Urinary Potassium Excretion
Can It Predict the Onset of Hypertension?

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See related article, pp 769–776

There are multiplicities of factors that have been proffered as physiological/dietary prompts for the new onset of hypertension. Such physiological factors generally center on changes in volume homeostasis, an excess of sympathetic nervous system activity, or either relative or absolute increases in various components of the renin–angiotensin–aldosterone system; however, population-based screening for changes in neurohumoral and volume-related factors associated with the new onset of hypertension is rarely done in clinical practice and for the most part, when attempted, has been sparingly predictive. Alternatively, at the individual patient level, the good clinician by virtue of an oftentimes thoughtfully applied algorithmic approach to treatment and simple neurohumoral testing can in a post hoc manner uncover the pathobiologic prompt to a newly developed hypertensive state.

Dietary factors actively involved in the genesis of hypertension have, however, received much more play because large population-based studies can be more readily initiated and outcomes tracked in a more longitudinally revealing manner. Of the many dietary factors invoked as causal in new-onset hypertension, sodium, potassium, magnesium, and calcium have been most commonly advanced as potentially etiologic and worthy of study. The details of many of these dietary studies have oftentimes been methodologically convoluted in that they have commonly relied on estimates of nutrient excretion or either spot or 12-hour overnight urine collections of these same nutrient cations and thus have been subject to critique. Alternatively, at the individual patient level, the good clinician by virtue of an oftentimes thoughtfully applied algorithmic approach to treatment and simple neurohumoral testing can in a post hoc manner uncover the pathobiologic prompt to a newly developed hypertensive state.

The 24-hour urine excretion of potassium is, moreover, preferable for studies such as these in that it eliminates the interpretive considerations relative to the circadian variation in urinary excretion of potassium. Of note, several renal potassium transporters have been identified that have a circadian rhythmicity consistent with the observed daily fluctuations in urinary potassium excretion, making this phenomenon one of the several that need to be summed in the interpretation of urine potassium excretion measured in a longitudinally comparative fashion. In that regard, there is a well-established decrease in urinary potassium excretion at night, an observation that reverses in patients with chronic kidney disease.

Assessing the time-wise intake of potassium by virtue of sequential 24-hour urine collections is not without other issues beyond the simple accuracy of the collection. To be able to reliably compare potassium content in urine collections obtained sequentially over time requires that potassium absorption be maintained as a constant percentage of intake; determinants of renal potassium handling remain comparable in their level of activity; cellular uptake of ingested potassium remains similar at the times of urine collection; and finally environmental conditions do not lead to varying and potentially excessive losses of potassium in sweat. Population-based studies such as the one performed by Kieneker et al are not designed to evaluate these influencing variables requiring that all 4 such variables be presumed to have been constant at the time of each urine collection. There is no certainty that this is the case until studied. For example, in other studies for as of yet not clearly established reasons, it has been shown that potassium excretion in black individuals, on both random diets and diets fixed for potassium intake, is commonly less than intake, making urine collections difficult to interpret if used in a singular fashion to approximate potassium intake.

The question remains as to whether increasing the potassium intake of the population shifts the blood pressure distribution curve in favor of less incident hypertension as has been suggested for lowering the sodium intake in the general population. Be that as it may, there remains no single factor that a high potassium intake changes that can be seen as a standard for blood pressure reduction or preventing the transition from a normotensive to a hypertensive state. Factors considered in that regard include a greater natriuretic response to an increased potassium intake as well as decreased vascular responsiveness to vasopressor substances and increased sensitivity of the baroreceptor reflex. In addition, it has been shown that potassium supplementation converts otherwise normotensive salt-sensitive nondippers to dippers in the absence of an effect on daytime blood pressure. The issue of night-time
blood pressure change was not intended for study by Kieneker et al., but one could speculate that in those with an implied higher potassium intake this might favorably influence overnight blood pressure. In so doing the impetus for daytime blood pressure increases, which might develop as a byproduct of higher nighttime readings or possibly a nocturnal nondipping state could conceivably be lessened.

Implicating intake/urinary excretion of potassium in the new onset of hypertension requires that other dietary nutrients be considered for their contribution to the developed state of hypertension. This same population in the PREVEND study has had the association of urinary magnesium excretion, as an indicator of intestinal magnesium absorption, also explored. In that regard, urinary magnesium excretion was found to be inversely associated with the risk of hypertension across the entire range of habitual dietary intake; this association remained intact after adjustment for a wide range of variables, including urinary excretion of sodium, potassium, and calcium. The fact that this and the potassium excretion studies being reported were observational means that confounding variables of a dietary nature may have had some play in the findings. Moreover, one must wonder as to how the individual patient and his/her blood pressure responded to the dietary cross-talk occurring between potassium and magnesium intake.

