Plasma glucose levels in the association between serum trans-β-carotene and obesity among children and adolescents

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Research

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Abstract

Background Results on the association between trans-β-carotene and obesity are less clear and little is known about how their relationship may be affected by plasma glucose levels.The present study aimed to evaluate the relationships between trans-β-carotene and obesity and to investigate whether plasma glucose levels had a modifying effect on these relationships.

Methods Children aged 6-18 years were selected from the National Health and Nutrition Examination Survey(NHANES) (2001–2006) (n =8030). The serum trans-β-carotene levels were divided into tertiles, and their associations with obesity were evaluated using multivariable-adjusted linear regression models adjusted for potential confounding factors. The interaction effects between trans-β-carotene levels and plasma glucose levels on obesity were further evaluated.

Results In the fully adjusted model, using serum trans-β-carotene as natural log-transformed continuous variable, the negative association between trans-β-carotene level and obesity were confirmed. In addition, plasma glucose levels significantly modified the inverse association between trans-β-carotene and obesity (p value for interaction: 0.09). A stronger association of trans-β-carotene levels with obesity was found in higher plasma glucose levels (more than100 mg/dl) than in lower plasma glucose levels. Further, a non-linear relationship was detected between trans-β-carotene and obesity in participants with higher plasma glucose levels, with an inflection point of 2.7 (trans-β-carotene =14.88 ug/dl). The effect sizes and confidence intervals for the left and right sides of the inflection point were 0.10 (0.00 to 0.2) and 6.7 (0.1 to 348.2), respectively.

Conclusion Our findings indicate that the association between trans-β-carotene concentration and obesity is stronger in individuals with higher plasma glucose population than in those with lower plasma glucose levels.

Introduction

The increasing prevalence of childhood obesity during the last decade has posed severe nutritional problems in the United States[1–3]. Obese children and adolescents have a higher risk of developing obesity-related comorbidities such as dyslipidemia and diabetes mellitus, which are major risks for cardiovascular events[4, 5]. Therefore, novel and effective therapies for obesity are urgently required.

Carotenoids like trans-β-carotene that cannot be synthesized by the human body are essential dietary constituents[6, 7]. The richest dietary sources of carotenoids are fresh fruits and vegetables. Human serum contains largely trans-β-carotene with only small or negligible amounts of 13-cis-β-carotene and 9-cis-β-Carotene after the ingestion of β-carotene isomers. Research shows that trans-β-carotene have a better bioavailability than the 9-cis-forms[8].Trans-β-carotene has been receiving great attention, certainly because it can be metabolized to its retinoic acid isomers, which plays a crucial role in vision and the formation of new cells and tissues. In addition to the functions already mentioned, the effect of trans-β-carotene on health, especially its role in human nutrition, is still a debatable topic. Previous studies have

shown a negative correlation between trans-β-carotene levels and obesity[9]. Similar results were noted that supplementation of a carotenoid mixture showed a significant increase in plasma trans-β-carotene levels[10]. But a different view also emerged: trans-β-carotene reduces obesity only when it is converted to vitamin A or something else, and that trans-β-carotene itself does not appear to play a direct role in gene expression or obesity[11].

Accordingly, the relationship between trans-β-carotene and obesity is complex and may be conducted by another, closely related factor.

Plasma glucose is a well-recognized risk factor for obesity. Hyperglycaemic glucose excursions are frequently observed in children with overweight and obesity[12]. Further, previous clinical trials have demonstrated that there is a negative correlation between baseline beta-carotene dietary intake and plasma concentrations with plasma glucose[10]. Animal experiments show that dietary β-carotene fortification inhibited the elevation in glucose concentrations, lipid metabolism, and inflammation in mice[13]. However, the presence of an interaction between trans-β-carotene and plasma glucose on obesity has rarely been considered. We assumed that the association between trans-β-carotene and obesity is stronger in individuals with higher plasma glucose population.

