Supporting muscle maintenance in patients undergoing hemodialysis

Impact

The goal of clinical research is to establish new facts, reach new conclusions, and improve the quality of clinical care for patients. In this paragraph, we will address how the work described in this thesis can improve clinical care for patients on chronic hemodialysis treatment.

Results and relevance of this thesis

Chronic kidney disease (CKD) is currently a public health problem with a global prevalence of 10% [1]. Yet, it is expected that its prevalence will further increase over the upcoming decades since risk factors for the development and progression of CKD, such as diabetes mellitus and hypertension, are becoming increasingly prevalent [1-3]. Consequently, the number of patients with the final stage of CKD, coined end-stage renal disease, who will require renal replacement therapy (dialysis) is also expected to increase. Hemodialysis is globally the most applied chronic renal replacement therapy when kidney transplantation is not (yet) possible. Over the past decades, the life expectancy of patients on hemodialysis and, as such, the period that they undergo this treatment, has increased substantially due to advances in hemodialysis techniques and management of comorbidities [4]. However, poor nutritional status has proven to be a persistent problem in patients on chronic hemodialysis treatment [5, 6]. A recent meta-analysis reported that protein-energy wasting (a state of malnutrition with insufficient dietary intake) is present in 28-54% of patients on dialysis treatment [7]. In addition, patients undergoing hemodialysis are generally frail and/or have severely reduced levels of physical functioning [8, 9]. Protein energy wasting, poor nutritional status, and frailty are closely associated with a reduced quality of life, increased morbidity, greater healthcare costs due to more hospitalizations, and higher mortality rates in patients on chronic hemodialysis treatment [10-13]. Therefore, it is essential to understand why poor nutritional status is so highly prevalent among this population and to develop effective interventions that can preserve muscle mass and function.

In this thesis, we report that a substantial amount of amino acids is removed from the body during hemodialysis, which has been shown to stimulate skeletal muscle protein breakdown [14]. For healthcare professionals involved in the clinical care for patients with CKD, it is relevant to understand that hemodialysis is a catabolic procedure and that anabolic interventions to counterbalance its effects should be part of their treatment plan. Interventions during hemodialysis (intradialytic) are time-efficient for patients and easy to supervise for healthcare professionals as patients are already present in the healthcare center. We showed that ample protein ingestion during hemodialysis can compensate for the removal of amino acids from the circulation. Furthermore, we showed that exercise performed prior to protein ingestion does not further enhance amino acid removal.

Previously, it had been suggested that intradialytic protein ingestion could reduce uremic toxin removal due to splanchnic blood pooling during hemodialysis [15]. In this thesis, we quantified uremic toxin removal throughout hemodialysis with protein ingestion for the first time and showed that protein feeding with or without prior exercise during hemodialysis did not compromise uremic toxin removal and actually increased urea removal. Therefore, intradialytic exercise and protein ingestion can be implemented to support muscle maintenance in this vulnerable population without compromising uremic toxin removal during hemodialysis.

Furthermore, we assessed the impact of co-ingestion of branched-chain ketoacids with protein during hemodialysis as a strategy to augment the anabolic properties of dietary protein without providing additional phosphate. Our results indicate that co-ingestion of ketoacids with protein during hemodialysis significantly reduces amino acid oxidation when compared to protein ingestion only, thereby likely improving the net protein balance. Therefore, adding ketoacids to protein supplementation during hemodialysis may represent an alternative strategy for additional protein ingestion to counteract the catabolic effects of hemodialysis.

