MENDELIAN RANDOMIZATION IN ENVIRONMENTAL EPIDEMIOLOGY

Bencko V, Novotný L
Charles University in Prague, 1st Faculty of Medicine, Institute of Hygiene and Epidemiology, Prague, Czech Republic

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Mendelian randomization principle (MRP) represents a chance for methodology of evaluation of the causal relations between external cause and disease. The use of the principle assumes the association between the disease and the genetic polymorphism studied reflects the biological relations between the suspected exposure and the disease, and is generally less prone to the phenomenon of confounding and reverse causation, which can impair the interpretation of results in conventional observational studies. Authors describe explanatory options of MRP using examples of isothiocyanate (ITC) versus lung carcinoma. Cruciferous vegetables (CV) – rich in ITCs, have been shown in animals to have strong chemopreventive properties against lung cancer. ITCs are thought to be eliminated by glutathione-S-transferase enzymes. Individuals who are homozygous for the inactive form of either or both genes GSTM1 and –T1, probably have higher ITCs concentrations because of their reduced elimination capacity. According the Mendelian principle genes are likely to be independent of other dietary and lifestyle factors, reducing the possibility of confounding from these sources. Our institute participated in investigation of this relation in a case-control study of 2,141 cases and 2,168 controls in six countries of central and Eastern Europe, a region that has traditionally high rates of CV consumption. The dietary component of the food frequency questionnaire listed 23 foods, of which three were CV (cabbage and a combination of brussels sprouts with broccoli). Neither GSTM1 nor GSTT1 PCR-based genotypes were related to potential confounding factors in the controls, such as country, age, smoking status, education, and dietary variables. Thus weekly consumption of CV protected against lung cancer in those who were GSTM1 null (odds ratio, OR = 0.67, 95% CI 0.49–0.91), GSTT1 null (0.63, 0.37–1.07), or both (0.28, 0.11–0.67). No protective effect was seen in people who were both GSTM1 and GSTT1 positive (0.88, 0.65–1.21). Similar protective results were noted for consumption of cabbage and a combination of broccoli and brussels sprouts. An overall protective effect of CV consumption: adjusted OR (0.78, 95% CI 0.64–0.96) was much the same for both cabbage consumption and for broccoli and brussels sprout consumption**.** The results also accord with those of several smaller studies of lung cancer, breast cancer, and colorectal adenomas, which showed a protective effect in GSTM1 and GSTT1 null carriers. Though the use of MRP has its limitations, it offers new possibilities to test causal relations and clearly shows that means invested into the Human genome project can contribute to the understanding and prevention of adverse effects of modifiable exposure to the human health.

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