Potassium and Cardiovascular Disease

Thiazide Diuretics, Potassium, and the Development of Diabetes
A Quantitative Review

Alan J. Zillich, Jay Garg, Sanjib Basu, George L. Bakris, Barry L. Carter

Abstract—National guidelines and a recent clinical trial have supported the use of thiazide diuretics as the preferred initial pharmacological treatment for hypertension. However, evidence from this and other clinical trials have also found an increased incidence of new onset diabetes among those patients receiving thiazide diuretics. The mechanisms responsible for the increased incidence of diabetes with thiazide diuretics have not been fully elucidated. This article provides a review of intervention studies that included data on the relation between thiazide-induced hypokalemia and glucose intolerance. We conducted a literature search from 1966 to June 2004 to identify clinical trials using thiazide diuretics where the metabolic effects on potassium and glucose are reported. A total of 59 clinical trials constituting 83 thiazide diuretic study arms were identified. Trial size, length, type of thiazide diuretic, and dose varied substantially among the studies. The association between average changes in potassium and glucose in the study arms is considered jointly in a weighted statistical model. The Pearson’s correlation coefficient, weighted by study sample size, for the relationship between glucose and potassium was $-0.54$ (95% CI, $-0.67$ to $-0.36$; $P<0.01$). A sensitivity analysis, which considered subset analyses and effect of covariates, as well as inverse-variance weighting, supported this finding. These data suggest that thiazide-induced hypokalemia is associated with increased blood glucose. Treatment of thiazide-induced hypokalemia may reverse glucose intolerance and possibly prevent the future development of diabetes. (Hypertension. 2006;48:219-224.)

Key Words: diuretics • potassium • glucose • diabetes mellitus • hypertension, experimental

Current national clinical practice guidelines and results from the Antihypertensive and Lipid Lowering treatment to prevent Heart Attack Trial (ALLHAT) support the use of thiazide diuretics as the initial pharmacotherapeutic agent for most patients with hypertension.1,2 However, examination of the ALLHAT findings has renewed a debate about the adverse metabolic effects associated with thiazide diuretics. In ALLHAT, the 4-year incidence of new-onset diabetes mellitus was significantly higher in the chlorthalidone group than in the amlodipine and lisinopril groups.3 However, the primary outcome of fatal and nonfatal myocardial infarction was no different between groups.1 Some have argued that the follow-up period of 4.9 years (range, 4 to 8 years) was not adequate to account for the occurrence of cardiovascular outcomes among those patients who developed diabetes while receiving antihypertensive treatment.3,4

Reports by Verdecchia et al5,6 seem to support this view. They observed that treatment with thiazide diuretics was an independent predictor of new diabetes among patients with hypertension, followed for a median of 6 years (range, 1 to 16 years). Furthermore, they found that the occurrence of new diabetes during the trial increased the risk of cardiovascular events to a level similar to that of patients who had diabetes and hypertension at the onset of the trial.6 Also, they calculated that 1 cardiovascular event associated with new-onset diabetes may be prevented if 385 to 449 patients are treated with “new” antihypertensive drugs (angiotensin-converting enzyme [ACE] inhibitors, calcium channel blockers [CCBs], and angiotensin receptor blockers) versus “old” (thiazides and $\beta$-blockers) antihypertensive drugs for 4 years.5

On the other hand, additional analysis from the ALLHAT did not find an increased risk of cardiovascular events among patients with impaired fasting glucose or diabetes who received thiazide diuretics compared with patients who received either ACE inhibitor or CCB.7 In addition, in a 14-year follow-up study of patients from the Systolic Hypertension in the Elderly Program (SHEP), the investigators did not find an increased risk of mortality among patients who developed diabetes during the trial while receiving chlorthalidone compared with patients who developed diabetes during the trial but received placebo.8 The controversy surrounding the association between thiazide diuretics and the development of diabetes requires further investigation.
It has been known for >40 years that thiazide diuretics can impair glucose tolerance, but a precise mechanism has not been elucidated. Several hypotheses have been postulated to explain this mechanism. One hypothesis ascribes that diuretic-induced hypokalemia, that is, serum potassium (K⁺) <3.5 mmol/L, causes an indirect reduction in insulin secretion leading to elevated serum glucose concentrations. It is possible that strategies that maintain normal potassium concentrations may prevent glucose intolerance and/or the development of diabetes, although this has not been investigated in a systematic manner.

