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Calibration of Dietary Data: "Folate and Nutrients Involved in the 1-Carbon Cycle in the Pretreatment of Patients for Colorectal Adenocarcinoma in a Referral Center for Oncology in Southeastern Brazil"

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Abstract

Objective: Calibrate the FFQ and evaluate its performance in relation to the consumption of energy, carbohydrate, protein, fat, alcohol, folate, vitamin B2, vitamin B6, vitamin B12, methionine, choline and betaine in the study population "Folate and nutrients involved in the 1-carbon cycle in the pretreatment of patients for colorectal adenocarcinoma in a referral center for oncology in southeastern Brazil.

Materials and methods: For calibration, we used three 24-hour dietary recalls (R24s; n=270) and the second FFQ (n=90) collected in a previous study. The R24 data were used as a reference method and subjected to linear regression, with β1 values used as a calibration factor for the FFQ data collected.

Results: Comparing the R24 data to observed FFQ data and observed FFQ data to calibrated FFQ data; the means were significantly different for all nutrients. When comparing calibrated FFQ data to R24 values, the means were statistically similar for carbohydrates, vitamin B2, vitamin B6, natural folate, synthetic folate, DFE diet and betaine.

Conclusion: The calibration coefficients were low, however the reference method used may not have been the best way to eliminate measurement errors found in the FFQ.

Keywords: Colorectal cancer; Dietary intake; Food frequency questionnaire; 24-hour food recall; Calibration

Introduction

The study "Folate and nutrients involved in the 1-carbon cycle in the pretreatment of patients for colorectal adenocarcinoma in a referral center for oncology in southeastern Brazil"' [1] is a work that aimed to assess the intake of folate and nutrients involved in the 1-carbon cycle in the pretreatment of patients for colorectal adenocarcinoma in a referral center for oncology in southeastern Brazil, using a food frequency questionnaire (FFQ) validated for patients with colorectal cancer. However, it is known that any dietary assessment method can lead to errors inherent in the estimation of food intake, and that no dietary measurement allows the estimate of true dietary intake of a group of individuals [2,3]. Thus, in virtue of these errors, this study may provide strategies for the analysis of the FFQs that have been used [4].

Calibration is a methodology that can be employed and is characterized by determining the correlation between two scales of measurement. It can be obtained through linear regression models which use a reference method purportedly free of errors [5]. We have as an aim to convert the results obtained in the FFQ into values closer to actual consumption [4] and therefore, to use in epidemiological studies that apply the FFQ to evaluate food intake [6,7]. Commonly, as the reference method may use a 24-hour dietary recall (R24) or food records, these studies purportedly approach more adequately the real value of food intake of the individual [8]. Calibration studies estimate the slopes of the regression lines (β) created for the nutrients and this value of β is used as a calibration factor for the values of the FFQ [6,7]. The objective of this study was to calibrate and assess the performance of the FFQ in relation to the consumption of energy, carbohydrate, protein, fat, alcohol, folate, vitamin B2, vitamin B6, vitamin B12, methionine, choline and betaine in the study population "Folate and nutrients involved in the 1-carbon cycle in the pretreatment of patients for colorectal adenocarcinoma in a referral center for oncology in southeastern Brazil."

Materials and Methods

For the study of calibration, we included 189 patients with newly diagnosed cases of colorectal adenocarcinoma from a colorectal tumor center of an oncology referral center in southeastern Brazil, from May 2011 to May 2012. We included patients with adenomatous lesions or adenocarcinoma of the colon or rectum, at any stage of the disease, with an indication for surgical intervention of the primary site and those who had not previously undergone surgery, radiotherapy and/or chemotherapy for colorectal tumor. These patients completed a validated FFQ in a previous study. Portions of this questionnaire were prepared based on the habitual dietary intake of residents from the municipality of São Paulo (Brazil) and was developed based on the R24 of 1477 adults, resulting in a questionnaire with 67 food items. Following validation for patients with colorectal tumors, the questionnaire now contains 110 food items [9]. The software Nutrition Data System for Research (NDSR) [10] was used to calculate the intake of energy and nutrients.

