Quality of dietary carbohydrate intake and micronutrient adequacy in a Mediterranean cohort: the SUN (Seguimiento Universidad de Navarra) project.

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Key words: Carbohydrate quality: Micronutrient adequacy: Mediterranean cohort

Abbreviations

CQI, Carbohydrate Quality Index; DRI, Dietary Recommended Intakes, EAR, Estimated Average Requirements; FQI, Fat Quality Index; GI, Glycemic Index; MeDiet, Mediterranean Diet; SUN, Seguimiento Universidad de Navarra.

ABSTRACT

Epidemiological research confirms that prevalence of suboptimal micronutrient intake across Europe is an emerging concern of public health. Our aim was to investigate the association between a new index of carbohydrate quality and micronutrient adequacy in the “Seguimiento Universidad de Navarra (SUN)” cohort. The baseline assessment expanded from 1999 to March 2012. We assessed 16841 participants who completed a validated 136-item semi-quantitative FFQ at baseline. We created a new index to evaluate the carbohydrate quality following 4 criteria: dietary fiber intake, glycemic index (GI), whole grains /total grains ratio and solid carbohydrates/ total carbohydrates ratio. Subjects were classified into quintiles according to this index. We evaluated the intake of: zinc, iodine, selenium, iron, calcium, potassium, phosphorus, magnesium, chromium and vitamins B_1, B_2, B_3, B_6, B_{12}, C, A, D, E and folic acid. The probability of intake adequacy was evaluated using the estimated average requirements (EAR)-cut point and the probabilistic approach. Logistic regression analysis was used to assess the nutritional adequacy according to the carbohydrate quality index (CQI).Participants in the highest quintile of CQI showed the lowest prevalence of inadequacy. A higher quality of carbohydrate intake was associated with lower risk of nutritional inadequacy in comparison with the lowest quintile of CQI (adjusted OR: 0·06; 95 % CI: 0·02, 0·16; *P* for trend <0·001. A higher CQI was strongly associated with a better micronutrient adequacy in a young Mediterranean cohort, stressing the importance of focusing nutritional education not only in carbohydrates quantity, but also in quality.

INTRODUCTION

Nutrient intake assessment is essential for planning dietary intervention at an individual level and it is a major component of public health and nutrition policy. However, epidemiological research related to dietary surveys or nutrient intake adequacy has been largely focused in over-consumption of certain nutrients, especially, fat, SFA, trans fatty acids (TFA), sugars, sodium, cholesterol, etc. according to nutrition goals and obesity or prevalent diet-related diseases [(1, 2)]

Micronutrient deficiencies constitute a health challenge in the WHO Regional Office for Europe [(3)] . In fact, epidemiological research confirms that prevalence of suboptimal micronutrient intakes across Europe is an emerging concern in terms of public health [(4)], but the different methods applied led to different prevalence estimates of micronutrient inadequacy [(5)].

Dietary patterns [(6)] and specific micronutrients have an important role in the development of chronic and degenerative diseases [(7-11)]. Dietary variety and dietary indexes have shown fair to moderate validity for measuring micronutrient intake adequacy [(12-14)]. Regarding the Mediterranean Diet (MeDiet), as adherence to this dietary pattern increases, the probability of not fulfilling the micronutrients recommendations sharply decreases [(15, 16)].

In relation with the role of macronutrients on adequacy of micronutrients, certain goals on *quantities* of fat and carbohydrate intake (28-30% of fat and 50-54% total energy, respectively) has been proposed as the "optimal" intakes in pregnant women [(17)].

Previous investigations have reviewed the associations between carbohydrates quantity and micronutrients adequacy but the evidence on its *quality* is sparse [(18-21)]. As recognized for fat [(22)], carbohydrates are also an heterogeneous class of nutrients and it has been suggested to refine recommendation for improving the quality of carbohydrate intake from a public health perspective [(23)].