Thus, the objective of this study was to investigate a possible effect modification by plasma glucose on the association between serum trans-β-carotene concentration and obesity in children and adolescents of 6 to 18 years old.

Subjects And Methods

We obtained the data from the National Health and Nutrition Examination Survey (NHANES, 2001–2006), which is designed to represent the non-institutionalized civilian populationin the USA[14]. Data from the NHANES 2001–2006 were selected because of the availability of simultaneous measurements of trans-β-carotene concentration and metabolism-related parameters. The initial population in our study consisted of 9,661 participants aged 6–18 years of age at the time of examination. Next, we excluded 1,631 children and adolescents from the analytic sample due to missing data on one or more covariates (final n = 8,030). The NCHS Research Ethics Review Board approved the NHANES protocol and consent was obtained from all participants.

Assessment Of Trans-β-carotene

Serum specimens were processed, stored and shipped to the Division of Laboratory Sciences, National Center for Environmental Health, and Centers for Disease Control and Prevention for analysis. Serum concentration of trans-β-carotene was measured using high performance liquid chromatography with photodiode array detection. Detailed information on specimen collection, processing instructions, and laboratory methods used in the survey is described in the NHANES Laboratory/Medical Technologists Procedures Manual[15].

Definitions Of Outcomes

Obese children and adolescents were selected according to the cut-off points based on sex and age. The 2007 World Health Organization (WHO) growth standards for children at age of 6–18 years was adopted to calculate age-and sex-specific height-for-age (HAZ), weight-for-age (WAZ) and BMI-for-age z-scores (BAZ) using WHO Anthro Plus for personal computers (version 1.0.3,2010)[16]. Normal weight was defined as a BMI z-score between − 2 standard deviations (SD) and 1 SD; overweight as z-score > 1 SD; and obesity as z-score > 2 SD[17].

Covariates

For more details about potential confounders in the NHANES, please refer to our previous studies[18, 19]. In our analyses, we considered the following covariates: information on age (years), sex (male or female), race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican American, or others), education levels (< high school, ≥high school), family poverty-income ratio (PIR), history of physician-diagnosed diabetes (yes/no). The above information was obtained by a standardized questionnaire during a home interview. We used both self-reported cigarette use and serum cotinine cutoff to define smoking status. Smokers were defined as self-reported current smokers and those with serum cotinine levels > 10 ng/mL; Non-smokers were defined as self-reported former and never smokers and those with serum cotinine levels ≤ 10 ng/mL[20]. We did not include alcohol drinking status because it could only be assessed in respondents aged ≥ 20 years[21].

According to National Cholesterol Education Program guidelines, We used standard cutoff values for levels of total cholesterol (TC)[22](≥ 200 mg/dl), high-density lipoprotein cholesterol (HDL-C)[23] (< 35 mg/dl), low density lipoprotein (LDL-C)[24] (≥ 130 mg/dl) and triglyceride (TG)[25](≥ 150 mg/dl) to define abnormal values[26–29]. When recommendations for cutoff values were inconsistent, we chose the more conservative definition. Glycated hemoglobin[30] ≥ 5.7% was defined as abnormal. Fasting blood glucose[31]values > 100 mg/dl were defined as abnormal. Additionally, we examined: 1) elevated C-reactive protein(CRP)[32] defined as > 0.211 mg/dl[33, 34], 2) homeostasis model assessment of insulin resistance(HOMA-IR) ≥ 3.29[35, 36].

