Original Article

Polyamines: total daily intake in adolescents compared to the intake estimated from the Swedish Nutrition Recommendations Objectified (SNO)

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Abstract

Background: Dietary polyamines have been shown to give a significant contribution to the body pool of polyamines. Knowing the levels of polyamines (putrescine, spermidine, and spermine) in different foods and the contribution of daily food choice to polyamine intake is of interest, due to the association of these bioactive amines to health and disease.
Objective: To estimate polyamine intake and food contribution to this intake in adolescents compared to a diet fulfilling the Swedish Nutrition Recommendations.
Design: A cross-sectional study of dietary intake in adolescents and an 'ideal diet' (Swedish nutrition recommendations objectified [SNO]) list of foods was used to compute polyamine intake using a database of polyamine contents of foods. For polyamine intake estimation, 7-day weighed food records collected from 93 adolescents were entered into dietetic software (Dietist XP) including data on polyamine contents of foods. The content of polyamines in foods recommended according to SNO was entered in the same way.
Results: The adolescents' mean daily polyamine intake was 316 ± 170 μmol/day, while the calculated contribution according to SNO was considerably higher with an average polyamine intake of 541 μmol/day. In both adolescent's intake and SNO, fruits contributed to almost half of the total polyamine intake. The reason why the intake among the adolescents was lower than the one calculated from SNO was mainly due to the low vegetable consumption in the adolescents group.
Conclusions: The average daily total polyamine intake was similar to that previously reported in Europe. With an 'ideal' diet according to Swedish nutrition recommendations, the intake of this bioactive non-nutrient would be higher than that reported by our adolescents and also higher than that previously reported from Europe.

Keywords: *putrescine*; *spermine*; *spermidine*; *bioactive amines*; *dietary polyamines*; *polyamine intake*

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Polyamines (spermine, spermidine, and putrescine) are aliphatic polycations, also named non-protein nitrogen compounds, which can be found in a wide variety of foods and in all mammalian cells (1, 2). Although they can be synthesized by intracellular *de novo* synthesis (3, 4), the external source of polyamines has a role in regulating this intracellular synthesis (1, 5–7).

Polyamines provided by food seem to be essential for the maintenance of normal growth and maturation of the intestinal tract (8, 9). Dietary polyamines are associated with cellular growth and differentiation. This association was reported to be due to polyamine interaction with DNA, RNA, and proteins (1, 10). Furthermore, exogenous polyamines modulate mucosal proliferation and absorption from diet (11). Hence, insufficient polyamine intake could hinder important health enhancing effects of polyamines such as induction of tolerance to dietary allergens (12). A high intake of spermine is associated with a decreased risk of food allergy among suckling rats as well as in children, due to the contribution of spermine

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to maturation of both the immune system (2, 13) and the small intestinal mucosa (14).

The role of polyamines in cellular growth and proliferation is possibly due to regulation of protein synthesis (15). This could be the reason why an increased intake of dietary polyamines has been shown to have a potentially favorable effect on postsurgery patients during wound healing and for growth and development of the neonatal digestive system (12). Dietary polyamines provide both antioxidant and anti-inflammatory properties (5, 16). The antioxidant activity of polyamines has been shown to be even stronger than that of some antioxidant vitamins (16).

The contribution of polyamines to cellular generation can be considered as an undesirable process in some pathological states. For instance, dietary polyamines were shown to induce carcinogenic growth in rat colon (17). In addition, high polyamine levels were observed in tumor cells (18, 19). *In vivo* studies showed that the undesirable polyamine uptake by the tumor cell is induced not only by endogenous polyamines but also by dietary source released into the circulation (19). Therefore, a polyamine reduced diet to control the tumors has been used in some studies where at least one previous list of polyamine rich foods has been produced due to a perceived need to reduce the intake in some risk groups (20).

In foods, polyamines are synthesized from amino acids such as arginine and ornithine, which act as precursors and undergo a decarboxylation process by action of putrefactive bacteria (21, 22). This explains the higher concentrations of polyamines in fermented food products such as sauerkraut, anchovy, some sausages, and cheeses (21, 23).