Stakeholders of this thesis

This thesis contributes to the scientific field of clinical nutrition and nephrology, as it provides insight in the impact of nutritional and physical activity interventions during hemodialysis. Furthermore, the scientific community may benefit from research methods that we applied during hemodialysis for the first time, such as sip feeding of test beverages containing a stable isotope amino acid tracer and quantifying the removal of protein-derived amino acids in the spent dialysate. This thesis will be of use for nephrologists and nurses working with kidney patients through providing a better understanding why patients on chronic hemodialysis treatment generally have poor nutritional status. In addition, it allows them to provide evidence-based recommendations (i.e. to supplement protein ingestion during hemodialysis and to stimulate physical activity) to patients. To implement nutritional and physical activity interventions in the clinical care for patients, involvement of dietitians and exercise professionals will be crucial. These healthcare professionals can also use the results of this thesis to provide evidence-based recommendations to patients on hemodialysis. Furthermore, the presented results are relevant to health care policy makers. Our work demonstrates the importance of patient-specific nutritional and physical activity interventions to support muscle maintenance patients with end-stage renal disease. In addition, such interventions to prevent frailty could reduce the high morbidity and hospitalization rates in this population and, as such, lower healthcare costs. At present, lifestyle interventions to support muscle maintenance are currently not incorporated in standard clinical guidelines for patients with CKD. For patients with end-stage renal disease, it is important to know and understand the side-effects of their hemodialysis treatment.

The results from this thesis provide them with tools to maintain, or even improve, their physical functioning and prevent frailty. It is important that patients are aware of the importance of proper dietary (protein) intake and sufficient physical activity to maintain their nutritional status, physical function, and general health. This will allow them to maintain functional independence and experience less adverse outcomes of their disease and its treatment and, as such, improve their quality of life.

The results presented have been communicated towards stakeholders through various forums. The research work described in this thesis has been established through a continuous collaboration of biomedical researchers, nephrologists, dietitians, exercise professionals, and patients. Five chapters of this thesis are openly accessible as published articles in peer-reviewed scientific journals and this thesis will be distributed to interested shareholders. In addition, we have presented our findings at (inter)national scientific conferences, workshops for healthcare professionals, and patient meetings. To simplify the translation of our results to clinical practice, we collaborated with seven other hospitals and the Knowledge Centre for Sport & Physical Activity to create a fact sheet about implementing physical activity interventions for patients on hemodialysis. Parts of this thesis were also summarized in layman language and published in a journal for dialysis nurses and the magazine of the Maastricht Organization for Patients with Kidney Disease (NvM).

General impact and future goals

Based on the results of the presented findings regarding protein ingestion during hemodialysis, the dialysis department of the Maastricht University Medical Center+ has changed their nutritional strategy as of February 2021 and now offers protein-rich foods to patients during hemodialysis. Furthermore, the findings regarding intradialytic physical activity were used to start a Dutch Kidney Foundation-funded project that resulted in the implementation of intradialytic cycling into routine care at the dialysis department of the Maastricht University Medical Center+. Thereafter, the Maastricht Organization for Patients with Kidney Disease (NvM) requested to expand this program to the dialysis department in Valkenburg. As a result, patients now have the opportunity to perform physical activity during their hemodialysis treatments.

The chapters of this thesis provide proof-of-principle evidence regarding nutritional and physical activity interventions during hemodialysis to support muscle maintenance. However, future research to establish evidence-based lifestyle interventions for all CKD stages is still required. To optimize the anabolic potential of intradialytic protein ingestion, the impact of protein dose, timing, and type should be further assessed. In addition, long-term effects of the nutritional and physical activity interventions described in this thesis remain to be evaluated. Lifestyle interventions to support muscle maintenance should preferably be already implemented prior to initiation of chronic hemodialysis treatment. In an earlier stage of CKD, it will be less complicated for patients to adopt lifestyle changes, which also may be more effective to increase muscle mass and function due to lower disease burden. Such a pre-habilitation strategy is not yet part of routine clinical care for patients with advanced CKD as evidence for its efficacy remains to be established. However, this population is underrepresented in product-development by companies and scientific research focusing on muscle maintenance, especially when compared to the work conducted in hemodialysis patients. Future studies should aim to provide insight in the etiology of accelerated muscle loss and the efficacy of lifestyle interventions to support muscle maintenance in patients at different stages of CKD.

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