Nephrol Dial Transplant (2020) 1–4
doi: 10.1093/ndt/gfaa268

ndt
Nephrology Dialysis Transplantation

The unsolved challenge of implementing sustained reductions of sodium intake in patients with chronic kidney disease

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According to current nutritional recommendations, patients with chronic kidney disease (CKD) should restrict their salt intake and eat <90–100 mmol sodium (Na) per day [5–6 g sodium chloride (NaCl)/day]. The scientific basis of this recommendation is the strong evidence of a beneficial effect of reducing salt intake on two major targets of CKD management, namely blood pressure (BP) and proteinuria. Indeed, when compared with patients with a high urinary Na excretion, CKD patients with a lower Na excretion (≤100 mmol/day) had better BP control and lower proteinuria [1, 2]. Experimentally there is also increasing evidence that a high Na intake may have a detrimental effect on renal function, independent of BP, through direct effects on inflammatory processes and immune balance [3, 4]. However, evidence that being on a low salt diet reduces mortality and slows the progression of renal diseases in CKD is still low, despite an increasing number of retrospective and prospective observational studies suggesting a favourable impact of low Na intake on mortality and on renal function decline as reviewed in a recent editorial [5].

Beyond the scientific controversy on the relevance of reducing Na intake in CKD patients, some experts have put forward practical worries justifying their reluctance to prescribe such a Na reduction. Their main concerns lie in the feasibility and ability to reduce Na intake by almost 40% to achieve recommended targets, the sustainability of this reduction and the lack of simple methods enabling physicians and patients to monitor Na intake. Indeed, in the absence of a 'Na feedback', it appears difficult to motivate patients, to maintain good adherence to the diet and to promote self-management.

In addition to these main limiting factors, several other barriers for patients' commitment to a low Na diet have been identified (Table 1) [6–8]. These include cultural aspects and beliefs and the high Na content of food products, the lack of Na feedback and of goal setting and discussing strategies for Na reduction and finally the absence of CKD-related symptoms [7]. In a Dutch survey, these latter factors were associated with age, level of education, number of comorbidities, perceived autonomy support, depressive symptoms and self-efficacy, but not with gender or kidney function [7].

In this issue of *Nephrology Dialysis Transplantation*, Panuccio *et al.* [9] present the results of a 6-month randomized multicentre study testing the effect of self-measurement of urinary chloride as a surrogate of Na intake compared with standard care on two primary outcome measures: adherence to a low Na diet (<100 mmol/day) and 24-h ambulatory BP. Several Italian nephrology centres contributed to this study and randomized 149 CKD patients with an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2; 138 patients completed the study. All patients received dietary instructions by a dietician and/or their nephrologist and dedicated documentation. The originality of this study was the use of chloride-reactive strips by patients of the active group in order to monitor their salt intake. This method had a 75.5% sensitivity and 82.6% specificity to adequately classify patients having a urinary Na >100 mmol/24 h. Patients in the active group used the strip once a week during the first month and every 2 weeks thereafter. They had to repeat the test if Na intake was >100 mmol/24 h. If a high value was confirmed a second time, then patients had to contact their centre in order to reinforce their dietary instructions.

The adherence to the salt monitoring was very good, with >80% of the strips used as prescribed, but the impact of the Na feedback on salt excretion was modest, with a mean decrease in Na excretion at 3 and 6 months of 16 mmol Na/day in the active group. The difference between the control and the intervention group (~35 mmol Na/day) was essentially due to a worsening of adherence to the Na restriction in the control group rather than to a major improvement in the active group. Indeed, the percentage of patients with urinary Na excretion <100 mmol/day was 20% at baseline and 12% at 6 months in the control group. In the active group, the percentage was already higher at baseline (28%) and at 6 months increased slightly to 30%. At 6 months there was no difference in 24-h ambulatory BP, eGFR and proteinuria between groups.

The results of this randomized prospective study are disappointing, as the lack of feedback on Na intake was one of the important limiting barriers identified by patients [7]. The use of a self-measurement technique providing patients

Table 1. Perceived barriers to the implementation of an effective and sustained reduction of Na intake in CKD patients (adapted from Burnier [5])

Considered as important by patients:
High Na content in products
Lack of Na feedback
Absence of personal goals
Absence of strategies to reduce Na
Experiencing no CKD-related symptoms
Considered as moderately important by patients:
Healthcare professionals are not patient-centred enough
Healthcare professionals have insufficient time to support me
Insufficient knowledge on how to reduce Na intake
Insufficient knowledge about Na content in products
Low Na food tastes bad
A low Na diet is unsocial
A low Na diet is time and energy consuming
Low Na products are expensive
Considered as somewhat important by patients:
Belief that reducing Na is not beneficial
Difficulty to refuse food when eating out
Other interfering factors:
Age
Level of education
Number of comorbidities
Autonomy support
Depressive symptoms
Self-efficacy

regular feedback on their Na excretion was expected to have a greater impact on adherence to the low salt diet. Apparently this was not the case, as the percentage of patients achieving the target Na excretion increased only marginally in the active group and remained far below the expected target. Unfortunately the low percentages of Italian CKD patients following nutritional recommendations on salt and achieving a Na excretion <100 mmol/day are in agreement with those published in other countries, such as the Netherlands (17%) [10] and Turkey (14.7%) [11]. In the UK, 17% of men and 55% of women with CKD Stage 3 had a 24-h urinary Na excretion <100 mmol/day [12].