Statistical analysis

Serum trans-β-carotene was not normally distributed, thus it was naturally log-transformed. We used population-weighted parametric and nonparametric tests when appropriate for studying the associations of baseline characteristics. We used weighted survey sampling logistic regression to examine the association between trans-β-carotene and obesity. Both non-adjusted and multivariate adjusted models were listed in the paper. Model 1 represented our crude model without covariate adjustment; model 2 was adjusted for demographic factors (Adjusted for age (years), sex, race/ethnicity (non-Hispanic white, non-Hispanic blacks, Mexican Americans, and others); model 3 was adjusted for model 2 variables plus

family PIR, education levels, serum cotinine status, diabetes; finally, the extended model 4 was further adjusted for potential confounders (model 3 plus TC,TG,HDL-C,LDL-C, HOMA-IR score, Glycohemoglobin, FBG,CRP), as our full model. We also used generalized additive model (GAM) to identify the non-linear relationship. If a non-linear correlation was observed, a two-piecewise linear regression model was performed to calculate the threshold effect of trans-β-carotene and obesity in terms of the smoothing plot. The subgroup analyses were performed using stratified linear regression models. After adjusting for the main effects of all confounding factors, each multiplicative interaction term in the multivariate logistic regression models was included in the full sample to estimate the p values for the interaction. Empower (R) (www.empowerstats.com, Inc. Boston MA) and the statistical software packages R (http://www.R-project.org, The R Foundation) were used for all statistical analyses and the NHANES complex sample design.

Results

Baseline characteristics of participants

Table 1 shows the characteristics of the subjects according to the tertiles of serum trans-β-carotene among the 8,330 participants aged 6–18 years in NHANES 2001–2006; 1,558 of them were obese (19.40 ± 0.85%) after being weighted to the US population. Serum trans-β-carotene level increased with increasing percentages of TC, LDL-C, but lower percentage of HDL-C, HOMA-IR, CRP. Subjects with higher Serum trans-β-carotene were found to be younger, in the low serum cotinine levels group, and less likely to be the Non-Hispanic Black.

Table 1

Characteristics of subjects according to the tertiles of serum trans-β-carotene in US children and adolescents, National Health and Nutrition Examination Survey, 2001–2006[a]

Characteristics	Total n = 8030	Tertiles 1	Tertiles 2	Tertiles 3	p for trend
Age,y	12.27(0.08)	13.66(0.1)	12(0.11)	11.36(0.1)	< 0.001
Age, %					
Age, ≥ 11yr	64.68(0.95)	80.94(1.18)	61.99(1.41)	53.41(1.35)	< 0.001
Age, < 11yr	35.32(0.95)	19.06(1.18)	38.01(1.41)	46.59(1.35)	
Gender, %					
Female	48.49(0.77)	47.03(1.1)	47.84(1.31)	50.32(1.42)	0.097
Male	51.51(0.77)	52.97(1.1)	52.16(1.31)	49.68(1.42)	
Height, cm	152.98(0.4)	160.66(0.53)	151.46(0.49)	147.88(0.55)	< 0.001
Weight, kg	51.82(0.44)	63.58(0.65)	49.53(0.54)	43.98(0.47)	< 0.001
Height-for-age z-scores, SD	0.61(0.02)	0.65(0.04)	0.59(0.03)	0.61(0.03)	0.448
Weight-for-age z-scores, SD	1.13(0.04)	1.87(0.1)	1.14(0.06)	0.86(0.05)	< 0.001
BMI-for-age z-scores, SD	0.82(0.03)	1.28(0.04)	0.77(0.05)	0.48(0.03)	< 0.001
Obesity, %	19.40(0.85)	36.05(1)	17.71(1.06)	9.65(0.72)	< 0.001
Ethnicity, %					
Non-Hispanic White	60.95(2.18)	59.5(3.04)	59.82(2.36)	63.2(2.13)	0.105
Non-Hispanic Black	14.8(1.42)	16(1.51)	15.55(1.59)	13.1(1.49)	0.020
Mexican American	12.34(1.19)	12.38(1.69)	12.49(1.22)	12.16(1.06)	0.851

NOTE. Results are mean (± SD), median (interquartile range), or percentage (n = number of individuals).

[a] Data were weighted according to the National Health and Nutrition Examination Survey protocol.