The Swedish nutrition recommendations translated to foods

The Swedish National Food Administration has translated their nutrition recommendations to foods in the resource 'Swedish nutrition recommendations objectified' (SNO) and formulated food lists contributing to 9.1 MJ and 11.5 MJ for females and males with low physical activity level, which provide the recommended levels of nutrients (24).

There is limited knowledge on the intake of polyamines and the main food sources. Some studies have analyzed the contents of polyamines in foods (1, 6, 25–32). The mean dietary intake of polyamines has been estimated in some countries such as Japan (32), United States (20), and United Kingdom (1). In this study, we wanted to identify the main sources of polyamines in the Swedish diet, compared to the Swedish 'ideal diet' (SNO). Also to provide a rough estimate of the mean putrescine, spermine, and spermidine intake in μmol/day in a group of adolescent volunteers' registered intake as well as based upon the SNO. Studies have shown that obese subjects tend to underreport their food intake significantly in comparison with non-obese subjects (33, 34). Therefore, we attempted to obtain 7-days dietary records from non-obese healthy adolescents in order to minimize food recording errors.

Methods

Dietist XP software package, version 3.0 (2007), was used for estimation of polyamine intake. This dietary program is linked to the Swedish Food Database (Livsmedelsverket-National Food Administration, 2007, Uppsala). This database as such covers around 1,600 foods and 52 nutrients. Dietist XP is designed to estimate macro- and micronutrients and energy intake. Using information from our review of literature to develop a polyamine database (35), data on content of polyamines in different foods was collected from different studies (1, 6, 25–32). These studies have reported values for each polyamine in different foods based on laboratory analysis. Using this information, polyamine contents for more than 250 selected foods were obtained. In the developed database, values for each polyamine were calculated and assigned for each type of food using a mean value for the published polyamine values that were gathered from different studies. These values were then entered in Dietist XP, supplementing the Swedish Food Database. Dietist XP was thereafter used for entering the dietary intake of the adolescents and for estimation of their polyamine intake.

Study subjects and dietary polyamine estimation

A cross-sectional study was conducted on 93 adolescent volunteers, mean age 17.4 and 17.5 years for males and females. Values for the mean body mass index (BMI) for both males and females were 21.6 ± 2.1 and 21.1 ± 1.8, respectively. The subjects were randomly selected from schools in Eskilstuna and Eksjö, Sweden, and were asked on a voluntary basis to record their dietary intake using 7-day food records. The amounts of food consumed were registered in grams or milliliters. The test participants were provided with food scales, and registration forms and instructions on how to record the intake were given by experienced nutritionists on the day before food intake was registered.

The entire 7-day dietary records for each participant were entered into the Dietist XP software and the total polyamine intake as well as individual polyamine intake in μmol per person per day was calculated. In Dietist XP, all values of polyamine contents are listed in mg/100 grams of food. Values for polyamine intake were converted into μmol/day based on the appropriate equation (mol = mass/molecular weight). The molecular weights for putrescine, spermine, and spermidine are 88.15 g/mol, 145.25 g/mol, and 202.34 g/mol, respectively.

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The contribution from each food group was estimated from the total intake of each individual.

Only seven records where the energy intake:basal metabolic rate (EI:BMR) was lower than 1.5 were excluded from the study as incomplete. The cutoff was derived using estimated BMR of the study subjects predicted from Schofield equations (36–38).

Estimation of food contribution to the polyamine intake

All foods were categorized into food groups according to the National Swedish Food Database classification of foods. Data on polyamine contents in foods were aggregated to provide an average value for each polyamine for each food group, which are fruits, vegetables, dried pulses, cheese, bread and cereals, meat/fish/eggs, and potatoes. This aggregation was made to compare the polyamine intake from these groups with the one calculated from the food groups in the SNO. Using Dietist XP, this aggregation was done first by estimating the food group intake for each individual in grams per day. Based on average values of polyamines that were given for each 100 g of the different food groups, the means of polyamine intake from the food groups were estimated in µmol per day for the adolescents as well as for the food groups given in the SNO.