Relationship Among Thiazides, Potassium, and Glucose

A decrease in K⁺ is a well-characterized effect of thiazide diuretics. It is estimated that ≤50% of patients receiving thiazide-type diuretics develop hypokalemia (defined as a serum K⁺ <3.5 mmol/L). The maximal potassium-depleting effect does not seem to be drug dependent or related to the total duration of exposure to the drug. However, there seems to be a dose-dependent effect regardless of thiazide diuretic used. Some reports suggest that doses of 12.5 to 25 mg daily of hydrochlorothiazide or chlorothalidone may produce less hypokalemia than doses of ≥50 mg daily. The mechanism responsible for this drug-induced hypokalemia involves increased renal excretion of potassium. In the distal convoluted tubule, thiazide diuretics deliver a high sodium load with a resulting physiological secretion of potassium. In addition, aldosterone is secreted in response to volume contraction, further promoting potassium excretion.

Conversely, an exact pathway has not been elucidated for thiazide-induced glucose intolerance. One theory posits that the relationship between hypokalemia and insulin secretion may be part of the mechanism. In a study by Rowe et al., an experimentally generated hypokalemia state produced impaired glucose tolerance secondary to impaired insulin secretion. Similarly, in an isolated perfused pancreas study, insulin release was decreased in a low-potassium state and increased in a high-potassium state. Finally, in a study of patients with chronic disease characterized by hypokalemia, Gorden et al. demonstrated that these patients have a higher ratio of proinsulin to insulin secretion. Proinsulin is less biologically active than insulin, resulting in higher serum glucose concentrations. These metabolic studies of potassium provide evidence for the effect of hypokalemia on glucose intolerance. The purpose of this article is to systematically evaluate clinical trials that used thiazide diuretics and reported the metabolic effects on potassium and glucose.

Methods

An extensive search was conducted using 3 different sources of medical literature. First, the Abridged Index Medicus from January 1966 to June 2004 was searched using the subject terms “diuretics, thiazide,” “hydrochlorothiazide,” or “chlorothalidone.” These terms were combined with the term “hypertension.” The search was limited to adult, human subject articles published in English language using the terms “controlled clinical trial” or “randomized controlled trial.” Second, the same search criteria were applied to the Cochrane Controlled Trial Database. Finally, the search criteria were extended to common journals related to hypertension research: Journal of Hypertension, Journal of Human Hypertension, Hypertension, American Journal of Hypertension, Journal of Clinical Hypertension, and Blood Pressure. The results from each data source were combined, and duplicate articles were removed.

Each article was examined according to the following inclusion and exclusion criteria: clinical trials had to be studies of patients with hypertension of ≥8 weeks duration and ≥10 subjects per arm. An 8-week treatment duration was chosen to allow sufficient time for the diuretic to exert effects on potassium. Trials must have had a thiazide-type diuretic used as a single agent or as primary initial therapy. Finally, the trials had to provide measurements of both potassium and glucose relative to either a baseline or placebo value. Trials that used combinations of antihypertensive agents or that did not attempt to separate results by type of diuretic or drug were excluded. Initially, abstracts were reviewed by 2 authors (A.J.Z. and J.G.) for inclusion/exclusion criteria. Then, all of the remaining full-text articles were reviewed according to inclusion/exclusion criteria. If no abstract was available, the full article was obtained for review. Articles that seemed to meet all of the criteria were selected for data extraction. During the extraction process, any remaining articles that subsequently did not meet inclusion criteria were discarded. All of the articles were reviewed and extracted by the same 2 investigators (A.J.Z. and J.G.), but there was no duplicate abstraction process.

A data extraction form was created to capture relevant information from each eligible study. Data on the trial design, size, and duration were extracted. For each arm of the studies, information was collected on the type of thiazide drug, initial dose, dose titration regimen, use of potassium supplements or potassium sparing agents, and metabolic effects on potassium and glucose. The study was conducted with exemption from an Institutional Review Board.

Data Analyses

For each study arm in the trials, the average changes in potassium and glucose were calculated from study summaries reported in the publications. For trials containing a placebo group, the changes in potassium and glucose were computed as the difference in final follow-up (end of study) laboratory value between the active minus the placebo group (placebo comparator trials). The change in potassium and glucose among trials with no placebo arm were calculated as the difference from baseline (beginning of study) to final follow-up (end of study) laboratory measurement (baseline comparator trials). The statistical analysis considered the change values for potassium and glucose as 2 outcome variables in a bivariate joint model. Because there is no standard approach for reporting this type of analysis, several data analytic techniques were used. Using several approaches ensures that the results found were not spurious.

