FULL-LENGTH ARTICLE NPub.org/ifylll

Association of Serum Magnesium Levels With Risk of Intracranial Aneurysm

A Mendelian Randomization Study

Susanna C. Larsson, PhD, and Dipender Gill, BMBCh, PhD

Cite as: *Neurology*® 2021;97:e341-e344. doi:10.1212/WNL.0000000000012244

Correspondence
Dr. Larsson
susanna.larsson@ki.se

Study Question

Is there an association between serum magnesium concentration and the risk of intracranial aneurysm?

What Is Known and What This Paper Adds

Serum magnesium concentrations have been implicated in regulating blood pressure and function of the vascular endothelium but whether increased serum magnesium concentrations affect the risk of intracranial aneurysm and related subarachnoid hemorrhage is not known. This investigation's results show that higher serum magnesium concentrations are associated with a reduced risk of intracranial aneurysm.

Methods

For this Mendelian randomization study, the investigators focused on 5 single-nucleotide polymorphisms (SNPs; rs4072037, rs7965584, rs3925584, rs13146355, and rs448378) that were associated with serum magnesium concentrations in a genome-wide association study involving 23,829 individuals of European ancestry. Genetic association estimates were obtained for intracranial aneurysm from a genome-wide association study involving 79,429 individuals of European ancestry (7,495 individuals with intracranial aneurysm and 71,934 control individuals) who belonged to 23 different cohorts. The inverse-variance weighted method was used in the primary analyses to obtain the causal estimates for serum magnesium concentrations and intracranial aneurysm.

Results and Study Limitations

Higher genetically predicted serum magnesium concentrations reduced the risk of intracranial aneurysm. The odds ratios per 0.1-mmol/L increment were 0.66 (95% confidence interval [CI], 0.49–0.91) for intracranial aneurysm in general, 0.57 (95% CI, 0.30–1.06) for unruptured intracranial aneurysm, and 0.67 (95% CI, 0.48–0.92) for aneurysmal subarachnoid hemorrhage. The present study's limitations include the possibility that the genetic proxies for serum magnesium concentrations influence aneurysm risks through alternative pathways that may violate the requisite assumptions of the Mendelian randomization approach. Furthermore, the investigators lacked the necessary data for a bidirectional Mendelian randomization analysis to investigate whether mechanisms that predispose an individual to intracranial aneurysm also influence circulating magnesium concentrations.

Table SNPs and Intracranial Aneurysm

SNP	β (standard error)
rs4072037	−0.038 (0.021)
rs7965584	−0.050 (0.022)
rs3925584	0.016 (0.022)
rs13146355	−0.026 (0.019)
rs448378	−0.036 (0.021)

Associations between SNPs and risk of intracranial aneurysm.

Study Funding and Competing Interests

This study was funded by the Swedish Research Council for Health, Working Life and Welfare; the British Heart Foundation Research Centre of Excellence at Imperial College London; and a National Institute for Health Research Clinical Lectureship at St. George's, University of London. Dr. Larsson has received funding from the Swedish Research Council and the Swedish Heart-Lung Foundation, outside this work. Dr. Gill is a part-time employee of Novo Nordisk. Go to Neurology.org/N for full disclosures.

A draft of the short-form article was written by M. Dalefield, a writer with Editage, a division of Cactus Communications. The corresponding author(s) of the full-length article and the journal editors edited and approved the final version.

Association of Serum Magnesium Levels With Risk of Intracranial Aneurysm: A Mendelian Randomization Study

Susanna C. Larsson and Dipender Gill

Neurology 2021;97;e341-e344 Published Online before print June 22, 2021
DOI 10.1212/WNL.0000000000012244