Nitrate intake and gastric cancer risk: results from the Netherlands cohort study

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1. Introduction

The high intake of nitrate has led to growing concern about the health risks, based on the risk of the metabolite of nitrate, nitrite. This concern focuses mainly on the risk of gastric cancer [1]. Nitrate is a natural compound of foods like vegetables and potatoes and in the Netherlands it is used as food additive in cheese and cured meats. It is also present in drinking water [2]. The proposed mechanism by which nitrate can be converted to carcinogenic N-nitroso compounds contains the following steps. After ingestion and absorption in the stomach, nitrate is secreted in the saliva in concentrated form. Oral bacteria can then reduce nitrate to nitrite. About 25% of ingested nitrate is recirculated into the saliva and about 20% of the salivary nitrate is reduced to nitrite by oral bacteria. Next, nitrite can react with nitrosatable compounds like amines, amides and aminoacids to N-nitroso compounds [3]. Ascorbic acid acts as inhibitor of the nitrosation reaction by reduction of nitrous acid (HNO₂) to nitric oxide (NO) and production of dehydro-ascorbic acid [4]. Apart from that, ascorbic acid has also been suggested to inhibit gastric carcinogenesis by acting as a scavenger of free radicals, thus preventing oxidative damage in gastric mucosa and mutations in DNA. We have studied the association between gastric cancer risk and nitrate intake from foods and drinking water, with special attention for vitamin C, in the Netherlands Cohort Study (NLCS) on nutrition and cancer.

2. Methods

The NLCS started in September 1986 in the Netherlands among 120,852 men and women aged 55–69 years. The usual consumption of food and beverages during the year preceding the start of the study was assessed at baseline with a 150-item semiquantitative food frequency questionnaire. A detailed description of the cohort study design has been reported elsewhere [5]. Food composition values for nitrate were derived from the Databank on contaminants in food.
from the State Institute for Quality Control of Agricultural Products (RIKILT, Wageningen). Nitrate contents in drinking water were also derived from the Databank on contaminants in food. Follow-up for cancer incidence consisted of record linkage with all regional cancer registries in the Netherlands and with a national pathology register (PALGA). This method of record linkage has been described previously [6]. For data-analysis a case-cohort approach is used [7], in which cases are derived from the entire cohort, while the person-years at risk are estimated from a randomly selected subcohort sample of 3500 subjects. The analysis is restricted to gastric cancer incidence from September 1986 through December 1990. In this period completeness of follow-up of the cohort was estimated to be at least 96% [8]. After these 4.3 years of follow-up 203 incident gastric cancer cases were detected. We excluded self-reported prevalent cancer cases other than skin cancer, cases with in situ carcinoma and cases without microscopically confirmed diagnosis. Also cases and subcohort members who did not answer the questions about dietary intake inventory were excluded. After these exclusions 177 gastric cancer cases were available for the analyses.

3. Results

In the subcohort the median daily nitrate intake was 99 mg NO$_3^-$ from foods as measured with the questionnaire (95th percentile 185 mg NO$_3^-$) and 4 mg NO$_3^-$ from drinking water (95th percentile 19 mg NO$_3^-$). After adjustment for age and sex, there was a significant inverse association between nitrate intake from foods (RR highest/lowest quintile 0.59, 95% Cl 0.37–0.94, trend-P = 0.01) and gastric cancer risk. We did not find an association between nitrate intake from drinking water and gastric cancer risk (RR highest/lowest quintile 1.05, 95% Cl 0.64–1.72, trend-P = 0.88). After additional adjustment for potential risk factors for gastric cancer (e.g. smoking habits, highest level of education, dietary intake of beta-carotene and vitamin C, family history of stomach cancer, prevalence of stomach disorders and use of refrigerator (number of years) or freezer (yes or no)), the rate ratio of gastric cancer for nitrate intake from foods in the highest quintile versus the lowest quintile was 0.62 (95% CI 0.31–1.22, trend-P = 0.09). The association between nitrate intake from drinking water did not change substantially either after the additional adjustment (RR highest/lowest quintile 1.02, 95% Cl 0.62–1.68, trend-P = 0.89). Furthermore, we categorized persons according to their nitrate intake from foods (low, medium, high) and intake of vitamin C (low, medium, high). In each tertile of vitamin C intake, people within the higher tertiles of nitrate intake had lower age- and sex-adjusted rate ratios for gastric cancer.

4. Conclusions

There is an inverse association between nitrate intake from foods and gastric cancer risk. This association was only partly due to the confounding effect from other risk factors for gastric cancer. There is no association between nitrate intake from drinking water and gastric cancer risk. After stratification for vitamin C intake, people with higher nitrate intake from foods still have lower rate ratios for gastric cancer. Therefore, we can conclude that, based on the current nitrate levels in the Netherlands, people within the highest categories of nitrate intake have no higher risk for gastric cancer.

References

