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Development of a Polyamine Database for Assessing Dietary Intake

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Abstract

Reducing the concentration of polyamines (spermine, spermidine, and putrescine) in the body pool may slow the cancer process. Because dietary spermine, spermidine, and putrescine contribute to the body pool of polyamines, quantifying them in the diet is important. Limited information about polyamine content of food is available, especially for diets in the United States. This brief report describes the development of a polyamine database linked to the Fred Hutchinson Cancer Center food frequency questionnaire (FFQ). Values for spermine, spermidine, and putrescine were calculated and reported per serving size (nmol/serving). Of the foods from the database that were evaluated, fresh and frozen corn contain the highest levels of putrescine (560,000 nmol/serving and 902,880 nmol/serving) and spermidine (137,682 nmol/serving and 221,111 nmol/serving), and green pea soup contains the highest concentration of spermine (36,988 nmol/serving). The polyamine database and FFQ were tested with a convenience sample (n=165). Average daily polyamine intakes from the sample were: 159,133 nmol/day putrescine, 54,697 nmol/day spermidine, and 35,698 nmol/day spermine. Orange and grapefruit juices contributed the greatest amount of putrescine (44,441 nmol/day) to the diet. Green peas contributed the greatest amount of spermidine (3,283 nmol/day) and ground meat contributed the greatest amount of spermine (2,186 nmol/day). Development of this database linked to an FFQ provides a means of estimating polyamine intake and contributes to investigations relating polyamines to cancer.

Polyamines (putrescine, spermidine, and spermine) are organic compounds that are found in every living cell, where they are involved in numerous biochemical and physiological activities, including cell proliferation and differentiation (1–5). The metabolic requirement for polyamines is particularly high in rapidly growing tissues, such as during normal growth and development, and in tumors (6–8). Recent studies have suggested that reducing the amount of polyamines in cells may help to slow the cancer process (9). Clinical trials are currently underway to investigate the effect of the polyamine synthesis inhibitor, difluoromethylornithine, on cancer progression, risk for recurrent polyps, and relevant

biomarkers (8). Whether foods that contribute to polyamine consumption affect cancer risk is also a topic ripe for exploration.

Until recently, it was believed that polyamines were derived exclusively from endogenous (internal) synthesis. It is now widely recognized that the polyamine body pool is maintained by three primary sources: synthesis within the body, production by microorganisms residing in the intestinal tract, and contribution from the diet (1,9–13). Studies in rats indicate that 10% of dietary putrescine, 40% of dietary spermidine, and 8% of dietary spermine are retained in body tissues (14). Thus, polyamines in the diet are among the determinants of the total body polyamine pool and may be a particularly important consideration in assessing adequacy of diets during early development and in evaluating responses to pharmaceutical agents, such as inhibitors of polyamine synthesis (eg, difluoromethylornithine), which are under study in clinical trials for cancer chemoprevention. Knowing the amount of polyamines that is typically provided by the diet is critical in interpreting the response to difluoromethylornithine in clinical trials testing the effect on cancer progression.

Despite the growing recognition of the potential importance of dietary polyamines for their effects on cancer progression, relatively little information on the polyamine content of foods is available (1,11,15–21). To date, the studies that have analyzed food content have generally been conducted outside the United States, so the foods (or estimated intakes) for which data are available may not be relevant or representative of the US diet. In addition, many of the foods in these studies were analyzed in the raw form or as single ingredients. As a result of the limited food-content data available, it has been very difficult to assess dietary polyamine intake.

The objectives of this project were to develop a polyamine database, with values for putrescine, spermidine, and spermine, and to link this database to a food frequency questionnaire (FFQ) developed by the Fred Hutchinson Cancer Research Center. Development of a polyamine database linked to an FFQ will aid in the identification of foods with substantial polyamine concentrations and will allow an assessment of dietary polyamine intake.

