High Sodium-Potassium Ratio Raises Death Risk

BY MARY ANN MOON

FROM ARCHIVES OF INTERNAL MEDICINE

A high sodium-potassium ratio appears to indicate a significantly increased risk of cardiovascular disease, ischemic heart disease, and all-cause mortality in the general population.

A high sodium-potassium ratio was more strongly related to mortality than was a high sodium level alone or a low potassium level alone in a study of a large, nationally representative sample of adults. In addition, the robust association was independent of age, sex, race/ethnicity, and other variables, said Quanhe Yang, Ph.D., of the office of public health genomics at the Centers for Disease Control and Prevention, Atlanta, and associates.

"From a public health point of view, reduced sodium intake accompanied by increased potassium intake could achieve greater health benefits than restricting sodium alone," they noted (Arch. Intern. Med. 2011;171:1183-91).

The link between high sodium consumption and hypertension is fairly well known, but the public is less aware that low potassium levels are even more strongly related to hypertension. Several recent studies have suggested that the ratio of sodium to potassium is an even more important risk factor for hypertension and cardiovascular disease than either component alone.

Dr. Yang and colleagues analyzed these associations using data from the Third National Health and Nutritional Examination Survey (NHANES III). They estimated the usual dietary intakes of sodium and potassium at baseline for 12,267 adults participating in the survey, then determined the subjects' mortality status during a median of 15 years of follow-up using the National Death Index.

During that time, there were 2,270 deaths, including 825 CVD deaths and 433 deaths from ischemic heart disease.

The risk of all-cause mortality increased linearly with increasing sodium-potassium ratio. The hazard ratio was 1.46 for the patients in the highest quartile of sodium-potassium ratio, compared with the lowest quartile.

A higher sodium-potassium ratio also was significantly associated with the risk of death from cardiovascular disease and from ischemic heart disease. The hazard ratios comparing the highest with the lowest quartiles were 1.46 for CVD mortality and 2.15 for ischemic heart disease mortality, the investigators said.

These links were robust regardless of subjects' sex, age, race/ethnicity, body mass index, hypertension status, physical activity level, or educational achievement.

"The observed stronger and more consistent association between the sodium-potassium ratio and mortality than between each nutrient separately and mortality may be due to complex interactions between potassium and sodium at cellular levels," the researchers said. "High sodium levels induce increased blood pressure and hypertension by stiffening endothelial cells, thickening and narrowing resistance arteries, and blocking nitric oxide synthesis, whereas higher potassium levels can counteract these effects by activating nitric oxide release."

No financial conflicts of interest were reported. ■

VIEW ON THE NEWS

Food Sources Are Probably Best

Optimizing potassium intake in the general population is of great public health importance, but there are "important questions regarding potential unintended negative consequences," said Dr. Lynn D. Silver and Dr. Thomas A. Farley.

It is unknown whether dietary or pharmacologic supplementation would have the same health benefits as potassium from traditional dietary sources. "Potassium in foods is accompanied by anions that are bicarbonate precursors, whereas potassium in pills and salt substitutes is generally potassium chloride," they noted.

Potassium supplements may help some patients, but they would put many others at risk for hyperkalemia – chiefly people with diabetes, renal failure, or heart failure, and people who take ACE inhibitors or spironolactone. "It is crucial that we understand the interplay of sodium and potassium in the diet and how to optimize intake in an increasingly processed food supply without generating harm," they said.

DR. SILVER and DR. FARLEY are with the New York City Department of Health and Mental Hygiene and reported no conflicts of interest. These remarks were taken from their editorial accompanying Dr. Yang's report (Arch. Intern. Med. 2011;171:1191-2).

Carvedilol Cut Intradialytic HT

BY KERRI WACHTER

FROM THE ANNUAL MEETING OF THE AMERICAN SOCIETY OF HYPERTENSION

NEW YORK – Patients treated with carvedilol not only had a reduced frequency of intradialytic hypertension, but also showed improvements in endothelial cell function, in a small study.

After 8 weeks of treatment with carvedilol, mean systolic postdialysis blood pressure dropped from 159 mm Hg at baseline to 142 mm Hg, reported Dr. Julia Inrig of the University of Texas Southwestern Medical Center in Dallas.

