A SYSTEMATIC REVIEW OF KNOWN INHIBITORS OF VASCULAR CALCIFICATION IN CHRONIC KIDNEY DISEASE

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Introduction

Approximately 13% of the population suffers from chronic kidney disease (CKD) globally. Furthermore, about half of the patients with CKD stages 4-5 encounter and eventually die from cardiovascular disease (CVD) [1]. The overwhelming part of the treatment for CKD stage 5 (end-stage renal disease - ESRD) patients for replacing kidney function is hemodialysis. The global number of individuals receiving dialysis treatment reached 2.7 million in 2016 and is estimated to reach 5.4 million by the year 2030 [2]. The occurrence of vascular calcification (VC), deposition of calcium salts in the form of hydroxyapatite in the vascular wall, increases with age in the general population, but is highly frequent and markedly accelerated in patients with CKD [3]. KDIGO (Kidney Disease: Improving Global Outcomes) CKD guidelines suggest considering the patients with advanced CKD (stages 3–5) and VC at the highest CVD risk [4]. More prevalent VC in CKD is believed to result from a disturbed balance between inhibitors and inducers of calcification. During dialysis therapy, uremic toxins are filtered out from the blood regularly. However, during the procedure, all the substances fitting the cut-off size of the dialysis membranes are transported to spent dialysate, among them many beneficial substances (including the inhibitors of vascular calcification). Washout of proteins e.g. albumin (MW 66 kDa) is considered to be a disadvantage of the more effective dialysis [5]. The cut-off value for the older type of membranes is about 3 000 Da, in the case of newer membranes it is around 15 000 Da and in super high-flux dialysis, it can reach 65 000 Da [6]. It is likely that many of VC inhibitors are removed during dialysis therapy, however it is not monitored. We performed a systematic review of literature to collect information about the substances with proved inhibitory effect on VC as a first step towards monitoring the inhibitors removal to make modifications or interventions to improve the inducers-inhibitors balance and thereby help improve these patients' quality of life.

Methods

An advanced search in PubMed and Web of Science was performed to identify existing research in August, 2023, and March, 2024. The systematic review was registered in the PROSPERO database. The search strategy is given in figure 1. Altogether, 177 papers were added to the extensive analysis. Vascular calcification inhibitors were divided in different categories and tables.

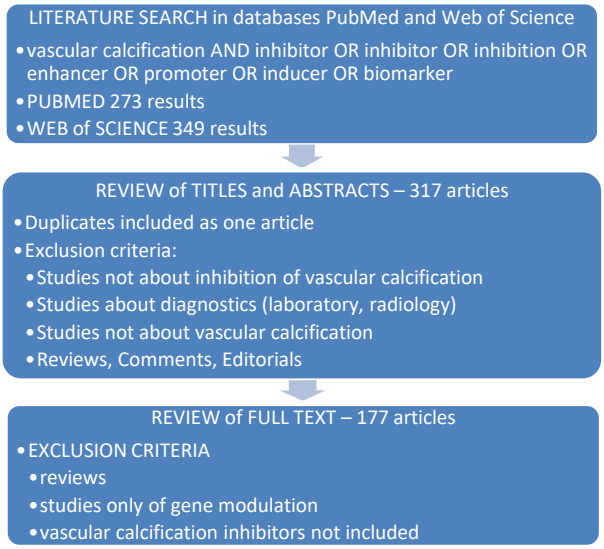

Figure 1: The search strategy.

Results

Endogenous inhibitors in patients with CKD are fetuin-A, matrix Gla protein, osteoprotegerin, osteopontin, vitamin D, sclerostin, FGF23, magnesium and klotho. Additionally, substances that have shown potential in further research, growth factors, medications, and plant-origin inhibitors were systematized.

Discussion

Measuring the levels of inhibitors that are most probably dialyzed or estimating how serum levels of VC inhibitors during hemodialysis are in relationship with removed uremic toxins would expand further knowledge towards patient-tailored treatment.

References

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