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Journal

NEUROLOGY, 58(7)

ISSN

0028-3878

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Publication Date

2002-04-09

P02.018

Plasma Total Cholesterol, LDL, HDL Levels and the Risk of Alzheimer Disease: The Baltimore Longitudinal Study of Aging

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OBJECTIVE: To examine the association of plasma levels of total cholesterol, low density lipoproteins (LDL), and high density lipoproteins (HDL) with the risk of developing Alzheimer disease (AD).

BACKGROUND: Several studies have suggested an increased risk of Alzheimer disease among subjects with high cholesterol levels during midlife. In addition, there is evidence that cholesterol lowering drugs (statins) may reduce the risk of dementia.

DESIGN/METHODS: Participants are volunteers in the Baltimore Longitudinal Study of Aging (BLSA), a multidisciplinary study of normal aging conducted by the National Institute on Aging. Cholesterol and lipid levels were collected from BLSA participants during their biennial visit between 1983 and 1998. Clinical diagnoses were made according to DSM-III-R criteria for dementia and NINCDS-ADRDA criteria for probable or possible AD. 988 BLSA participants who were older than 60 years of age and had plasma cholesterol and lipid levels were included in the analyses. We used Cox proportional hazards models to estimate the relative risk (RR) and confidence intervals (CI) of developing AD associated with plasma levels (mg/dl) of total cholesterol, LDL, HDL, and LDL/HDL ratio at different time periods up to 9 years before the diagnosis of AD. Separate analyses were performed for each of the intervals before diagnosis. Chronological age was used as the time scale in the Cox models. The most recent cholesterol and lipid level within each interval was included as a time-dependent variable in the models. The analyses adjusted for gender, education, and use of cholesterol lowering drugs (statins).

RESULTS: High levels of LDL or a high ratio of LDL/HDL years before diagnosis was associated with an increased risk of AD. 7 to 9 years before diagnosis the RR for LDL levels > 160 mg/dl vs. < 130 mg/dl was 2.65 (95%CI=1.33–5.31, p=.006) while the RR for an LDL/HDL ratio > 3 was 1.82 (95%CI=1.02–3.25, p=0.04). 5 to 7 years before diagnosis, there was also a significant increase in the risk of AD in subjects with a high ratio of LDL/HDL levels (RR=1.76, 95%CI=1.04–2.99, p=.04). We also found an increased risk of AD among subjects with low levels of HDL and among subjects with high cholesterol levels 7 to 9 years before diagnosis but this increase was not statistically significant. The RR for HDL levels < 50 mg/dl was 1.62 (95%CI=0.86–3.33, p=0.14) and the RR for total cholesterol levels > 200 mg/dl was 1.60 (95%CI=0.89–2.90, p=.12). Adjustment for use of statins did not have an effect on the association between risk of AD and lipid levels up to 5 years before diagnosis. Statin information was not available at longer intervals before diagnosis because of the infrequent use of these compounds in those time periods. Adjustment for presence or absence of an ε4 allele of Apolipoprotein E did not change the association.

CONCLUSIONS: Our findings support previous suggestions that high levels of LDL or a high ratio of LDL/HDL may increase the risk of AD years later. Total cholesterol or HDL levels appear to be less relevant to AD but further studies are necessary.

Supported by: extramural grants AG05146 and AG08325 and the Intramural Research Program of the National Institute on Aging

Disclosure: Maria M Corrada has nothing to disclose.