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Calibration of Dietary Data

We used the three R24s (n=270) and the second FFQ (n=90) collected in the study of LAMEZA (2010) [9]. The FFQ and R24s were also converted into nutrients and energy values according to the Table of the U.S. Department of Agriculture [11]. Furthermore, the values were adjusted by the **Multiple Source Method [12] with the objective to diminish the** variation in food consumption [13]**.**

Statistical Analysis

Statistical analysis was performed through the software STATA [14]. The significance level adopted was 5%. First, the distribution of dietary variables of the R24s and the FFQ from the study of LAMEZA (2010) [9] was verified using the Kolmogorov-Smirnov test. As the nutrients showed asymmetry, variables were converted to natural logarithm. Assuming that the random errors present in the measurement of the R24 are independent of those in the FFQ and that there is a linear relationship between the values obtained by the FFQ and those obtained from the R24, we estimated the dietary intake level of energy and nutrients predicted by R24 (reference method and the dependent variable) in relation to the measurement of the FFQ (independent variable) from the calibration method for simple linear regression, using the R24 as the dependent variable and the FFQ as the independent variable [8,15].

$$R24h = \hat{\beta}_0 + \hat{\beta}_1 (\text{QFA}) \quad (1)$$

The $\hat{\beta}_1$ slope estimated by linear regression analysis is called the calibration coefficient. The FFQ data from this study were calibrated with equations estimated by regression analysis generated from the data from the study of Lameza [9]. After the calibration procedure, the presence of outliers was verified using a box plot graph. Thus, of the 195 individuals evaluated in this study, 6 were excluded from the dietary assessment, resulting in a total of 189 patients included in the dietary analyses. According Cade et al. a sample size between 50 and 100 subjects, is desirable to test a hypothesis in validation studies [16]. In addition, an adjustment was made for the energy of nutrients obtained by the R24 and calibrated FFQ. The geometric means and CI95% were calculated for the FFQ data before and after calibration, as well as for R24 deattenuated. The Mann-Whitney *U* test was used to identify differences between the means of the R24 and both the observed and calibrated FFQ (Tables 1 and 2).

Nutrients	FFQ observed (n=189)	R24 (n=90)
Energy (kcal)	2953.32 (2805.28-3109.17)	1773.33 (1746.56-1800.51)
Fat (g)	96.23 (91.14-101.60)	68.58 (67.23-69.97)
Carbohydrate (g)	390.86 (365.65-417.80)	205.17 (202.10-208.29)
Protein (g)	113.26 (107.09-119.78)	79.56 (78.54-80.58)
Alcohol (g)	0.82 (0.58-1.18)	0.26 (0.22-0.30)
Vitamin B2 (mg)	2.30 (2.18-2.42)	1.56 (1.54-1.57)
Vitamin B6 (mg)	2.63 (2.46-2.81)	1.50 (1.47-1.54)
Vitamin B12 (μg)	6.87 (6.40-7.38)	4.38 (4.26-4.51)
Methionine (g)	2.47 (2.32-2.62)	1.81 (1.78-1.84)
Natural folate (μg)	344.42 (324.22-365.88)	215.68 (212.03-219.39)
Synthetic folate (μg)	120.95 (109.98-133.01)	76.59 (74.63-78.60)
DFE diet[1] (μg)	576.33 (543.14-611.54)	362.01 (359.90-364.14)
Choline (mg)	416.87 (394.30-440.73)	285.28 (281.44-289.18)
Betaine (mg)	210.74 (193.38-229.65)	130.80 (129.38-132.23)

R24- 24-hour dietary recall used in the study of LAMEZA (2010)
FFQ- Food Frequency Questionnaire
CI95%- 95% confidence interval
DFE- Dietary Folate Equivalent
1DFE diet=natural folate + 1.7 × (synthetic folate in diet)

Table 1: Geometric means and CI95% of the values of observed FFQ, R24 without energy-adjustment and R24 with energy-adjustment.

