non-surgical interventions. However, many of the studies included in this review were limited by small participant numbers, high risk of bias and inconsistent reporting of outcome measures leading to the overall quality of the evidence to be very low. This means that we cannot be sure that future studies would find similar results.

Conclusions
The evidence is not very certain but suggests that compared with usual care or control those who participated in weight loss interventions may experience some health benefits including improvements in body weight. Whether these benefits help reduce
cardiovascular outcomes and the risk of death remains uncertain and require further study.


8. **Pharmacological interventions versus placebo, no treatment or usual care for osteoporosis in people with chronic kidney disease stages 3-5D**

*What is the issue?*
Patients with chronic kidney disease (CKD) have an increased risk of osteoporosis (weakened bone strength), which can often lead to bone fracture. Several drugs are available for the treatment of osteoporosis; however, it is unknown whether these drugs are equally effective and safe in patients with CKD because bone strength impairment in these patients occurs via a different mechanism.

*What did we do?*
Data were collected from studies including patients with osteoporosis and CKD stages 3-5, and those undergoing dialysis (stage 5D) with data available on fracture, change in the bone mineral density (BMD; a bone strength index), and adverse events. We included seven studies with available evidence up to 25 January 2021, comparing anti-osteoporotic drugs (abaloparatide, alendronate, denosumab, raloxifene, and teriparatide) with placebo (a dummy drug), in 9,164 postmenopausal women. We performed a meta-analysis to assess the effects of these anti-osteoporotic drugs.

*What did we find?*
In postmenopausal women with CKD stages 3-4, anti-osteoporotic drugs may reduce vertebral fracture in low certainty evidence. Anti-osteoporotic drugs probably make little or no difference to clinical fracture and adverse events in moderate certainty evidence. In postmenopausal with CKD stages 5 or 5D, it is uncertain whether anti-osteoporotic drug reduces the risk of clinical fracture and death, and anti-osteoporotic drug may slightly improve BMD at the lumbar spine in low certainty evidence. It is uncertain whether anti-osteoporotic drug improve BMD at the femoral neck.
Conclusions
Among postmenopausal women with CKD stages 3-4, anti-osteoporotic drugs may reduce the risk of vertebral fracture. Among patients with CKD stages 5 and 5D, anti-osteoporotic drug may slightly improve bone strength. However, these conclusions are based on limited data and therefore uncertain.


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