Effect of Intensive Versus Standard Blood Pressure Control on Depression and Health-Related Quality of Life in Type 2 Diabetes The ACCORD trial

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Journal Title: Diabetes Care
Volume: Volume 35, Number 7
Publisher: AMER DIABETES ASSOC | 2012-07-01, Pages 1479-1481
Type of Work: Article
Publisher DOI: 10.2337/dc11-1868
Permanent URL: https://pid.emory.edu/ark:/25593/s5jc9

Final published version: http://dx.doi.org/10.2337/dc11-1868

Accessed November 10, 2017 12:34 PM EST
Effect of Intensive Versus Standard Blood Pressure Control on Depression and Health-Related Quality of Life in Type 2 Diabetes

The ACCORD trial

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OBJECTIVE—We tested the hypothesis that intensive (systolic blood pressure [SBP] <120 mmHg) rather than standard (SBP 130–139 mmHg) blood pressure (BP) control improves health-related quality of life (HRQL) in those with type 2 diabetes.

RESEARCH DESIGN AND METHODS—Subjects were 1,028 ACCORD (Action to Control Cardiovascular Risk in Diabetes) BP trial HRQL substudy participants who completed baseline and one or more 12-, 36-, or 48-month HRQL evaluations. Multivariable linear regression assessed impact of BP treatment assignment on change in HRQL.

RESULTS—Over 4 years of follow-up, no significant differences occurred in five of six HRQL measures. Those assigned to intensive (vs. standard) BP control had statistically significant worsening of the Medical Outcomes Study 36-item short-form health survey (SF36) physical component scores (β = 0.8 vs. −0.2, P = 0.02), but magnitude of change was not clinically significant. Findings persisted across all prespecified subgroups.

CONCLUSIONS—Intensive BP control in the ACCORD trial did not have a clinically significant impact, either positive or negative, on depression or patient-reported HRQL.

Diabetes Care 35:1479–1481, 2012

In those with type 2 diabetes (T2DM), adequate blood pressure (BP) control may enhance control of hypertension (HT)-related symptoms and reduce the risk of major vascular events that impair health-related quality of life (HRQL) (1,2). However, the net impact of BP treatment on HRQL in patients with T2DM is determined by the balance of treatment burden, hypotension-related adverse events, and BP medication side effects on the one hand and potential reductions of cardiovascular disease (CVD) and microvascular events on the other (3).

In the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial, intensive BP control did not reduce the main prespecified, composite macrovascular outcome, or reduce mortality or myocardial infarctions, although intensive BP treatment did reduce the rate of strokes (4,5). In light of mixed clinical results, the impact of BP interventions on HRQL may inform the selection of optimal BP targets by clinicians and patients.

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The opinions and interpretations expressed in this article do not necessarily reflect those of the study’s sponsors or funding agencies.

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and at 12, 36, and 48 months throughout the ACCORD clinic visits. All measures that were completed before 30 June 2009 were used in the analysis. Completion varied somewhat across instruments.

Each HRQOL or depression measure was a dependent variable considered in a separate linear model for repeated measures; no formal adjustments were made for multiple tests. All models included BP trial assignment, glucose trial assignment, and presence or absence of cardiovascular events at baseline. To test whether the effect of the BP treatment arm assignment varied across time, we included an interaction term for BP treatment arm by time. A second set of models tested each HRQOL or depression outcome as outlined above but included sex, race, and age at baseline. Finally, we analyzed prespecified subgroups based on age, race/ethnicity, prior CVD, glucose trial assignment, number of BP medications taken just prior to randomization, baseline diastolic BP, and baseline systolic BP levels.

RESULTS—Participants randomly assigned to the intensive and standard BP treatment arms of ACCORD had similar baseline demographic and clinical characteristics, except that the proportion of subjects on statin therapy at baseline was 64.2% in the intensive BP treatment arm and 71.2% in the standard BP versus intensive BP treatment arms (P = 0.02). At baseline, the six prespecified HRQOL and depression outcome measures were not statistically different between subjects randomized to intensive versus standard BP treatment.