Nutrients	Simple linear regression β_1 (CI95%) in log	β_0	p	R^2a
Energy (kcal)	0.27 (0.14-0.39)	5.30	0.001*	0.16
Fat (g)	0.34 (0.18-0.49)	2.65	0.001*	0.17
Energy-adjusted	0.05 (-0.02-0.13)	3.86	0.14	0.01
Carbohydrate (g)	0.21 (0.11-0.32)	4.02	0.001*	0.14
Energy-adjusted	0.08 (0.01-0.14)	4.81	0.01*	0.05
Protein (g)	0.21 (0.09-0.32)	3.36	0.00*	0.11
Energy-adjusted	0.06 (-0.01-0.13)	4.02	0.09	0.02
Alcohol (g)	0.40 (0.20-0.59)	-1.26	0.001*	0.17
Energy-adjusted	0.28 (0.10-0.47)	-1.41	0.001*	0.10
Vitamin B2 (mg)	0.16 (0.59-0.27)	0.30	0.001*	0.08
Energy-adjusted	0.10 (0.03-0.18)	0.33	0.001*	0.07
Vitamin B6 (mg)	0.31 (0.08-0.53)	0.10	0.001*	0.06
Energy-adjusted	0.32 (0.13-0.52)	0.08	0.001*	0.10
Vitamin B12 (μg)	0.37 (0.22-0.52)	0.74	0.001*	0.20
Energy-adjusted	0.29 (0.15-0.42)	0.87	0.001*	0.16
Methionine (g)	0.25 (0.13-0.37)	0.35	0.001*	0.16
Energy-adjusted	0.11 (0.02-0.19)	0.44	0.01*	0.05
Natural folate (μg)	0.27 (0.15-0.38)	3.78	0.001*	0.19
Energy-adjusted	0.26 (0.15-0.37)	3.81	0.001*	0.20
Synthetic folate (μg)	0.26 (0.05-0.46)	3.07	0.01*	0.05
Energy-adjusted	0.15 (-0.02-0.33)	3.57	0.09	0.02
DFE diet[1] (μg)	0.09 (-0.02-0.20)	5.30	0.12	0.01
Energy-adjusted	0.05 (-0.04-0.15)	5.55	0.28	0.00
Choline (mg)	0.22 (0.11-0.33)	4.28	0.001*	0.15
Energy-adjusted	0.13 (0.05-0.21)	4.82	0.001*	0.09
Betaine (mg)	0.12 (-0.03-0.27)	4.22	0.12	0.01
Energy-adjusted	0.12 (-0.01-0.27)	4.18	0.07	0.02

FFQ-Food Frequency Questionnaire
Log-natural logarithm
CI95%-95% confidence interval
DFE-Dietary Folate Equivalent
1DFE diet=natural folate + 1.7 × (synthetic folate in diet)
* p<0.05

Table 2: Calibration coefficients of nutrients assessed and simple linear regression models considered for the calibration of FFQ data in the pretreatment of patients for colorectal cancer.

Ethical Aspects

This study was approved by the research ethics committee of Fundação Antonio Prudente under number 1542/11.

Results

Table 3 presents the geometric means and CI95% of observed and calibrated FFQ values. For all nutrients, the observed values obtained in FFQ were higher compared to the values of R24. Comparing R24 data with the observed FFQ data, means are significantly different ($p<0.001$) for all nutrients.

The coefficients of the equation for calibration of nutrient intake data are presented in Table 2. The coefficients ranged from 0.09 for DFE diet to 0.40 for alcohol. The power of the models (R^2a) ranged from 0.01 for DFE diet and betaine to 0.20 for vitamin B12. However, when nutrients were energy-adjusted, the calibration coefficients ranged from 0.05 for the DFE diet and fat to 0.32 for vitamin B6. The power of the models (R^2a) with adjusted nutrients ranged from 0.00 for DFE diet to 0.20 for natural folate.

