COCHRANE RENAL GROUP
A REVIEW GROUP OF THE COCHRANE COLLABORATION

November 2014

New reviews, protocols and titles

New and updated reviews May to October 2014

Between May and October 2014 (issues 5 to 10) we published 14 reviews (8 new; four updates with changed conclusions and two updates):

New

- Androgens for the anaemia of chronic kidney disease in adults
- Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers for preserving residual kidney function in peritoneal dialysis patients
- Astragalus (a traditional Chinese medicine) for treating chronic kidney disease
- Continuous renal replacement therapy (CRRT) for rhabdomyolysis
- Early referral to specialist nephrology services for preventing the progression to end-stage kidney disease
- Oral adsorbents for preventing or delaying the progression of chronic kidney disease
- Steroid avoidance or withdrawal for pancreas and pancreas with kidney transplant recipients
- Topical corticosteroids for treating phimosis in boys

Updated and conclusions changed:

- Antibiotics for acute pyelonephritis in children
- Frequency of administration of erythropoiesis-stimulating agents for the anaemia of end-stage kidney disease in dialysis patients
- HMG CoA reductase inhibitors (statins) for people with chronic kidney disease not requiring dialysis
- Immunosuppressive treatment for idiopathic membranous nephropathy in adults with nephrotic syndrome

Updated

- Bicarbonate versus lactate solutions for acute peritoneal dialysis
- Double bag or Y-set versus standard transfer systems for continuous ambulatory peritoneal dialysis in end-stage kidney disease

Did you know? Cochrane reviews are published on the understanding that they will be updated every two years

In this issue:

New protocols

We published nine new protocols in issues 5 to 10 in 2014:

- Acetylcysteine for preventing contrast-induced nephropathy
- Antibiotics for asymptomatic bacteriuria in kidney transplant recipients
- Calcium channel blockers as medical expulsive therapy for ureteric stones
- Dialysate sodium levels for chronic haemodialysis
- Diuretics for people with chronic kidney disease
- Early versus delayed erythropoietin for the anaemia of end-stage kidney disease
- Effects of peri-operative nonsteroidal anti-inflammatory drugs on postoperative kidney function for adults with normal kidney function
- Medical and dietary interventions for preventing recurrent urinary stones in children
- Omega-3 fatty acids for vascular access outcomes in patients with chronic kidney disease

Titles registered

We have registered three review titles between May and October 2014:

- Erythropoeitin (rHuEPO) for anaemia in predialysis patients
- Bioimpedance and blood volume monitoring for guiding fluid management in people with chronic kidney disease requiring dialysis
- Low molecular weight heparin (LMWH) versus unfractionated heparin (UFH) for haemodialysis anticoagulation

Renal Group news

Ruth Mitchell retires

I joined the Cochrane Renal Group as Trials Search Coordinator (TSC) in August 2000, soon after its relocation from France to Sydney.

Work at the Renal Group proved to be of great variety and was often challenging. The core activities—development of our specialised register, and of search strategies and search assistance for our review authors, plus the annual production of the Renal Health Library—were all undertaken in collaboration with fellow TSC Gail Higgins.

However, our Co-ed Jonathan Craig ensured that other challenges appeared, such as preparation of a regular current awareness column of recent RCTs for the *American Journal of Kidney Diseases*, work for several kidney guidelines groups, and an increasing involvement in the development of Cochrane diagnostic test accuracy reviews. This included several years' work on the Cochrane register of DTA studies which led to the preparation and presentation of many workshops at Cochrane Colloquia related to searching for DTA studies in collaboration with fellow TSCs and other Cochrane colleagues.

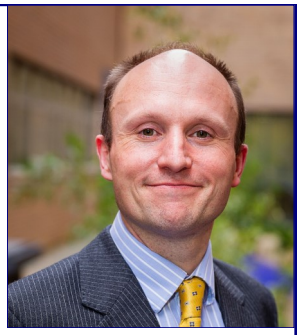
None of this work would have been as enjoyable as it (mostly) was without the collegiality and friendship of Renal Group staff, editors and review authors, and of the many TSCs and other Cochrane colleagues I got to know over the past 14 years. Thank you all!

I am working one day a week on largely non-Cochrane related research. I am also enjoying local bush care activities, art classes, sewing, choral singing, catching up with family and friends, and chasing brush turkeys out of my garden.

Ruth Mitchell

Renal group news (Cont'd)

New Editor joins the Cochrane Renal Group



In July this year, **Colin Wilson** joined the Renal Group Editorial team. Colin is a Consultant Transplant and Hepatobiliary Surgeon based at the Institute of Transplantation in Newcastle-upon-Tyne, United Kingdom. The Institute of Transplantation is a novel multidisciplinary concept combining both thoracic and abdominal transplantation in the same purpose-designed building attached to the Freeman Hospital.

Colin has an academic position at the University of Newcastle with research interests in warm perfusion for organ preservation. His initial interest in meta-analysis and systematic review was stimulated by research into the risks and benefits of ureteric stents in kidney transplantation. In his clinical practice Colin is actively involved in kidney, pancreas and liver transplantation and has published in all of these areas.

Vale Jim Dellit

We were deeply saddened by news of the loss of Jim Dellit, who was a consumer representative on the Cochrane Renal Group's Advisory Board for six years. Jim was a respected consumer advocate and participated as a contributor for several Renal Group reviews. Jim offered very insightful and thoughtful perspectives from the consumer viewpoint on the Cochrane Collaboration, the Renal Group and medical consumers.

Jim's involvement and contributions to the work of the Renal Group was highly valued—he is sadly missed.

The Cochrane Colloquium 2014, Hyderabad, India

Although participant attendance at the 2014 Colloquium was slightly fewer in number than previous years, the enthusiasm of participants more than compensated.

The city of Hyderabad—which may be the largest Indian city least visited by travellers—is a city of 8 million people with abundant cultural, historical, scenic and culinary delights and the harmonious confusion of a hectic 24/7 global city. The city—a technical hub for India—provided excellent facilities and a warm welcome for delegates.

The Colloquium—organised by the South Asian Cochrane Centre based in Vellore, provided a varied, thoughtful and provocative program. The meeting's theme centred on public health issues. There were passionate messages and stories from presenters—many from the region—that reminded many of us about the importance of evidence to inform public health programs. The interests of tech-oriented people were well supported, particularly by the pre-Colloquium Tech Symposium, which is becoming a fixture for meetings.

The social program provided abundant opportunities for mixing meeting and dancing—what would a meeting in India be without Bollywood night?

See more (including Cochranites in full Bollywood dance routine mode) at https://www.cochrane.org/features/hyderabad-colloquium-numbers

The 2015 Cochrane Colloquium will be held in Vienna, Austria from 3 to 7 October.

Renal group news (Cont'd)

ISN/Cochrane—Podcasts

In October this year, *ISN Education* announced the release of a new feature: the Cochrane Library on Treatment for Lupus Nephritis. This resource was put together by Lorna Henderson and Angela Webster of the Cochrane Renal Group and combines literature, presentations, audio podcasts and resources on the treatment of Lupus Nephritis.

This library is the first of a number of future reviews to be published thanks to this new partnership between the Cochrane Renal Group and *ISN Education*:

www.theisn.org/glomerular-disease/education-by-topic/glomerular-disease/cochrane-library-treatment-for-lupus-nephritis/itemid-1385

2013 Impact Factor for Cochrane Database of Systematic Reviews

The 2013 impact factor for the *Cochrane Database of Systematic Reviews* (*CDSR*) is **5.939**. This is an increase on the 2012 impact factor, which was 5.785. The impact factor for the Cochrane Renal Group is 3.800

Some highlights of the 2013 impact factor include:

- The *CDSR* is ranked 10 of the 150 journals in the Medicine, General & Internal category
- The total number of times the *CDSR* was cited increased from 34,230 in 2012 to 39,856 meaning the *CDSR* receives the 6th highest number of citations in its category
- The 5 year impact factor is 6.706, an increase on 6.553 last year
- The total number of citable items (new and updated reviews) included in the 2013 impact factor calculation was 1660. The average number of citable items included in the 2013 impact factor of the other journals in the top 10 of the Medicine, General & Internal category was 370.

