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Effects of Magnesium Supplementation on Clinical and Biochemical Outcomes in Patients with Chronic Kidney Disease: A Systematic Review of Randomized Controlled Trials

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Keywords:
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Abstract

Chronic kidney disease (CKD) is associated with metabolic and cardiovascular complications, as well as mineral and bone disorders. Hypomagnesemia occurs in some patients with CKD and has been associated with disease progression and increased mortality. Magnesium supplementation may improve various clinical and biochemical outcomes; however, findings across studies remain inconsistent. A systematic literature search was conducted using electronic databases, including PubMed and Embase, to identify randomized controlled trials (RCTs) evaluating oral magnesium supplementation in adults with CKD. The outcomes assessed included vascular parameters, kidney function, metabolic outcomes, mineral and bone metabolism parameters, inflammatory markers, and safety. Ten RCTs met the eligibility criteria, including seven studies involving patients with nondialysis-dependent CKD and three involving patients undergoing hemodialysis. Intervention durations ranged from 8 weeks to 2 years. Magnesium supplementation demonstrated potential benefits for certain vascular outcomes, particularly carotid intima-media thickness (cIMT) and serum calcification propensity, as measured by the T50 test, as well as selected metabolic parameters. However, its effects on coronary artery calcification (CAC) progression, kidney function, mineral and bone metabolism, inflammation, and oxidative stress were inconsistent across studies. No cases of severe symptomatic hypermagnesemia were reported, although gastrointestinal adverse effects, particularly diarrhea, were among the most frequently reported adverse events. Oral magnesium supplementation may provide benefits for selected vascular and metabolic outcomes in patients with CKD. However, the available evidence remains inconsistent and insufficient to support routine magnesium supplementation in all patients with CKD.

INTRODUCTION

Chronic kidney disease (CKD) is a major global health concern that contributes significantly to morbidity and mortality. In 2023, approximately 788 million adults worldwide were estimated to have CKD, and approximately 1.48 million deaths were attributed to the disease. CKD is also strongly associated with an increased risk of cardiovascular disease, metabolic disturbances, and CKD-related mineral and bone disorders (Mark et al., 2025).

In addition to declining kidney function, CKD is frequently accompanied by metabolic and mineral disturbances that may adversely affect patient outcomes (Shroff et al., 2022). Magnesium has received increasing attention because of its essential roles in energy metabolism, glucose homeostasis, vascular function, and mineral and bone metabolism (Jahnen-Dechent & Ketteler, 2012; Panta & Regmi, 2024).

The kidneys play a central role in maintaining magnesium homeostasis. In patients with CKD, a reduced glomerular filtration rate may impair renal magnesium excretion; however, hypomagnesemia can still occur because of inadequate dietary intake, certain medications, diabetes mellitus, proteinuria, and impaired renal tubular magnesium reabsorption (Cunningham et al., 2012; Oka et al., 2019). Hypomagnesemia is a clinically relevant electrolyte disturbance in patients with CKD (Abdel-Hameed et al., 2022). Its prevalence has been reported to be 14.7% among patients with predialysis CKD (Oka et al., 2019) and 29.1% among those with CKD stages 3–5 (Biyik et al., 2020), although estimates vary according to the study population and disease severity.

Low serum magnesium concentrations in patients with CKD have been associated with kidney disease progression, increased mortality, and elevated cardiovascular risk (Azem et al., 2020; Sakaguchi et al., 2012; Yin et al., 2023). Magnesium may also inhibit calcium-phosphate crystal formation and osteogenic differentiation of vascular smooth muscle cells, potentially reducing vascular calcification, a common complication of CKD (Sakaguchi, 2022).

Several randomized controlled trials (RCTs) have evaluated magnesium supplementation in patients with CKD and reported potential benefits for various vascular, metabolic, and kidney-related outcomes (Vermeulen & Vervloet, 2023; Zhan et al., 2023). However, the available findings remain inconsistent. Although magnesium supplementation may improve certain surrogate markers, including serum calcification propensity and vascular parameters, these improvements have not consistently translated into favorable structural vascular outcomes or improved kidney function. Furthermore, existing studies differ in CKD stage, dialysis status, magnesium formulation and dosage, intervention duration, and assessed outcomes. This heterogeneity limits the comparability of findings and prevents definitive conclusions regarding the clinical benefits of magnesium supplementation in patients with CKD.

