

Whole Food Interventions and Nutrient Displacement: Tomato Sauce Entrees for Prostate Cancer Patients

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Abstract

This study sought to determine changes in self-selected diets in response to a high energy tomato pasta entrée. Thirty men, mostly African-American, who were diagnosed with prostate cancer and also scheduled for prostatectomy were enrolled in the study. Dietary intakes were obtained by 24 hr diet recall for 3 days before the intervention and 3 days in week 2 during the intervention. Tomato pasta entrees were formulated to contain 30 mg of lycopene with roughly the same macronutrient composition and averaged 771 kcal/entrée. Mean adherence to lycopene dose was 82% and, days when the entrée was consumed, the mean adherence to lycopene was 90%. Lycopene intake in their self-selected diet decreased from 5 to 1 mg/day which lowered the exposure to lycopene, planned during the intervention. The men were able to decompensate for most of the added energy to their diet, but there was still a mean increase in total intake of 242 kcal/day ($p=0.04$), which did not result in weight gain over the short period of the study. There were no significant changes in the percent of energy from protein, fat or carbohydrates, but dietary cholesterol increased from 341 to 472 mg/day ($p=0.0002$). Mean intakes of vitamins A and C, and folate were not significantly different and were above the EAR. Vitamin E intake decreased, but, because of the variance in intake, the decrease was not statistically significant. Possible deterioration of diet quality should be a consideration when recommending whole food interventions for the prevention of chronic disease or the amelioration of physiological dysfunction.

Key words: tomato sauce, lycopene, food intervention, nutrient displacement, prostate cancer

INTRODUCTION

Prostate cancer is the second most common cancer among men and has surpassed lung cancer to become the second leading cause of male cancer death in the United States (1). Risk for prostate cancer has been shown to be lower in individuals who have lower intakes of meat, fat and energy, and increased fruit and vegetable intake (2-4). A leading hypothesis is that carotenoids, a family of photo-sensitive plant pigments, serve as antioxidants in preventing free radical damage to critical cellular components including the epithelial cells of the prostate (5,6). Lycopene, a member of the carotenoid family, is found almost exclusively in tomato and tomato products, and is responsible for their red color. Epidemiological studies suggest that intake of lycopene or other compounds in tomatoes may reduce prostate cancer risk (7-10). Among 72 studies reviewed, 57 reported inverse associations between tomato intake or blood lycopene levels and the risk of cancer at a defined anatomic site. Thirty-five of these inverse associations were statistically significant (8,11). However, in re-

sponse to an application for a qualified health claim for the decreased risk of cancer with higher consumption of lycopene or tomato products, the United States Food and Drug Administration (FDA) applied their new systematic rules for significant scientific agreement and came to the conclusion that there was a weak case for tomato products but not for lycopene. The review panel disregarded all diet and plasma lycopene associations because (1) diet collection techniques were uncertain measures of actual intake, (2) lycopene-containing foods contain other "nutrients" that might affect the etiology of cancer and (3) plasma lycopene levels are poorly correlated with lycopene intake and can be affected by other factors such as smoking status, time of year, and serum cholesterol levels (12).

Prior to the FDA evaluation, we had hypothesized that a higher consumption of tomato products would modulate biomarkers for prostate cancer not only because of their lycopene content but also their other bioactive compounds. We found that the consumption of the tomato sauce entrée increased lycopene in the prostate 3 fold, decreased DNA damage in leukocytes and prostate >

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20% and serum prostate specific antigen (PSA) levels about 18% and increase prostate cancer cell apoptosis in 32 men with prostate cancer scheduled for prostatectomy (13-15).

The most popular tomato products, such as tomato sauce pasta entrée and pizza are energy dense and contain a high percent of fat. We wondered whether the introduction of such products would lead to increased energy intake and a displacement of important micro-nutrients in self-selected diets. Whole food recommendations as a public health measure could have unintended consequences if issues of displacement are not seriously considered. Surprisingly, although the issue of displacement is a widely recognized concern among nutritionists, it is a poorly researched area (16). A thorough search of the literature found that the only primary data in studies that collected dietary information during controlled whole food supplementation investigations were those that looked at the addition of nuts and whole-grain cereals. Unfortunately, most food supplementation studies do not report shifts in nutrient intakes before and after the intervention or between the intervention and control groups. We report here the macro- and micro-nutrient changes in the self-selected diets of the men cited in the above study (13-15), resulting from the daily consumption of the tomato entrée.

MATERIALS AND METHODS

Subjects

Thirty-two patients diagnosed with adenocarcinoma of the prostate and scheduled for prostatectomy were recruited from the urology clinic of the Westside Veterans

Administration Medical Center, Chicago, IL (WSVA, USA). Details of the study design, methods, recruitment and exclusion criteria have been published (13). All patients gave informed consent prior to their participation in the study, as approved by the University of Illinois Institutional Review Board (IRB) and the research review board of the WSVA.