However, to our knowledge there are no studies that have examined at the same time, the relationship between the overall dietary quality of carbohydrates or other indexes of macronutrient quality and nutritional adequacy. We tested the following hypothesis: a higher carbohydrate quality is associated with a higher micronutrient adequacy. Thus, our aim was to define a framework for assessing the quality of carbohydrate intake and to investigate the association between the CQI and the intake adequacy of 19 micronutrients in the SUN cohort study. Additionally we also assessed the association between fat quality index (FQI) and a MeDiet pattern and nutritional adequacy.

SUBJECTS AND METHODS

Study population

The SUN Project is a multipurpose and dynamic cohort designed to study the prospective association of diet and the occurrence of major chronic diseases [24]. Details on the cohort design, recruitment strategy and follow-up methods are available elsewhere [25]. Briefly, the recruitment of participants started in December 1999 and it is permanently open. All participants are Spanish university graduates, with a high educational level. Information is collected using self-administered questionnaires sent by postal or electronic mail every 2 years. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Institutional Review Board of the University of Navarra. Voluntary completion of the baseline questionnaire was considered as informed verbal consent. For this analysis, participants with data in FFQ at baseline or who answered the baseline questionnaire before March 2012 were eligible (n=21478). Among them, we excluded subjects who were outside of predefined limits for total energy intake: <3349 kJ/d (800 kcal/d) for men or <2093 kJ/d (500 kcal/d) for women, >16747 kJ/d (4000 kcal/d) for men or >14654 kJ/d (3500 kcal/d) for women(n=2034), and those who were outside of predefined values of any micronutrient intake (at three or more standard deviations from both sides of the mean) (n=2583). Participants who reported implausibly high or low energy intake were not included in the analyses because these levels of intake are unlikely to be true[36]. Extreme values of micronutrient intake were also not included to avoid under-estimating or over-estimating the prevalence of inadequacy. Therefore, the final sample comprised 16841 participants.

Our estimated sample size for a two-sample comparison of proportions (highest versus lowest quintile of CQI) was based on the following assumptions: alpha = 0.05 (two-sided), statistical power = 90%. A proportion of participants with inadequacy = 0.15 in the category with the highest inadequacy, and proportion= 0.10 in the quintile with the best adequacy. Under these assumptions the sample size needed was 918 participants in each quintile.

Exposure assessment

Dietary intake was assessed using a baseline semi-quantitative FFQ repeatedly validated in Spain [26, 27]. It showed a reasonably good validity for assessing fat intake and also for carbohydrates intake [28] . Nutrient intakes of 136 food items were calculated as frequency multiplied by nutrient composition of specified portion size for each food item, using an ad hoc computer program developed for this purpose. There were 9 options for the average frequency of consumption (from never/almost never to at least 6 times per day). Trained dieticians updated the nutrient data bank using the available information from the food composition tables for Spain [29, 30] . Furthermore, the average intake of micronutrients from dietary supplements was added to the intake from foods, taking into account the consumption declared over the past year.

We used baseline dietary intake data to identify a new index. The CQI was defined summing up the following four criteria: dietary fiber intake (g/d), GI, whole grains /total grains ratio and finally, solid carbohydrates/total carbohydrates ratio (Table 1). For this last criterion, we considered only the amount of CHO from each food. Total grains were calculated summing whole grains, refined grains and its products. For each of these 4 components, participants were categorized into quintiles and received a value (ranging from 1 to 5) according to each quintile. Finally, we constructed by summing all values the CQI (ranging from 4 to 20) and it was also categorized roughly into quintiles.

On the other hand, we used two indexes to compare the results in relation to CQI and micronutrient adequacy: the FQI and a priori MeDiet score. To calculate the FQI, we used the ratio MUFA+PUFA /SFA+TFA (Table 1). According to this score (ranging from 0·62 to 5·92) participants were categorized into quintiles. Finally, we used an a priori score to appraise MeDiet as proposed by Trichopoulou et al[31] to assess the association between the adherence to this dietary pattern and nutritional adequacy. With the exception of alcohol, sample sex-specific median cut-off points for eight items were used. For beneficial components (fruits and nuts, cereal, fish, vegetables and legumes), subjects whose consumption was below the median were assigned a value of 0, and subjects whose consumption was at or above the median were assigned a value of

1. For components presumed to be detrimental (meat, poultry, and dairy products), subjects whose consumption was below the median were assigned a value of 1, and subjects whose consumption was at or above the median were assigned a value of 0. Finally, for ethanol, a value of 1 was assigned to men who consumed between 10 and 50 g per day and to women who consumed between 5 and 25 g per day.