Given these uncertainties, this systematic review aimed to comprehensively synthesize evidence from RCTs evaluating the effects of magnesium supplementation on clinical and biochemical outcomes in patients with CKD. The rationale for this review was supported by the substantial global burden of CKD, the clinical relevance of magnesium disturbances, and the fragmented and conflicting findings from existing RCTs. This review sought to contribute to the literature by comparing the direction and magnitude of treatment effects across studies, categorizing findings according to dialysis status and outcome domain, and systematically assessing the risk of bias using the revised Cochrane risk-of-bias tool for randomized trials (RoB 2). By integrating these findings, the review aimed to identify potential differences in treatment responses across patient subgroups, highlight existing evidence gaps, and inform priorities for future clinical research.

METHOD

This study uses a systematic review method prepared based on the guidelines of PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).

Eligibility

The study included in this systematic review was a randomized controlled trial (RCT) that evaluated magnesium supplementation in adult patients aged ≥18 years with CKD, both non-dialysis CKD and patients undergoing dialysis. Interventions received were oral

magnesium supplementation, including magnesium oxide, citrate, hydroxide, carbonate, or other oral magnesium formulations, with a placebo, standard care, or no magnesium supplementation.

Studies must report at least one clinical or biochemical outcome, including magnesium levels, renal function, albuminuria or proteinuria, vascular and cardiovascular parameters, glucose and lipid metabolism, mineral and bone parameters, inflammatory biomarkers, or side effects of magnesium supplementation.

Observational studies, quasi-randomized studies, case reports, case series, reviews, experimental animal studies, as well as studies using magnesium only as a component of dialysis fluid or phosphate binder are excluded from this review

Search Strategy

Literature searches were conducted on major online databases: PubMed, Embase, Web of Science, and ClinicalTrials.gov. Keywords were used systematically with a combination of terms related to magnesium and CKD, including "magnesium," "magnesium supplementation," "magnesium oxide," "magnesium citrate," "magnesium hydroxide," "magnesium carbonate," "chronic kidney disease," "chronic renal failure," "renal insufficiency," "nephropathy," "hemodialysis," "dialysis," and "randomized controlled trial." There is no publication year limit. References from included articles are also manually searched for additional relevant research.

Research Selection Process

Initial search results were filtered by title and abstract. Articles that were not topically relevant or did not meet the study design criteria were immediately eliminated. Potentially relevant articles were analyzed in full-text form to ensure conformity to the inclusion criteria. The selection process was conducted by two reviewers independently, with discussions to resolve the non-conformities. The PRISMA diagram was used to systematically illustrate the study selection flow.

Data Extraction

Data from studies that met the criteria were extracted into a comparative table that included the name of the author and year of publication, the country of the study, the study design, the number of samples, the characteristics of the participants, the stage of CKD, dialysis status, the type and dose of magnesium, the duration of the intervention, the comparison group, and the reported outcomes.

Study outcomes were grouped into magnesium status, renal output, vascular and cardiovascular output, metabolic parameters, mineral and bone parameters, inflammatory biomarkers, and safety outputs. The main outcomes of each study and the incidence of side effects were also recorded.

Data Synthesis

Given the variation in CKD stage, magnesium formulation and dose, duration of intervention, and type of outcomes assessed, data will be synthesized narratively and descriptive-comparatively. Studies were grouped based on CKD status, namely non-dialysis CKD and dialysis CKD, as well as by the evaluated output domain.

The synthesis was carried out by comparing the direction and magnitude of the effects of magnesium supplementation between studies and considering the characteristics of the population and the intervention of each study.

Risk of bias in each RCT was assessed using Cochrane Risk of Bias 2 (RoB 2) which included a randomisation process, deviation from the planned intervention, missing output data, outcome measurement, and selection of reported outcomes. The overall risk of bias was categorized as low risk of bias, some concerns, or high risk of bias.

RESULTS AND DISCUSSION

Research Characteristics

A total of 10 RCTs evaluated oral magnesium supplementation in adult patients with chronic kidney disease (CKD).