Experimental design

Patients consumed the tomato pasta entrée daily for a mean of 19.8 ± 0.6 days before prostatectomy. Three 24 hr diet recalls were collected in person or by telephone before the intervention and three recalls were collected in the second week of the intervention. Dietary data were available for 30 patients at the time of the dietary analysis. Blood and prostate biopsies were collected before supplementation and blood was collected the day before prostatectomy and resected tissue was obtained at the time of the prostatectomy. Men chose from 5 entrées designed to contain 30 mg of lycopene contained in 200 g of Hunt's Traditional Spaghetti Sauce and roughly similar in macronutrient and antioxidant content. Table 1 represents the individual nutrient analysis of each tomato sauce entrée.

Data analysis

Nutrient calculations of energy, macronutrients, micronutrients, and cholesterol were performed using the Nutrition Data System for Research (NDS-R) (software version 4.01, developed by the Nutrition Coordinating Center, University of Minnesota, Minneapolis, MN, USA, Food and Nutrient Database 29, released December, 1998). Compliance to pasta entrée consumption was estimated daily by providing patients with

Table 1. Nutrient analysis of tomato sauce entrees

| | Sausage lasagna | Stuffed shells | Baked rigatoni | Penne pasta | Mexican lasagna |
|-----------------------------|-----------------|----------------|----------------|-------------|-----------------|
| Weight (gm) | 485 | 418 | 418 | 367 | 391 |
| Energy (kcal) | 957 | 714 | 723 | 601 | 638 |
| Total CHO (g) | 47 | 49 | 57 | 55 | 97 |
| % CHO | 20 | 28 | 31 | 73 | 61 |
| Total fat (g) | 59 | 38 | 37 | 6 | 19 |
| % Fat | 55 | 48 | 46 | 17 | 27 |
| Protein (g) | 61 | 46 | 42 | 10 | 22 |
| % Protein | 26 | 26 | 23 | 13 | 14 |
| Cholesterol (mg) | 416 | 344 | 130 | 7 | 24 |
| Vitamin E (mg) | 4.6 | 4.3 | 3.8 | 3.2 | 5.5 |
| Vitamin C (mg) | 27 | 33 | 26 | 27 | 32 |
| Vitamin A (RE) | 546 | 477 | 461 | 210 | 269 |
| Folate (μ g) | 71 | 63 | 45 | 30 | 51 |
| Total fiber (gm) | 4 | 4 | 5 | 5 | 9 |
| Lycopene (mg) | 30 | 30 | 30 | 30 | 30 |
| β -Carotene (mg) | 1.1 | 1.1 | 1.1 | 1.1 | 1.1 |
| α -Carotene (mg) | 0.02 | 0.02 | 0.02 | 0.02 | 0.02 |
| Lutein (mg) | 0.2 | 0.2 | 0.2 | 0.2 | 0.2 |
| β -Cryptoxanthin (mg) | 0 | 0 | 0 | 0 | 0 |

paper grids of the entrée dish divided off in quadrants. Patients check all the quadrants consumed that day for each day of the study. Following dietary data collection, all individual food records were entered into NDS-R and evaluated for differences in diet intake between the two assessment periods. Additional information of entrée consumption for the recall days was incorporated to provide total nutrient intakes. The 3-day mean of lycopene in patients' diets was measured at baseline and during the tomato entrée intervention to determine whether participation would result in increases or decreases in self-selected dietary lycopene consumption. Records of lycopene-containing foods were compiled for each patient, and each food's lycopene content was calculated using the database of carotenoid containing foods on the web page of the United States Department of Agriculture (www.nal.usda.gov/fnic/foodcomp/Data).

Statistical analysis

Paired t-tests were performed to evaluate before and during (intervention) mean differences in macro- and micronutrient which included energy, fat, carbohydrate, protein, percent fat change, percent protein change, vitamins A, C, E and folate. Paired t-tests were also performed to determine within-group increases of serum lycopene levels before vs. after the intervention, and changes in prostate lycopene levels before (prostate biopsy) vs. after the intervention (resected tissue). A p-value of <0.05 was considered statistically significant.

