INPLASY PROTOCOL

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None declared.

Correcting metabolic acidosis and the nutritional status of patients with non-dialysis dependent chronic kidney disease: a systematic review and meta-analysis

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Review question / Objective: **What is the effect of correcting metabolic acidosis on different nutritional status parameters in patients with CKD.**
Information sources: **The search was conducted in MEDLINE and the Cochrane Library from inception to December 2022. Two investigators extracted the data independently. Titles and abstracts were screened based on predefined inclusion and exclusion criteria in the protocol. Similarly, full-text articles were screened using a predefined form to extract data. These included year of publication, study design and setting, population characteristics, description of intervention and control conditions, number of patients, and baseline and follow-up outcomes of interest. We requested any relevant missing information from original study authors and received the raw data from one author.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 May 2023 and was last updated on 23 May 2023 (registration number INPLASY202350085).

INTRODUCTION

Review question / Objective: **What is the effect of correcting metabolic acidosis on different nutritional status parameters in patients with CKD.**

Rationale: **Multiple CKD-related factors increase protein breakdown and decrease protein synthesis, leading to loss of muscle mass. Metabolic acidosis is one of these factors. Metabolic acidosis has unfavorable effects on the nutritional status of patients with non-dialysis dependent chronic kidney disease (CKD) including the loss of muscle mass and functionality, but the effects of correction are uncertain. Metabolic acidosis is common in patients with**

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advanced CKD, especially when glomerular filtration rate (GFR) falls below 30 mL/min per 1.73 m2. A systematic review of intervention studies, including randomized controlled trials, on the effect of correcting metabolic acidosis on nutritional status of patients with CKD is pivotal for clinical practice, but is currently lacking.

Condition being studied: Metabolic acidosis, chronic kidney disease, nutritional status.

METHODS

Search strategy: The search was conducted in MEDLINE and the Cochrane Library from inception to December 2022
Search strategy:
("metabolic acidosis" OR "renal acidosis" OR "acid-base balance") AND ("chronic kidney failure" OR CKD OR "kidney failure") AND ("nutritional status" OR "nutritional parameters" OR “malnutrition” OR “muscle” OR "muscle mass" OR "muscle function" OR "protein wast*" OR "protein metabolism" OR "lean tissue mass" OR "FFM" OR "fat free mass" OR "body weight" OR "physical function" OR "protein intake").

Participant or population: Adult patients (≥18 years of age) with non-dialysis dependent CKD.

Intervention: Any type of intervention focused on correcting metabolic acidosis.

Comparator: A control group with or without placebo.

Study designs to be included: Randomized controlled trials, clinical trial, cross-over.

Eligibility criteria: Studies were eligible for inclusion if they included adult patients (≥18 years of age) with non-dialysis dependent CKD, used any type of intervention focused on correcting metabolic acidosis compared with a control group with or without placebo, and if they reported any kind of parameter that indicated nutritional status.

Information sources: The search was conducted in MEDLINE and the Cochrane Library from inception to December 2022. Two investigators extracted the data independently. Titles and abstracts were screened based on predefined inclusion and exclusion criteria in the protocol. Similarly, full-text articles were screened using a predefined form to extract data. These included year of publication, study design and setting, population characteristics, description of intervention and control conditions, number of patients, and baseline and follow-up outcomes of interest. We requested any relevant missing information from original study authors and received the raw data from one author.

Main outcome(s): We retrieved data from 12 intervention studies including 1995 patients, with a mean age of 63.7±11.7 years, 58% male and mean estimated glomerular filtration rate of 29.8±8.8 mL/min per 1.73 m2. Eleven studies performed an intervention with oral sodium bicarbonate compared with either placebo or with standard care and one study compared veverimer, an oral HCl-binding polymer, with placebo. The mean change in serum bicarbonate was +3.6 mEq/L in the intervention group and +0.4 mEq/L in the control group. Correcting metabolic acidosis significantly improved muscle mass assessed by mid-arm muscle circumference (SMD 0.35 [95% CI 0.16-0.54], P<0.001) and functionality assessed with the sit-to-stand test (SMD -0.31 [95% CI -0.52 -0.11], P=0.003). We found no statistically significant effects on dietary protein intake, handgrip strength, serum albumin and prealbumin concentrations, and blood urea nitrogen.

Data management: IBM SPSS Statistics version 28. Review Manager 5.4.1.

Quality assessment / Risk of bias analysis: The risk of bias was separately assessed by W.V. and E.B. using the Cochrane risk of bias tools for randomized trials and non-randomized studies of interventions. The risk of bias was scored as ‘low risk’, ‘some concern’, or ‘high risk’. Discrepancies were

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discussed and resolved through mutual agreement.
Publication bias was assessed through funnel plots for all meta-analyses and Egger test for the meta-analyses with at least 5 studies included using IBM SPSS Statistics version 28.

Strategy of data synthesis: When ≥ 2 comparable studies assessed an objective parameter that indicated one of the domains of nutritional status, and when means ± standard deviations (SDs) were provided or could be calculated, we included these in subsequent meta-analyses. Random effects models were applied to obtain pooled standardized mean difference (SMD) and 95% confidence intervals (CIs), and were reported as main results. Pooled results were shown in forest plots. Data were gathered and analysed using Review Manager 5.4.1. We quantified heterogeneity using the I2 metric and used chi-squared to test its statistical significance. I2 ≥ 75% alongside a statistically significant heterogeneity was considered to indicate considerable heterogeneity. Results were considered statistically significant at P<0.05.

Subgroup analysis: Not applicable.

Sensitivity analysis: Not applicable.

Language restriction: Yes, English language.

Country(ies) involved: The Netherlands.

Keywords: Nutritional Status, Muscle, Physical function, Kidney disease, Metabolic acidosis.

Dissemination plans: Manuscript under review.

Contributions of each author:
Author 1 - Wesley Visser - Designed research; Conducted research; Provided essential reagents; Analyzed data / performed statistical analysis. Wrote paper. All authors have read and approved the final manuscript.

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