Considerations for the Assessment of Salt Intake by Urinary Sodium Excretion in Hypertensive Patients

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Do and colleagues[1] have evaluated the effectiveness of the Eat Less Salt intervention in a Vietnamese population, collecting spot urine samples for estimation of 24-hour sodium excretion before and after informed reduction of sodium intake.

It is well-known that hypertension has important implications both on the expense of health and on the future risk of illness. A major factor involved in hypertension is salt intake associated with genetic predisposing factors. Increased dietary sodium intake is a modifiable risk factor for cardiovascular disease. The monitoring of population sodium intake is a key part of any salt reduction intervention. However, the extent and methods used for assessment of sodium intake in Southeast Asia is currently unclear.[2] Dietary data suggest that sodium intake in most Southeast Asian countries exceeded the World Health Organization recommendation of 2 g/d,[3] and even healthy patients have frequently lower renin values compared with those in western countries, as a result of different sodium intake. The greatest proportion of dietary sodium comes from salt added in home cooking, soy sauce, and commercially processed foods.[4] The results of the study by Do and colleagues[1] show a correlation between reduced sodium intake and sodium excretion using spot urine samples. Moreover, they demonstrated that a community-based intervention on salt reduction behavior can reduce the risk related to high sodium intake.

Collection of 24-hour urine is widely considered the best method for assessment of sodium intake.[5] It is known that about 90% of ingested sodium is excreted in the urine in 24 hours. The remaining 10% is excreted through sweat and feces, which could play an important role in situations of hot climates, increased physical activity, diarrhea, and vomiting. Assessment of completeness of 24-hour urine collection is more precise measuring urinary creatinine or administering para-aminobenzoic acid.[6] This latter method may be challenging for patients because it requires administration several times during the 24-hour collection.

Recently, many authors have tried to demonstrate that 24-hour sodium excretion can be estimated using spot urine samples, which are easily collected and cannot account for inaccuracy of collection and losses.[7] Sodium concentration in spot urine represents the sodium intake in the short period preceding the collection; for that reason, the sodium excretion can vary during the day depending on sodium intake. Spot urine samples, however, have increased individual variability depending not only on sodium ingestion in the previous hours but also water ingestion and regulation of hormonal and nonhormonal factors involved in sodium concentration. The determination should be standardized by collecting urine samples at the same period of the day to compare the excretion in the same patient.

The estimation of sodium intake from measurement of sodium excretion is feasible in the general population, in particular in studies aimed to investigate a sample of patients before and after a dietetic intervention, considering that all the factors involved in the sodium regulation do not change over a short period of time.

In hypertensive patients, the estimation of sodium intake from spot urine could be misleading and should be associated with the measurement of plasma renin and aldosterone, plasma, and urinary osmolality to exclude plasma dilution caused by increased water intake or treatments that change sodium excretion. It is also known that renin and aldosterone are dependent on the standing or lying position and therefore these factors should also be considered.

HOMEOSTATIC EQUILIBRIUM OF SODIUM AND WATER

The excretion of sodium and potassium is related to several factors that are involved in keeping sodium and potassium concentration normal in serum, tissues, and urine.

The most important regulators of this homeostatic equilibrium are salt/water intake and excretion and related hormonal regulators such as renin-angiotensin-aldosterone system (RAAS), estrogens, cortisol, vitamin D, progesterone, and antidiuretic hormones. A physiological assessment of these factors is associated with their normality, while any change results in compensation by one or more regulators. When the compensation is not more efficient, a state of disease will appear.

For example, an increase in water ingestion results in its increased excretion, as a result of reduction in the RAAS and antidiuretic hormone. The decrease in aldosterone is a defense considering the deleterious

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effects of aldosterone itself at the level of mineralocorticoid receptors in kidney, lymphocyte, heart, and vessels.[8] However, long-term increased water ingestion leads to further water retention and plasma volume expansion as a result of impaired urinary concentrating ability.

Increased sodium intake can result in water retention, hypertension, and suppression of the RAAS. Most experimental animal studies on the deleterious effects of aldosterone in hyperaldosteronism have used the aldosterone and sodium model. However, in patients with increased salt intake, the mechanism of defense is the reduction of the RAAS. This mechanism can block the inflammatory and atherogenic effects of increased aldosterone associated with sodium. The only clinical situations associated with an increase in mineralocorticoids and volume expansion are primary aldosteronism and pseudohyperaldosteronism.[9] The inflammatory effect of aldosterone is also evident in patients treated with thiazides and amiloride,[10] while aldosterone receptor blockers are able to prevent cardiovascular risk.[11,12] Thiazides and furosemide can reduce blood pressure but they increase aldosterone, and mineralocorticoid receptors are not blocked as occurs with spironolactone derivatives.