Cochrane Commentaries—*Nephrology*

In 2013 in conjunction with the journal *Nephrology* we produced several short commentaries on new and updated reviews. This project has been co-ordinated and edited by Angela Webster. The commentaries published in 2013 were:

1. *Induction and maintenance treatment of proliferative lupus nephritis. Nephrology 2013 18: 71-2. Philip Masson*
2. *Antiviral medications for preventing cytomegalovirus disease (CMV) in solid organ transplant recipients. Nephrology 2013; 18:237-8. Maleeka Ladhani*
3. *Pre-emptive treatment for cytomegalovirus viraemia to prevent cytomegalovirus disease in solid organ transplant recipients. Nephrology 2013; 18: 235-6. Maleeka Ladhani*
4. *High-flux versus low-flux haemodialysis membranes for end-stage kidney disease. Nephrology 2013; 18: 313-4. Suetonia Palmer and Giovanni Strippoli*
5. *Cranberries for the prevention of urinary tract infections. Nephrology 2013 18: 388-9. Ruth Jepson*
6. *Antiplatelet agents for chronic kidney disease. Nephrology 2013; 18: 474-6. Suetonia Palmer, Valeria Saglimbene and Giovanni FM Strippoli*
7. *Antioxidants for chronic kidney disease. Nephrology 2013; 18: 576-8. Min Jun*

Exploring Research Priorities in Chronic Kidney Disease

A national workshop was convened on February 7, 2014 in Sydney, to explore research priorities in chronic kidney disease.

The participants were people living with chronic kidney disease, family, caregivers, nephrologists, nurses, and allied health professionals. Participants travelled from New South Wales, Victoria, Queensland, Northern Territory, South Australia, Western Australia and the Australian Capital Territory.

A total of 58 participants worked together to formulate, discuss and rank research questions:

- Identifying questions
- Choosing priority questions
- Voting by CKD stage
- Ranking the top 20 questions ➔

RESEARCH PRIORITIES - YOUR TOP 20

1. How effective are lifestyle programs (diet, exercise and smoking cessation) for preventing deterioration in kidney function in patients with early CKD?
2. What interventions can improve long term post-transplant outcomes (drugs, lifestyle)?
3. What strategies will improve donor family consent to deceased donation taking different cultural groups into account?
4. What strategies help patients maintain work while on HD?
5. What can we do to improve and individualise drug therapy in terms of better management of side effects?
6. What are the effective interventions for post HD fatigue?
7. What psychological interventions would improve the psychological health for transition between kidney stages
8. How do we improve health outcomes in young transplant recipients?
9. What are the best interventions to improve the decision making process of people faced with HD?
10. Does active implementation of clinical practice guidelines in general practice improve kidney health in patients with early CKD?
11. How can we best provide support services to be integrated to patients, carers, and families to improve mental health in PD?
12. Do interventions that increase knowledge of support services and early referral practices increase quality of life in patients and carers?
13. Does implementing a personalised care plan increase quality of life for patients on HD and carers?
14. Does provision of culturally appropriate information about early CKD modify acknowledgement, medication adherence, and health service uptake in patients with early CKD?
15. What is the best diet and nutrition to improve general health outcomes for PD patients?
16. What interventions are most effective to reduce inter-dialytic weight gain?
17. Are electronic and social media an effective modality to deliver health promotion about CKD in the general population?
18. How can we best deliver staff education to reduce patient complications in PD?
19. What kinds of exercise programs are safe and most effective for PD patients?
20. How can technology be used to improve patient self-monitoring in PD?

Kidney Health Australia (KHA)

"This priority setting exercise will prove most useful in assisting the choice of themes selected by the Australian Kidney Research Foundation for its initial focus. The views of patients in the direction of research support have been under represented in the past and this exercise helps redress that position."

- Tim Mathew, Medical Director

Australasian Kidney Trials Network (AKTN)

"The day proved very insightful. When patients and their caregivers were present in the process of assigning priorities, the outcomes of the discussion were very different compared to those arrived at by health professionals in isolation. The AKTN will be taking this into consideration in trial design: the need for attention to quality of life, symptom control, non-pharmacological interventions such as exercise, diet and nutrition, attention to cultural needs and the emphasis on psychological well-being, and psycho-social support delivery were the clearest messages on the day."

- Carmel Hawley, Chair and Operations Secretariat

Cochrane Renal Group (CRG)

"The priorities developed by the workshop will help us to ensure our systematic reviews of research evidence address topics of concern to consumers, and ultimately show which areas of research should be pursued."

- Jonathan Craig, Coordinating Editor

"I'm hoping that other groups and other disease areas will learn from the experience that we've had here today and that more agencies will be performing priority setting exercises. I think policy makers and funding agencies will find it extremely useful."

- Dr Davina Ghersi
National Health and Medical Research Council

Recent abstracts (*new*)

Androgens for the anaemia of chronic kidney disease in adults

Qianchun Yang , Minawaer Abudou , Xi Sheng Xie and Taixiang Wu

Background

Anaemia occurs when blood contains fewer red blood cells and lower haemoglobin levels than normal, and is a common complication among adults with chronic kidney disease (CKD). Although a number of approaches are applied to correct anaemia in adults with CKD, the use of androgen therapy is controversial.

Objectives

The aim of this review was to determine the benefits and harms of androgens for the treatment of anaemia in adult patients with CKD.

Search methods

We searched CENTRAL, the Cochrane Renal Group's Specialised Register, the Chinese Biomedicine Database (CBM), CNKI, VIP and reference lists of articles without language restriction. The most recent search was conducted in August 2014.

Selection criteria

All randomised controlled trials (RCTs) that assessed the use of androgens for treating anaemia of CKD in adults were eligible for inclusion.

Data collection and analysis

Two authors independently extracted data and assessed risk of bias in the included studies. Meta-analyses were performed using relative risk (RR) for dichotomous outcomes and mean differences (MD) for continuous outcomes, with 95% confidence intervals (CI).

Main results

We included eight studies that reported data from 181 participants. Study quality was assessed as moderate in six studies, one was low quality, and one was high quality. The small number of included studies, and low participant numbers adversely influenced evidence quality overall.

We found limited evidence (1 study, 24 participants) to indicate that oxymetholone can increase haemoglobin (Hb) (MD 1.90 g/dL, 95% CI 1.66 to 2.14), haematocrit (HCT) (MD 27.10%, 95% CI 26.49 to 27.71), change in albumin (MD 4.91 g/L, 95% CI 3.69 to 6.13), alanine aminotransferase (ALT) (MD 54.50 U/L, 95% CI 43.94 to 65.06), and aspartate aminotransferase (AST) (MD 47.33 U/L, 95% CI 37.69 to 56.97); and decrease high-density lipoprotein (HDL) (MD -15.66 mg/dL, 95% CI -24.84 to -6.48). We also found that compared with erythropoietin alone, nandrolone decanoate plus erythropoietin may increase HCT (3 studies, 73 participants: MD 2.54%, 95% CI 0.96 to 4.12). Compared with erythropoietin (1 study, 27 participants), limited evidence was found to suggest that nandrolone decanoate can increase plasma total protein (MD 0.40 g/L, 95% CI 0.13 to 0.67), albumin (MD 0.20 g/L, 95% CI 0.01 to 0.39), and transferrin (MD 45.00 mg/dL, 95% CI 12.61 to 77.39) levels. Compared with no therapy (remnant kidney), evidence was found to suggest that nandrolone decanoate can increase Hb (2 studies, 33 participants: MD 1.04 g/dL, 95% CI 0.66 to 1.41) and HCT (1 study, 24 participants: MD 3.70%, 95% CI 0.68 to 6.72). Compared with no therapy (anephric), evidence was found (1 study, 5 participants) to suggest that nandrolone decanoate can increase Hb (MD 1.30 g/dL, 95% CI 0.57 to 2.03), but nandrolone decanoate did not increase HCT (MD 2.00%, 95% CI -0.85 to 4.85).