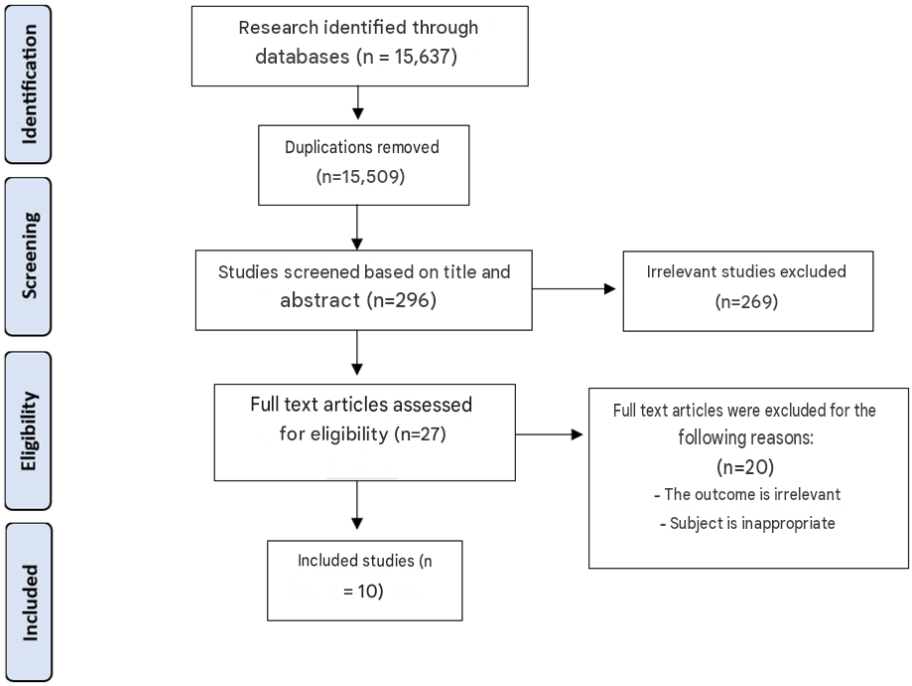


Figure 1. Schematic of research literature search strategy

Seven studies were conducted in non-dialysis CKD patients and three studies in patients undergoing hemodialysis. The study sample size ranged from 19 to 148 people, with the duration of intervention ranging from 8 weeks to 2 years.

The study population showed considerable heterogeneity. Non-dialysis CKD studies primarily involved CKD G3–G4, while some studies specifically involved patients with diabetic nephropathy, hypomagnesemia, obesity, or prediabetes.

Table 1. Risk of bias assessment of RCT (Risk of Bias 2.0) research

Research (RCT)	Randomization	Deviation from the intervention	Lost data	External measurement	Selection of Reported Externalities	Overall Bias
Turgut et al. (2008)	Some concerns	Some concerns	Low	Some concerns	Some concerns	Some concerns
Mortazavi et al. (2013)	Some concerns	Low	Low	Low	Some concerns	Some concerns
Bressendorff et al. (2017)	Low	Low	Low	Low	Low	Low

Research (RCT)	Randomization	Deviation from the intervention	Lost data	External measurement	Selection of Reported Externalities	Overall Bias
Toprak et al. (2017)	Some concerns	Low	Some concerns	Low	Some concerns	Some concerns
Sakaguchi et al. (2019)	Low	Some concerns	Some concerns	Low	Some concerns	Some concerns
Talari et al. (2019)	Low	Low	Low	Low	Low	Low
Sadeghian et al. (2020)	Some concerns	Low	Low	Low	Low	Some concerns
Bressendorff et al. (2023)	Low	Low	Some concerns	Low	Low	Some concerns
Halawa et al. (2023)	Some concerns	Some concerns	Some concerns	Low	Low	Some concerns
Pendón-Ruiz de Mier et al. (2024)	Some concerns	Some concerns	Low	Low	Some concerns	Some concerns

Table 2. Extraction of research data

Research	Population and number of samples	Intervention groups	Control group	Duration	Main exterior	Main results
Turgut et al. (2008)	Hemodialysis, (n=47)	Mg citrate 610 mg every 2 days	Calcium acetate as *a phosphate binder* without Mg supplementation	2 months	cIMT, Mg, PTH, Ca, P	The left cIMT decreased from 0.97±0.30 to 0.70±0.20 mm (p=0.001) and the right from 0.95±0.30 to 0.78±0.30 mm (p=0.002). Control did not change significantly. PTH decreased from 392.7±346.4 to 214.8±142.7 pg/mL (p=0.003).
Mortazavi et al. (2013)	Hemodialysis (n=54)	Mg oxide 440 mg, 3×/week (n=29)	Placebo on the same schedule (n=25)	6 months	cIMT, FMD, CRP	cIMT decreased from 0.84±0.13 to 0.76±0.13 mm (p=0.001), while in placebo it increased from 0.73±0.13 to 0.79±0.12 mm (p=0.003). There was no significant improvement in FMD or CRP.
Bressendorff et al. (2017)	CKD G3–G4 (n=36)	Slow-release Mg hydroxide: elemental Mg 15 mmol/day or 30 mmol/day	Matching placebo	8 weeks	T50, serum Mg, intracellular Mg	At 30 mmol/day, T50 increased from 256±60 to 296±64 minutes, a change of about +40 minutes. The difference in change to placebo at week 8 was 56.2 minutes (95% CI 9.5–102.9; p=0.02). Serum Mg increased, but

