Dietary Salt Restriction and MDP for Cardiometabolic Health

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The dietary restriction of salt intake and the adhesion to Mediterranean dietary pattern (MDP) are among the most recommended lifestyle modifications for the prevention of cardiovascular diseases. A large amount of evidence supports these recommendations. Likewise, findings from observational and clinical studies suggest a causal role of excess salt intake in blood pressure increase, cardiovascular organ damage, and the incidence of cardiovascular diseases. In this context, it is also conceivable that the beneficial effects of these two dietary patterns overlap because Mediterranean dietary patterns are typically characterized by a large consumption of plant-based foods with low sodium content. However, there is little data on this issue, and heterogeneous results are available on the relationship between adherence to salt restriction and to Mediterranean dietary patterns.

Keywords: salt ; sodium ; Mediterranean dietary pattern ; cardiovascular risk ; blood pressure

1. Overview

Non-communicable diseases (NCDs) and, in particular, cardiovascular diseases (CVD) are the leading causes of death globally [1], and their reduction is a health priority [2]. In turn, high blood pressure (BP) and unhealthy diets are major causes of CVD [1][2].

In this context, the role of dietary salt (i.e., sodium chloride) has been extensively studied in relation to its effects on CVD. In particular, a large body of evidence supports a causal role of excess salt intake in the increase in BP with age, in the development of hypertension [3], and, eventually, in the incidence of CVD [3][4]. Epidemiological evidence regarding the strong relationship between salt intake, BP, and hypertension was provided over 30 years ago [5], and was confirmed thereafter by numerous studies [6][7]. In particular, recent results of the CARDIA study indicated that in a sample of initially normotensive young participants (mean age: 30 years), an average salt consumption of 14 g per day was associated with a 53% higher risk of hypertension than with a consumption of approximately 3 g per day over a 25-year follow-up period [8].

Excess salt intake has detrimental effects on endothelial function, contributes to the salt sensitivity of BP, activates the sympathetic nervous system, and is involved in the inflammatory response, modulating innate and adaptive immunity [9] [10]. There is experimental evidence of structural and functional alterations induced by high-salt regimens in the arterial wall above and beyond the effect of high BP [10].

The results of intervention studies are in agreement with observational and experimental data. For instance, robust evidence regarding the effect of changes of dietary salt intake on BP was provided by a seminal study, which showed a significant increment of BP after switching a group of chimpanzees from their habitual low-salt diet to a high-salt diet for six months, and then a switch of BP back to normal when they returned to their usual low-salt regimen [11]. Thereafter, several controlled clinical trials examining the effect of dietary salt intake on BP have been conducted in humans, and their results have been the object of meta-analyses showing a favorable effect of salt intake reduction on BP in different settings (e.g., participants with and without hypertension, diabetic patients, and patients with renal disorders) [12][13][14][15] [16][17].

In addition to the effects on BP, many studies have indicated that elevated salt intake may promote target organ damage and, conversely, several clinical trials have shown that salt restriction leads to an improvement in arterial stiffness [18], urinary albumin excretion [19], central blood pressure [18], and left ventricular mass [20][21][22].

Given the well-proven relationship between high BP and coronary, cerebrovascular, and renal outcomes, it is expected that salt intake in turn affects the incidence of cardiovascular disorders. Indeed, many longitudinal studies have detected a

direct association between salt intake and CVD, and in particular with stroke risk [3][23][24].

Recently, the Mediterranean diet has been recognized as one of the dietary models more in keeping with the model of planetary diet conceived by the EAT–Lancet Commission as a diet for the Anthropocene [25]. The potential beneficial effects of a high level of adhesion to the Mediterranean dietary pattern (MDP) on CVD were hypothesized as early as in the 1950s [26]. That observation has inspired countless studies in which a higher degree of adhesion to the MDP was associated with a reduced risk of all-cause mortality and CVD [27][28]. In this regard, a recent meta-analysis of the effects of seven popular structured dietary patterns has shown that only the MDP substantially reduces all-cause mortality, non-fatal myocardial infarction, and stroke rates [28]. The benefit toward the risk of stroke was also reported by a previous meta-analysis showing that a higher adhesion to the MDP was associated with a lower risk of stroke in both Mediterranean and non-Mediterranean populations, and for both the ischemic and hemorrhagic types of stroke [29]. Likewise, yet another meta-analysis of 16 prospective cohort studies including only women detected a significant association between a higher adherence to the MDP and a lower incidence of total cardiovascular and coronary events, as well as total mortality, and a weaker association between MDP adhesion and the risk of stroke [30]. A very recent observational study, including approximately 2000 middle-aged male and female Greek participants, showed that those who sustained a high degree of adhesion to the MDP over the years had the lowest 20-year CVD risk [31]. In agreement with these results, other prospective cohort studies provided evidence that high adherence to the MDP improves survival in people with a history of CVD [32]. In keeping with the evidence on the relationship between MDP and the risk of cardiovascular events, several studies have also provided evidence of the association between the MDP and numerous cardiovascular risk factors. Thus, adhesion to the MDP was associated with beneficial changes in body weight, waist circumference, BP, insulin resistance, lipid profile, and flow-mediated arteriolar dilation [33]. The favorable effect of the MDP on BP was also found by two meta-analyses that detected a lower average systolic BP in participants with a higher degree of adhesion to the MDP compared to the lower-adhesion group [34][35]. In line with these results are those of another meta-analysis including 58 studies with finding of significantly lower values of waist circumference and serum triglyceride, and higher values of HDL-cholesterol in the high-adhesion MDP individuals [36]. Finally, based on 16 prospective studies, a systematic review found that the greatest adhesion to the MDP was significantly associated with a reduced risk of type 2 diabetes through a non-linear relationship [37].

2. Epidemiological Evidence

The first strong epidemiological evidence of the direct association between salt intake and BP was provided by the results of the INTERSALT study, showing that the higher the habitual salt intake, the higher the average BP increase with age and the prevalence of hypertension in different populations around the world [5]. The detrimental effect of salt intake on cardiovascular risk was documented by several meta-analyses, in which an unequivocal association was detected with CVD, and in particular with stroke risk. The first of such meta-analyses, including prospective studies of samples of general populations, indicated a direct and significant association between higher salt intake and incidence of CVD [4]. The analysis, including 170,000 participants and more than 11,000 vascular events, showed a 23% greater risk of stroke and a 17% greater risk of total cardiovascular events for an average difference in salt intake of 5 g of salt per day. Further meta-analyses substantially confirmed these trends, despite some differences in the number of studies included in the analyses [3][23].

By the same token, looking at the epidemiological evidence on MDP, a number of prospective studies were carried out on the association between adhesion to the MDP and health outcomes. A recent systematic review has suggested that a high degree of adhesion to the MDP was associated with lower mortality rates in samples of general populations and in patients with previous CVD [27]. In addition, a separate evaluation of six prospective studies indicated that, following MDP, the risk of CVD (i.e., coronary artery disease, stroke, and cardiovascular mortality) decreased; in particular, the reduction in risk ranged from a hazard ratio of 0.44 to 0.71. The association was found when the adhesion to the MDP was expressed both as a continuous and as a dichotomous variable.

Despite this consolidated individual role of low salt intake and MDP adherence in CVD, and the potential synergistic effect of the combination of the two dietary measures, few investigations explored this issue. Nevertheless, a few studies tried to assess the relationship between adhesion to the MDP and of the salt content of the diet in this context.

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