Response to Effect of Fenofibrate on Vascular Endothelial Function: Statistical Appraisal and its Validity

We recently published an original research article reporting that short-term fenofibrate improves flow-mediated dilation (FMD) in healthy normolipidemic older adults. By assessing the response to vitamin C infusion before and after fenofibrate treatment, we determined that the mechanism for the improvements in FMD was reduced oxidative stress. We also assessed the influence of changes in clinical characteristics on the improvements in FMD. On the basis of these analyses, we concluded that oxidative stress was the primary mechanism for the improvements in FMD in response to fenofibrate.

In a letter to the editor, Dr Kawada recently stated concerns about our statistical analyses. Specifically, there was a concern that the distributions for circulating factors may not be normal. In response, we would like to emphasize that bivariate correlations were performed on the change in these factors from baseline to 2 or 7 days of fenofibrate treatment, not with the raw values. Although it is true that the raw values for circulating factors may not be normally distributed, this is not necessarily the case for the changes over time. To address Dr Kawada’s concern, we analyzed the normality of all variables used in correlation analyses, including the change in FMD, blood pressure, and circulating factors. Using the Shapiro–Wilk test, we found that all factors had a normal distribution except the 2-day change in C-reactive protein and the 7-day change in triglycerides. However, after log transformation, these variables were not related to the change in brachial FMD for those respective time periods (2-day C-reactive protein: r=0.35, P=0.35, r=−0.30, P=0.19), consistent with the results in the original publication.

In our original article, we performed a linear regression to examine the relationship between changes in clinical characteristics and the effect of treatment and changes in potentially modulating factors with FMD and its changes. On the basis of the results of these new analyses, we confirm our original conclusions that the improvements in FMD with fenofibrate are independent of changes in clinical factors in this study. However, as we previously mentioned, the variability of some measures, particularly circulating triglycerides, may limit our ability to accurately assess their contributions to improvements in FMD. Thus, studies with larger sample sizes may be needed to more definitively determine the influences of changes in clinical characteristics on vascular function with fenofibrate treatment.

Table. Linear Regression Analysis for the Influence of Fenofibrate Treatment, Blood Pressure, and Cholesterol on the Change in Flow-Mediated Dilation After 7 Days

<table>
<thead>
<tr>
<th>Variable</th>
<th>β</th>
<th>r²</th>
<th>P Value</th>
<th>Tolerance</th>
<th>VIF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment group</td>
<td>0.514</td>
<td>0.130</td>
<td>0.049</td>
<td>0.491</td>
<td>2.037</td>
</tr>
<tr>
<td>Change in SBP</td>
<td>−0.315</td>
<td>0.042</td>
<td>0.245</td>
<td>0.417</td>
<td>2.398</td>
</tr>
<tr>
<td>Change in DBP</td>
<td>−0.159</td>
<td>0.011</td>
<td>0.543</td>
<td>0.436</td>
<td>2.294</td>
</tr>
<tr>
<td>Change in TC</td>
<td>0.194</td>
<td>0.012</td>
<td>0.523</td>
<td>0.322</td>
<td>3.104</td>
</tr>
<tr>
<td>Change in LDL-C</td>
<td>−0.083</td>
<td>0.003</td>
<td>0.766</td>
<td>0.377</td>
<td>2.652</td>
</tr>
</tbody>
</table>

β indicates standardized beta coefficient; DBP, diastolic blood pressure; LDL-C, low-density lipoprotein cholesterol; r², squared part coefficient; SBP, systolic blood pressure; TC, total cholesterol; and VIF, variance inflation factor.

Disclosures

None.

Ashley E. Walker
Rachelle E. Kaplon
Sara Marian S. Lucking
Molly J. Russell-Nowlan
Douglas R. Seals
Department of Integrative Physiology
University of Colorado Denver
Boulder, CO

Robert H. Eckel
Division of Endocrinology, Metabolism, and Diabetes
Department of Medicine
University of Colorado Denver
Aurora, CO

Response to Effect of Fenofibrate on Vascular Endothelial Function: Statistical Appraisal and its Validity
Ashley E. Walker, Rachelle E. Kaplon, Sara Marian S. Lucking, Molly J. Russell-Nowlan, Douglas R. Seals and Robert H. Eckel

Hypertension. 2013;61:e56; originally published online April 15, 2013;
doi: 10.1161/HYPERTENSIONAHA.113.01310

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/61/6/e56

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/