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Inconsistent efficacy of low protein diet for diabetic nephropathy

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Abstract

Angiotensin-Converting Enzyme inhibitors (ACEIs) and Angiotensin Receptor Blockers (ARBs) initially used to treat hypertension. They can use to treat diabetes, Chronic Renal Insufficiency (CRI)(RI), Congestive Heart Failure (CHF)(HF), and myocardial infarction (MI). They recorded to have some Adverse Effects (AEs) such as Acute Renal Failure (ARF) due to the lack of appropriate timelines monitoring scheme. The following Systematic Review (SR) will focus on the AEs of the administration of ACEIs/ARBs without appropriate timelines monitoring on adult patients as the specific population under study as per the prevailing literature provides. The data sources include a search for English language literature in the Cochrane database (2015-2019), MEDLINE, and the American Heart Association Journal Database (AHA). The search terms in the above databases included ACEIs /ARBs, adults, clinical trials, laboratory trials, random trails, humans, and timeline monitoring. The study selection included literature with random control trials of patients with the above diseases and how the appropriate monitoring of ACEIs/ARBs had any effects on the angiotensin system in adults. The data extraction is based on eight sources while keeping in mind the data fields used and the quality of the studies conducted. The data synthesis criteria observed a pool of patients larger than 50,000 included in each study that was put under the administration of ACEIs/ARBs for a year while noting the appropriate timelines monitoring of ACEIs/ARBs on the potassium and creatinine and how they affect the patients if they are not properly monitored. The SR of these laboratory studies confirms that under appropriate timelines monitoring of the administration of ACEIs/ARBs, apart from treating the above diseases, have very limited AEs on the renin-angiotensin-aldosterone system of the patients under observation.

Keywords: Diabetic nephropathy•low protein diet • Diabetes Practice Guidelines 2019 (JDS2019) • 2019 dietary consensus report (ADA2019) • Geriatric Nutritional Risk Index (GNRI)

Introduction

Diabetes has been recently increasing worldwide, and the discussion concerning diabetic nephropathy has been continued. The adequate diet has been protein restriction for long [1,2]. However, several research of meta-analyses of Randomized Controlled Trials (RCTs) have not shown the consistent efficacy of low protein diet [3,4]. Then, there have been controversies about protein restriction [5].

Regarding patients with diabetic nephropathy, hemodialysis and Chronic Kidney Disease (CKD), the nutritional status would be important. It can be evaluated by the GNRI, which is useful for various pathophysiology [6]. It can assess the relationship among GNRI, Dialysis Malnutrition Score (DMS) and Subjective Global Assessment (SGA) [7].

American Diabetes Association (ADA) presented nutrition recommendations (ADA2013), in which it denied the efficacy of protein restriction for nephropathy [8]. It was not recommended that those patients limit protein intake less than the general population. The reason included no changes of glycemic control, cardiovascular disease risk, or reduced Glomerular Filtration Rate (GFR) [8]. There were two studies of meta-analyses resulting no clear beneficial effects on renal parameters from low-protein diets [9,10]. This dietary principle was also followed in the 2019 dietary consensus report (ADA2019) [11].

On the other hand, CKD Clinical Guidelines 2018 by Japan Diabetes Association (JDA) have partly recommended low protein diet for diabetic nephropathy and CKD. The recommended grade for CKD2018 was B1. After that, there has been some changes in the Diabetes Practice Guidelines 2019 (JDS2019) [12]. It included that i) protein restriction may be effective, but ii) clinical evidence is not sufficient, and iii) further evaluation would be necessary for the degree of protein restriction, the starting time to restrict and nutritional safety. Consequently, there are currently different managements of protein restriction for nephropathy and CKD in Japan and United States.

Recently, an impressive paper was reported [13]. The study was undertaken for 449 T2DM with nephropathy, and the relationship among Dietary Protein Intake (DPI), renal outcome, and nutritional status was studied. The primary and secondary endpoints were set as initiation of Renal Replacement Therapy (RRT) and mortality. Malnutrition was defined as the GNRI of ≤ 98. As a result, decreased DPI was shown with lower incidence of RRT with Hazard Ratio (HR) of 0.81. Then, this study suggested beneficial efficacy of a low-protein diet for nephropathy [13].

In relation to this report, there was a previous paper that a low-protein diet had potentially beneficial renal effects for diabetic nephropathy with the method of randomized crossover trial [14]. When investigating the effects of a low-protein diet, the study protocol may be rather difficult for adhering to the therapy [3]. It is indeed that RCTs would be ideal, but other method such as observational study or randomized crossover trial may be actually adequate for successful continuation and follow up the case and multiple biomarkers. Some report had measured 24 h urinary nitrogen excretion as the basic assessment method [15].

Furthermore, nutritional status such as total protein and albumin is important. Evaluation of the Geriatric GNRI is also required, and GNRI is calculated as (14.89 x serum albumin (g/dL)) + (41.7 x present body weight (kg)/standard body weight (kg)) [16]. Undernutrition was diagnosed at the borderline of a GNRI at less than 98 [13]. In the undernourished population, the adjusted HR of death before starting RRT for every 0.1 lower protein intake per kg of standard body weight was 2.26 [15].

As mentioned above, it is necessary to evaluate what kind of methods and biomarkers would be selected concerning the study of a low-protein diet for diabetic nephropathy.

Although there were reports of supporting the significance of a low-protein diet [13,14], ADA 2013/2019 showed no recommendation of limiting protein for diabetic nephropathy. In contrast, JDA 2013/2016 and JDA-CKD guideline 2018 showed partly recommendation of limiting protein. CKD 2018 presented recommendation in the level of grade B1.

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An important data in these documents is the rate of eGFR decline per year. In T1DM, it was 16.9--25.0/min/1.73 m2 per year. Recently, the rate of eGFR reduction in T1DM and T2DM with stage 3 nephropathy was around 3.0-3.3 mL/min/1.73 m2 [17]. In contrast, no relationship was observed between protein intake and the decrease rate of eGFR [15]. A low protein diet would be effective, when the compliance of the research is good [3]. The inconsistency of efficacy of a low protein diet was found in T2DM [18]. Long-term study of very low-protein diet in Modification of Diet in Renal Disease (MDRD) Study revealed that the diet did not delay progression to kidney failure [19].

On the other hand, the author and colleagues have continued clinical research for T2DM, associated with low carbohydrate diet [20,21]. We have also continued reports concerning hemodialysis (HD) patients with medical biomarkers [22,23].

Conclusion

Finally, the implication of protein restriction for nephropathy was described. There are various results concerning clinical efficacy of protein limitation. However, it seems a better option to follow protein restriction about 0.3-0.6 g/kg for patients with CKD. For clinical research concerning nephropathy and adequate diet, accumulating much data would be necessary in the future.

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