However, oxymetholone was not found to reduce blood urea nitrogen (BUN), serum creatinine (SCr), cholesterol, or triglycerides; or increase plasma total protein, prealbumin, or transferrin. No evidence was found to indicate that nandrolone decanoate increased prealbumin or decreased BUN, SCr, AST, ALT, cholesterol, triglycerides, HDL or low-density lipoprotein (LDL). Adverse events associated with androgen therapy were reported infrequently.

Authors' conclusions

We found insufficient evidence to confirm that use of androgens for adults with CKD-related anaemia is beneficial.

Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers for preserving residual kidney function in peritoneal dialysis patients

Ling Zhang , Xiaoxi Zeng , Ping Fu and Hong Mei Wu

Background

Angiotensin-converting enzyme inhibitors (ACEis) and angiotensin receptor blockers (ARBs) are widely used in peritoneal dialysis (PD) patients, yet controversy exists about their impact on residual kidney function.

Objectives

This review aimed to evaluate the benefits and harms of ACEis and ARBs for preserving residual kidney function in PD patients.

Search methods

The Cochrane Renal Group's specialised register, Cochrane Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE (OvidSP interface), Chinese Biomedical Literature

Recent abstracts (*new*)

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Database (CBM), China National Knowledge Infrastructure (CNKI) and other resources were searched by applying a prespecified comprehensive search strategy. Date of last search: 01 May 2014.

Selection criteria

Randomised controlled trials (RCTs) and quasi-RCTs comparing ACEis or ARBs with placebo, other antihypertensive drugs or each other in PD patients were included.

Data collection and analysis

Screening, selection, data extraction and quality assessments for each retrieved article were carried out by two authors using standardised forms. Authors were contacted when published data were incomplete. Statistical analyses were performed using the random effects model and results expressed as risk ratio (RR) with 95% confidence intervals (CI). Heterogeneity among studies was explored using the Cochran Q statistic and the I^2 test, subgroup analyses and random effects meta-regression.

Main results

Six open-label studies (257 patients) were identified. One study compared ACEi with other antihypertensive drugs, three compared ARBs with other antihypertensive drugs, and two studies compared an ARB with an ACEi. Long-term use (≥ 12 months) of an ARB showed significantly benefit of preserving residual kidney function in continuous ambulatory PD (CAPD) patients (MD 1.11 mL/min/1.73 m^2, 95% CI 0.38 to 1.83), although there was no significant benefit when an ARB were used short-term (≤ six months). One study showed that compared with other antihypertensive drugs, long-term use (12 months) of the ACEi ramipril showed a significant reduction in the decline of residual kidney function in patients on CAPD (MD -0.93 mL/min/1.73m^2, 95% CI -0.75 to -0.11), and delayed the progression to complete anuria (RR 0.64, 95% CI 0.41 to 0.99). There was no significant difference in serum potassium, urinary protein excretion, Kt/V, weekly creatinine clearance and blood pressure for ARBs versus other antihypertensive drugs. Compared with other antihypertensive drugs, ramipril showed no difference in mortality and cardiovascular events. Compared with an ACEi, ARBs did not show any difference in residual kidney function.

The selection bias assessment was low in four studies and unclear in two. Five studies were open-label; however the primary outcome (residual kidney function) was obtained objectively from laboratory tests, and were not likely to be influenced by the lack of blinding. Reporting bias was unclear in all six studies.

Authors' conclusions

Compared with other antihypertensive drugs, long-term use (≥ 12 months) of ACEis or ARBs showed additional benefits of preserving residual kidney function in CAPD patients. There was no significant difference on residual kidney function preservation between ARBs and ACEis. However, limited by the small number of RCTs enrolling small number of participants, there is currently insufficient evidence to support the use of an ACEi or an ARB as first line antihypertensive therapy in PD patients.

Astragalus (a traditional Chinese medicine) for treating chronic kidney disease

Hong Wei Zhang , Zhi Xiu Lin , Chuanshan Xu , Connie Leung and Lai Sum Chan

Background

Astragalus (Radix Astragali, huang qi) is the dried root of Astragalus membranaceus (Fisch.) Bge. var. mongholicus (Bge.) Hsiao or Astragalus membranaceus (Fisch.) Bge. (Family Leguminosae). It is one of the most widely used herbs in traditional Chinese medicine for treating kidney diseases. Evidence is needed to help clinicians and patients make judgments about its use for managing chronic kidney disease (CKD).

Objectives

This review evaluated the benefits and potential harms of Astragalus for the treatment of people with CKD.

Search methods

We searched the Cochrane Renal Group's Specialised Register to 10 July 2014 through contact with the Trials' Search Co-ordinator using search terms relevant to this review. We also searched CINAHL, AMED, Current Controlled Trials, OpenSIGLE, and Chinese databases including CBM, CMCC, TCMLARS, Chinese Dissertation Database, CMAC and Index to Chinese Periodical Literature.

Selection criteria

Randomised controlled trials (RCTs) and quasi-RCTs comparing Astragalus, used alone as a crude herb or an extract, with placebo, no treatment, or conventional interventions were eligible for inclusion.

Data collection and analysis

Two authors independently extracted data and assessed risk of bias in the included studies. Meta-analyses were performed using relative risk (RR) for dichotomous outcomes and mean differences (MD) for continuous outcomes, with 95% confidence intervals (CI).

Recent abstracts (*new*)

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Main results

We included 22 studies that involved 1323 participants, of whom 241 were receiving dialysis treatment. Risk of bias was assessed as high in six studies, and unclear in the remaining 16 studies. Study quality was low overall.

Our nominated primary outcomes of time to requirement for renal replacement therapy (RRT) or initiation of dialysis and all-cause mortality were not reported in any of the included studies.

Results concerning the effects of Astragalus on kidney function were inconsistent. Astragalus significantly increased CrCl at end of treatment (4 studies, 306 participants: MD 5.75 mL/min, 95% CI 3.16 to 8.34; I^2 = 0%), decreased SCr (13 studies, 775 participants: MD -21.39 µmol/L, 95% CI -34.78 to -8; I^2 = 70%) and especially in those whose baseline SCr was < 133 µmol/L in particular (3 studies, 187 participants: MD -2.52 µmol/l, 95% CI -8.47 to 3.42; I^2 = 0%). Astragalus significantly decreased 24 hour proteinuria at end of treatment (10 studies, 640 participants; MD -0.53 g/24 h, 95% CI -0.79 to -0.26; I^2 = 90%); significantly increased haemoglobin levels overall (4 studies, 222 participants): MD 9.51 g/L, 95% CI 4.90 to 14.11; I^2 = 0%) and in haemodialysis patients in particular (3 studies, 142 participants: MD 11.20 g/L, 95% CI 5.81 to 16.59; I^2 = 0%). Astragalus significantly increased serum albumin (9 studies, 522 participants: MD 3.55 g/L, 95% CI 2.33 to 4.78; I^2 = 65%). This significant increase was seen in both dialysis (3 studies, 152 participants): MD 4.04 g/L, 95% CI 1.91 to 6.16; I^2 = 72%) and non-dialysis patients (6 studies, 370 participants: MD 3.24 g/L, 95% CI 1.70 to 4.77; I^2 = 61%). Astragalus significantly decreased systolic blood pressure (2 studies, 77 participants: MD -16.65 mm Hg, 95% CI -28.83 to -4.47; I^2 = 50%), and diastolic blood pressure (2 studies, 77 participants: MD -6.02 mm Hg, 95% CI -10.59 to -1.46; I^2 = 0%).

Six of 22 included studies reported no adverse effects were observed; while the remaining 16 studies did not report adverse effects.