An unweighted Pearson correlation, the nonparametric Spearman correlation, as well as the Pearson correlation weighted according to sample size of the thiazide treated study arms are reported along with the associated P values. Separate subgroup analyses of the placebo comparator trials and the baseline comparator trials were also considered. We assumed that the changes in potassium and glucose for each subject have homogeneous variances and covariance (a bivariate normal distribution) across all of the baseline comparator studies. In addition, the partial correlation between potassium and glucose, after adjusting for the covariates age and gender, and weighted by the study sample size, was obtained. Trial arms that did not provide information on patient age or gender were excluded from this partial correlation analysis.

Specific variances for potassium and glucose are available only for a subset of the studies. Therefore, an inverse variance weighted model was calculated only for those studies for which the variance data were available. Because both potassium and glucose have to be appropriately weighted by their respective variances (different weights for potassium and glucose), a maximum likelihood-based approach was used under a bivariate normal distribution assumption. A paired samples setup was used for the baseline comparator arms using the variance of the changes from baseline. Variance between placebo and active arms was used in a 2 independent samples setup for the placebo comparator trials. Correlation estimates and 95% confidence limits are presented with a significant P value defined as <0.05. In addition, estimated correlations for changes in potassium and glucose were calculated using 2 different bivariate random effects models. These models can incorporate
between-study variations as well as within-study variations. However, it should be noted that the available data on study averages (average changes in potassium and glucose) can be used to estimate only the between-study variances and covariances for the model. Therefore, in the first random effects model, the within-study variances are set to equal the observed study variances only for the studies in which such variance data are available. The within-study correlation (between potassium and glucose) is assumed to be identical to the between-study correlation. The second random effects model used all of the trial arms and obtained a pooled estimate of the within-study variances for potassium and glucose. This model assumed homogeneous variances for subjects in all of the studies in addition to the within-study correlation being identical to the between-study correlation.

Finally, 2 additional subanalyses were conducted to test the effects of dose and potassium supplementation. First, trials using >50 mg of hydrochlorothiazide (or the equivalent) were excluded. This ensured that “high-dose” trials were not the primary driver of any effects of potassium on glucose. Second, a comparison of trial arms was conducted between those studies that used any potassium supplements and/or potassium sparing agents with those studies that did not use any potassium enhancements. This analyses was performed to determine whether correction of hypokalemia could mitigate the effects on glucose. The correlation estimates were transformed via Fisher’s z transformation and then compared using a z test. All of the data were analyzed using SAS.

### Results

The initial search produced 780 possible trials for further evaluation. Figure 1 shows the trial flow and reasons for exclusion. Overall, the most common reasons for exclusion were combination therapy rather than a diuretic only arm (n=199), no report of potassium and/or glucose: 190, trial design not according to protocol: 199, and no report of potassium and/or glucose: 42.

Figure 1. Flow diagram for reasons trials were excluded. *Consisted of trials using combination therapy where thiazide diuretic was not the primary agent; †Consisted of trials that were not prospective, sufficient size, duration, adult, or hypertensive population.