METHODS

Database Development

The Fred Hutchinson Cancer Center FFQ is one of several FFQs used in major studies of diet and disease risk in the United States, including the sample examined in this report. The polyamine intake data generated from this FFQ have the potential to be applied to other studies. The Fred Hutchinson Cancer Center FFQ food definitions and database were used to identify approximately 370 foods to be the focus of the polyamine food-content database. The primary nutrient database for this FFQ is the University of Minnesota Nutrition Database (Nutrition Data Systems for Research software, 2005, Minneapolis, MN). An extensive search of the literature produced polyamine content data for approximately 117 of the 370 foods for which polyamine content data were needed, with published values for putrescine, spermidine, and spermine. The polyamine levels of the 253 remaining food items were determined via imputation based on methods reported by Schakel and colleagues (22). Methods used for nutrient estimation of the database included: (a) using values from a different but similar food, (b) calculating values from different forms of the same food, (c) calculating values from other components in the same food, (d) calculating values from household recipes, and (e) assuming a zero value.

Values for each food item in the polyamine database were calculated as nmol/g, nmol/100 g, and nmol/serving, and serving size and gram weights were based on values used in the Fred Hutchinson Cancer Center FFQ database. Polyamine values (nmol/100 g) for the selected foods were merged into the Fred Hutchinson Cancer Center FFQ database. To test the newly

developed database within the Fred Hutchinson Cancer Center FFQ programming, we examined data from a convenience sample of FFQs from the first 165 subjects enrolled in an ongoing multicenter, randomized, double-blind, placebo-controlled phase III chemoprevention trial in the United States that is examining the effect of difluoromethylornithine administration on adenoma recurrence and relevant biomarkers (8). Participants recruited for this study were male and female, aged 40 to 80 years, with a history of one or more resected adenomas. The institutional review boards of all the participating institutions approved procedures for that study, and written informed consent was obtained from all the study participants prior to enrollment.

Data Analysis

Average daily consumption of putrescine, spermidine, and spermine from the convenience sample, as provided by analysis of the Fred Hutchinson Cancer Center FFQs, were calculated. Polyamine values for each FFQ line item were also averaged to calculate the mean nmol/day of polyamine that each item contributed to the total intake of the convenience sample. Foods were ranked from highest to lowest dietary contributors of polyamines in the sample.

RESULTS AND DISCUSSION

Table 1 shows the 10 FFQ foods with the highest amounts per serving for each polyamine in our database. Values for polyamines have been traditionally reported per gram weight; however, when identifying foods that are large and small contributors of polyamines to the total intakes, it is important to consider the weight and serving size of the food. For example, popcorn would appear to be a potentially important contributor of putrescine in the polyamine database when examining values based on nmol/g, but when foods are ranked per serving, the potential contribution of popcorn is attenuated (one medium serving of popcorn is equivalent to 1 cup or 12.8 g). As another example, when examining values based on nmol/g of beer, it may not appear to be a potentially important contributor of putrescine. However, when foods are ranked per serving, beer apparently is a potentially important contributor.

The top dietary contributors of polyamines (nmol/day) for the convenience sample analysis are shown in Table 2. Notably, food ranked as low in polyamine content when examined as nmol/g or nmol/serving has the potential to become a major contributor to the diet if it is consumed in large amounts or multiple times during the day.

Estimates of polyamine intake have been made for several countries, including the United Kingdom, Italy, Spain, Finland, Sweden, and the Netherlands (21). The average estimated polyamine intakes for adults in countries surveyed to date are: 211,910 nmol/day putrescine, 86,959 nmol/day spermidine, and 54,704 nmol/day spermine. Average daily polyamine intakes from our convenience sample were: 159,133 nmol/day putrescine, 54,697 nmol/day spermidine, and 35,698 nmol/day spermine.

Differential estimates for polyamine intake, when comparing our values with those reported from other countries, may result, in part, from differential methods used to collect dietary data in addition to true variations in the diet. We used the FFQ approach, and the other estimates were generally obtained via food intake surveys and interview-based approaches. The different ways the food items were grouped or recorded in the different countries during data collection could greatly affect the calculated total polyamine levels (21). Also, the convenience sample in this project was not recruited to be representative of a healthy population.

The development of this polyamine database linked with an FFQ is a first step to estimating polyamine content in the diet. A future step will address validating the estimates of intake. This

will include measuring tissue polyamines and nondietary influencing factors that would affect interpretations of the observed relationships.