Abbreviations:

BMI body mass index, HDL-C high-density lipoprotein cholesterol, LDL-C low-density lipoprotein cholesterol, CRP C-reactive protein, TC total cholesterol, TG triglyceride, HOMA-IR homeostasis model assessment of insulin resistance; HS High school, PIR, poverty income ratio, FPG, fasting plasma glucose.

Characteristics	Total n = 8030	Tertiles 1	Tertiles 2	Tertiles 3	p for trend
Other Race/Ethnicity	6.17(0.74)	5.39(0.96)	6.22(0.92)	6.78(1.06)	0.243
Cotinine, %					
Cotinine, > 10 ng/mL	7.62(0.5)	14.25(1.17)	7.34(0.8)	2.28(0.3)	< 0.0001
Cotinine, ≤ 10 ng/mL	92.38(0.5)	85.75(1.17)	92.66(0.8)	97.72(0.3)	
PIR, %					
PIR, ≥1	78.77(1.09)	75.64(1.5)	79.21(1.2)	81(1.43)	0.002
PIR, <1	21.23(1.09)	24.36(1.5)	20.79(1.2)	19(1.43)	
Education, %					
Education, ≥HS	5.49(0.48)	7.68(0.8)	4.88(0.58)	4.21(0.6)	< 0.001
Education, <HS	94.51(0.48)	92.32(0.8)	95.12(0.58)	95.79(0.6)	
Diabetes, %	0.45(0.09)	0.42(0.13)	0.28(0.1)	0.63(0.2)	0.340
TC, ≥ 200 mg/dL	9.92(0.57)	6.35(0.69)	9.54(0.98)	13.29(0.87)	< 0.001
TG, ≥ 150 mg/dL	11.21(0.91)	14.77(1.75)	8.31(1.36)	10.48(1.5)	0.080
LDL-C, ≥ 130 mg/dL	6.9(0.63)	3.58(0.55)	7.5(1.31)	9.51(1.25)	< 0.001
HDL-C, < 35 mg/dL	5.43(0.4)	10.47(0.92)	4.25(0.74)	2.11(0.56)	< 0.001
Glycohemoglobin, > 5.7%	1.74(0.2)	2.11(0.4)	1.52(0.31)	1.47(0.35)	0.231
FPG, ≥ 100 mg/dL	14.92(1.28)	15.11(1.61)	14.04(1.84)	15.56(2.54)	0.906
HOMA-IR, ≥ 3.29	25(1.44)	33.4(2.32)	22.32(2.19)	16.29(1.81)	< 0.001
CRP, ≥ 0.211 mg/dL	15.56(0.6)	23.32(0.9)	14.36(1.03)	10.11(0.71)	< 0.001

NOTE. Results are mean (± SD), median (interquartile range), or percentage (n = number of individuals).

[a] Data were weighted according to the National Health and Nutrition Examination Survey protocol.

Abbreviations:

BMI body mass index, HDL-C high-density lipoprotein cholesterol, LDL-C low-density lipoprotein cholesterol, CRP C-reactive protein, TC total cholesterol, TG triglyceride, HOMA-IR homeostasis model assessment of insulin resistance; HS High school, PIR, poverty income ratio, FPG, fasting plasma glucose.

The Results Of Relationship Between Trans-β-carotene And Obesity

In the multiple linear regression analysis, serum trans-β-carotene level was significantly associated with obesity after being adjusted for confounding factors (Table 2). The non-adjusted and adjusted models are also set out in Table 2. In crude model, trans-β-carotene showed a negative correlation with obesity (0.32,95%CI: 0.28–0.37). In the adjusted model I (adjusted for age, sex, race/ethnicity), the result had not obviously changed (0.32, 95%CI: 0.28–0.37). In addition, we detected the same negative correlation in fully adjusted model (adjustment variables: age, sex, race/ethnicity, family PIR, education levels, serum cotinine status, diabetes, TC, TG, HDL-C, LDL-C, HOMA-IR score, Glycohemoglobin, FBG, CRP) (0.42, 95%CI: 0.29–0.61). For the sensitivity analysis, we also handled trans-β-carotene as Categorical variable (tertiles) and found the same trend (p for trend = 0.002). The higher tertile of serum trans-β-carotene level was significantly associated with reduction of obesity compared with the lower tertile after adjustment for all confounding factors (compared to 1st tertile, 2nd tertile: OR = 0.50, 95% CI, 0.31–0.81; 3rd tertile: OR = 0.30, 95% CI, 0.17–0.55).