#### TABLE 1. Summary of Thiazide Diuretic Trials Included in the Systematic Review (n=59 Trials)

<table>
<thead>
<tr>
<th>Characteristics of the Trials</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total subjects</td>
<td>58 520</td>
</tr>
<tr>
<td>Total subjects, mean (±SD)</td>
<td>991.9 (±4377.9)</td>
</tr>
<tr>
<td>Subjects exposed to diuretic</td>
<td>26 625</td>
</tr>
<tr>
<td>Subjects exposed to diuretic, mean (±SD)</td>
<td>451.3 (±2008.0)</td>
</tr>
<tr>
<td>No. of diuretics arms*</td>
<td>83</td>
</tr>
<tr>
<td>Bendroflumethiazide</td>
<td>7</td>
</tr>
<tr>
<td>Chlorothalidone</td>
<td>23</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>41</td>
</tr>
<tr>
<td>Metolazone</td>
<td>5</td>
</tr>
<tr>
<td>Chlorthalidize</td>
<td>3</td>
</tr>
<tr>
<td>Weeks of follow-up</td>
<td>2645</td>
</tr>
<tr>
<td>Weeks of follow-up, mean (±SD)</td>
<td>451.3 (±2008.0)</td>
</tr>
<tr>
<td>Blinded, n (%)</td>
<td>55 (93.2)</td>
</tr>
<tr>
<td>Double</td>
<td>50</td>
</tr>
<tr>
<td>Single</td>
<td>5</td>
</tr>
<tr>
<td>Placebo-controlled, n (%)</td>
<td>20 (33.9)</td>
</tr>
<tr>
<td>Active-controlled, n (%)</td>
<td>39 (66.1)</td>
</tr>
<tr>
<td>Randomized, n (%)</td>
<td>58 (98.3)</td>
</tr>
<tr>
<td>Reported on the incidence of new onset diabetes, n (%)</td>
<td>4 (6.8)</td>
</tr>
<tr>
<td>Any K+ supplementation allowed, n (%)†</td>
<td>16 (27.2)</td>
</tr>
<tr>
<td>Average change in potassium, mean (±SD), meq/L</td>
<td>−0.41 (±0.24)</td>
</tr>
<tr>
<td>Average change in glucose, mean (±SD), mg/dL</td>
<td>7.07 (±7.38)</td>
</tr>
</tbody>
</table>

Data are number unless otherwise specified.

*Trial arms do not add to 83. An additional 4 arms used ethacrynic acid, ticrynafen, clorexolone, and trichlormethiazide.

†Any potassium supplementation was inferred from study methods. Any study that explicitly stated a protocol for use of potassium supplements or treatment of hypokalemia were included. This included any use of potassium-sparing diuretics as add-on medications.
thiazide. Of note, there were 2 study arms with very large sample sizes (2363 and 15255, respectively).

Figure 2 presents an unadjusted scatter plot of each trial arm. The trial arms are plotted according to descending order of the change in potassium with a corresponding increase in glucose. There is a clear linear trend relating a decrease in potassium and glucose are plotted along the vertical axes.

Table 2 reports results (correlation estimates, P values, and 95% CIs) of the correlation analyses between changes in potassium and changes in glucose. The unweighted Pearson and nonparametric Spearman rank correlation from all 83 of the arms is −0.28 and −0.37, respectively. For the 52 baseline comparator arms, these values are −0.18 and −0.33; for the 31 placebo comparator studies, the values are −0.31 and −0.58. If the 2 largest studies (active arm sizes of 2363 and 15255) are dropped, both the Pearson and Spearman correlations of the remaining 81 studies stay relatively unchanged at −0.28 and −0.36, respectively. In addition, excluding the 20 “high-dose” trial arms, the Pearson correlation is −0.30, and the Spearman correlation is −0.43.

The weighted correlation (weighted by sample sizes) for all (n=83) of the studies, baseline comparators trials only (n=52), and placebo comparators trials only (n=31) are −0.54, −0.58, and −0.42, respectively. In a sensitivity analysis, when the 2 largest studies are dropped, the weighted correlation estimates for the remaining (n=81) studies is −0.35 (95% CI, −0.53 to −0.14; P=0.001), and the same for the remaining (n=50) baseline comparator studies is −0.38 (95% CI, −0.59 to −0.11; P=0.006). Here, because the correlation estimates are weighted by sample size, dropping the 2 largest studies has a strong impact; however, the correlation estimates still show a strong negative relationship. On the other hand, when the 20 high-dose trial arms were excluded, the weighted correlation estimate was unchanged (−0.55; 95% CI, −0.70 to −0.35; P<0.0001), indicating that the high-dose trials had relatively little impact.

Similar inverse relationships are shown for the weighted correlation analysis with adjustments for covariates; however, the number of arms for the analysis is decreased because of missing covariate data for almost half of the trial arms. Results from the inverse variance weighted correlation approach produced smaller correlation estimates but tight CIs. All of the correlation estimates are, however, still negative and significantly (P<0.01) different from 0.

In the first random-effects analysis, the within-study variances are set to equal the observed study variances for 38 studies in which such variance data were available. This approach yielded a correlation estimate of −0.32 (95% CI, −0.60 to −0.03; P=0.03). In the second random-effects

![Figure 2](http://hyper.ahajournals.org/)

**Figure 2.** Trial arms are plotted on the horizontal axis in descending order according to the change in potassium. For each trial arm, the paired data points for the change in potassium and glucose are plotted along the vertical axes.