Research	Population and number of samples	Interventio n groups	Control group	Durati on	Main exterior	Main results
						intracellular Mg did not change.
Toprak et al. (2017)	mild–moderate CKD, hypomagnesemia, obesity and prediabetes (n=128 per group)	Mg oral, elemental mg 365 mg/day	Placebo once a day	3 months	HOMA-IR and metabolic parameters	Compared to placebo, Mg resulted in greater decreases in HOMA-IR (−31.9% vs −3.3%; p<0.001), insulin (−29.6% vs −2.66%; p<0.001) and HbA1c (−6.6% vs −0.16%; p<0.001). Serum Mg increased +0.21±0.18 vs −0.04±0.05 mg/dL (p<0.001).
Sakaguchi et al. (2019)	CKD G3–G4 with CAC risk factors (n=123)	Initial Mg oxide 330 mg/day (198 mg elemental Mg), titrated for serum Mg 2.5–3.0 mg/dL	Standard CKD therapy without MgO; allocation of AST-120 is carried out factorially independently	2 years	CAC score changes	Median CAC progression was lower with MgO: 11.3% vs 39.5% in control (p<0.001). *Rapid CAC progression* ≥15%/year occurred at 23.9% vs 62.0% (p<0.001). There was no difference in thoracic aortic calcification progression (24.2% vs 29.0%; p=0.89).
Talari et al. (2019)	Diabetes + hemodialysis, n=54	Mg oxide 250 mg/day (n=27)	Matching placebo (n=27)	24 weeks	cIMT and metabolic parameters	Compared to placebo, Mg decreased mean left cIMT β=−0.04 mm (95% CI −0.06 to −0.02; p<0.001), HOMA-IR β=−0.56 (p=0.001), HbA1c β=−0.74% (p<0.001), LDL β=−0.29 mmol/L (p=0.01), hs-CRP β=−1.57 mg/L (p<0.001) and MDA β=−0.26 µmol/L (p=0.04).
Sadeghian et al. (2020)	T2DM with *early diabetic nephropathy* and hypomagnesemia (n=80)	Mg oxide 250 mg/day (n=40)	Placebo (n=40)	12 weeks	Kidney function, insulin resistance, metabolic	The decrease in microalbuminuria was numerically greater at Mg (−14±9.9 vs −3.1±2.2 mg/L) but not significant (p=0.09). HOMA-IR increased more at Mg (+1.9±4.0 vs +0.2±2.2; p=0.04). There were no significant differences in HbA1c, creatinine or BUN.

Research	Population and number of samples	Intervention groups	Control group	Duration	Main exterior	Main results
Bressendorff et al. (2023), MAGiCAL-CKD	eGFR 15–45 mL/min/1.73 m², n=148	Mg hydroxide 15 mmol 2×/day (n=75)	Matching placebo (n=73)	12 months	CAC progression	The CAC increased by 33.3% in the Mg group and 31.2% in the placebo. The difference in CAC after adjustment was only 0.9% (95% CI −10.2 to 13.4; p=0.438) so it showed no protective effect. Plasma Mg increased significantly in the intervention group.
Halawa et al. (2023)	Diabetic nephropathy, n=60; 54 subjects until the study is completed	Standard therapy + Mg citrate 2.25 g/day, equivalent to 360 mg elemental Mg (n=30)	Standard therapy only (n=30)	12 weeks	UACR; eGFR, metabolic, QoL	The median change in UACR was greater with Mg: −6.87% vs −0.9% (p=0.001). The percentage change in eGFR was also greater (+21.74% vs about 0%; p=0.001). There was no significant difference in HbA1c/HOMA-IR changes, but lipid and QoL profiles improved in the Mg group.
Pendón-Ruiz de Mier et al. (2024)	CKD G3–G4, n=19	Mg carbonate 360 mg/day (n=7)	Standard treatment without Mg supplementation (n=12)	15 months	BMD, vascular calcification, PWV	There was no difference in changes in PWV (+0.19±0.83 vs −0.03±1.49 m/s; p=0.755), vertebral BMD (+9 vs +6 mg/cm²; p=0.692), femoral neck (−28 vs −6 mg/cm²; p=0.231) or hip (−11 vs +3 mg/cm²; p=0.430). There was no significant progression *of vascular calcification* based on the Adragao index.