Table 2

Association of serum trans-β-carotene level with obesity in NHANES 2001–2006 (n = 8030). [a]

	Odds ratio (95% CI) P			
	Model 1	Model 2	Model 3	Model 4
Trans-β-carotene level (ug/dl) ln transform				
ln (trans-β-carotene, ug/dl)	0.32(0.28,0.37) <0.001	0.29(0.25,0.33) <0.001	0.28(0.24,0.32) <0.001	0.42(0.29,0.61) <0.001
Trans-β-carotene Level (ug/dl)				
Tertiles 1	1.00 (referent)	1.00 (referent)	1.00 (referent)	1.00 (referent)
Tertiles 2	0.44(0.38,0.52) <0.001	0.40(0.34,0.48) <0.001	0.39(0.33,0.47) <0.001	0.50(0.31,0.81) 0.018
Tertiles 3	0.22(0.18,0.27) <0.001	0.19(0.16,0.23) <0.001	0.19(0.16,0.23) <0.001	0.30(0.17,0.55) 0.003
p for trend	< 0.001	< 0.001	< 0.001	0.002

[a] Data were weighted according to the National Health and Nutrition Examination Survey protocol.

Table 3

Effect sizes of serum trans-β-carotene level and obesity between two groups.

	FPG < 100 (mg/dl)	FPG ≥ 100 (mg/dl)
Crude model (β, 95%CI, P)		
Trans-β-carotene level (ug/dl) ln transform		
ln (trans-β-carotene, ug/dl)	0.39 (0.32, 0.47) < 0.001	0.20 (0.13, 0.32) < 0.001
Trans-β-carotene Level (ug/dl)		
Tertiles 1	1.00 (referent)	1.00 (referent)
Tertiles 2	0.48 (0.37, 0.62) < 0.001	0.20 (0.11, 0.36) < 0.001
Tertiles 3	0.32 (0.24, 0.42) < 0.001	0.10 (0.05,0.20) < 0.001
p for trend	< 0.001	< 0.001
Model I (β,95%CI, P)		
Trans-β-carotene level (ug/dl) ln transform		
ln (trans-β-carotene, ug/dl)	0.36 (0.29, 0.44) < 0.001	0.18 (0.11, 0.30) < 0.001
Trans-β-carotene Level (ug/dl)		
Tertiles 1	1.00 (referent)	1.00 (referent)
Tertiles 2	0.45 (0.35, 0.59) < 0.001	0.18 (0.10, 0.33) < 0.001
Tertiles 3	0.30 (0.22, 0.40) < 0.001	0.09 (0.18, 0.38) < 0.001
p for trend	< 0.001	< 0.001
Model II (β, 95%CI, P)		
Trans-β-carotene level (ug/dl) ln transform		
ln (trans-β-carotene, ug/dl)	0.36 (0.29, 0.44) < 0.001	0.17 (0.10, 0.29) < 0.001
Trans-β-carotene Level (ug/dl)		
Tertiles 1	1.00 (referent)	1.00 (referent)
Tertiles 2	0.44 (0.34, 0.58) < 0.001	0.20 (0.11, 0.37) < 0.001
Tertiles 3	0.31 (0.23, 0.42) < 0.001	0.07 (0.03, 0.16) < 0.001
p for trend	< 0.001	< 0.001
Model III (β, 95%CI, P)		
Trans-β-carotene level (ug/dl) ln transform		