<table>
<thead>
<tr>
<th>Description</th>
<th>All Studies</th>
<th>Baseline Comparator</th>
<th>Placebo Comparator</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unweighted Pearson</td>
<td>N=83</td>
<td>−0.28† (−0.47 to −0.07)</td>
<td>N=52</td>
</tr>
<tr>
<td>Unweighted Spearman</td>
<td>N=83</td>
<td>−0.37† (−0.54 to −0.17)</td>
<td>N=52</td>
</tr>
<tr>
<td>Weighted by sample size§</td>
<td>N=83</td>
<td>−0.54† (−0.67 to −0.36)</td>
<td>N=52</td>
</tr>
<tr>
<td>Adjusted by covariates and weighted by sample size</td>
<td>N=42</td>
<td>−0.62‡ (−0.78 to −0.37)</td>
<td>N=33</td>
</tr>
<tr>
<td>Weighted by inverse variance¶</td>
<td>N=38</td>
<td>−0.09† (−0.10 to −0.08)</td>
<td>N=20</td>
</tr>
<tr>
<td>Random effects model #</td>
<td>N=38</td>
<td>−0.32‡ (−0.60 to −0.03)</td>
<td>N=20</td>
</tr>
<tr>
<td>Random effects model 2**</td>
<td>N=83</td>
<td>−0.40‡ (−0.62 to −0.17)</td>
<td>N=52</td>
</tr>
</tbody>
</table>

*N value represents the number of trial arms for the given correlation analysis. Trial arms sizes differ because of either fully or partially missing data required for the given analysis.
†P<0.01.
‡P<0.05.
§Weighted according to the sample size of the trial arm.
¶Covariates used are average age of subjects and the percentage of males in the trial arm.
#Maximum likelihood based approach was used with a bivariate normal distribution assumption. A paired samples setup was used for the baseline comparator arms using the variance of the changes from baseline. Variance between placebo and active arms was used in a 2 independent samples setup for the placebo comparator arms.
**Pooled estimate of the within-study variances for potassium and glucose. This model assumed homogenous variances for subjects in all studies.

In addition, the within-study correlation (between potassium and glucose) is assumed to be identical to the between-study correlation.
analysis, using a pooled approach produced an estimated correlation of $-0.40$ (95% CI, $-0.62$ to $-0.17$; $P=0.0007$) for all 83 of the studies. The baseline comparator and placebo comparator subset analyses are listed in Table 2.

Finally, 23 of the 83 arms reported use of potassium supplements. A comparison of these 23 studies to the remaining group of 60 studies is reported in Table 3. The group that received potassium supplementation reports, on average, a smaller decrease of potassium ($-0.23$ meq versus $-0.37$ meq), a smaller increase in glucose ($3.26$ mg/dL versus $6.01$ mg/dL), and a stronger negative correlation ($r=-0.72$) compared with the remaining group ($r=-0.34$). The resulting $P$ value of 0.03 provides strong evidence for a significant difference.

### Discussion

The findings from our analyses of 59 clinical trials containing 83 trial arms demonstrate a significant inverse relationship where lower potassium values are associated with higher glucose values. The findings were consistent after weighting the trials according to sample size and adjusting for age and gender. In addition, separate sensitivity analyses of the trials according to baseline and placebo comparator arms, as well as dropping the 2 largest trial arms, confirmed the inverse relationship between potassium and glucose.

Recent clinical trial results have numerous authors debating the use of thiazide diuretics as first-line therapy for hypertension, because they are associated with increases in the incidence of new-onset diabetes. In ALLHAT, development of diabetes occurred significantly more in the thiazide group with an absolute difference of $1.8\%$ to $3.5\%$ relative to the lisinopril and amlodipine groups ($P<0.05$). In other clinical trials, the absolute difference of new-onset diabetes was $2.1\%$ and $1.6\%$ higher in the thiazide diuretics groups compared with ACE inhibitor or CCB groups. Of interest, the final K+ measurements in ALLHAT were statistically different between the diuretic arm ($4.1$ meq/L) and both the CCB arm ($4.4$ meq/L) and the ACE inhibitor arm ($4.5$ meq/L).