Sodium is the principal electrolyte present in the human body and its intracellular and extracellular content is mainly regulated by aldosterone. The individual regulation of sodium and water balance is a genetic characteristic related to race, sex, and epigenetic factors. Patients at increased risk for low-renin hypertension are African American and Asiatic populations. In the first case, a genetic tendency to sodium retention predisposes to low-renin essential hypertension. In the SEA population, low-renin and low-aldosterone hypertension is more related to overconsumption of salt contained in foods.[13]

In the study by Do and colleagues, the average population in Vietnam has salt excretion values around 3 g higher than the World Health Organization's recommended salt intake of 5 g.[1,3] The difference remained after the intervention, showing that more specific behavioral intervention could further reduce salt intake and thus cardiovascular risk.

The evaluation of sodium excretion from spot urine is feasible in patients who do not have hypertension or do not take medications. In the study by Do and colleagues,[1] only 8% of patients were taking hypotensive drugs and only 26% were hypertensive. The change in sodium after the intervention was smaller using spot urine than 24-hour urine collection.[1] This is likely because of the different sodium excretion during the day depending on intake and values of aldosterone. During the night, aldosterone and cortisol levels are low, and sodium excretion is lower than during the day.

Other factors that could disturb the measurement of sodium excretion from spot urine are age and sex. It is well-known that older people have lower renin and aldosterone values as a result of sclerosis of the juxtaglomerular apparatus. There are no data on sex-related differences; however, it is well reported that salt intake is higher in men than in women and perhaps a separate evaluation could provide more information on these differences.

CONCLUSIONS

The estimation of sodium intake to evaluate sodium excretion is helpful in the general population, while in pathological conditions or in patients treated for hypertension or with drugs that interfer with the RAAS, the evaluation is difficult. Other factors to be considered are race, age, sex, amount of water ingested, and use of hormonal contraceptives.

In hypertensive patients, the RAAS should also be assessed and related to water and salt ingestion. In patients with increased salt intake, the reduction of renin and aldosterone is a mechanism of defense against the proinflammatory and proatherogenic effects of hyperaldosteronism associated with sodium. The only clinical situations associated with increase in mineralocorticoids and volume expansion are primary aldosteronism and pseudohyperaldosteronism.

The study by Do and colleagues[1] demonstrates that a decrease in sodium intake can ameliorate the general situation and reduce the prevalence of hypertension. The authors did not evaluate cardiovascular risk but other studies have reported a reduction in the risk by reducing sodium intake in populations at risk.

The importance of the study is not only the evaluation of sodium excretion by spot urine, but the finding that a reduction in sodium intake ameliorates blood pressure values.

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References

1. Do HTP, Santos JA, Trieu K, et al. Effectiveness of a Communication for Behavioral Impact (COMBI) intervention to reduce salt intake in a Vietnamese Province based on estimations from spot urine samples. *J Clin Hypertens (Greenwich)*. 2016;18:1135–1142.
2. Batcagan-Abueg AP, Lee JJ, Chan P, et al. Salt intakes and salt reduction initiatives in Southeast Asia: a review. *Asia Pac J Clin Nutr*. 2013;22:490–504.
3. World Health Organization. *Guideline: sodium intake for adults and children*. Switzerland: World Health Organization; Geneva; 2012.
4. Anderson CA, Appel LJ, Okuda N, et al. Dietary sources of sodium in China, Japan, the United Kingdom, and the United States, women and men aged 40 to 59 years: the INTERMAP study. *J Am Diet Assoc*. 2010;110:736–745.
5. McLean RM. Measuring population sodium intake: a review of methods. *Nutrients*. 2014;6:4651–4662.
6. Johansson G, Bingham S, Vahter M. A method to compensate for incomplete 24-hour urine collections in nutritional epidemiology studies. *Public Health Nutr*. 1999;2:587–591.
7. Huang L, Crino M, Wu JH, et al. Mean population salt intake estimated from 24-h urine samples and spot urine samples: a systematic review and meta-analysis. *Int J Epidemiol*. 2016;45:239–250.
8. Wehling M, Armanini D, Strasser T, Weber PC. Effect of aldosterone on sodium and potassium concentrations in human mononuclear leukocytes. *Am J Physiol*. 1987;252:E505–E508.
9. Armanini D, Calò L, Fiore C. Salt and aldosterone do not get along with each other: implication of mineralocorticoid receptors in the profibrotic action of aldosterone. *Kidney Int*. 2012;81:118.

10. Armanini D, Bordin L, Clari G. Serum potassium, thiazides, aldosterone, and mineralocorticoid receptors. *Hypertension*. 2012; 60:e9.
11. Armanini D, Sabbadin C, Donà G, et al. Aldosterone receptor blockers spironolactone and canrenone: two multivalent drugs. *Expert Opin Pharmacother*. 2014;15:909–912.
12. Sabbadin C, Calò LA, Armanini D. The story of spironolactones from 1957 to now: from sodium balance to inflammation. *G Ital Nefrol*. 2016;33(S66).
13. Sabbadin C, Armanini D. Syndromes that mimic an excess of mineralocorticoids. *High Blood Press Cardiovasc Prev*. 2016;23:231–235.