The group of fruits included all fruits and berries consumed including fruit juice. The group vegetables referred to all green vegetables, green beans, peas, carrots, and roots except for potato, which was counted separately. The group pulses included dried beans and peas. The group of meat and meat products covered all types of meat, fish, and eggs. The bread and cereal group included all types of bread, grains, and corn products. For the dairy group, cheese was counted separately. Within the cheese group, the aggregation was made on the most commonly used cheeses by the study participants due to the wide differences in polyamine contents between different types of cheese.

Data analysis

All statistical analyses were performed using Statistical Package for Social Science (SPSS version 17.0, 2008, SPSS Inc.). Means and standard deviations of dietary polyamine (putrescine, spermine, and spermidine) intake in µmol/person/day were calculated. The *t*-test was conducted for gender differences in terms of energy, food, and polyamine intake. Testing the difference in the energy intake between day 1 and day 7 was performed using paired-sample *t*-test.

Results

Polyamine intake of adolescent volunteers

The foods consumed by the Swedish adolescents shown in g/day per food group and the mean intake of

Table 1. Food group consumed by adolescents (mean ± SD) and polyamines intake (mean ± SD) estimated from each food group

	Male					Female				
Food group	Food (g/d)	Range (g/d)	PUT (µmol/d)	SPD (µmol/d)	SPM (µmol/d)	Food (g/d)	Range	PUT (µmol/d)	SPD (µmol/d)	SPM (µmol/d)
Fruit and fruit juice	309.9 ± 192.5	26–818	160.75 ± 105.5	43.37 ± 27.5	9.4 ± 6.0	313.6 ± 210.3	11–974	167.9 ± 112.3	45.3 ± 30.3	9.88 ± 6.42
Vegetables	82.3 ± 42.8	19–174	3.74 ± 1.1	19.2 ± 9.6	11.36 ± 4.9	84.4 ± 41.9	14–200	3.74 ± 1.1	19.76 ± 9.6	11.66 ± 5.43
Pulses, dried	5.7 ± 9.0	0–44.6	0.2 ± 0.4	1.3 ± 2.4	0.7 ± 1.3	6 ± 8.5	0–32	0.2 ± 0.4	1.3 ± 2.2	0.7 ± 1.2
Bread and cereals	254.4 ± 115.3	74–484	9.75 ± 4.4	22.7 ± 9.6	7.9 ± 3.46	166.8 ± 77.5	14–340	6.3 ± 2.9	14.87 ± 6.88	4.94 ± 1.97
Meat and meat products	105.4 ± 57.5	0–238	11 ± 5.6	4.0 ± 2.0	15.3 ± 8.4	69.3 ± 43.3	0–237	7.14 ± 4.42	2.61 ± 1.37	9.88 ± 5.93
Cheese	23.8 ± 19.5	0–88	4 ± 3.2	15.83 ± 12.0	3.4 ± 2.47	24.8 ± 15.7	0–74.5	4.2 ± 2.2	16.18 ± 9.63	3.65 ± 1.97
Potatoes	163.4 ± 89.8	61–454	20.87 ± 11.3	18.6 ± 9.6	3 ± 1.48	95.8 ± 58.9	14–226.8	11.34 ± 6.8	10.87 ± 6.2	1.73 ± 0.98
Total polyamine	–	–	210.3 ± 131.5	125 ± 72.7	51 ± 28	–	–	200.8 ± 130.1	110.9 ± 66.2	42.4 ± 23.9

Abbreviations: PUT, putrescine; SPD, spermidine; SPM, spermine.