This project has some limitations. The subjects selected for this project are not representative of the general population. In addition, subjects were all adults and variations in intakes over a life span could not be measured. Imputation methods used in this project to estimate the polyamine content are less desirable than obtaining replicate content analysis in a laboratory setting.

CONCLUSIONS

Currently there is limited information on polyamine content of foods. Dietary polyamines promote carcinogenesis in experimental animal studies, and reduction of tissue polyamines appears to reduce cancer growth in humans. A polyamine database linked to an FFQ will provide a method of estimating polyamine intake, including overall intake and foods that are dietary sources of these bioactive compounds. In the future, this database may enable estimation of polyamine intakes, and may be useful in evaluating the influence of dietary polyamines on cancer outcomes in ongoing chemoprevention clinical trials.

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Table 1

Top 10 foods on the Fred Hutchinson Cancer Research Center food frequency questionnaire with the highest polyamine content

Food item	Serving size	Polyamine (nmol) per serving size
Putrescine		
Corn (fresh/canned)	½ cup	560,000/902,880 ^a
Grapefruit juice	1 cup	276,640
Oranges	1 medium	174,230
Orange juice	1 cup	154,629
Grits	1 cup	99,728
Crab (canned)	½ cup	93,555
Grapefruit	½ medium	90,176
Cream of potato soup	1 cup	70,930
Tortilla chips	1 small bag	56,717
Tomato and V8 ^b juice	1 cup	56,181
Spermidine		
Corn (fresh/canned)	½ cup	137,682/221,111 ^a
Green pea soup	1 cup	65,552
Pear	1 medium	60,756
Cheese enchilada	1 medium	48,770
Tempeh	3 oz	42,618
Soy burgers	1	39,616
Peas (fresh/canned)	½ cup	35,9 20/38,165 ^a
Lentil soup	1 cup	37,117
Pasta with meat sauce	1 cup	36,059
Tofu hotdog	1	27,121
Spermine		
Green pea soup	1 cup	36,988
Chicken liver	4 oz	33,226
Chili with meat and beans	1 cup	26,441
Chicken breast (grilled/roasted)	1 large	21,560/24,420 ^a
Black bean soup	1 cup	23,786
Peas, fresh	1 medium	23,572
Peas (fresh/canned)	½ cup	20,840/22,143 ^a
Bean with bacon soup	1 cup	22,062
Ground turkey	3 oz	21,535
Tempeh	3 oz	20,565

^aThese two figures provide values for the food in the two different forms described.

^bCampbell Soup Co, Camden, NJ.

Table 2

Top 10 major dietary contributors of polyamines as assessed by the Fred Hutchinson Cancer Research Center food frequency questionnaire

Food item	Polyamine contribution (nmol/day)
Putrescine	
Orange juice and grapefruit juice	44,441
Oranges, grapefruit, and tangerines (not including juice)	17,613
Fresh tomatoes	10,042
Bananas	7,344
Beer (all types)	6,374
Corn and hominy	5,832
Cheese (eg, American, cheddar)	5,592
Potato chips, tortilla chips, corn chips, puffs, and pretzels	4,595
Burritos, tacos, tostadas, and quesadillas	4,411
Green pepper and green chilies	4,343
Spermidine	
Green peas	3,283
Cheese, such as American and cheddar	3,124
Lasagna and pasta with meat sauce	2,900
Potatoes (boiled, baked, and mashed)	2,388
Burritos, tacos, tostadas, and quesadillas	1,890
Dark breads (including dark bagels and rolls)	1,736
Green salad (lettuce or spinach)	1,535
Low- or reduced-fat cheese	1,456
Corn and hominy	2,765
Broccoli	1,347
Spermine	
Ground meat	2,186
Lunch meats (eg, ham, turkey, bologna, and salami)	1,977
Green peas	1,905
Lasagna and pasta with meat sauce	1,443
Peanut butter, peanuts, and other nuts and seeds	1,237
Rice, noodles, and other grains	1,136
Chili with meat and beans	1,027
Bean soups such as pea, lentil, and black bean	747
Cheese (eg, American, cheddar)	670
Stew, pot pie, and casseroles with meat or chicken	656