Three other studies were conducted on CKD G5D patients undergoing hemodialysis. The magnesium formulations used included magnesium hydroxide, magnesium oxide, magnesium citrate, and magnesium carbonate. The comparison group was placebo, standard therapy without magnesium supplementation, or active therapy without added magnesium. Outcomes evaluated included vascular and cardiovascular parameters, renal function, metabolic and glycemic parameters, mineral and bone metabolism, magnesium status, inflammation and oxidative stress, and safety.

Bias Risk Assessment

Risk of bias assessment was conducted using Cochrane Risk of Bias 2 (RoB 2) based on the main outcomes of each study. The five domains assessed included the randomisation process, deviation from planned interventions, missing output data, outcome measurement, and selection of reported outcomes.

Overall, two studies were rated as having a low risk of bias, while eight studies showed some concerns. None of the studies were classified as high risk of bias overall (Table 1). The most frequent sources of concern came from limited reporting of randomization or allocation concealment methods, open-label design, missing output data, and lack of information about pre-defined analyses.

External Vascular

Vascular output was the domain most frequently evaluated. In hemodialysis patients, Turgut et al. (2008) reported that the left cIMT decreased from 0.97±0.30 to 0.70±0.20 mm ($p=0.001$) and the right cIMT from 0.95±0.30 to 0.78±0.30 mm ($p=0.002$) after two months of magnesium citrate supplementation, while there was no significant change in the control group.

Mortazavi et al. (2013) showed a decrease in cIMT from 0.84±0.13 to 0.76±0.13 mm ($p=0.001$) in the magnesium oxide group, while the placebo group increased from 0.73±0.13 to 0.79±0.12 mm ($p=0.003$) after six months. However, there was no significant improvement in flow-mediated dilation or CRP. Talari et al. (2019) also found a decrease in mean left cIMT compared to placebo of $\beta=-0.04$ mm (95% CI −0.06 to −0.02; $p<0.001$), as well as a decrease in maximum left cIMT and mean right cIMT.

In CKD G3–G4, Bressendorff et al. (2017) showed an increase in serum calcification propensity time (T50). In the 30 mmol/day elemental magnesium group, T50 increased from 256±60 to 296±64 minutes, with a difference in change compared to placebo of 56.2 minutes (95% CI 9.5–102.9; $p=0.02$).

Results for coronary artery calcification (CAC) were inconsistent. Sakaguchi et al. (2019) found a two-year median CAC progression of 11.3% in the magnesium group compared to 39.5% in the control ($p<0.001$). The proportion of patients with CAC progression ≥15% per year was also lower in the magnesium group (23.9% vs 62.0%; $p<0.001$).

The MAGiCAL-CKD trial (Bressendorff et al., 2023) found no benefit on CAC progression. After 12 months, CAC increased by 33.3% in the magnesium group and 31.2% in the placebo, with an adjusted between-group difference of 0.9% (95% CI −10.2 to 13.4; $p=0.438$). The MagicalBone study (Pendón-Ruiz de Mier et al., 2024) also showed no difference in PWV change between the magnesium and control groups (+0.19±0.83 vs −0.03±1.49 m/s; $p=0.755$) nor a significant change in vascular calcification based on the Adragao index.

External Kidney

renal discharge was evaluated in a more limited number of studies. In diabetic nephropathy patients, Sadeghian et al. (2020) found a numerically greater reduction in microalbuminuria in the magnesium group than in placebo (−14±9.9 vs −3.1±2.2 mg/L), but the difference did not reach statistical significance ($p=0.09$). No significant differences were found in serum creatinine or BUN.

In contrast, Halawa et al. (2023) reported a greater median decrease in UACR in the magnesium citrate group than in the control (−6.87% vs −0.9%; $p=0.001$). eGFR also showed better changes in the magnesium group after 12 weeks ($p=0.001$).