We also used the MeDiet score to assess the association between the adherence to this dietary pattern and nutritional adequacy. The range was 0 point to minimum adherence to 9 points to maximum adherence. Finally, we categorized all participants into quintiles according to MeDiet score.

Outcome assessment

We aimed to summarize micronutrient adequacy across the following 19 micronutrients with known public health relevance: zinc, iodine, selenium, iron, calcium, potassium, phosphorus, magnesium, chromium and vitamins B_1, B_2, B_3, B_6, B_{12}, C, A, D, E and folic acid. The probability of intake adequacy was calculated comparing the intakes of those nutrients to EAR when these were available or adequate intake, if not, as proposed by Institute of Medicine [32] .

On the other hand, nutrient intake adequacy for 16 nutrients (all but chromium, potassium and iron) was also evaluated using the probabilistic approach [33]. With this approach the probability of adequacy for usual intake of a nutrient was calculated from a z score, as follows: z score = (estimated nutrient intake - EAR)/SD of the EAR. Besides, when we calculated the probability of adequacy for iron intake, the distribution intake was log transformed.

Assessment of other variables

The baseline assessment also gathered information on socio-demographic and anthropometric variables, lifestyle and health-related habits and medical history. Self-reported BMI was calculated as weight (in kilograms)/ the square of height (in meters). Self-reported anthropometrics were previously validated in a subsample of the cohort [34]. Information regarding physical activity during leisure-time was gathered at baseline with a specific questionnaire previously validated in Spain [35]. We obtained a value of overall weekly MET- hours for each participant taken into account the weekly time spent in each activity.

Statistical analysis

We compared the baseline characteristics of participants according to 5 categories of dietary quality scores. We calculated means (SD) or percentages for each variable across the 5 categories. Chi-square tests or ANOVA were used to assess the statistical significance of the differences among proportions or means, respectively. Pearson's correlation coefficients were calculated to identify the relationship between 3 diet quality scores and between each dietary index and its components.

We used non-conditional logistic regression models to assess the relationship between CQI, FQI or MeDiet score, and the risk of inadequate nutrient intakes using the EAR cut-point and the probabilistic approach. In all analyses, the lowest quintile was used as the reference category. Crude OR and multivariate-adjusted OR were estimated in the following analyses: a) failing to comply with 4 or more recommendations and b) with 8 or more unmet recommendations. For each quality score we fitted 3 multivariable-adjusted models controlling for the following potential confounders or sources of bias: a) age (continuous), sex and educational level (4 categories), b) additionally adjusting for total energy intake and total carbohydrates or fat intake (continuous) and c) additionally adjusted for MeDiet score (continuous)[31], BMI (continuous), physical activity (continuous), smoking status (3 categories), and dietary supplement use (yes/no). Tests of linear trend across successive quintiles of three diet quality scores were conducted assigning the median value to each quintile category and treating the variables as continuous.

Analyses were performed with STATA version 12 (STATA Corp., TX, USA). All *P* values are two-tailed and statistical significance was set at the conventional cut-off of $P < 0{\cdot}05$.

RESULTS

Baseline characteristics of the study participants according to extreme quintiles of CQI and FQI are presented in Table 2 and Table S1 (available online) respectively. Subjects with higher CQI (fifth quintile, Q5) were more likely to be women, more physically active and to have history of hypertension or diabetes (Table 2). CQI was also directly associated with a higher adherence to a MeDiet pattern, and consumption of fruits, vegetables, legumes, fish, olive oil and nuts. However, the differences in macronutrients intake were minimum for all of them. Besides, all the values for micronutrient intakes increase with the increasing quintiles of CQI (P<0·001).

