REVIEW

Substitution Analysis in Nutrition Sciences: A Tutorial

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Abstract

Evaluating the effects of nutrients in our diet needs to enter more than one nutrient item (or food groups) in a single statistical unit. Accordingly, not only we consider the effects of a nutrient in health-related subjects, but also we find out the consequences of replacing and deleting nutrients. In nutritional epidemiology, substitutional analysis is used to evaluate the effects of various nutrients on a specific outcome. In the substitutional analysis, when some nutrients or foods are included in a single statistical model, investigation of the effects of several nutrients on the specific outcome is more achievable. The objective of this paper was to provide a detailed examination of the key aspects of substitutional analysis in nutritional sciences.

Keywords: Substitution analysis- dietary intake- nutritional epidemiology

Introduction

Investigating the role of nutrition sciences in human health as well as their role in the incidence of various diseases has a long history [1]. However, focusing on the role of a nutrient and ignoring the intakes of other nutrients that may affect our desired outcome reduce the precision and generalizability of the results [2]. Typically, adding a nutrient in the diet may lead to elimination of other nutrients and perceived impact of added food can be caused by the effects of eliminated nutrients than those adding [2]. So, it is better to consider the effect of eliminated nutrients in the diet when evaluating the effects of food intake. Accordingly in evaluating the effects of nutrients in our diet, more than one nutrient item (or food groups) should be entered in a single statistical unit. Through this method, not only we consider the effects of a nutrient in health-related subjects, but also we find out the consequences of replacing and deleting nutrients in our outcome. For this reason, in recent years, it has been tried to make an epidemiological model to study the effects of using single nutrients on health outcome and compare it with other nutrients [3-4]. For example, a recent study evaluated the effects of carbohydrate on the risk of type 2 diabetes with considering the intake of other macronutrients [5]. They concluded that if 3% of total calorie from protein sources replaced with the same iso-calorie carbohydrate sources, risk of diabetes decreased by 16%. Comparative study of the role of nutrients is called substitutional analysis [2].

In this way, the difference between the coefficients of the regression parameters entered in the multivariate model is used to estimate relative risks (RR) and 95% confidence interval is considered for replacement of a nutrient used in place of other food [2]. This method can be utilized interchangeably to replace nutrients and food items. For example, we can use it to estimate the percentage of energy intake that yield from each macronutrient. By entering three macronutrients in a model, we can compare their effects. This model enables us to obtain more comprehensive interpretation when adding one nutrient and decreasing other macronutrients. If P, C, and F respectively represent the percentage of energy intake yield from protein, carbohydrate, and fat, and m poses as a confounding factor, the model will be as follows:

$$Y0 = pP + fF + cC + m$$

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In this model, if one serving of carbohydrate is replaced with one serving of fat, the model is:

Ynew= pP + f (F-1) + c (C+1) + m = Y0 + (c-f) Substitute Analysis was proposed for the first time by Walter Willet in 1997 to replace carbohydrate intake with the same calories come from fat and protein [6]. In his study, the effect of carbohydrate was different from the effects of each of two other groups (protein or fat). Mostly, substitute analysis is done using combined data from cohort studies and data aggregation [7]. The exposure-disease association is evaluated by Cox proportional hazards model [8].

Definition and examples of the substituted analysis in nutrition

In nutritional epidemiology, substitutional analysis is used to evaluate the effects of various nutrients on a specific outcome [9]. Faerch et al. (2005) evaluated the effects of dietary factors on the incidences of diabetes in adults in both sex. The aim of this study was to determine whether using substitutional analysis can increase the achievements of previous studies or not. This study used data from Danish research, "inter 99 studies". They compared dietary intake of 262 non-diabetic people with 4,627 diabetic patients by using two different types of logistic regression after adjustment for confounders. The first model included single dietary factors and the second model was based on the replacement of macronutrients with each other. In the first model dietary intake of carbohydrates, fiber, and coffee had inverse association with diabetes (P > 0.01). Total fat and saturated fat intake had a direct correlation with diabetes (P > 0.05). The results of substitutional model showed that when 3% of calorie intake of carbohydrate was replaced for fat, alcohol or protein, the likelihood of developing diabetes dropped by 7%, 10%, and 16%, respectively (P > 0.05). Therefore, the use of substitute model would gain more information on the relation between nutrients intake and the risk of diabetes [5]. Another study by Song et al was done to investigate the relation between plant or animal sources of protein intake and the mortality risk [10]. This study used data from 131,342 participants from two cohort studies (Nurse's health study and Health Staff Follow-up Study). Dietary intakes of animal and plant sources protein were assessed using food frequency questionnaire. Intake of animal proteins was linked with higher mortality rate of heart disease.