Nutrients	FFQ observed	FFQ calibrated		p
		Non-energy-adjusted nutrients[b]	Energy-adjusted nutrients[c]	
Energy (kcal)	2953.32 (2805.28-3109.17)	1758.05 (1733.68-1782.77)	-	<0.05*[ab]
Fat (g)	96.23 (91.14-101.60)	67.89 (66.63-69.16)	62.14 (61.94-62.33)	<0.05*[ab,ac,bc]
Carbohydrate (g)	390.86 (365.65-417.80)	203.77 (200.85-206.73)	200.20 (199.14-201.28)	<0.05*[ab,ac,bc]
Protein (g)	113.26 (107.09-119.78)	79.06 (78.12-80.00)	75.85 (75.58-76.13)	<0.05*[ab,ac,bc]
Alcohol (g)	0.82 (0.58-1.18)	0.26 (0.22-0.30)	0.22 (0.20-0.25)	<0.05*[ab,ac,bc]
Vitamin B2 (mg)	2.30 (2.18-2.42)	1.55 (1.54-1.56)	1.53 (1.52-1.54)	<0.05*[ab,ac,bc]
Vitamin B6 (mg)	2.63 (2.46-2.81)	1.49 (1.46-1.52)	1.49 (1.46-1.53)	<0.05*[ab,ac]
Vitamin B12 (µg)	6.87 (6.40-7.38)	4.32 (4.21-4.44)	4.21 (4.12-4.30)	<0.05*[ab,ac]
Methionine (g)	2.47 (2.32-2.62)	1.80 (1.77-1.83)	1.72 (1.71-1.73)	<0.05*[ab,ac,bc]
Natural folate (µg)	344.42 (324.22-365.88)	214.27 (210.79-217.80)	214.26 (210.85-217.72)	<0.05*[ab,ac]
Synthetic folate (µg)	120.95 (109.98-133.01)	75.76 (73.90-77.67)	75.45 (74.35-76.57)	<0.05*[ab,ac]
DFE diet[1] (µg)	576.33 (543.14-611.54)	360.99 (359.04-362.96)	360.67 (359.53-361.80)	<0.05*[ab,ac]
Choline (mg)	416.87 (394.30-440.73)	283.44 (279.89-287.04)	276.54 (274.52-278.58)	<0.05*[ab,ac,bc]
Betaine (mg)	210.74 (193.38-229.65)	130.30 (128.96-131.65)	130.31 (128.80-131.76)	<0.05*[ab,ac]

FFQ-Food Frequency Questionnaire
CI95%-95% confidence interval
DFE-Dietary Folate Equivalent
[1]DFE diet=natural folate + 1.7 × (synthetic folate in diet)
* p<0.05

Table 3: Geometric means and CI95% of the values of observed FFQ, calibrated FFQ without energy-adjustment, calibrated FFQ with energy-adjustment, R24 without energy-adjustment and R24 with energy-adjustment.

Table 3 presents the geometric means and CI95% of observed FFQ and calibrated FFQ values. Comparing the values of observed FFQ to the values of calibrated FFQ, the means are significantly different ($p<0.001$) for all nutrients, independent of energy adjustment. There were also significant differences for carbohydrate, fat, protein, alcohol, vitamin B2, methionine and choline when comparing the results of energy-adjusted calibrated FFQ to calibrated FFQ without energy adjustment. Note that with the calibration of data, there was a decrease in the variation in dietary intake, as evidenced by a reduction in confidence intervals (Table 3).

Discussion

This study aimed to calibrate the FFQ used in the study Ferrari et al. [1]. Generally, calibration is indicated in studies whose data have an approximately normal distribution. In this study, dietary data showed asymmetry. However, when the variables are converted to natural logarithm, there appears to be no fundamental requirement of normality [17] and for this reason, in this study, dietary data were first converted into natural logarithm.