Table S1 (available online) shows that FQI was positively associated with be older, more active, to have a history of hypertension, diabetes or dyslipemia, adherence to the MeDiet, carbohydrate and fat intake and with consumption of fruits, vegetables, fish, grains, olive oil and nuts. For all micronutrients under study, a higher dietary intake of micronutrients was observed between subjects in higher FQI, except for iodine, calcium, phosphorus and vitamin B_3.

The prevalence of inadequate intake below EAR for each nutrient according to each score is presented in Table S2 (available online). A highest quintile of CQI or MeDiet score showed the lowest prevalence of inadequate dietary intake for every vitamin and mineral. Contrarily, the number of participants with non-compliance of EAR for iodine, calcium, phosphorus and vitamins B_2, B_3 and B_{12} was highest in the fifth quintile of FQI. The mean prevalence of inadequacy was between 19 and 58% for calcium, phosphorus, magnesium and folic acid, and above 93% for vitamin D and E.

Tables 3 and 4 present the risk of not meeting ≥4 or ≥8 Dietary Recommended Intakes (DRI) according to quintiles of CQI or FQI using the probabilistic approach. Participants in the quintile of poorest quality of CQI had a 17·5 fold risk of failing to meet ≥8 DRI (Table 3). A higher CQI showed a strong inverse association with the risk of unmet DRI. In the adjusted model, the OR (95% CI) for successive quintiles of CQI was 1.00 (reference), 0·49 (0·33-0·73), 0·31 (0·19-0·48), 0·15 (0·08-0·29) and 0·06 (0·02-0·16) for failing ≥8 DRI after adjusting for the main potential confounders (P for trend < 0·001). When we repeated the analyses for failing to meet ≥4 DRI, the results were basically the same.

When we assessed the association between FQI and not achieving ≥4 or ≥8 DRI, we found a direct association in both models after adjusting for age, sex, educational level, energy intake, total fat intake and MeDiet score, BMI, physical activity, smoking status and dietary supplement use (Table 4). Thus, the OR (95%) for the fifth quintile for failing to meet ≥8 was (OR: 3·64; 95% CI: 2·15, 6·17); *P* for trend < 0·001.

We have repeated the results using deciles to calculate the CQI and the a priori MeDiet Score (Figure 1 and 2 respectively) and they indicate the robustness of our findings.

OR and 95% CI for unmet EAR in ≥8 nutrients across quintiles of CQI are shown in Figure S1 (available online). A lower risk of inadequate intake was observed among participants in the highest quintile of CQI after adjusting for several potential confounders (OR: 0·10; 95% CI: 0·06, 0·19). On the other hand, a higher FQI was significantly associated with a higher risk of not achieving the EAR in ≥9 micronutrients in comparison with the lowest category of FQI: (OR: 3·26; 95% CI: 2·22, 4 ·77) (Figure S2, available online). On the contrary, a higher MeDiet score was associated with a high likelihood of meeting the EAR of ≥9 micronutrients (Figure S3, available online). In the three analyses the *P* value for trend was significant (*P*<0·001).

The number of nutrients with intakes not meeting the EAR was lower in the extreme quintile of CQI or MeDiet score and higher in the fifth quintile of FQI (Figure 3, Figure 4 and S4 respectively).

Figure 5 shows relative risks of intakes not meeting the EAR according to the joint classification by CQI and FQI. A higher quality of carbohydrate intake tended to be associated with a lower risk of unmet requirements for ≥9 nutrients micronutrients in comparison with the lowest category of FQI in the three intake groups of FQI.

The correlation coefficients between the GI, fiber intake, whole grains /total grains ratio and solid carbohydrates/ total carbohydrates ratio were -0·34, +0·58, +0·63, and +0·33. The correlation coefficients between MUFA, PUFA, SFA, and TFA with FQI were +0·19, +0·29, -0·35 and -0·42. Finally, the correlations between diet quality scores were: 0.12 between CQI and FQI, 0·36 between CQI and MeDiet score, and 0·48 between MeDiet score and FQI.