(HR, 1.08 per 10% energy increment; 95%CI, 1.01-1.16; P = .04). Plant protein intake was associated with a decreased risk of various diseases mortalities, especially heart disease mortality.

(HR,0.88 per 3% energy increment; 95%CI, 0.80-0.97; P for trend = .007). When the plant protein intake with 3% calories was replaced with processed animal protein, unprocessed animal protein, or egg, hazard ratio (HR) of death from various causes would be 0.66, 0.88, and 0.81, respectively. It was concluded that the source of dietary protein played a significant role in the risk of death.

Borgi et al evaluated the relationship between intake of potatoes and hypertension [11]. In the aforementioned study, 62,175 women from Nurse's Health Study and 36,803 men from health staff study without hypertension were included. HR for 4 or more baked potatoes or mashed potatoes servings per day was 1.11. (95% confidence interval 0.96 to 1.28; P for trend=0.05), for French fries was 1.17, and for potato chips was 0.97 (0.87 to 1.08; P for trend=0.98). In the substitutional analysis, substitution of one unit of a baked, boiled or mashed potato with non-starchy vegetables reduced the risk of hypertension (hazard ratio 0.93, 0.89 to 0.96 respectively).

Five assumptions for using substitutional analysis in nutritional sciences

In the substitutional analysis, when some nutrients or foods are included in a single statistical model, investigation of the effects of several nutrients on the specific outcome is more achievable. For example, a substitutional analysis revealed that replacing potatoes with non-starchy vegetables lowered blood pressure. Therefore, in nutritional interventions, a dietary guideline included a non-starch vegetables instead of potato can have some advantages. When choosing food alternatives for a substitutional analysis, these five critical assumptions should be considered.

1- Selecting foods should be in accordance with the the results of previous studies. For example, previous studies demonstrated the relationship between fat and carbohydrate intakes and diabetic incidence, then we could consider these two macro-nutrient groups in substitutional analysis [5].

2- Food items included in substitutional analysis should be different from each other in terms of their food ingredients affecting desired outcome. To illustrate this difference, we can use the example of starchy and non-starchy vegetables which their starch ingredients are completely different and these may cause different effects in the incidence of hypertension [11]. So, it is recommended to consider the possible mechanisms of action of each food before choosing them for the substitutional analysis.

3- Food items for substitutional analysis should be selected from the replaceable choices so that the results could be useful for future studies. For example, we can apply the substitutional analysis results which show that replacing saturated fatty acids (SFA) with polyunsaturated fatty acids (PUFA) may significantly reduce the risk of coronary heart disease [7]. In this regard, replacing PUFA consumption by SFA could be a possible dietary intervention.

4- If the substitutional analysis considered macronutrients, its better to use isocaloric amounts of these nutrients to replace with each other to avoid the effects of change in energy intake. For example, 3% of energy intake from carbohydrate could be replaced with fat in isocaloric values [3].

5- Adjustment for all related confounders is crucial. For example, if the analysis of the relation between PUFA and SFA replacement with coronary heart disease is evaluated, factors such as age, smoking status, body mass index, effective drugs against high blood pressure,

family history, using vitamin E supplements, alcohol consumption, and physical activity should be assumed and adjusted [7].

Substitutional analysis provides a good opportunity to assess dietary intake. Investigation of the effects of several nutrients on the specific outcome is more achievable in the substitutional analysis. Conducting a substitutional analysis can enhance the likelihood of the associations between dietary intake and health related outcomes. Substitutional analysis should be well designed; selected foods should be associated with the outcome, selected food items should be different from each other in terms of their food ingredients, food items should be selected from the replaceable choices, isocaloric amounts of the nutrients should be used to be replaced with each other, and adjustment for all related confounders is crucial.

Conflict of Interest

There is no conflict of interest to be reported.

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