Authors' conclusions

Although Astragalus as an adjunctive treatment to conventional therapies was found to offer some promising effects in reducing proteinuria and increasing haemoglobin and serum albumin, suboptimal methodological quality and poor reporting meant that definitive conclusions could not be made based on available evidence.

Continuous renal replacement therapy (CRRT) for rhabdomyolysis

Xiaoxi Zeng , Ling Zhang , Taixiang Wu and Ping Fu

Background

Rhabdomyolysis is a condition that is characterised by the breakdown of skeletal muscle tissue and leakage of intracellular myocyte contents into circulating blood. Rhabdomyolysis can lead to acute kidney injury (AKI) and is a potentially life-threatening condition. Studies have indicated that continuous renal replacement therapy (CRRT) may provide benefits for people with rhabdomyolysis by removing potentially damaging myoglobin and stabilising haemodynamic and metabolic status.

Objectives

We aimed to: i) assess the efficacy of CRRT in removing myoglobin; ii) investigate the influence of CRRT on mortality and kidney-related outcomes; and iii) evaluate the safety of CRRT for the treatment of people with rhabdomyolysis.

Search methods

We searched the Cochrane Renal Group's Specialised Register to 6 January 2014 through contact with the Trials' Search Co-ordinator using search terms relevant to this review. We also searched China National Knowledge Infrastructure (from 1 January 1979 to 16 April 2013) and the Chinese Clinical Trials Register (to 16 April 2013).

Selection criteria

All randomised controlled trials (RCTs) and quasi-RCTs that investigated clinical outcomes of CRRT for people with rhabdomyolysis were included.

Data collection and analysis

Two authors independently assessed studies for inclusion and extracted data. We derived risk ratios (RR) for dichotomous data and mean differences (MD) for continuous data with 95% confidence intervals (CI). Methodological risk of bias was assessed using the Cochrane risk of bias tool.

Main results

Of the three included studies (101 participants), one evaluated continuous arteriovenous haemodialysis and two investigated continuous venovenous haemofiltration; all included conventional therapy as control.

We found significant decreases in myoglobin in patients among whom CRRT therapy was initiated on days four, eight, and 10 (day 4: MD -11.00 (µg/L), 95% CI -20.65 to -

Recent abstracts (*new*) *...Cont'd*

1.35; Day 8: MD -23.00 (µg/L), 95% CI -30.92 to -15.08; day 10: MD -341.87 (µg/L), 95% CI -626.15 to -57.59) compared with those who underwent conventional therapy.

Although CRRT was associated with improved serum creatinine, blood urea nitrogen, and potassium levels; reduced duration of the oliguria phase; and was associated with reduced time in hospital, no significant differences were found in mortality rates compared with conventional therapy (RR 0.17, 95% CI 0.02 to 1.37). The included studies did not report on long-term outcomes or prevention of AKI.

Overall, we found that study quality was suboptimal: blinding and randomisation allocation were not reported by any of the included studies, leading to the possibility of selection, performance and detection bias.

Authors' conclusions

Although CRRT may provide some benefits for people with rhabdomyolysis, the poor methodological quality of the included studies and lack of data relating to clinically important outcomes limited our findings about the effectiveness of CRRT for people with rhabdomyolysis.

There was insufficient evidence to discern any likely benefits of CRRT over conventional therapy for people with rhabdomyolysis and prevention of rhabdomyolysis-induced AKI.

Early referral to specialist nephrology services for preventing the progression to end-stage kidney disease

Neil A Smart , Gudrun Dieberg , Maleeka Ladhani and Thomas Titus

Background

Early referral of patients with chronic kidney disease (CKD) is believed to help with interventions to address risk factors to slow down the rate of progression of kidney failure to end-stage kidney disease (ESKD) and the need for dialysis, hospitalisation and mortality.

Objectives

We sought to evaluate the benefits (reduced hospitalisation and mortality; increased quality of life) and harms (increased hospitalisations and mortality, decreased quality of life) of early versus late referral to specialist nephrology services in CKD patients who are progressing to ESKD and RRT. In this review, referral is defined as the time period between first nephrology evaluation and initiation of dialysis; early referral is more than one to six months, whereas late referral is less than one to six

Conferences

January 28-30, 2015
The 17th International Conference on Dialysis, Advances in Kidney Disease, New Orleans, LA, USA
www.renalresearch.com/RRI/index.htm

March 13 —17, 2015
ISN World Congress of Nephrology 2015, Cape Town, South Africa
www.wcn2015.org

May 2—6, 2015
American Transplant Congress, Philadelphia, Pennyslvania, USA
http://2015.atcmeeting.org/

May 15 —19, 2015
American Urological Association Annual Meeting, New Orleans, LA, USA
www.auanet.org/education/aua-annual-meeting.cfm

May 28—31, 2015
52nd ERA-EDTA Congress, London, UK
www.era-edta2015.org/en-US/home

June 21—23, 2015
TSANZ Annual Scientific Meeting, Canberra, ACT, Australia
www.tsanz.com.au/meetings/index.asp

September 7—9, 2015
ANZSN Annual Scientific Meeting, Canberra, ACT, Australia (Update Course 5th & 6th September)
www.nephrology.edu.au/meetings/Index.asp

October 3—7, 2015
Cochrane Colloquium 2015, Vienna, Austria
www.cochrane.org/events/colloquia

November 3 - 8 2015
ASN Kidney Week, San Diego Convention Centre, San Diego, CA, USA
www.asn-online.org/education/kidneyweek/archives/future.aspx

Recent abstracts (*new*)

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months prior to starting dialysis. All-cause mortality and hospitalisation and quality of life were measured by the visual analogue scale and SF-36. SF-36 and KDQoL are validated measurement instruments for kidney diseases.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) (The Cochrane Library, 2012; Issue 1) which contains the Cochrane Renal Group's Specialised Register; MEDLINE (1966 to February 2012), EMBASE (1980 to February 2012). Search terms were approved by the Trial Search Co-ordinator.

Selection criteria

Randomised controlled trials (RCTs), quasi-RCTs, prospective and retrospective longitudinal cohort studies were eligible for inclusion.

Data collection and analysis

Two authors independently assessed study quality and extracted data. Events relating to adverse effects were collected from the studies.

Main results

No RCTs or quasi-RCTs were identified. There were 40 longitudinal cohort studies providing data on 63,887 participants; 43,209 (68%) who were referred early and 20,678 (32%) referred late.

Comparative mortality was higher in patients referred to specialist services late versus those referred early. Risk ratios (RR) for mortality reductions in patients referred early were evident at three months (RR 0.61, 95% CI 0.55 to 0.67; I^2 = 84%) and remained at five years (RR 0.66, 95% CI 0.60 to 0.71; I^2 = 87%). Initial hospitalisation was 9.12 days shorter with early referral (95% CI -10.92 to -7.32 days; I^2 = 82%) compared to late referral. Pooled analysis showed patients referred early were more likely than late referrals to initiate RRT with peritoneal dialysis (RR 1.74, 95% CI 1.64 to 1.84; I^2 = 92%).

Patients referred early were less likely to receive temporary vascular access (RR 0.47, 95% CL 0.45 to 0.50; I^2 = 97%) than those referred late. Patients referred early were more likely to receive permanent vascular access (RR 3.22, 95% CI 2.92 to 3.55; I^2 = 97%). Systolic blood pressure (BP) was significantly lower in early versus late referrals (MD -3.09 mm Hg, 95% CI -5.23 to -0.95; I^2 = 85%); diastolic BP was significantly lower in early versus late referrals (MD -1.64 mm Hg, 95% CI -2.77 to -0.51; I^2 = 82%). EPO use was significantly higher in those referred early (RR 2.92, 95% CI 2.42 to 3.52; I^2 = 0%). eGFR was higher in early referrals (MD 0.42 mL/min/1.73 m^2, 95% CI 0.28 to 0.56; I^2 = 95%). Diabetes prevalence was similar in patients referred early and late (RR 1.05, 95% CI 0.96 to 1.15; I^2 = 87%) as was ischaemic heart disease (RR 1.05, 95% CI 0.97 to 1.13; I^2 = 74%), peripheral vascular disease (RR 0.99, 95% CI 0.84 to 1.17; I^2 = 90%), and congestive heart failure (RR 1.00, 95% CI 0.86 to 1.15; I^2 = 92%). Inability to walk was less prevalent in early referrals (RR 0.66, 95% CI 0.51 to 0.86). Prevalence of chronic obstructive pulmonary disease was similar in those referred early and late (RR 0.89, 95% CI 0.70 to 1.14; I^2 = 94%) as was cerebrovascular disease (RR 0.90, 95% CI 0.74 to 1.11; I^2 = 83%).