DISCUSSION

To the best of our knowledge, our study is the first analysis to investigate the association between two new scores of carbohydrate or fat quality and the adequacy of micronutrient intake. Participants of this Mediterranean young cohort who had a high CQI or adherence to a MeDiet were at lower risk of micronutrient inadequacy. These findings could contribute to develop prevention and nutritional education strategies focused not only in amount of macronutrients intake [37, 38], but also on quality of macronutrients, particularly carbohydrate.Moreover, in this context this seems more important than the quality of fat.

Previous studies have focused in studying how diet quality, dietary patterns or variety of foods, are validated methods to measure micronutrient intake adequacy [12-14] . In the SUN cohort, it has been confirmed before that higher adherence to a MeDiet pattern was associated with a lower prevalence of inadequacy for the intake of zinc, iodine, magnesium, iron, selenium and vitamins E, B_1, A, C and folic acid[15]. In this work, we also demonstrate that a better profile of micronutrient intake was associated with MeDiet measured by using an a priori MeDiet score. In fact, we found that global prevalence of nutrient intake inadequacy as higher for calcium, potassium, magnesium and vitamins D and E and lower to phosphorus and vitamin B_3. In general, these results are consistent with the evidence in Spain [39-42] and Europe [4, 43, 44].

As expected, participants with better quality of carbohydrates referred higher consumption of fruits, vegetables, legumes, nuts, but less grains. Furthermore, those in the higher quintile of CQI, were more likely to meet micronutrient recommendations. In absolute terms, intake of carbohydrates (% total energy) was quite similar across quintiles of CQI, ranging from 42·7% to 43·4%, suggesting that it is not quantity of carbohydrates but quality, what is really important when assessing micronutrient adequacy. In fact, the quantity of protein and fat were very similar in all groups. A possible explanation for this result is that whole grains and low GI foods are particularly rich in micronutrients, while major sources of liquid carbohydrates, particularly sugar-sweetened beverages, are mostly less nutritious foods. These drinks, have been linked to obesity and other cardiometabolic problems, and it has been recently recommended global legislative initiatives and prizing instruments, as public policies to change consumption patterns [45, 46].

Systematic reviews offer no conclusive evidence of relationship between added sugars and micronutrients intake [19] and does not allow establishing an optimal level of added sugars intake for micronutrient adequacy [18, 47]. With respect to dietary glycemic load, two interesting works have recently demonstrated that a higher GI diet predicts a greater risk of not meeting recommendations for several micronutrients in pregnant women[21], children and adolescents [20].

There is a very limited evidence for the association between fat quality and the compliance with the DRI, although low fat diets could increase the risk of inadequate intakes for essential fatty acids and fat-soluble vitamin [48]. Several mechanisms might be proposed to explain the strong and positive association between fat quality and the nutritional inadequacy. The protein intake was significantly low among participants with better fat quality in comparison with those with worse quality, probably because the consumption of dairy products and meats was also significantly low. In fact, when we additionally adjusted for protein intake (% of total energy), no association was found between the FQI and nutritional adequacy (OR for the fifth quintile: 0·95; 95% CI: 0·52-1·76; *P* for trend: 0·883). This outcome is in agreement with other investigation in adolescents, which showed the importance of consuming meat and dairy products in order to meet a broad range of micronutrient guidelines [14].

On the other hand, we found that a higher adherence to the MeDiet pattern was associated with a higher likelihood of meeting the dietary recommendations of micronutrients and with a lower number of nutrients with dietary intakes unmet. The main explanation for these results might be that the traditional MeDiet, rich in minerals, vitamins, antioxidants, fiber (from vegetable food), *n*-3 fatty acids (from fish and sea food) and unsaturated fatty acids (from olive oil and nuts), has an appropriate balance in the intake of both macronutrients and essential micronutrients, while energy-dense or nutrient-poor foods such as processed meats, processed meals and fast food, is particularly low[49].