Table 1 shows the results of repeated HRQOL and depression outcome measure analyses by intensive versus standard BP treatment arm at last available follow-up. Mean follow-up time from randomization to last HRQOL assessment was 1,362 days (median 1,461 days, or 4.0 years). No differences between intensive BP and standard BP treatment group were noted in the change in PHQ-9 scores, SF36 mental component scores, number of symptoms, mean symptom distress, or treatment satisfaction. However, SF36 physical component scores decreased more from baseline to follow-up among the intensive BP treatment group relative to the standard BP treatment group (−0.8 vs. −0.2 units; P = 0.02), suggesting worse perceived physical function over time in the intensive BP treatment group.

Results, including the statistically significantly worse SF36 physical component scores, persisted across prespecified subgroups based on age, sex, race, baseline CVD status, glucose trial assignment, BP tertiles at baseline, and baseline number of BP medications (data not shown).

CONCLUSIONS—Intensive BP control neither improved nor worsened most measures of health-related quality of life. Although intensive BP control subjects had significantly worse SF36 physical component scores, the magnitude of this difference (less than one point out of 100 on the SF36 physical component score) is less than the five-point change generally considered the minimal clinically important difference for this scale (9). Thus, this degree of difference in SF36 physical component scores, although statistically significant, was not clinically significant.

A recent meta-analysis of 20 studies (using various SF questionnaire versions) reported physical health scores that were 2.43 points lower in hypertensive compared with normotensive patients, but the studies included were heterogeneous (12). The Treatment of Mild Hypertension Study (TOMHS) showed that among adults with HT and no diabetes, actively treated HT patients had better HRQOL than those treated with placebo, although the effects of specific classes of HT medications were mixed (2). However, HRQOL data for those with diabetes and comorbid HT are limited. The few observational studies examining the effects of coexisting morbidities (e.g., diabetes and other non-BP cardiovascular risk factors) have shown no consistent pattern of association for BP (and/or HT) and HRQOL (13–15). Furthermore, no prior, large, randomized trial has achieved SBP <120 mmHg, so no prior assessment of the impact of such low BP levels on the HRQOL of patients with HT is available. Whether the results presented may change with longer-term follow-up is of interest, and follow-up of ACCORD subgroups is underway.

Acknowledgments—This study was funded by the National Heart, Lung, and Blood Institute (N01-HC-095183 and other contracts), National Institute of Diabetes and Digestive and Kidney Diseases, and Centers for Disease Control and Prevention.

No potential conflicts of interest relevant to this article were reported.

P.J.O., M.K.A., and M.D.S. researched data and wrote the manuscript. K.M.V.N., R.A., L.F., D.L.S., J.M.S.-H., L.A.K., and K.L.M. reviewed and edited the manuscript and contributed to conclusions and introduction. P.F. and D.G.H. researched and analyzed data and contributed to research design and methods and results. P.J.O. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Parts of this study were presented orally at the 71st Scientific Sessions of the American Diabetes Association, San Diego, California, 24–28 June 2011.

References


Table 1—Results of repeated-measures analyses of HRQOL and PHQ-9 outcomes by glycemia arm measures taken at years 1, 3, and 4

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intensive</th>
<th>Standard</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF36 physical component score (SE)</td>
<td>−0.8 (0.19)</td>
<td>−0.2 (0.19)</td>
<td>0.02</td>
</tr>
<tr>
<td>SF36 mental component score (SE)</td>
<td>0.5 (0.39)</td>
<td>0.4 (0.40)</td>
<td>0.77</td>
</tr>
<tr>
<td>Sum of diabetes symptoms (SE)</td>
<td>−1.4 (0.34)</td>
<td>−1.1 (0.35)</td>
<td>0.48</td>
</tr>
<tr>
<td>Diabetes symptom distress (SE)</td>
<td>−0.04 (0.02)</td>
<td>−0.04 (0.02)</td>
<td>0.98</td>
</tr>
<tr>
<td>Diabetes treatment satisfaction (SE)</td>
<td>13.3 (0.54)</td>
<td>13.1 (0.55)</td>
<td>0.84</td>
</tr>
<tr>
<td>PHQ-9 continuous score (SE)</td>
<td>−1.1 (0.14)</td>
<td>−0.9 (0.14)</td>
<td>0.29</td>
</tr>
</tbody>
</table>
15. U.K. Prospective Diabetes Study Group. Quality of life in type 2 diabetic patients is affected by complications but not by intensive policies to improve blood glucose or blood pressure control (UKPDS 37). Diabetes Care 1999;22:1125–1136