	FPG < 100 (mg/dl)	FPG ≥ 100 (mg/dl)
ln (trans-β-carotene, ug/dl)	0.50 (0.37, 0.69) < 0.001	0.10 (0.03, 0.31) < 0.001
Trans-β-carotene Level (ug/dl)		
Tertiles 1	1.00 (referent)	1.00 (referent)
Tertiles 2	0.54 (0.36, 0.82) 0.003	0.07 (0.02, 0.24) < 0.001
Tertiles 3	0.46 (0.29, 0.73) 0.001	0.04 (0.01, 0.26) < 0.001
p for trend	< 0.001	< 0.001

The Subgroup Analyses

Interaction tests were carried out to examine the effect of relevant stratification factors on the relationship between trans-β-carotene and obesity. A significant interaction (P = 0.01) between trans-β-carotene and plasma glucose was observed. The effect sizes of trans-β-carotene and obesity showed a significant difference between two plasma glucose groups. A stronger association between trans-β-carotene and obesity was found in higher plasma glucose levels (more than100 mg/dl)(OR = 0.10; 95% CI, 0.03–0.31).With each one-unit of natural log-transformed serum trans-β-carotene unit, there was an 90% decrease in obesity among high-plasma glucose population. For sensitivity analysis, a higher serum trans-β-carotene level was significantly associated with a reduced probability of obesity in higher plasma glucose levels (compared to 1st tertile, 2nd- tertile: OR = 0.07, 95% CI, 0.02–0.24; 3rd tertile: OR = 0.04, 95% CI, 0.01–0.26).

The Analyses Of Linear Relationship

Because trans-β-carotene was a continuous variable, analyses of linear relationship were necessary. In the present study (Fig. 1A), we found that the relationship between trans-β-carotene and obesity was linear (adjustment variables: age, sex, race/ethnicity, family PIR, education levels, serum cotinine status, diabetes, TC,TG,HDL-C,LDL-C, HOMA-IR score ,Glycohemoglobin, FBG,CRP)(0.45, 95%CI: 0.34–0.60). We also used generalized additive model to identify the linear relationship, and the inflection point was 2.34 (likelihood ratio test p = 0.198). However, the relationship between trans-β-carotene and obesity is non-linear at higher plasma glucose level(Fig. 1B). We also utilized GAM to identify the non-linear relationship and the inflection point was 2.7 (trans-β-carotene = 14.88 ug/dl) (likelihood ratio test p = 0.012) (Table 4). By two-piecewise linear regression model, effect sizes and confidence intervals for the left and right sides of the inflection point were 0.10 (0.00 to 0.2) and 6.7 (0.1 to 348.2), respectively.

Table 4

Results of two-piecewise linear regression model in higher plasma glucose level group.

Inflection point of ln (trans-β-carotene, ug/dl)	Effect size (β)	95%CI	P value
< 2.7	0.1	(0.00, 0.2)	< 0.001
≥ 2.7	6.7	(0.1, 348.2)	0.345
Adjusted for age, sex, race/ethnicity (non-Hispanic white, non-Hispanic blacks, Mexican Americans, and others), family PIR, education levels, serum cotinine status, diabetes, TC, TG, HDL-C, LDL-C, HOMA-IR score, glycohemoglobin, CRP;			

Discussion

In this large, nationally representative sample of children and adolescents aged 6 to 18 years old, plasma glucose significantly modified the inverse association between trans-β-carotene and obesity, which was stronger in individuals with higher plasma glucose population than in those with lower plasma glucose levels. As showed in the fully adjusted model, trans-β-carotene was associated with obesity even by sensitivity analysis. Indeed, this indicated 58% decrease in the odds of obesity for per one ln mg/dl increase in trans-β-carotene level. In addition, significant interaction was observed between trans-β-carotene level and obesity. Subjects with high-plasma glucose levels (more than100 mg/dl) had a 90% decrease in the odds of obesity for per 1ln mg/dl increase in trans-β-carotene level. Notably, using generalized additive model, the association between trans-β-carotene level and obesity was nonlinear at high levels of plasma glucose groups (likelihood ratio test p = 0.01).