The quality of the included studies was assessed as being low to moderate based on the Newcastle-Ottawa Scale. Slight differences in the definition of early versus late referral infer some risk of bias. Generally, heterogeneity in most of the analyses was high.

Authors' conclusions

Our analysis showed reduced mortality and mortality and hospitalisation, better uptake of peritoneal dialysis and earlier placement of arteriovenous fistulae for patients with chronic kidney disease who were referred early to a nephrologist. Differences in mortality and hospitalisation data between the two groups were not explained by differences in prevalence of comorbid disease or serum phosphate. However, early referral was associated with better preparation and placement of dialysis access.

Oral adsorbents for preventing or delaying the progression of chronic kidney disease

Hong Mei Wu , Hong Juan Sun , Feng Wang , Ming Yang , Bi Rong Dong and Guan J Liu

Background

Chronic kidney disease (CKD) is a worldwide public health problem which is at high increased risk of cardiovascular disease (CVD) and renal failure. Deterioration of kidney function causes an increase in circulating toxins, which, in turn promotes the progression of CKD. Oral adsorbents with capacity to adsorb and remove substances including uraemic toxins from the intestine could be effective in minimising kidney injury.

Objectives

To investigate the benefits and harms of oral adsorbents for preventing or delaying the progression of CKD.

Recent abstracts (*new*)

...Cont'd

Search methods

We searched the Cochrane Renal Group's Specialised Register (to 22 September 2014) through contact with the Trials' Search Co-ordinator using search terms relevant to this review. The following four Chinese medical databases were also searched: China Biological Medicine Database (1979 to May 2012); Chinese Science and Technique Journals Database (to May 2012); China National Infrastructure (to May 2012); Wan Fang database (to May 2012).

Selection criteria

Randomised controlled trials (RCTs) and quasi-RCTs comparing any oral adsorbents for preventing or delaying the progression of CKD.

Data collection and analysis

Two authors independently assessed and extracted information. Information was collected on methods, participants, interventions and outcomes (incidence of end -stage kidney disease (ESKD), mortality, quality of life and adverse events). Results were expressed as risk ratios (RR) for dichotomous outcomes or as mean differences (MD) for continuous data with 95% confidence intervals (CI). Adverse events were expressed as risk differences (RD).

Main results

Fifteen studies (1590 patients) conducted in Japan, China, and the USA were identified. The risk of bias of the included studies was moderate or high and the sample sizes were small.

Three studies compared oral AST-120 plus routine treatment with placebo plus routine treatment; however data on our outcome measures of interest were not reported in two studies. These studies did not assess or did not provide data for our primary outcomes of interest (incidence of ESKD; time to ESKD; all-cause mortality). There was no significant difference in the changes of serum creatinine (SCr), slope of 1/SCr over time and creatinine clearance (CrCl) between AST-120 and placebo for patients with CKD.

Eight studies compared oral AST-120 plus routine treatment with routine treatment alone; data on our outcome measures of interest were not reported in one study. There was no significant difference in incidence of ESKD, all-cause mortality and the change in health-related quality of life between AST-120 and routine treatment for patients with CKD. AST-120 showed beneficial effects on delaying the decline of kidney function measured by using the slope of change in estimated CrCl (SMD 0.39, 95% CI 0.21 to 0.5) and the mean changes of glomerular filtration rate (GFR) (MD -0.76 mL/min/mo, 95% CI -0.82 to -0.70) for patients with CKD; AST-120 was not superior to routine treatment in retarding the decline of kidney function measured by using the 1/SCr slope over time, occurrence of increase in SCr concentration, doubling of SCr concentration, changes in GFR from baseline (mL/min/1.73 m^2) and slope of the eGFR curve (mL/min/mo) for patients with CKD.

Three studies compared oral Ai Xi Te plus routine treatment with routine treatment alone. These studies did not assess our primary outcomes of interest. Compared with routine treatment, Ai Xi Te had positive effects on reducing SCr (MD -113.40 (μmol/L), 95% CI -188.69 to -38.10) and retarding the decline of CrCl (MD 9.74 (mL/min), 95% CI 4.28 to 15.21) for patients with CKD.

One study compared oral Niaoduqing granules plus routine treatment with routine treatment alone, but did not assess our primary outcomes of interest. Compared with routine treatment, Niaoduqing granules had positive effects on reducing SCr (MD -135.60 (μmol/L), 95% CI -198.03 to -73.17) and CrCl (MD 13.30 (mL/min), 95% CI 5.69 to 20.91).

The most commonly reported adverse events associated with AST-120 and Ai Xi Te were gastrointestinal symptoms however no serious adverse events were reported.

Authors' conclusions

Few studies reported our primary outcomes of interest. For our secondary outcomes, there is evidence of limited quality that AST-120, Ai Xi Te and Niaoduqing granules may have positive effects on delaying the decline of kidney function. There were no serious adverse events for any of the interventions in patients with CKD. Given the lack of information for our primary outcomes, the low methodological quality of most studies, and the small sample sizes, there is no strong evidence on the effectiveness of these oral adsorbents.

Steroid avoidance or withdrawal for pancreas and pancreas with kidney transplant recipients

Nuria Montero , Angela C Webster , Ana Royuela , Javier Zamora , Marta Crespo Barrio and Julio Pascual

Background

Pancreas or kidney-pancreas transplantation improves survival and quality of life for people with type 1 diabetes mellitus and kidney failure. Immunosuppression after transplantation is associated with complications. Steroids

Recent abstracts (*new*)

...Cont'd

have adverse effects on cardiovascular risk factors such as hypertension, hyperglycaemia or hyperlipidaemia, increase risk of infection, obesity, cataracts, myopathy, bone metabolism alterations, dermatologic problems and cushingoid appearance. Whether avoiding steroids changes outcomes is unclear.

Objectives

We aimed to assess the safety and efficacy of steroid early withdrawal (treatment for less than 14 days after transplantation), late withdrawal (after 14 days after transplantation) or steroid avoidance in patients receiving a pancreas (including a vascularized organ) alone (PTA), simultaneous with a kidney (SPK) or after kidney transplantation (PAK).

Search methods

We searched the Cochrane Renal Group's Specialised Register (to 18 June 2014) through contact with the Trials' Search Co-ordinator. We handsearched: reference lists of nephrology textbooks, relevant studies, recent publications and clinical practice guidelines; abstracts from international transplantation society scientific meetings; and sent emails and letters seeking information about unpublished or incomplete studies to known investigators.

Selection criteria

We included randomised controlled trials (RCTs) or cohort studies of steroid avoidance (including early withdrawal) versus steroid maintenance or versus late withdrawal in pancreas or pancreas with kidney transplant recipients. We defined steroid avoidance as complete avoidance of steroid immunosuppression, early steroid withdrawal as steroid treatment for less than 14 days after transplantation and late withdrawal as steroid withdrawal after 14 days after transplantation.

Data collection and analysis

Two authors independently assessed the retrieved titles and abstracts, and where necessary the full text reports to determine which studies satisfied the inclusion criteria. Authors of included studies were contacted to obtain missing information. Statistical analyses were performed using random effects models and results expressed as risk ratio (RR) or mean difference (MD) with 95% confidence interval (CI). Cohort studies were not meta-analysed, but their findings summarised descriptively.