In summary, the work of Kieneker et al. provides support for what is a developing consensus that an increased potassium intake favorably influences both hypertension and the natural trajectory of blood pressure increase in the general population as well as the risk of incident stroke. Moreover, there seems to be no adverse effects from an increased potassium intake as related to lipid concentrations, catecholamine levels, or renal function as long as the patient so treated does not have renal disease in which case the risk of hyperkalemia becomes a relative deterrent to such an approach. Intervention trials including potassium consumption as high as 400 mmol per day from food for several weeks and 115 mmol per day for up to a year reported no adverse effects from increased potassium intake.

This study, however, does not and cannot provide insight into what is an optimal potassium intake/urinary potassium excretion, and even the cut points for urinary potassium excretion offered have to be taken with a grain of salt as to their generalizability in that a homogeneous, nonethnically diverse population was being evaluated in the PREVEND study.

Disclosures

None

References

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尿钾排泄
能否预测高血压的发生？

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研究已发现多种引起新发高血压的生理/饮食因素。此类生理学因素通常集中在体液平衡的改变，交感神经系统过度激活、肾素-血管紧张素-醛固酮系统各种成分的相对或绝对增加。然而，以人群为基础的调查与新发高血压有关的神经体液和容量相关因素的变化很少在临床实践开展，而在此为数不多的研究中，大多数的预测价值极少。另外，在患者个体水平，优秀的临床医生能够借助全面的日常应用治疗流程以及简单的神经体液检测，以事后分析（post hoc）方式来发现新发高血压状态的病理学因素。

然而，与高血压发生密切相关的时间因素已有更多研究成果，因为以人群为基础的大型研究更容易开展，纵向呈现形式更易于记录结局指标与新发高血压病因相关的众多膳食因素中，钠、钾、镁和钙是最常见的潜在病因以及值得研究的致病因素。许多膳食研究的方法学细节错综复杂，因为这些研究主要依靠营养素排泄估计值，或者随意采集或12小时夜收集成尿液中的营养蛋白质，这些研究也因为这些估计值的隐含变量受到质疑。在这一方面，Kieneker等[3]对于一项前瞻性基于人群的队列研究——肾脏和血管终末期疾病的预防（Prevention of Renal and Vascular End-Stage Disease，PREVEND），选择了一种更严格的研究形式，采用评价尿液营养素/离子液排泄或的金标准即收集24 h尿液，在551例28~75岁的血压正常个体的队列中，以时间方式中位随访7.6年，以确定尿钾排泄与高血压发生风险之间的关系。

此外，对于此类研究而言，采用24小时尿钾排泄更为可靠，可以不需要考虑有关尿钾排泄的昼夜变异[3]。需要注意的是，现已确定有数个肾脏的钾转运蛋白具有昼夜节律性，与所观察到的尿钾排泄每日波动相一致。基于该现象，在对采用纵向比较方式测量的尿钾排泄进行解释分析时，需要将此考虑进去[4]。在这一方面，已经确认夜间尿钾排泄会降低，而在慢性肾病患者中则观察到相反的情况[5]。

通过连续24小时尿液收集来评估尿钾排入情况，除了尿液收集的简便准确之外，并没有其他问题。为了比较连续收集尿液中实时钾含量的可靠性，需要维持钾吸收与排入的恒定，肾脏处理钾的影响因素在检测期间保持可比性：消化吸收的钾在尿液收集时应保持具体水平；最后，环境条件相对恒定，并没有引起尿液钾的变化以及过度丢失的可能性。诸如Kieneker等[3]进行的这类基于人群的研究，设计目的并非为了评估这些信息变量，所有4个变量应该在每次尿液收集时假设为保持恒定，但并不确定进行研究时情况确为如此。例如，在尚无明确原因的其他研究中，结果显示钾摄入无论是随机膳食还是固定膳食，每人个体的钾排泄通常低于摄入量，如果采用单一的方法粗略估计钾的摄入量时，对尿液收集结果的诠释就变得相当困难[4]。

问题在于人群的钾摄入增加是否会增加血压分布曲线转变为有利于高血压发病率较低的状态，如同在一般人群中降低钠的摄入所显示的结果，即便如此，高钾摄入的改变仍然并非单纯因素，不能将其视为降低血压或者预防从正常血压向高血压状态转变的标准方法。在这一方面考虑的因素包括：钾摄入增加所引起的水分钠排泄反应提高，对血管加压物质的血管反应性降低，对压力感受性反射的敏感性增加。此外，研究已显示进行钾补充可以改善敏感性血压正常者的血压从非杓型转变为杓型，而对间歇性血压无作用[7]。Kieneker等[3]的研究并未针对夜间血压这一问题，但
blood pressure change was not intended for study by Kieneker et al, but one could speculate that in those with an implied higher potassium intake this might favorably influence overnight blood pressure. In so doing the impetus for daytime blood pressure increases, which might develop as a byproduct of higher nighttime readings or possibly a nocturnal non-dipping state could conceivably be lessened.

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