Our results are in accordance with results of another previous study using data from NHANES 2001–2004, in which has been suggested that trans-β-carotene were significantly inversely associated with children's body mass index[9]. Other relevant reports also showed that serum levels of β-carotene were significantly lower in obese children opposed to those found in normal weight children[37]. We provide further evidence for the finding that a significant interaction between trans-β-carotene and plasma glucose on obesity. To our knowledge, this potential relationship has not previously been assessed. Biologically, obesity-related insulin resistance provides a potential link between trans-β-carotene and obesity. Obese children with insulin resistance suffer an additional oxidative stress and thus, their antioxidant mechanisms become overwhelmed and struggle to manage acute stressors[38]. The main feature of β-carotene is its low polarity and large number of double bonds, which contribute to its powerful antioxidant properties[39]. Interestingly, in mice, a diet supplemented with β-carotene can reduce oxidative stress, adipocyte size and the circulating leptin level in a BCMO1-dependent manner[11]. Therefore, the most reasonable explanation for the significant effect modification by plasma glucose on the association between trans-β-carotene and obesity observed in this study could be oxidative stress, which in turn may play a role in the pathogenesis of obesity.

In addition, it is of note that the current study demonstrated a nonlinear relationship between trans-β-carotene and obesity. In this study, we used not only the generalized linear model to evaluate the linear

relationship between trans-β-carotene and obesity, but also the generalized additive model to distinguish the linear relationship. The relationship between trans-β-carotene and obesity was non-linear in participants with higher plasma glucose levels. The risk of obesity decreased when trans-β-carotene level hit the turning point (14.88 ug/dl). When trans-β-carotene level exceeded 14.88 ug/dl, the association of trans-β-carotene and the risk of obesity no longer existed at higher levels of plasma glucose groups, yet such a pattern was not observed in lower levels of plasma glucose groups. The effect sizes and confidence intervals for the left and right sides of the inflection point were 0.10 (0.00 to 0.2) and 6.7 (0.1 to 348.2), respectively. No such case to our knowledge has been reported in the literature. This result suggests that excessive trans-β-carotene supplementation may not help to reduce obesity in high-plasma glucose status. Further, our results provide a valuable reference value (14.88 ug/dl) for designing additional clinical trials that use trans-β-carotene as a method of therapy. Finally, since this study is an observational study involving unavoidable potential confounding, we used strict statistical adjustment to minimize residual confounding. We did detect this relationship after adjusting other confounding factors, such as HDL-C, LDL-C and glycohemoglobin, that had not been adjusted by previous studies[9, 37].

However, our study also had some limitations. First, we used an analytical cross-sectional study and therefore could not establish temporal relationships or infer causality. Second, our studies focused on the intricate relationship of trans-β-carotene, plasma glucose, obesity and did not address the value of other carotenoids (such as lutein, zeaxanthin, α-cryptoxanthin, β-cryptoxanthin, and α-carotene and β-carotene, etc). Third, we were unable to assess the circadian rhythm of trans-β-carotene levels and exact timing of blood collection for each participant. Forth, there are many tools that have been used to evaluate childhood obesity, such as weight for age (WFA), weight for length (WFL), BMI, BMI-z. However, these indicators are not ideal indicators for evaluating childhood obesity. The use of BMI as the predictor of children's obesity has long been controversial. However, depending on the WHO standard[17], the BMI-z score could eliminate the effects of age and gender to better assess childhood obesity. This method has been widely used in clinical practice for the estimation of childhood obesity. Therefore, in this study, we decided to use BMI-z as the outcome variable. Finally, as the study population only contains children in the US, the results of this study may not be applicable in other biographic ethic groups.

Conclusion

In conclusion, our results suggest that individuals with higher plasma glucose levels who are trans-β-carotene deficient are even more likely to have a higher risk of developing obesity than their counterparts with lower plasma glucose levels. Further studies are required to investigate the causal association and whether trans-β-carotene supplementation can be used to prevent childhood obesity.