Main results

Three RCTs enrolling 144 participants met our inclusion criteria. Two compared steroid avoidance versus late steroid withdrawal and one compared late steroid withdrawal versus steroid maintenance. All studies included SPK and only one also included PTA. All studies had an overall moderate risk of bias and presented only short-term results (six to 12 months). Two studies (89 participants) compared steroid avoidance or early steroid withdrawal versus late steroid withdrawal. There was no clear evidence of an impact on mortality (2 studies, 89 participants: RR 1.64, 95% CI 0.21 to 12.75), risk of kidney loss censored for death (2 studies, 89 participants: RR 0.35, 95% CI 0.04 to 3.09), risk of pancreas loss censored for death (2 studies, 89 participants: RR 1.05, 95% CI 0.36 to 3.04), or acute kidney rejection (1 study, 49 participants: RR 2.08, 95% CI 0.20 to 21.50), however results were uncertain and consistent with no difference or important benefit or harm of steroid avoidance/early steroid withdrawal. The study that compared late steroid withdrawal versus steroid maintenance observed no deaths, no graft loss or acute kidney rejection at six months in either group and reported uncertain effects on acute pancreas rejection (RR 0.88, 95% CI 0.06 to 13.35). Of the possible adverse effects only infection was reported by one study. There were significantly more UTIs reported in the late withdrawal group compared to the steroid avoidance group (1 study, 25 patients: RR 0.41, 95% CI 0.26 to 0.66).

We also identified 13 cohort studies and one RCT which randomised tacrolimus versus cyclosporin. These studies in general showed that steroid-sparing and withdrawal strategies had benefits in lowering HbAc1 and risk of infections (BK virus and CMV disease) and improved blood pressure control without increasing the risk of rejection. However, two studies found an increased incidence of acute pancreas rejection (HR 2.8, 95% CI 0.89 to 8.81, P = 0.066 in one study and 43.3% in the steroid withdrawal group versus 9.3% in the steroid maintenance, P < 0.05 at three years in the other) and one study found an increased incidence of acute kidney rejection (18.7% in the steroid withdrawal group versus 2.8% in the steroid maintenance, P < 0.05) at three years.

Authors' conclusions

There is currently insufficient evidence for the benefits and harms of steroid withdrawal in pancreas transplantation in the three RCTs (144 patients) identified. The results showed uncertain results for short-term risk of rejection, mortality, or graft survival in steroid-sparing strategies in a very small number of patients over a short period of follow-up. Overall the data was sparse, so no firm conclusions are possible. Moreover, the 13 observational studies findings generally concur with the evidence found in the RCTs.

Recent abstracts (*new*)

...Cont'd

Topical corticosteroids for treating phimosis in boys

Gladys Moreno , Javiera Corbalán , Blanca Peñaloza and Tomas Pantoja

Background

Until recently, phimosis has been treated surgically by circumcision or prepuceplasty; however, recent reports of non-invasive treatment using topical corticosteroids applied for four to eight weeks have been favourable. The efficacy and safety of topical corticosteroids for treating phimosis in boys has not been previously systematically reviewed.

Objectives

We aimed to 1) compare the effectiveness of the use of topical corticosteroid ointment applied to the distal stenotic portion of the prepuce in the resolution of phimosis in boys compared with the use of placebo or no treatment, and 2) determine the rate of partial resolution (improvement) of phimosis, rate of re-stenosis after initial resolution or improvement of phimosis, and the rate of adverse events of topical corticosteroid treatment in boys with phimosis.

Search methods

We searched the Cochrane Renal Group's Specialised Register through contact with the Trials' Search Co-ordinator using search terms relevant to this review. Date of last search: 16 June 2014.

Selection criteria

We included all randomised controlled trials (RCTs) that compared use of any topical corticosteroid ointment with placebo ointment or no treatment for boys with phimosis.

Data collection and analysis

Two authors independently assessed titles, abstracts and the full-text of eligible studies, extracted data relating to the review's primary and secondary outcomes, and assessed studies' risk of bias. Statistical analyses were performed using the random-effects model and results were expressed as risk ratios (RR) for dichotomous outcomes with 95% confidence intervals (CI). We contacted authors of primary articles asking for details of study design and specific outcome data.

Main results

We included 12 studies that enrolled 1395 boys in this review. We found that both types of corticosteroids investigated and treatment duration varied among studies. Compared with placebo, corticosteroids significantly increased complete or partial clinical resolution of phimosis (12 studies, 1395 participants: RR 2.45, 95% CI 1.84 to 3.26). Our analysis of studies that compared different types of corticosteroids found that these therapies also significantly increased complete clinical resolution of phimosis (8 studies, 858 participants: RR 3.42, 95% CI 2.08 to 5.62). Although nine studies (978 participants) reported that assessment of adverse effects were planned in the study design, these outcomes were not reported.

Overall, we found that inadequate reporting made assessing risk of bias challenging in many of the included studies.Selection bias, performance and detection bias was unclear in the majority of the included studies: two studies had adequate sequence generation, none reported allocation concealment; two studies had adequate blinding of participants and personnel and one had high risk of bias; one study blinded outcome assessors. Attrition bias was low in 8/12 studies and reporting bias was unclear in 11 studies and high in one study.

Authors' conclusions

Topical corticosteroids offer an effective alternative for treating phimosis in boys. Although sub optimal reporting among the included studies meant that the size of the effect remains uncertain, corticosteroids appear to be a safe, less invasive first-line treatment option before undertaking surgery to correct phimosis in boys.

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Recent abstracts (*updated and conclusions changed*)

Antibiotics for acute pyelonephritis in children

Yvonne Strohmeier , Elisabeth M Hodson , Narelle S Willis , Angela C Webster and Jonathan C Craig

Background

Urinary tract infection (UTI) is one of the most common bacterial infections in infants. The most severe form of UTI is acute pyelonephritis, which results in significant acute morbidity and may cause permanent kidney damage. There remains uncertainty regarding the optimum antibiotic regimen, route of administration and duration of treatment. This is an update of a review that was first published in 2003 and updated in 2005 and 2007.

Objectives

To evaluate the benefits and harms of antibiotics used to treat children with acute pyelonephritis. The aspects of therapy considered were 1) different antibiotics, 2) different dosing regimens of the same antibiotic, 3) different duration of treatment, and 4) different routes of administration.

Search methods

We searched the Cochrane Renal Group's Specialised Register, CENTRAL, MEDLINE, EMBASE, reference lists of articles and conference proceedings without language restriction to 10 April 2014.

Selection criteria

Randomised and quasi-randomised controlled trials comparing different antibiotic agents, routes, frequencies or durations of therapy in children aged 0 to 18 years with proven UTI and acute pyelonephritis were selected.

Data collection and analysis

Four authors independently assessed study quality and extracted data. Statistical analyses were performed using the random-effects model and the results expressed as risk ratio (RR) for dichotomous outcomes or mean difference (MD) for continuous data with 95% confidence intervals (CI).

Main results

This updated review included 27 studies (4452 children). This update included evidence from three new studies, and following re-evaluation, a previously excluded study was included because it now met our inclusion criteria.