Studies with colorectal cancer which used calibrated FFQ data were not found in the literature. Thus, data will be presented of calibration studies whose target audience is not patients with colorectal tumors.

According to Rosner et al. ideal is for the slopes of the lines, namely calibration factors, to be approximately 1. In this case, it can be said that the mean food consumption estimated through the FFQ is equal to the mean estimated by the reference method [15]. In this study, a calibration coefficient proximate to the desired value was not verified, indicating that the FFQ expressed biases. The use of the FFQ may not bring the correct estimates of habitual food intake because the patient may not remember what and how much of a certain food was consumed in a given time period, have trouble properly reporting the frequency and sizes of portions consumed and even their food intake can be influenced by important psychological factors [18]. Consequently, this method of assessment of dietary intake may be biased and not correctly reflect estimates of relative risks in studies aimed at assessing the relationship between diet and disease [19,20]. In this study, the calibration coefficients ranged between 0.09 and 0.40. These data are similar to values of the calibration study of Teixeira et al. [21] that showed values of β_1 between 0.06 for total fat and 0.45 for fibers. Moreover, after multiple linear regression, the authors found calibration coefficients between 0.03 for total fat and 0.45 for fibers. This study, which aimed to assess the calibration factors through linear regression of the FFQ data used in the HIM-Brazil study, also used the FFQ that was developed based on the study "Survey of Health of the State of São Paulo (ISA- SP) - Household Survey of Health of the Base Population in the Municipalities of São Paulo, 1999-2000 ", reflecting that the FFQ is consistent. In the present study, we found a low calibration coefficient for proteins (β_1=0.21), carbohydrates (β_1=0.21) and energy (β_1=0.27), demonstrating the presence of significant biases. With respect to energy, the study of Teixeira et al. [20] found β_1=0.28. In a cohort study conducted in northern Sweden that used a method evaluating the calibration from the linear regression of a FFQ with 84 food items, a value of β_1=0.41 was observed for males and β_1=0.45 for females [22]. In this study, as to proteins, we observed a result very close to the value of 0.20 found in the study of Slater et al. [23]. This, which was the first calibration study conducted in Brazil, used a database of 79 adolescents from the municipality of São Paulo who answered a FFQ in 1999. As a reference method, the values used were obtained from at least three R24s. Another cohort study conducted in the same area (northern Sweden) that used a method evaluating the calibration from the linear regression of a FFQ with 84 food items, found a calibration coefficient between 0.30 for protein and 0.59 for vitamin C [21]. In the study of Teixeira et al. [22] the β_1 value found for protein was 0.15. Regarding carbohydrates in this study, considerable bias was also seen, supporting the study of Teixeira et al. [21] that found a calibration coefficient of 0.20, but differing from the work of Slater et al. [23], which found a value of 0.41. Fat, which was among the macronutrients, showed the highest calibration coefficients. This value differs from that found in the study of Slater et al. [23], which found a calibration coefficient of 0.22 for fat, and a study by Teixeira et al. [21] that found a β_1 value of 0.06 for total fat. In relation to DFE diet, the calibration coefficient in this study was low, resembling the study of Teixeira et al. [21] in which a β_1 value of 0.28 was obtained, with CI95% from 0.13 to 0.42.

In this study, the other nutrients assessed had low calibration coefficients, the highest found for vitamin B6 (β_1=0.31), B12 (β_1=0.37) and alcohol (β_1=0.40). We have not found any studies in the literature that evaluated calibration factors for these micronutrients. For alcohol, the calibration coefficient was moderate, with the highest coefficient found in the present study. In the study by Johansson et al. [22], alcohol also had the highest calibration coefficient when compared with other nutrients. It is important to point out that for the assessment of alcohol consumption, it is likely that the use of a FFQ instead of just one R24 would reflect intake more accurately by encompassing daily, weekly, monthly and yearly intake versus only daily intake from a R24. DFE diet and betaine regression models were not statistically significant, which suggests the impractcably of calibration for these nutrients. Although the calibration coefficients are far from 1, after calibration, the data showed a decrease in standard deviation and confidence interval, the same as in the studies of Kaaks et al. [24], Kipnis et al. [25], Hoffmann et al. [26], Kynast-Wolf et al. [4], Slater et al. [23] and Voci et al. [27]. According to Kynast-Wolf et al. [4], this occurs because, assuming that there is a linearity between the values found in the reference method and the FFQ, the extreme values obtained are reached and therefore tend to reduce the standard deviation [5]. However, the calibration by linear regression cannot approximate the FFQ values of the reference method and individual level [27].