Declarations

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Author Contributions

Xuming Mo conceived and designed the study. Xiaodong Zang analysed and interpreted the data, and wrote the manuscript. Hui Liu and Junqiang Zheng conducted data collection and statistical analyses. Ming Fan, Xian Shen, Zhaocong Yang, Jirong Qi prepared tables 1-4 and figures 1. Xuming Mo was responsible for the accuracy of all content in the proof. All authors reviewed the manuscript.

Conflicts of Interest

The authors declare that they have no competing interests.

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Figures

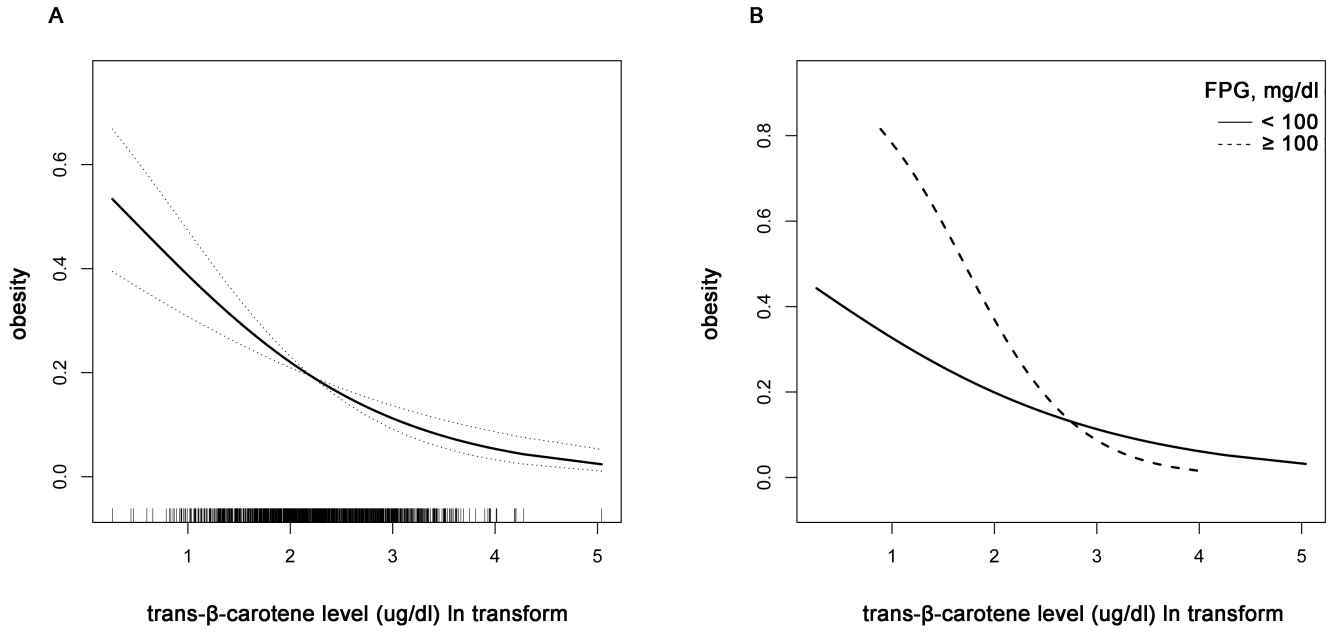

Figure 1

Result of Smooth curve fitting. A :linear relationship between trans-β-carotene and obesity was observed among overall study population. B: a nonlinear relationship between trans-β-carotene level and obesity was observed in individuals with higher plasma glucose (adjustment variables: age, sex, race/ethnicity (non-Hispanic white, non-Hispanic blacks, Mexican Americans, and others),family PIR, education levels, serum cotinine status, diabetes, TC, TG, HDL-C, LDL-C, HOMA-IR score ,Glycohemoglobin, FBG, CRP).