Glycemic Control and Hypoglycemia: Is the Loser the Winner?: Response to Perlmuter et al.

The Harvard community has made this article openly available. Please share how this access benefits you. Your story matters

Citation

Published Version
doi:10.2337/dc08-2264

Citable link
http://nrs.harvard.edu/urn-3:HUL.InstRepos:12153019

Terms of Use
This article was downloaded from Harvard University's DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA
hypoglycemia and cognitive performance
tween subsequent episodes of severe
lescence, there was no relationship be-
Complications Trial (DCCT) during ado-
ported that within the cohort of subjects
effects of severe hypoglycemia and raised
T
Loser the Winner?
Glycemic Control and
Hypoglycemia: Is the
Loser the Winner?
Response to Perlmutter et al.
The editorial by Perlmutter et al. (1) in
the October 2008 issue of Diabetes Care commented on the long-term effects of severe hypoglycemia and raised concerns about our study (2), which reported that within the cohort of subjects who entered the Diabetes Control and Complications Trial (DCCT) during adolescence, there was no relationship between subsequent episodes of severe hypoglycemia and cognitive performance measured ~20 years after study entry. Below, we outline their five major concerns and provide supporting information.

One concern of Perlmutter et al. was the exclusion of potential participants from the DCCT if they had a history of severe hypoglycemia, thus limiting generalizability. However, a history of severe hypoglycemia was not an absolute exclusion criterion for participation in the DCCT. Indeed, 24% of the 175 participants had previously experienced 1–5 episodes of severe hypoglycemia with loss of consciousness before entry into the DCCT.

The editorial by Perlmutter et al. also suggested that nonparticipation may have been due to cognitive deterioration or severe hypoglycemic events. However, the 56 nonparticipants remained active in the Epidemiology of Diabetes Interventions and Complications (EDIC) protocol, and data are available on their frequency of severe hypoglycemia. The frequency distribution of severe hypoglycemia episodes is similar between the 56 nonparticipants and the 175 participants (5 vs. 9%, respectively). Therefore, dropout due to cognitive deterioration is unlikely. A comparison of cognitive performance between baseline and DCCT year 5 for both groups showed the same scores on seven domains, with participants scoring modestly better only on problem solving (P = 0.01).

Perlmutter et al. asserted that baseline data for the dropouts would have been useful: There were no differences in demographic or clinical characteristics between the 175 participants and the 56 nonparticipants at baseline. Complete baseline data are available upon request.

Perlmutter et al. also stated that our article was unclear regarding the ages of the individuals during each severe hypoglycemic episode: By EDIC year 12, there were 294 events in 87 subjects (33 events, ages 13–16 years; 71, 17–19 years; 152, 20–29 years; and 38, 30–39 years). As noted on page 1936 of our article, the timing of severe hypoglycemic events did not affect performance on any of the eight cognitive domains evaluated.

Finally, Perlmutter et al. expressed concern regarding the synergistic effects of hyperglycemia and hypoglycemia and stated that statistical support for these effects was not reported. The synergistic effects of hypoglycemia and hyperglycemia on cognitive function were evaluated using the interaction term in an ANCOVA model. We found no statistically significant effect.

In conclusion, our research question related to the long-term effects of severe hypoglycemic episodes on cognitive performance associated with intensive insulin therapy during the DCCT and post-DCCT period. Our results indicate that for patients similar to those of the DCCT adolescent cohort, intensive diabetes therapy can be implemented without undue concern for development of long-term cognitive deficits during the follow-up period. Despite this finding, intensive diabetes therapy must be practiced with caution because severe hypoglycemia can cause short-term cognitive impairment that affects ability to carry out daily activities and can lead to seizure or coma. Moreover, effects of hypoglycemia at a younger age were not assessed. In sum, the goal of achieving tight glycemic control while avoiding severe hypoglycemia is appropriate for adolescent patients.

GAIL MUSEN, PHD1,2
ALAN M. JACOBSON, MD1,2
CHRISTOPHER M. RYAN, PHD3
PATRICIA A. CLEARY, MS4
BARBARA H. WABERSKI, MS4
KATIE WEINGER, EDD5,2
WILLIAM DAHMS, MD5
MEG BAYLESS, RN6
NANCY SILVERS, RN7
JUDITH HARTH, RN7
NEIL WHITE, MD, CDE8
FOR THE DIABETES CONTROL AND
COMPLICATIONS TRIAL/EPIDEMIOLOGY OF
DIABETES INTERVENTIONS AND
COMPLICATIONS (DCCT/EDIC) RESEARCH GROUP*

From the 1Joslin Diabetes Center, Boston, Massachusetts; the 2Department of Psychiatry, Harvard Medical School, Boston, Massachusetts; the 3Department of Psychiatry, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; the 4Biostatistics Center, George Washington University, Washington, D.C.; 5Rainbow Babies and Children’s Hospital, Case Western Reserve University, Cleveland, Ohio; 6Diabetes Clinical Research & Programs, University of Iowa, Iowa City, Iowa; 7St. Joseph’s Health Care London, University of Western Ontario, London, Ontario, Canada; and the 8Department of Pediatric Endocrinology and Metabolism, Washington University in St. Louis, St. Louis, Missouri.

*Corresponding author: Gail Musen, gail.musen@joslin.harvard.edu


Acknowledgments — Funding for this study was provided by NIH grant 5RO1-DK-062218-02 and contracts with the Division of Diabetes, Endocrinology, and Metabolic Diseases of the National Institute of Diabetes and Digestive and Kidney Diseases and by the General Clinical Research Centers Program, National Center for Research Resources.

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

References