In the study by Sakaguchi et al. (2019), the change in eGFR over two years did not differ significantly between magnesium oxide and controls (p=0.50), whereas Pendón-Ruiz de Mier et al. (2024) showed no significant change in renal function during the intervention period.

External Metabolic

Toprak et al. (2017) reported that in mild–moderate CKD patients with hypomagnesemia, obesity, and prediabetes, magnesium supplementation resulted in a greater reduction in HOMA-IR than placebo (−31.9% vs −3.3%; p<0.001). Decreases were also found in insulin (−29.6% vs −2.66%; p<0.001) and HbA1c (−6.6% vs −0.16%; p<0.001).

In diabetic patients undergoing hemodialysis, Talari et al. (2019) reported a decrease in insulin of β=−9.42 pmol/L (95% CI −14.94 to −3.90; p=0.001), HOMA-IR of β=−0.56 (95% CI −0.89 to −0.24; p=0.001), and HbA1c of β=−0.74% (95% CI −1.10 to −0.39; p<0.001). Total cholesterol and LDL-cholesterol were also significantly decreased compared to placebo.

However, different results were found by Sadeghian et al. (2020). There was no significant improvement in HbA1c or fasting glucose, while changes in insulin resistance were worse in the magnesium group than in the placebo group (p=0.04). Halawa et al. (2023) also found no significant difference in changes in the glycemic index, although there was an improvement in lipid profile in the magnesium group.

Mineral and Bones Exterior

Turgut et al. (2008) reported a decrease in PTH from 392.7±346.4 to 214.8±142.7 pg/mL (p=0.003) in the magnesium citrate group, while the change in the control group was not significant. No significant changes were found in calcium, phosphorus, or calcium-phosphorus products.

Pendón-Ruiz de Mier et al. (2024) found no difference in changes in bone mineral density between the magnesium and control groups in vertebrae (p=0.692), femoral neck (p=0.231), and hip (p=0.430) after 15 months. Halawa et al. (2023) reported a greater decrease in serum osteocalcin in the magnesium citrate group (p=0.001), but the study did not directly evaluate BMD.

Inflammation and Oxidative Stress

Effects on inflammation and oxidative stress showed inconsistent results. Talari et al. (2019) reported a decrease in hs-CRP compared to placebo of β=−1.57 mg/L (95% CI −2.06 to −1.08; p<0.001) and malondialdehyde of β=−0.26 μmol/L (p=0.04). Total antioxidant capacity increased by β=168.91 mmol/L (95% CI 113.92–223.89; p<0.001).

In contrast, Mortazavi et al. (2013) showed no significant changes in CRP after six months of magnesium supplementation, whereas Sadeghian et al. (2020) also found no meaningful effect on inflammatory biomarkers in diabetic nephropathy patients.

Security

No severe symptomatic hypermagnesemia was found in RCTs evaluating oral magnesium supplementation. In the study by Bressendorff et al. (2017), magnesium supplementation for eight weeks was well tolerated and no serious adverse events were found associated with the intervention.

Gastrointestinal effects were the most consistent occurrence at higher doses or long-term use. In the study by Sakaguchi et al. (2019), the dropout rate was higher in the magnesium group than in the control group (27% vs. 17%), mainly due to diarrhea.

In the MAGiCAL-CKD RCT (Bressendorff et al., 2023), 35 participants (47%) in the magnesium group experienced loose stool or diarrhea compared to 9 participants (12%) in the placebo. There were no participants with plasma magnesium >1.50 mmol/L. A total of 23 serious adverse events occurred in the magnesium group and 13 in the placebo; six major adverse cardiovascular events occurred in the magnesium group and none in the placebo. However, the researchers stated that these serious events were not considered to be directly related to the study drug.

Talari et al. (2019) reported no supplementation-related side effects for 24 weeks, whereas Halawa et al. (2023) reported mild side effects that did not require intervention or discontinuation of therapy. Pendón-Ruiz de Mier et al. (2024) found no episodes of hypermagnesemia during 15 months of magnesium carbonate supplementation.

Magnesium supplementation in patients with chronic kidney disease (CKD) has the potential to improve some vascular and metabolic outputs, but inter-RCT results are still inconsistent. Benefits are most commonly seen in surrogate vascular outcomes, such as carotid intima-media thickness (cIMT) and serum calcification propensity (T50), while effects on coronary artery calcification (CAC), renal function, and mineral-bone output remain uncertain. These findings are consistent with previous studies that have shown the potential benefits of magnesium on vascular parameters, but have not provided consistent evidence of structural vascular calcification (Zhan et al., 2023).