We are "very interested in this phenomenon of intradialytic hypertension," she said at the meeting. When most patients come for dialysis, there is a gradual reduction in their systolic blood pressure. "However, up to 20% of patients have this gradual increase in their systolic blood pressure during their dialysis. So they leave their dialysis session much more hypertensive than when they showed up, despite similar amounts of fluid removed."

In addition, "we've identified that this is an important prognostic indicator." In a cohort of 450 dialysis patients, those with increased BP during dialysis were nearly twice as likely to be hospitalized or die by 6 months (Kidney Int. 2007;71:454-61).

The researchers in the Mechanisms and Treatment of Intradialytic Hypertension (MATCH) pilot study prospectively enrolled 25 hemodialysis patients with intradialytic hypertension into an open-label intervention study. Once patients were accepted into the study, they underwent baseline testing, including 44-hour ambulatory blood pressure, lipids, albumin, sodium, and C-reactive protein, as well as postdialysis endothelin-1, asymmetric dimethylarginine, endothelial progenitor cells, pulse-wave velocity, and brachial artery flow. In 8 weeks, the baseline lab work was repeated.

Patients were started on carvedilol 6.25 mg twice daily, and eventually titrated to 50 mg twice daily. "Our goal was to reach a delta [systolic] blood pressure less than zero with regard to their postdialysis blood pressure no longer increasing," said Dr. Inrig. However, she and her colleagues were also targeting a postdialysis systolic BP of less than 130 mm Hg as an alternative goal.

The average patient age was 54 years, and the group was 80% male. Roughly two-thirds of the population was Hispanic (64%), and more than a third was black (36%). Almost all (88%) had diabetes, and 32% had cardiovascular disease. Many were on ACE inhibitors or angiotensin II receptor blockers (64%), beta-blockers (68%), or calcium channel blockers (60%) at baseline.

Mean predialysis BP was roughly the same regardless of carvedilol treatment (144 mm Hg vs. 146 mm Hg). The frequency of intradialytic hypertension declined from 77% of hemodialysis sessions at baseline to 28% by the study's end, a significant difference.

Carvedilol treatment showed a trend toward improvement of brachial artery flow–mediated dilation. However there was no change in C-reactive protein or pulse-wave velocity.

"With regard to safety, patients tolerated carvedilol fairly well," said Dr. Inrig. There was a low incidence of side effects.

Dr. Inrig has received an investigator-initiated research grant from Genzyme, and has participated in industry-sponsored research for Keryx Biopharmaceuticals. ■

Inhaled Treprostinil Aids Children With PAH

BY MIRIAM E. TUCKER

FROM AN INTERNATIONAL CONFERENCE OF THE AMERICAN THORACIC SOCIETY

DENVER – Inhaled treprostinil was well tolerated and tied to gains in exercise capacity and functional class when added to background therapy in a retrospective study of 18 children with pulmonary arterial hypertension.

Inhaled treprostinil (iTRE; brand name, Tyvaso) was approved in 2009 but has not been previously studied in children with PAH, said Dr. Erika B. Rosenzweig, director of the pulmonary hypertension center at Columbia University Medical Center in New York.

This study included 6 girls and 12 boys with PAH who were seen at either the Columbia center or the Children's Hospital in Aurora, Colo., during September 2009–January 2011. They had a mean age of 11 years, a mean weight of 42 kg, and a mean body mass index of 19.4 kg/m^2. A total of 11 patients had idiopathic PAH and 7 had associated PAH, including 5 with congenital heart defects. All were on background therapy at the time of iTRE initiation. All patients received three to nine breaths, with 6 mcg per breath of iTRE, four times daily. The mean treatment duration was 11.5 months (range, 2-20 months). Four patients discontinued iTRE, including three because of bronchospasm, and one because of noncompliance with all medications (who died 3 months later). Side effects requiring down-titration included cough in one patient and nausea/emesis in two, Dr. Rosenzweig noted at the conference.

World Health Organization functional class improvements were seen in 11 of the 18 children. Of the seven children who were able to complete the 6-minute walk test, the mean improvement was from 446 to 472 meters, a significant difference. Of four who completed cardiopulmonary exercise testing, the mean workload improved from 59 to 74 watts and mean peak oxygen consumption from 20 to 22 mL/kg per minute. Neither of those findings was statistically significant.

Dr. Rosenzweig has received research support and consulting fees from for United Therapeutics, the maker of Tyvaso. ■