Once again, the results of Panuccio *et al.*'s study [9] emphasize the major difficulty to implement a sustained and effective reduction in salt intake in patients with or without CKD. In Europe, the mean salt intake of the general population ranges between 9 and 13 g/day in men and 7–11 g/day in women, and these figures are similar in CKD patients. Thus, to meet the recommended target, dietary interventions should decrease salt intake by at least 3–5 g/day. Decreases of this order of magnitude have been obtained in short-term studies lasting only a couple of weeks [1], but so far evidence that such substantial reductions of Na intake can be maintained beyond 3–6 months in CKD patients is still lacking. In Panuccio *et al.*'s study [9], Na intake decreased by ~1–1.5 g/day at 6 months, but baseline Na intake was already lower than in the general Italian population (8.5 g NaCl/day), probably reflecting the impact of nephrologists' interventions before patients' enrolment. Dutch investigators reported similar reductions in Na intake (1–2 g NaCl/day) in their long-term studies, but with the use of greater patient support [13, 14]. In hypertensive patients, a reduction of 38 mmol Na/day was obtained at 3 years, but baseline Na excretion was relatively high (187 mmol/24 h) [15]. In the Multifactorial Approach and Superior Treatment Efficacy in Renal Patients with the Aid of Nurse Practitioners study, no change in urinary Na excretion was observed after 4.6 years of follow-up despite multiple nurse interventions on risk factors including Na intake [16]. In a more recent study from Korea, implementation of an intensive low salt diet education programme in CKD patients also failed to produce a marked reduction in salt intake after 36 months of follow-up [17]. As previously described, the favourable changes observed during the first weeks vanished thereafter. These results are challenging and one wonders whether a sustained reduction in Na intake is feasible and if the recommendation is truly applicable in clinical practice.

The question arises as to what nephrologists should do to increase their chances of long-term success when prescribing a reduction of Na intake to their patients? The involvement of dieticians and the use of educational and motivating documents are definitively needed, but they do not appear to be sufficient to maintain improvements over years. In addition, they are not always applicable outside reference nephrology centres. An alternative would be to promote a high potassium (K) intake, which has been shown to counteract the effects of a high Na intake, but nephrologists are rather prudent towards this approach as renal function declines [18]. Regular monitoring of urinary Na excretion, or of the Na:K or Cl:K ratio, should help patient adherence with dietary prescriptions by providing a regular feedback. However, the key issue is the choice of the monitoring system. Repeated 24-h urine collections are cumbersome and not appreciated by patients. Morning urine samples are easier to obtain, but calculation of Na intake based on spot urine has been criticized in response to the use of formulas extrapolating Na intake. Moreover, this approach does not enable self-assessment, as Na measurement has to be done in a laboratory and patients cannot do calculations themselves. The use of reactive urinary strips appears to be the easiest and cheapest method to monitor urinary Na excretion on a regular basis. It is convenient for the patient and hence favours self-assessment. The initial reading devices were relatively complex and not always very accurate, but they were found helpful to reduce Na intake [19, 20]. The urinary chloride monitoring system, as used by Panuccio *et al.* [9], correlated well with urinary Na excretion but poorly with the previous day's intake of dietary Na as measured by the food record [19]. Interestingly, as reported recently for 24-h urine collections [21], it was estimated that five overnight urine samples would be required to estimate food record Na to within ±25 mmol in individuals with relatively stable diets. This observation confirms an early finding that 24-h urinary Na excretion has a significant rhythmicity even when subjects are on a fixed controlled Na intake for several weeks [22]. Nevertheless, Panuccio *et al.* [9] should be commended for having designed this study and this approach deserves further improvements and validation. In this respect, the rapid development of the 'lab on chip technology' might contribute to refining the system [23].

Finally, can digital developments help CKD patients reduce their salt intake in a long-lasting way? Today, many digital

health tools are designed to support healthcare professionals as well as patients, offering a wide range of functions. In addition to facilitating the patient–physician relationship, these applications (apps) can offer easy-to-use educational and monitoring tools to inform patients and physicians, with a final aim of ensuring better adherence to medical prescriptions. This strategy should be particularly suitable for the management of chronic conditions such as CKD. In the context of Na recommendations, many smartphone applications are available, essentially focused upstream of the salt consumption by helping patients to make the best choice of low Na–containing foods and hence improving their awareness of dietary salt consumption [24–26]. For example, in the SaltSwitch randomized controlled trial conducted in New Zealand, patients used an app to scan the barcode of packaged foods. After scanning, they receive an immediate traffic light nutrition label on the screen, along with suggestions for lower salt alternatives [25]. This application was tested in a 4-week study and its use resulted in a reduction of salt purchases of 0.7 g/day/person. Whether this approach would lead to a significant and sustained reduction of salt intake is yet unknown. In another recent study [26], investigators assessed the effect of a just-in-time adaptive mobile app intervention, LowSalt4Life, on reducing Na intake in adults with hypertension. In this 8-week, single-centre, randomized study, the use of the app induced a reduction of 24-h urinary Na excretion of ∼630 mg/day. Taken together, these data suggest that digital health tools have some potential benefits to help patients reduce their salt intake. However, this strategy remains poorly explored and there is a need for additional clinical investigations to demonstrate its efficacy as a long-term tool for patients.

In conclusion, obtaining a significant and sustained reduction of salt intake in CKD patients is a very difficult (and quite discouraging) task. An effective way to reduce salt consumption would be to lower the Na content of processed foods, which represent 75% of salt sources in western civilization. One could also make healthy food more affordable than unhealthy products. Unfortunately this is in the hands of the industry, which is usually unwilling to do so, thus nephrology societies should take a strong stand against the industry's refusal to lower Na content in processed foods. Meanwhile, we must continue our efforts to convince patients and their nephrologists that reducing Na intake is beneficial for their health and encourage them with the hope that new efficient tools will become available in the near future.

CONFLICT OF INTEREST STATEMENT

None declared.

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Received: 6.9.2020; Editorial decision: 28.9.2020