The potential vascular effects of magnesium have a biological basis because magnesium may inhibit the formation of calcium-phosphate crystals and osteogenic transformation of vascular smooth muscle cells (Sakaguchi, 2022). Some RCTs showed improved cIMT in haemodialysis patients and increased T50 in CKD G3–G4 (Bressendorff et al., 2017; Mortazavi et al., 2013; Talari et al., 2019; Turgut et al., 2008; Vermeulen & Vervloet, 2023). However, results on CAC differed between studies. Sakaguchi et al. (2019) found a lower progression of CAC after magnesium oxide, while the MAGiCAL-CKD RCT showed no slowdown in CAC even though plasma magnesium levels increased (Bressendorff et al., 2023). These differences may be related to variation in study design, sample size, duration of intervention, magnesium formulation and dose, degree of CKD, and initial calcification load. This suggests that improvement in surrogate biochemical markers does not necessarily translate into structural or clinical vascular benefits.

Evidence on renal output is still more limited. Halawa et al. (2023) reported improvements in UACR and eGFR in diabetic nephropathy, while Sadeghian et al. (2020) found no significant improvements in kidney function. Other RCTs also did not show consistent changes in eGFR (Pendón-Ruiz de Mier et al., 2024; Sakaguchi et al., 2019). Thus, although hypomagnesemia is observationally associated with CKD progression and higher mortality (Azem et al., 2020), the current RCT evidence is insufficient to conclude that magnesium supplementation provides a renoprotective effect.

Results on metabolic parameters also varyed. Toprak et al. (2017) and Talari et al. (2019) showed improvements in HOMA-IR, insulin, and HbA1c, while Sadeghian et al. (2020) and Halawa et al. (2023) showed no similar glycemic benefits. One possible cause is differences in early magnesium status. Studies with more positive metabolic outcomes have mostly involved patients with hypomagnesemia or obvious metabolic disorders, so correction of magnesium deficiency may provide greater benefits than supplementation in patients without deficiency.

Evidence on PTH, bone mineral density, inflammation, and oxidative stress is also limited and inconsistent (Mortazavi et al., 2013; Pendón-Ruiz de Mier et al., 2024; Talari et al., 2019; Turgut et al., 2008).

Safety aspects need to be considered because magnesium excretion ability decreases with progression of CKD (Cunningham et al., 2012). The available RCTs do not consistently show a consistent incidence of severe symptomatic hypermagnesemia, but gastrointestinal disorders, especially diarrhea, are fairly frequently reported and may lead to discontinuation of therapy (Bressendorff et al., 2023; Sakaguchi et al., 2019). Therefore, the safety findings in existing studies cannot be directly generalized to all stages of CKD, particularly CKD G4–G5 or dialysis patients. Dose selection, initial magnesium status, and monitoring of magnesium levels remain important.

These studies were limited due to the high heterogeneity in CKD stages, dialysis status, magnesium formulation and dose, duration of intervention, and type of outcomes used. Most studies had relatively small sample sizes and used surrogate outcomes, while evidence on patient-important outcomes such as progression to kidney failure, cardiovascular events, hospitalization, and mortality was very limited. Some RCTs had a good double-blind placebo-controlled design, while others were open-label, had loss of subjects during the study, or incomplete randomisation reporting (Bressendorff et al., 2017; Sakaguchi et al., 2019; Toprak et al., 2017). Multicentre RCTs with larger sample sizes, with stratification based on CKD stage and initial magnesium levels, standardized doses are needed to determine the population most likely to benefit from magnesium supplementation.

CONCLUSION

Oral magnesium supplementation in patients with chronic kidney disease (CKD) may provide benefits for certain vascular and metabolic outcomes. However, its effects on kidney function, vascular calcification, mineral and bone metabolism, and inflammatory markers remain inconsistent. Magnesium supplementation appears to be generally well tolerated, with diarrhea being the most frequently reported adverse effect. Nevertheless, the available evidence is insufficient to support routine magnesium supplementation in all patients with CKD. Further well-designed randomized controlled trials are needed to establish its long-term efficacy and safety and identify patient subgroups most likely to benefit from supplementation.

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