Risk of bias was assessed as low for sequence generation (12 studies), allocation concealment (six studies), blinding of outcome assessors (17 studies), incomplete outcome reporting (19 studies) and selective outcome reporting (13 studies). No study was blinded for participants or investigators. The 27 included studies evaluated 12 different comparisons. No significant differences were found in duration of fever (2 studies, 808 children: MD 2.05 hours, 95% CI -0.84 to 4.94), persistent UTI at 72 hours after commencing therapy (2 studies, 542 children: RR 1.10, 95% CI 0.07 to 17.41) or persistent kidney damage at six to 12 months (4 studies, 943 children: RR 0.82, 95% CI 0.59 to 1.12) between oral antibiotic therapy (10 to 14 days) and intravenous (IV) therapy (3 days) followed by oral therapy (10 days). Similarly, no significant differences in persistent bacteriuria at the end of treatment (4 studies, 305 children: RR 0.78, 95% CI 0.24 to 2.55) or persistent kidney damage (4 studies, 726 children: RR 1.01, 95% CI 0.80 to 1.29) were found between IV therapy (three to four days) followed by oral therapy and IV therapy (seven to 14 days). No significant differences in efficacy were found between daily and thrice daily administration of aminoglycosides (1 study, 179 children, persistent clinical symptoms at three days: RR 1.98, 95% CI 0.37 to 10.53). Adverse events were mild and uncommon and rarely resulted in discontinuation of treatment.

Authors' conclusions

This updated review increases the body of evidence that oral antibiotics alone are as effective as a short course (three to four days) of IV antibiotics followed by oral therapy for a total treatment duration of 10 to 14 days for the treatment of acute pyelonephritis in children. When IV antibiotics are given, a short course (two to four days) of IV therapy followed by oral therapy is as effective as a longer course (seven to 10 days) of IV therapy. If IV therapy with aminoglycosides is chosen, single daily dosing is safe and effective. Insufficient data are available to extrapolate these findings to children aged less than one month of age or to children with dilating vesicoureteric reflux (grades III-V). Further studies are required to determine the optimal total duration of antibiotic therapy required for acute pyelonephritis.

Frequency of administration of erythropoiesis-stimulating agents for the anaemia of end-stage kidney disease in dialysis patients

Deirdre Hahn , June D Cody and Elisabeth M Hodson

Background

The benefits of erythropoiesis-stimulating agents (ESA) for dialysis patients have been demonstrated. However, it remains unclear whether the efficacy and safety of new, longer-acting ESA given less frequently is equivalent to recombinant human erythropoietin (rHuEPO) preparations. This is an update of a review first published in 2002 and last updated in 2005.

Recent abstracts (*updated and conclusions changed*)

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Objectives

This review aimed to establish the optimal frequency of ESA administration in terms of effectiveness (correction of anaemia, and freedom from adverse events) and efficiency (optimal resource use) of different ESA dose regimens.

Search methods

We searched the Cochrane Renal Group's Specialised Register to 21 March 2013 through contact with the Trials' Search Co-ordinator using search terms relevant to this review.

Selection criteria

We included randomised control trials (RCTs) comparing different frequencies of ESA administration in dialysis patients.

Data collection and analysis

Two authors independently assessed study eligibility, risk of bias and extracted data. Results were expressed as risk ratio (RR) or risk differences (RD) with 95% confidence intervals (CI) for dichotomous outcomes. For continuous outcomes the mean difference (MD) or standardised mean difference (SMD) with 95% confidence intervals (CI) was used. Statistical analyses were performed using the random-effects model.

Main results

This review included 33 studies (5526 participants), 22 of which were added for this update. Risk of bias was generally high; only nine studies were assessed at low risk of bias for sequence generation and 14 studies for allocation concealment. Although only four studies were placebo-controlled, all were considered to be at low risk of performance or detection bias because the primary outcome of haemoglobin level was a laboratory-derived assessment and unlikely to be influenced by lack of blinding. We found that 16 studies were at low risk of attrition bias and five were at low risk of selection bias; only one study reporting sources of support was not funded by a pharmaceutical company.

We compared four different interventions: Continuous erythropoietin receptor agonists (CERA) versus other ESA (darbepoetin or rHuEPO); different frequencies of darbepoetin administration; darbepoetin versus rHuEPO; and different frequencies of rHuEPO administration.

There were no significant differences in maintaining final haemoglobin between CERA administered at two weekly intervals (4 studies, 1762 participants: MD 0.08 g/dL, 95% CI -0.04 to 0.21) or four weekly intervals (two studies, 1245 participants: MD -0.03 g/dL, 95% CI -0.17 to 0.12) compared with rHuEPO administered at two to three weekly intervals. In one study comparing CERA administered every two weeks with darbepoetin administered once/week, there was no significant difference in final haemoglobin (313 participants: MD 0.30 g/dL, 95% CI 0.05 to 0.55). In comparisons of once/week with once every two weeks darbepoetin (two studies, 356 participants: MD 0.04 g/dL, 95% CI -0.45 to 0.52) and once every two weeks with monthly darbepoetin (one study, 64 participants: MD 0.40 g/dL, 95% CI -0.37 to 1.17) there were no significant differences in final haemoglobin levels. There was marked heterogeneity among studies comparing weekly darbepoetin with once every two weeks and was possibly related to different administration protocols. Eight studies compared weekly darbepoetin with rHuEPO given two to three times/ week; no statistical difference in final haemoglobin was demonstrated (6 studies, 1638 participants: MD 0.02 g/dL, 95% CI -0.09 to 0.12). Fourteen studies compared different frequencies of rHuEPO. No statistical difference was demonstrated in final haemoglobin (7 studies, 393 participants: SMD -0.17 g/dL, 95% CI -0.39 to 0.05). Adverse events did not differ significantly within comparisons; however, mortality and quality of life were poorly reported, particularly in earlier publications.

Authors' conclusions

Longer-acting ESA (darbepoetin and CERA) administered at one to four week intervals are non-inferior to rHuEPO given one to three times/week in terms of achieving haemoglobin targets without any significant differences in adverse events in haemodialysis patients. Additional RCTs are required to evaluate different frequencies of ESA in peritoneal and paediatric dialysis patients and to compare different longer-acting ESA (such as darbepoetin compared with CERA).

HMG CoA reductase inhibitors (statins) for people with chronic kidney disease not requiring dialysis

Suetonia C Palmer , Sankar D Navaneethan , Jonathan C Craig , David W Johnson , Vlado Perkovic , Jorgen Hegbrant and Giovanni FM Strippoli

Background

Cardiovascular disease (CVD) is the most frequent cause of death in people with early stages of chronic kidney disease (CKD), for whom the absolute risk of cardiovascular events is similar to people who have existing coronary artery disease. This is an update of a review published in 2009, and includes evidence from 27 new studies (25,068 participants) in addition to the 26 studies (20,324 participants) assessed previously; and excludes three previously included studies (107 participants). This updated review includes 50 studies (45,285 participants); of these 38 (37,274 participants) were meta-analysed.

Recent abstracts (*updated and conclusions changed*)

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Objectives

To evaluate the benefits (such as reductions in all-cause and cardiovascular mortality, major cardiovascular events, MI and stroke; and slow progression of CKD to end-stage kidney disease (ESKD)) and harms (muscle and liver dysfunction, withdrawal, and cancer) of statins compared with placebo, no treatment, standard care or another statin in adults with CKD who were not on dialysis.

Search methods

We searched the Cochrane Renal Group's Specialised Register to 5 June 2012 through contact with the Trials' Search Co-ordinator using search terms relevant to this review.

Selection criteria

Randomised controlled trials (RCTs) and quasi-RCTs that compared the effects of statins with placebo, no treatment, standard care, or other statins, on mortality, cardiovascular events, kidney function, toxicity, and lipid levels in adults with CKD not on dialysis were the focus of our literature searches.

Data collection and analysis

Two or more authors independently extracted data and assessed study risk of bias. Treatment effects were expressed as mean difference (MD) for continuous outcomes (lipids, creatinine clearance and proteinuria) and risk ratio (RR) for dichotomous outcomes (major cardiovascular events, all-cause mortality, cardiovascular mortality, fatal or non-fatal myocardial infarction (MI), fatal or non-fatal stroke, ESKD, elevated liver enzymes, rhabdomyolysis, cancer and withdrawal rates) with 95% confidence intervals (CI).

Main results

We included 50 studies (45,285 participants): 47 studies (39,820 participants) compared statins with placebo or no treatment and three studies (5547 participants) compared two different statin regimens in adults with CKD who were not yet on dialysis. We were able to meta-analyse 38 studies (37,274 participants).