RESULTS AND DISCUSSION

Table 2 presents demographic and anthropometric information. Mean daily nutrient intakes before and during pasta entrée consumption are presented in Table 3. Adherence to the intervention was characterized by number of days that patients consumed at least 25% of the tomato pasta entrée divided by the number of intervention days and was $90.0 \pm 2.0\%$. Adherence to dose was estimated as daily reported entrée intake \times lycopene content divided by the total lycopene content of each entrée \times the number of intervention days. Mean adherence to dose was 81.6%. Excellent adherence was corroborated by a rise of serum total lycopene of 97.2% and prostate lycopene of 1.94%. Mean lycopene intake from the patients' self-selected diet decreased from 5 mg/day to 1 mg/day. This decrease was most evident in men with higher consumptions of lycopene on the days when 24 hr recalls were obtained. Mean energy intake increased by 242 kcal during the entrée consumption period. Since mean intake from entrées was 771 kcal/day representing 1/3 of their total energy intake the men were

Table 2. Characteristics of the study patients with adenocarcinoma of the prostate¹⁾

| | Group (n = 30) |
|--|-----------------|
| Age (yr) | 63.7 \pm 6.1 |
| Height (cm) | 175.7 \pm 7.7 |
| Weight (kg) | 87.0 \pm 17.7 |
| % of body fat | 20.9 \pm 5.4 |
| Body mass index (kg/m ²) | 28.0 \pm 4.9 |
| Smoking status ²⁾ | 10/30 |
| Ethnicity | |
| African-American (%) | 75 |
| Other (%) ³⁾ | 25 |
| Marital Status (n) | % |
| Married (11) | 36.6 |
| Divorced (8) | 26.6 |
| Separated (3) | 10 |
| Widowed (4) | 13.3 |
| Never married (4) | 13.3 |
| Education (n) | % |
| % \leq 9th grade (3) | 10 |
| % \geq 9th < 12th (8) | 26.6 |
| % \geq High school (19) | 63.3 |
| No of intervention days | 19.8 \pm 0.6 |
| Compliant days, % | 90.0 \pm 2.0 |
| Compliant to total dose, % | 81.7 \pm 21.5 |
| Self-selected lycopene consumed before the study, mg/day | 5.0 \pm 7.3 |
| Self-selected lycopene consumed during the study, mg/day | 1.0 \pm 0 |
| Total lycopene consumed during the study, mg/day | 26.8 \pm 2.2 |

¹⁾Mean \pm SE.

²⁾Current smoker.

³⁾4 Anglo-Americans, 1 Latino-American, 1 Indian-American.

able to adjust their energy intake by a mean of 529 kcal. Body weight did not increase during the 3 wk period. If the mean 242 kcal/day increase was a valid estimate we might have expected to see a body weight increase of 1.3 lbs (4,598/3500 kcal) during the 20 days of intervention. The limitations of the diet assessments do not allow an accurate estimate of the extent of energy decompensation due to the whole food intervention but what is evident is that the men were able to decompensate for most of the energy added to their diets through dietary self-selection. The macronutrient composition of the diet did not change during the intervention but mean cholesterol intake increased by 131 g due to the high cholesterol content of sausage lasagna and stuffed shells, the most favored entrées. Other whole food supplementation studies have shown that high energy foods can be added to the diet without producing weight gain. Only a few have documented intakes from self-selected diets before and after intervention. Chisolm et al. (17) added walnuts to the diet (478 kcal/day) for 8 wks

Table 3. Body weight, serum/prostate lycopene concentration and daily nutrient intake, before and during intervention

| Total group (n=30) | Before (Mean \pm SE ¹⁾) | During (Mean \pm SE ¹⁾) | EAR ²⁾ | p-value ³⁾ |
|--|---------------------------------------|---------------------------------------|-------------------|-----------------------|
| Energy (kcal) | 2096 \pm 132 | 2338 \pm 122 | | 0.04 |
| MEE ideal (BMR \times 1.3) | 1978 \pm 33 | | | |
| Body weight (lb) | 192 \pm 7.2 | 191 \pm 7.1 | | NS |
| Macronutrients | | | | |
| Carbohydrate (g) | 243 \pm 16 | 266 \pm 17 | | 0.14 |
| protein (g) | 79 \pm 5.1 | 93 \pm 5.5 | 57.3 | 0.01 |
| fat (g) | 92 \pm 7.5 | 103 \pm 5.7 | | 0.07 |
| Protein (%) | 15.4 \pm 0.6 | 16.1 \pm 0.6 | | NS |
| Fat (%) | 38.7 \pm 1.4 | 39.8 \pm 0.9 | 20~35 | NS |
| Cholesterol (mg) ⁴⁾ | 341 \pm 39.2 | 472 \pm 33.1 | | 0.0002 |
| Micronutrients | | | | |
| Vitamin A (μ g) | 1285 \pm 174 | 1497 \pm 218 | 625 | NS |
| Vitamin E (mg) | 19 \pm 9.4 | 13.5 \pm 1.7 | 12 | NS |
| Vitamin C (mg) | 128.7 \pm 20.2 | 137.8 \pm 21.6 | 75 | NS |
| Folate (μ g) | 295.8 \pm 35 | 308.4 \pm 45.7 | 400 | NS |
| Serum/Tissue Biochemistry | | | | |
| Serum total lycopene (nM) ⁵⁾ | 638 \pm 60 | 1258 \pm 95 | | 0.0001 |
| Prostate total lycopene (nmol/g) ⁵⁾ | 0.279 \pm 0.450 | 0.820 \pm 0.119 | | 0.001 |

¹⁾Mean \pm SE (standard error).