We acknowledge that our study has some limitations. First, we used a self-reported FFQ, which has measurement errors and might not be the best method to assess some micronutrients (e.g. selenium, iron or folic acid). For example, food contents of selenium vary according to soil contents, so FFQ assessments of selenium are typically include a fair degree of measurement error unreliable [50]. However, FFQ is the most practical and feasible approach to evaluate food habits in large epidemiological studies. Besides, our sample is comprised by highly educated volunteers so the data have fairly adequate quality. Second, we used to translate food consumption into micronutrient intake two well-known Spanish-food composition tables that might be a source of variation in our findings. Third, as in any observational study some residual confounding might not been totally excluded. However, we performed the analyses adjusting for the main known confounders of the nutritional adequacy and for this reason we do not consider residual confounding as a likely important cause of the observed findings. Fourth, the total dietary intake of micronutrients could be probably underestimated since we have not calculated the average intake of vitamins and minerals from all sources of the nutrients. Thus, we have included in data analysis to assess the risk of inadequate intake the intake from foods and from dietary supplements, without considering fortified foods or medication which participants might be consumed. Fifth, our results show the probability of adequacy but not express nutrient deficiencies or if the diet of this population is adequate. In fact, the real nutritional deficiency should be confirmed by biomarkers of nutrient intake. And sixth, a potential weakness of the SUN cohort is that all participants were university graduates, and therefore, they cannot be considered in any way as representative of the general population. Our participants were more likely to be homogeneous in terms of their background diet than participants would be if a similar study were conducted in a representative sample of the general population. This homogeneity of participants in the SUN cohort regarding their background diet can limit the generalizability of our findings and also may have reduced the between-subject variability in dietary exposures, because they belong to a single educational and socioecomic stratum. On the other hand, this fact can be also viewed as an advantage because this homogeneity regarding the background diet of our participants could also have actually enhanced the validity of our study, because this homogeneity reduced the potential confounding related to socioeconomic level, educational status and variability in participants background diet. In any case, we adjusted our results for total energy intake, and other confounders related to this background diet. In addition, analyses assessing CQI and FQI were also adjusted for the overall dietary pattern (MeDiet) and the amount of CHO or fat intake, respectively.

The strengths of this study are that we are using data of a well-known Mediterranean cohort (the SUN study) with a relatively large sample size and a high response rate. In addition, we were able to adjust for numerous potential confounders. Moreover, dietary intake was measured using a previously validated FFQ in highly- educated cohort with a high quality of self-reported data[26, 27]. Our results are very similar using two different methods to estimate nutrient intake adequacy: the probabilistic approach and the EAR cut-point value. The use of this last approach as a reference for estimating nutritional adequacy compared to the DRI value, will not lead to an overestimation of the prevalence of dietary inadequacy. Finally, the two new dietary quality scores used in this study, the CQI and the FQI that to our knowledge have not been used before, included several of the proposed recommendations to assess nutrient intake adequacy [51].

In conclusion, a higher CQI was strongly associated with a better micronutrient adequacy in this young Mediterranean cohort. These findings suggest the usefulness of measuring carbohydrate quality taking into account fiber and proportion of whole grains and liquid carbohydrates. Furthermore, our results could be translated to a universal dietary advice: increasing the consumption of whole grains and fiber intake, and decreasing the dietary added sugar and liquid carbohydrates, will reduce not only the negative effects of liquid-carbohydrates on health, but also will improve micronutrient adequacy.

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AUTHOR´S CONTRIBUTION TO MANUSCRIPT

The authors' responsibilities were as follows: IZ, SS, JAM and MAM design research; IZ, AST, SS and MAM conducted research; CFA, MBR, MAM provide essential materials; IZ, AST, SS and MAM analyzed data or performed statistical analysis; IZ and SS had primary responsibility for final content. All authors read and approved the final manuscript.

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