The risk of bias in the included studies was high. Seven studies comparing statins with placebo or no treatment had lower risk of bias overall; and were conducted according to published protocols, outcomes were adjudicated by a committee, specified outcomes were reported, and analyses were conducted using intention-to-treat methods. In placebo or no treatment controlled studies, adverse events were reported in 32 studies (68%) and systematically evaluated in 16 studies (34%).

Compared with placebo, statin therapy consistently prevented major cardiovascular events (13 studies, 36,033 participants; RR 0.72, 95% CI 0.66 to 0.79), all-cause mortality (10 studies, 28,276 participants; RR 0.79, 95% CI 0.69 to 0.91), cardiovascular death (7 studies, 19,059 participants; RR 0.77, 95% CI 0.69 to 0.87) and MI (8 studies, 9018 participants; RR 0.55, 95% CI 0.42 to 0.72). Statins had uncertain effects on stroke (5 studies, 8658 participants; RR 0.62, 95% CI 0.35 to 1.12).

Potential harms from statin therapy were limited by lack of systematic reporting and were uncertain in analyses that had few events: elevated creatine kinase (7 studies, 4514 participants; RR 0.84, 95% CI 0.20 to 3.48), liver function abnormalities (7 studies, RR 0.76, 95% CI 0.39 to 1.50), withdrawal due to adverse events (13 studies, 4219 participants; RR 1.16, 95% CI 0.84 to 1.60), and cancer (2 studies, 5581 participants; RR 1.03, 95% CI 0.82 to 130).

Statins had uncertain effects on progression of CKD. Data for relative effects of intensive cholesterol lowering in people with early stages of kidney disease were sparse. Statins clearly reduced risks of death, major cardiovascular events, and MI in people with CKD who did not have CVD at baseline (primary prevention).

Authors' conclusions

Statins consistently lower death and major cardiovascular events by 20% in people with CKD not requiring dialysis. Statin-related effects on stroke and kidney function were found to be uncertain and adverse effects of treatment are incompletely understood. Statins have an important role in primary prevention of cardiovascular events and mortality in people who have CKD.

Immunosuppressive treatment for idiopathic membranous nephropathy in adults with nephrotic syndrome

Yizhi Chen , Arrigo Schieppati , Xiangmei Chen , Guangyan Cai , Javier Zamora , Giovanni A Giuliano , Norbert Braun and Annalisa Perna

Background

Idiopathic membranous nephropathy (IMN) is the most common form of nephrotic syndrome in adults. The disease shows a benign or indolent course in the majority of patients, with a rate of spontaneous complete or partial remission of nephrotic syndrome as high as 30% or more. Despite this, 30% to 40% of patients progress toward end-stage kidney disease (ESKD) within five to 15 years. The efficacy and safety of immunosuppression for IMN with nephrotic syndrome are still controversial. This is an update of a Cochrane review first published in 2004.

Objectives

The aim of this review was to evaluate the safety and efficacy of immunosuppressive treatments for adult patients

Recent abstracts (*updated and conclusions changed*)

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with IMN and nephrotic syndrome. Moreover it was attempted to identify the best therapeutic regimen, when to start immunosuppression and whether the above therapies should be given to all adult patients at high risk of progression to ESKD or only restricted to those with impaired kidney function.

Search methods

We searched Cochrane Renal Group Specialised Register, Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, Chinese databases, reference lists of articles, and clinical trial registries to June 2014. We also contacted principal investigators of some of the studies for additional information.

Selection criteria

Randomised controlled trials (RCTs) investigating the effects of immunosuppression in adults with IMN and nephrotic syndrome.

Data collection and analysis

Study selection, data extraction, quality assessment, and data synthesis were performed using the Cochrane-recommended methods. Summary estimates of effect were obtained using a random-effects model, and results were expressed as risk ratios (RR) and their 95% confidence intervals (CI) for dichotomous outcomes, and mean difference (MD) and 95% CI for continuous outcomes.

Main results

Thirty nine studies with 1825 patients were included, 36 of these could be included in our meta-analyses. The data from two studies could not be extracted and one study was terminated due to poor accrual. Immunosuppression significantly reduced all-cause mortality or risk of ESKD ((15 studies, 791 patients): RR 0.58 (95% CI 0.36 to 0.95, P = 0.03) and risk of ESKD ((15 studies, 791 patients): RR 0.55, 95% CI 0.31 to 0.95, P = 0.03), increased complete or partial remission ((16 studies, 864 patients): RR 1.31, 95% CI 1.01 to 1.70, P = 0.04), and decreased proteinuria ((9 studies,(393 patients): MD -0.95 g/24 h, 95% CI -1.81 to -0.09, P = 0.03) at the end of follow-up (range 6 to 120 months). However this regimen was associated with more discontinuations or hospitalisations ((16 studies, 880 studies): RR 5.35, 95% CI 2.19 to 13.02), P = 0.0002). Combined corticosteroids and alkylating agents significantly reduced death or risk of ESKD ((8 studies, 448 patients): RR 0.44, 95% CI 0.26 to 0.75, P = 0.002) and ESKD ((8 studies, 448 patients): RR 0.45, 95% CI 0.25 to 0.81, P = 0.008), increased complete or partial remission ((7 studies, 422 patients): RR 1.46, 95% CI 1.13 to 1.89, P = 0.004) and complete remission ((7 studies, 422 patients): RR 2.32, 95% CI 1.61 to 3.32, P < 0.00001), and decreased proteinuria ((6 studies, 279 patients): MD -1.25 g/24 h, 95% CI -1.93 to -0.57, P = 0.0003) at the end of follow-up (range 9 to 120 months). In a population with an assumed risk of death or ESKD of 181/1000 patients, this regimen would be expected to reduce the number of patients experiencing death or ESKD to 80/1000 patients (range 47 to 136). In a population with an assumed complete or partial remission of 408/1000 patients, this regimen would be expected to increase the number of patients experiencing complete or partial remission to 596/1000 patients (range 462 to 772). However this combined regimen was associated with a significantly higher risk of discontinuation or hospitalisation due to adverse effects ((4 studies, 303 patients): RR 4.20, 95% CI 1.15 to 15.32, P = 0.03). Whether this combined therapy should be indicated in all adult patients at high risk of progression to ESKD or only restricted to those with deteriorating kidney function still remained unclear. Cyclophosphamide was safer than chlorambucil ((3 studies, 147 patients): RR 0.48, 95% CI 0.26 to 0.90, P = 0.02). There was no clear evidence to support the use of either corticosteroid or alkylating agent monotherapy. Cyclosporine and mycophenolate mofetil failed to show superiority over alkylating agents. Tacrolimus and adrenocorticotropic hormone significantly reduced proteinuria. The numbers of corresponding studies related to tacrolimus, mycophenolate mofetil, adrenocorticotropic hormone, azathioprine, mizoribine, and Tripterygium wilfordii are still too sparse to draw final conclusions.

Authors' conclusions

In this update, a combined alkylating agent and corticosteroid regimen had short- and long-term benefits on adult IMN with nephrotic syndrome. Among alkylating agents, cyclophosphamide was safer than chlorambucil. This regimen was significantly associated with more withdrawals or hospitalisations. It should be emphasised that the number of included studies with high-quality design was relatively small and most of included studies did not have adequate follow-up and enough power to assess the prespecified definite endpoints. Although a six-month course of alternating monthly cycles of corticosteroids and cyclophosphamide was recommended by the KDIGO Clinical Practice Guideline 2012 as the initial therapy for adult IMN with nephrotic syndrome, clinicians should inform their patients of the lack of high-quality evidence for these benefits as well as the well-recognised adverse effects of this therapy. Cyclosporine or tacrolimus was recommended by the KDIGO Clinical Practice Guideline 2012 as the alternative regimen for adult IMN with nephrotic syndrome; however, there was no evidence that calcineurin inhibitors could alter the combined outcome of death or ESKD.

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