When comparing theR24 data from the Lameza study [9] to the observed FFQ data of this study, the means of all nutrients were significantly different. After calibration of the data, the mean values of energy, fat, protein, alcohol, vitamin B12, methionine and choline remained significantly different compared to R24. When assessing the means of observed and calibrated FFQ, all nutrient values were significantly different. This means that there was an approximation of the FFQ data from this study to R24 data of Lameza [9], considered as the reference method.

Even with low calibration coefficients, it cannot be said that the FFQ is not able to correctly reflect the habitual food intake, since according to Edwards et al. [28] and Voci et al. [29], using an inadequate reference method may further increase bias. In an attempt to improve the assessment of dietary intake, some authors suggest that other strategies are used, such as the use of biomarkers, existing only for some nutrients [21,28]. In the studies cited for comparison of data so far, the calibration coefficients were generated from R24 and FFQ applied in each study. However, in this work, the calibration coefficients were obtained through the FFQ and R24 used in the study of Lameza [9]. Although the study population is composed of patients with adenocarcinoma of the colon and rectum, in the study Lameza [9], participating patients could be at any stage of treatment, unlike the present study, where only patients in pretreatment of colorectal tumors were recruited. It is known that after the diagnosis of cancer, the patient is subjected to antitumor therapy, which may include surgical treatment, chemotherapy, radiotherapy, or even a combination of these modalities. These interventions can interfere directly in the patient's nutritional state, due to changes in taste, swallowing, food intake, digestion and absorption of nutrients [30-33]. For these reasons, when using the calibration coefficients obtained with the values of the Lameza [9] study on the observed data obtained in the present study, it may be that the proposed methodology is not as adequate as if a R24 were used beyond the FFQ applied. The methodology applied here was not found in the literature. Although the correlation coefficients are low, it cannot be said that it is indicated only the FFQ be used for the assessment of food consumption, as in this study, the reference method used may not have been the best way to eliminate the measurement errors found in the FFQ.

Conclusion

With the development of this study, it was possible to conclude that calibration is a methodology that allows a reduction in measurement error, since the mean values obtained by the FFQ approached the mean values obtained in the reference method. However, the use of this methodology needs to be further evaluated. This study opted for the use of the R24 as the reference method used in the validation study of the FFQ applied here, namely, a reference method that came from a population with the same clinical diagnosis which, it is hoped, leads to a minimization of measurement errors by correcting the data through calibration. However, these populations were encountered at different times of cancer treatment. First of all, methods of references used in studies of dietary assessment are frequently based on recalls of food intake of the individual. Second, it is worth emphasizing that even though the population consisted of patients with colorectal adenocarcinoma, for the validation study, the patient could be at any stage of treatment, unlike the criteria used in this study, in which the FFQ was administered to patients in pretreatment for tumors of the colon and rectum. For these reasons, although the correlation coefficients are low, it cannot be said that the exclusive use of the FFQ for assessing dietary intake is not recommended, since this study, the reference method used may not have been the best way to eliminate the measurement errors found in the FFQ. Thus, it is suggested that for studies that aim to analyze the relationship between diet and disease, uncorrected and corrected data for calibration can be used comparatively. It is noteworthy that even when it is of interest to assess the prevalence of inadequate nutrient intake, besides the application of the FFQ, some other method of quantitative assessment of food consumption is used, as the R24 or food record.

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