Reviewer's report

Title: Primary care patient willingness for genetic testing for salt-sensitive hypertension: a cross sectional study

Version: 1 Date: 11 September 2013

Reviewer: RICHARD KONES MD PhD

Reviewer's report:

Hypertension is a prevalent and potent risk factor for future cardiovascular disease (CVD) (1), and control of hypertension in the general population, despite recent improvements, remains at about 50%. The link between sodium intake and blood pressure is strong (2), particularly in the subset of patients whose hypertension is “salt-sensitive.” Although there are many sources for the shortfall in blood pressure control, patients’ awareness, attitudes and behaviors contribute significantly.

In an effort to assist in identifying individuals who would benefit from future therapies, Okayama et al sought to determine the willingness of patients to undergo genetic testing for salt-sensitivity in a primary care population. The study design was cross-sectional and employed a questionnaire for self-reporting by outpatients. They found that half their patients would chose genetic testing, which was a function of age>50 years (y), educational level, family history of hypertension, and concern or “worry” about high blood pressure.

The authors note the “promise of personalized medicine, with the potential to enhance human health through more effective prevention” and suggest that “primary care physicians should provide patients with advice on genetic testing, as well as address their anxieties and concerns related to developing hypertension.”

Major revisions

The broader subject of this paper—identification and personalization of patients at high risk for intensive therapy—is highly relevant. The purpose and methods in this study are clearly stated. The paper would be enhanced if the discussion were expanded to put the findings in perspective. True, the promise of personalized medicine is early identification of high-risk individuals prior in order to target therapy and prevent clinical expression of disease. A cogent, specific, and directed statement about the significance of the findings leading to the conclusion would be welcome.

In this case, will identification of 50%, or even 100%, of patients who are salt-sensitive actually lead to such therapy, given the current practice milieu? What are the barriers? Will improved motivation among positive patients translate into clinically meaningful, cost-effective, changes in outcomes? The bridges from raised awareness to actual changes in behavior, for instance, especially with
respect to physician guideline compliance, or patient adherence, are vast and not easily crossed. While no one is able to predict the future, what do currently available data suggest about the answers to these questions?

In the section concerning limitations, a comment about self-reported data and the patient population might be considered. Self-reporting may introduce considerable error in data presentation. Patients who are highly educated perform differently with respect to reporting and healthy behaviors. Hypertension is also prevalent among patients younger than age 50—how will the greater willingness of older patients to have genetic testing influence the significance of the findings?

How generalizable are the reported data to other populations? A comment might be warranted in the limitations section about the cultural, dietary, and genetic differences that might diminish or reinforce the applicability of results to Western and other countries. Would the relative heterogeneity, for instance, of the United States population be a factor?

The advice primary care physicians should give to patients with hypertension and about genetic testing might be more specific, rather than general.

Notes

1. About 33% of Americans, and up to 40% of the global population, have hypertension. About 82% are aware of their condition, 75% are using antihypertensive medications, but only 53% of those have their BP controlled. African-Americans have a higher prevalence of 44%, primarily attributable to a higher risk burden rather than racial differences, but their disease is of greater severity. Of all risk factors, uncontrolled hypertension is associated with the largest adjusted population-attributable fraction for CVD and all-cause mortality. In the USA, hypertension contributes to nearly 1000 deaths daily; the World Health Organization (WHO) estimates that hypertension contributes to nearly 9.4 million deaths annually, accounting to about 62% of cases of cerebrovascular disease and 49% of instances of ischemic heart disease. The prevalence of prehypertension (untreated systolic BP of 120-139 mm Hg or untreated diastolic BP of 80-89 mm Hg and not having been told they had hypertension on 2 occasions) in adults is 36.3% but varies with age and ethnicity. In American children and adolescents the prevalence ranges from 3%-5%. Progression to hypertension occurs in up to 7% of cases. Resistant hypertension in adults, with a prevalence of some 20%-30% of hypertensive patients, will, upon careful further examination, be treatable in a significant proportion of such patients.

2. Reducing sodium intake by 1,200 mg/day in the USA would lower the annual number of new instances of coronary heart disease (CHD) by 50%, acute myocardial infarction by 54.5%, stroke by 48.5%, and total all-cause mortality by 47.8%. Computer simulations predict a reduction of CVD mortality of up to 17%-20% over a decade if the daily American Heart Association-recommended 1500 mg sodium consumption were achieved, amounting to an absolute saving of 500,000-1.2 million CVD deaths, or 100,000-190,000 CHD deaths over a decade. A reduction of 40% in sodium take could result in 25%-30% fewer
deaths, and a 4% annual fall in sodium consumption over 10y, corresponding to #2200 mg/day, might produce a fall in CHD/stroke mortality of 4%-10% and of total mortality by 1.5%-3%, about half the effect of the 40% reduction.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.