²⁾Estimated average requirement, dietary reference intakes for men \geq 51 yrs, Institute of Medicine, National Academy Press.

³⁾Comparisons for before and during entrée consumption are for two-tailed ANOVA tests performed on log-transformed data.

⁴⁾No UL for cholesterol was set because even low dietary cholesterol may be harmful in some people. An increase of 100 mg/day is predicted to result in a 0.5~1.0 mmol/L increase in total serum cholesterol, with 80% found in the LDL fraction (23).

⁵⁾Mean \pm SD (standard deviation).

and saw negligible total energy intake increases but found an 8% increase in dietary fat and a reciprocal 6% and 2% decrease in dietary carbohydrate and protein, respectively. Spiller et al. (18) added almonds to the diet (621 kcal/day) for 9 wks and saw a negligible increase in total energy intake, a 9% and 3% increase in dietary fat and protein, respectively, and an 8% decrease in dietary carbohydrate. Kirk et al. (19) added cereal to the diet (217 kcal/day) for 4 wks and found no change in total energy intake, a 5.5% and 0.2% increase in dietary carbohydrate and protein, respectively, and a 5.4% decrease in dietary fat. Our estimated 11.5% increase in total energy intake during our tomato pasta entrée intervention may provide some indication of how much individuals will decompensate for food additions to their usual self-selected diet, since our supplementation provided more energy the studies cited. One long-term study did show a slight increase in energy intake. Jaceldo-Siegl et al. (20) provided 52 g/day (308 kcal/day) of almonds for a 6 month period after a 6 month study period with no almond supplementation. They saw a 7.7% ($p=0.003$) increase in energy consumption during almond supplementation, but also health-promoting shifts in all classes of dietary fats, fiber, animal protein and a number of micronutrients.

Dietary vitamins A and C and folate intake met the DRI nutrient recommendations and were not affected by the whole food intervention. This was likely due to the

fact that the entrées provided good levels of vitamins A, C and folate, although vitamin E content was low. The decrease in mean daily vitamin E intake was not statistically significant because of large dietary variance.

Underreporting of energy intake has been shown to be a fairly common occurrence among patients providing food intake data (21,22). To determine whether underreporting may have occurred in these older men, Minimum Energy Expenditures (MEE) were calculated for patients based on ideal weights using the Metropolitan Life tables. Patient BMR's (using Harris Benedict) were multiplied by a 1.3 activity factor (minimal energy expenditure consistent with daily life) to determine MEE. Comparisons showed that 14/30 patients were apparent under-reporters on the days that 24 hr recalls were collected. When the dietary data was compared for the 16 good reporters and the 14 under-reporters there were no statistically significant differences in diet changes in response to the tomato pasta entrée consumption. Both under-reporters and good reporters increased their cholesterol intake, but macronutrient composition and micronutrient consumption were unchanged. However, the good reporters were more likely to report higher energy consumption while consuming the study entrées. To determine whether the mostly African-American men in our study were more likely to under-report their food intakes, we compared our results to population studies reporting the diets of African-American men of com-

parable age. Mean energy consumption of our good and under-reporters were $2,104 \pm 215$ and $2,086 \pm 151$ kcal, respectively, while the NHANES reference population of African-American men with a mean age of 64.5 yrs was $1,882 \pm 94$ kcal (23). Shimakawa et al. (24) reported a mean intake of $1,731 \pm 663$ kcal in 1,567 African-American men with a mean age of 54 yrs and Norris et al. (25) reported a mean of $2,026 \pm 140$ kcal in 159 men with a mean age of 56 yrs. Even our under-reporters were able to report more of their food intake compared to comparable populations of African-American men.

CONCLUSIONS

Overall, good compliance to entrée consumption was observed in all subjects, as evidenced by increases in plasma and prostate lycopene concentrations. However, lycopene intake in self-selected diets decreased, which lowered the estimate of the intended dose of bioactive compound. Subjects were able to lower their self-selected energy consumption in response to the imposition of a high energy whole food without a gain in weight over a short intervention period, but there may be a limit is how much energy for which they can decompensate, since energy intakes were higher during the intervention period. Consumption of cholesterol-rich tomato pasta entrees increased cholesterol intake in most subjects, which may put them at risk for coronary heart disease. Macronutrient distribution did not change, but this was largely a function of the balanced nature of the entrée provided. Micronutrient intakes were not statistically different, but there were negative trends, especially for vitamin E, that point to a need to be concerned about the deterioration of overall diet quality when whole foods are recommended to be incorporated into diets.

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