What has been lost in many of these discussions is the relationship between glucose intolerance and hypokalemia that has been known for $>40$ years. The first reports appeared in the 1950s, and several investigators confirmed that glucose intolerance occurred in the face of hypokalemia. In 1964, Rapoport and Hurd found that glucose intolerance could be minimized if hypokalemia was reversed. More recently, in a 3-year study by Amery et al., diuretic-treated patients experienced a $3$ mg/dL rise in fasting blood sugar for each year in the trial. The absolute level of fasting blood sugar was negatively correlated with K+ after 2 and 3 years of follow-up ($P<0.05$). The highest fasting blood sugars occurred with potassium concentrations $<3.9$ mmol/L, indicating that maintaining potassium above $4.0$ mmol/L may prevent glucose intolerance. Results from a study by Gorden provide support for this concept among normal volunteers. These patients were subjected to a hypokalemic state, which produced a glucose intolerance that was reversed with potassium supplementation. Among patients treated with diuretics for hypertension, the Swedish Trial in Old Patients With Hypertension (STOP) supports this concept. The investigators found no significant change in blood glucose or potassium in the group receiving a potassium-sparing diuretic in combination with hydrochlorothiazide compared with placebo. Our analyses support this concept as well. Among the trial arms that used any potassium supplementation/sparing agent, there was a relatively smaller increase in serum glucose, which correlated more strongly with a relatively smaller decrease in potassium. Conversely, among the trials that did not supplement potassium, there was a relatively larger rise in serum glucose, which correlated less strongly with a larger decrease in potassium. Collectively, these data suggest that potassium supplementation with thiazide diuretics may obviate the associated rise in blood glucose.

The results from this study must be interpreted with some caution because there are several limitations. Notably, we extracted pooled data from clinical trials on both potassium and glucose, reducing the potential for effect size and individual variation. In addition, the method for collecting and sampling both potassium and glucose varied across the studies. Variability in the timing of collection, fasting versus nonfasting, and type of samples, plasma or whole blood, would affect the data in this study. Similarly, some trials included patients with diabetes, other trials excluded patients with diabetes, whereas other trials did not specifically mention the presence or absence of diabetes. Finally, information was not always conclusive about the treatment, or rather, the lack of treatment for hypokalemia in the studies. Medication dosage regimens and adherence to the regimen also varied across the studies and may have influenced both the potassium and glucose values. To minimize some of the inherent limitations, we conducted several data analytic techniques to account for missing data and performed various sensitivity analyses. In addition, our analyses calculated correlations between potassium and glucose, demonstrating association but not causality. A test for causality for the effect of thiazide-induced hypokalemia on glucose intolerance must come from a randomized trial; yet, this type of study may not be conducted. Nonetheless, our study pooled results from multiple studies to derive a more robust association.

### Perspectives

Our analyses show a strong relationship between hypokalemia and glucose intolerance in 59 thiazide diuretic clinical
trials. This study, as well as others, suggests that treatment of thiazide-induced hypokalemia could lessen glucose intolerance and possibly the development of diabetes. However, no prospective clinical trials have reported the development of diabetes as a function of potassium levels. Perhaps a retrospective examination of large clinical trials, such as ALLHAT or SHEP, could provide a more definitive answer. However, the data should be examined using a paired analysis of patients’ potassium with blood glucose. In clinical trials, the effects on potassium and blood glucose have been reported as means measured during 1 or more time periods in the trial, thus diluting the potential relationship between potassium and glucose. Ultimately, a prospective clinical trial is needed to test the change in the development of diabetes as a function of intervention on K+.

At this time, it is reasonable to target K+ ≥4.0 mmol/L among all of the patients taking thiazide diuretics. Maintenance cations to control blood pressure,2 the addition of an ACE inhibitor or angiotensin receptor blocker to a thiazide diuretic may maintain potassium homeostasis, because studies have shown that this combination can prevent hypokalemia.32–34

Disclosures

J.G. has been a paid consultant for Genetech. B.L.C. is a member of the NHLBI-ALLHAT speakers bureau. The remaining authors report no conflicts.

References


Thiazide Diuretics, Potassium, and the Development of Diabetes: A Quantitative Review
Alan J. Zillich, Jay Garg, Sanjib Basu, George L. Bakris and Barry L. Carter

Hypertension. 2006;48:219-224; originally published online June 26, 2006;
doi: 10.1161/01.HYP.0000231552.10054.aa

Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2006 American Heart Association, Inc. All rights reserved.
Print ISSN: 0194-911X. Online ISSN: 1524-4563

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://hyper.ahajournals.org/content/48/2/219

Data Supplement (unedited) at:
http://hyper.ahajournals.org/content/suppl/2006/06/26/01.HYP.0000231552.10054.aa.DC1

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Hypertension can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Hypertension is online at:
http://hyper.ahajournals.org/subscriptions/