Table 2. Daily recommended food intake (g/day) according to SNO and the estimated polyamine values of intake (μmol/food in g/day)

	Male				Female			
Food groups	(g/day)	PUT	SPD	SPM	(g/day)	PUT	SPD	SPM
Fruits and fruit juice	364	193.5	52.7	11.3	300	160.5	43.4	9.4
Vegetables	309	14.1	73	42.7	250	11.4	59	34.6
Pulses, dried	10	0.5	2.5	1.4	13	0.6	3.3	1.8
Bread, cereals, rice, and pasta	384	14.8	34.3	12	302	11.6	27	9.4
Meat, poultry, fish, and eggs	224	23.3	8.8	33.3	175	18.2	7.0	26
Cheese	22	3.4	14.4	3.3	20	3	13.1	3.0
Potatoes	210	26.8	24	3.8	175	22.4	20	3.2
Total polyamine	—	276.4	209.7	107.8	—	227.7	172.8	87.4

polyamine from each food group are shown in Table 1, whereas Table 2 shows the SNO foods in g/day as well as the estimated values for each polyamine that would be provided by each food group. About half of the total polyamine intake (48%) was provided by fruit, and the rest were shared almost equally between the other food groups (Fig. 1).

Percentages of contribution from different food items to the daily intake of putrescine are also shown in Fig. 1. Fruits provided more than two-thirds of putrescine intake and about one-third of the spermidine intake. Meat and vegetables were the most significant contributors to spermine intake. The average daily polyamine intake was estimated to be 316 μmol/day (337 μmol/day for males and 303 μmol/day for females) in the study of adolescents. This total value was based on the mean values for putrescine, spermidine, and spermine daily intake from food (215.5 μmol, 66 μmol, and 34.5 μmol, respectively).

The energy intake of the adolescents was on average 12.3 MJ/day (14.9 MJ/day for males and 10.6 MJ/day for females; $p < 0.001$). Testing the difference in the energy

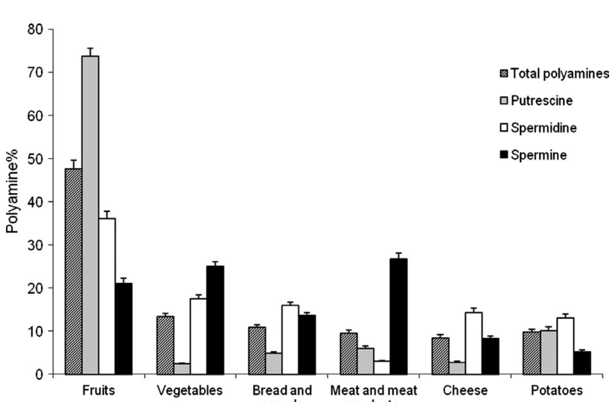

Fig. 1. Food contribution to the daily total and each polyamine (putrescine, spermine, and spermidine) intake expressed as percentage. Error bars represent Standard Error of Mean (SEM).

intake between day 1 (11.8 MJ) and day 7 (11.4 MJ) showed no statistical significance ($p = 0.2$).

Among the adolescents, gender differences in spermidine and spermine intake ($p < 0.001$) were found. These differences corresponded to a higher spermidine and spermine intake among males (75.7 and 43 μmol/day) than females (60.6 and 30.3 μmol/day).

Polyamine contribution from Swedish Nutrition Recommendations Objectified (SNO)

According to the SNO, the list of foods constructed to meet the Swedish nutrition recommendations, the average total intake of polyamines from this nutrient-wise ideal diet would be on average 541 μmol/day representing 594 μmol/day and 488 μmol/day for males and females, respectively. The main contribution to the putrescine intake from the ideal diet would come from fruit (70%), vegetables and fruits together would contribute to 60% spermidine intake, while the 60% of spermine intake would be provided from vegetables and meat products. The SNO for males provided more total polyamines than for females.

If the Swedish nutrition recommendations are followed, such as in the case of SNO, about half of the total daily polyamine intake would for both genders be provided from fruit. The least contributor would be dry pulses with less than 1% of the total intake. Out of the total polyamine intake, 47% would come from putrescine, whereas spermidine and spermine would represent, respectively, 35% and 18% of the total daily polyamine intake. All the results for food contribution to each polyamine were similar for both males and females.

Discussion

Total intake of polyamines

The most important contributor to the total polyamine intake in the adolescent diet and in the SNO was the group of fruits. Apart from the high mean intake of fruit and cheese among both male and female adolescents, the

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mean intake of all the other food groups was lower in the study participants, both males and females, in comparison with the recommended ideal diet of the SNO. In addition, it has been shown that vegetables contain higher concentrations of spermidine and spermine than fruits (1, 39). The mean intake of vegetables in the study group (Table 1) was far below the one recommended in the SNO (Table 2). This explains the adolescents' lower intake of spermidine than that estimated from the SNO. Similarly, the adolescents' lower bread and cereals intake contributed to low spermidine intake in comparison with the one estimated from SNO. These differences in the intake of these two food groups between adolescents and the SNO contributed most to the high polyamine intake according to SNO.

The contribution of different foods to the total daily polyamine intake has previously been reported in a few studies (1, 32, 39). In the UK (1), fruits were also the major contributor but with only 24% of the total polyamine intake, while in Japan (32), 26% of polyamines came from vegetables as a major contributor to the total polyamine intake.

In the present study, the contribution of fruits to half of the total polyamine intake was a result of the high intake of fruits in the study group (Table 1) compared to the intakes reported from the British and Japanese studies.

In the SNO, there was a similar contribution of the fruits to the total polyamine intake (Table 2); however, the 8% contribution of cheese to the total polyamine daily intake of the adolescents (Fig. 1) compared to the lower percentage of contribution in the SNO is explained by the adolescents' high mean cheese intake and lower average consumption of the other food groups.

The total average polyamine intake for the whole group (316 μmol/day) was higher than the values estimated in Japan (200 μmol/person/day) (32) and in the US (250 μmol/person/day) (20), but still within the range reported in some European countries (300–390 μmol/person/day) (1, 39). The higher intake among the Swedish group compared to the one reported in Japan can be explained by the difference in types of foods consumed. This figure agrees with the previous explanation of the difference due to the higher intake of rice in the Japanese groups (32) compared to the Swedish group. The relatively high polyamine intake from fruit in the current study shows that a high fruit intake can lead to high polyamine consumption.

Intake of the separate polyamines

Despite the differences in food intake between the SNO and the adolescents, when using the SNO list to estimate polyamine intake we could see that the relative contribution of these three polyamines to the total polyamine intake were quite similar to the actual intake in this current study as well as to the percentages reported for polyamines intake from the US study (20). In our study, the high percentage that came from putrescine among the adolescents was due to the high mean intake of fruits for both genders as shown in Table 1. When each fruit intake was estimated to see which contributed most to putrescine, about 56% of the actual fruit intake came from orange (35 g/d) and orange juice (138 ml/d) consumption. This intake contributed to about 80% of the actual mean intake of putrescine (49.6 μmol and 125.2 μmol from orange and orange juice, respectively). In addition, by taking the contents of spermidine and spermine into account, orange and orange juice alone contributed to 56% of the total polyamine intake. The high contribution of fruits to the putrescine intake was in line with previous studies (1, 20). Furthermore, putrescine, for which fruits were the most important food contributor, as shown in Fig. 1, constituted about 68% of the total polyamine intake. Spermidine and spermine, on the other hand, accounted for 21% and 11% of the total polyamine intake, respectively. These values were similar to those calculated in the American study where the percentages of the contribution of putrescine, spermidine, and spermine to the total polyamine intake were 64%, 22%, and 14%, respectively (20).

Alcoholic beverages like beer have been previously reported to contain fair mounts of polyamines, particularly putrescine (12, 32). In this study only 11 adolescents have reported a mean intake of 54.4 ± 42.7 g of beer/day. This amount would only provide this particular group with 2.4 μmol/d putrescine, 0.3 μmol/d spermidine, and 0.05 μmol/d spermine.

The percentages of contribution of different food items to the daily intake of putrescine, spermidine, and spermine among the adolescents are shown in Fig. 1. Despite the relatively low amounts of spermidine in fruits, these were still the major contributors to the total spermidine intake and the third food contributor to spermine after the meat and the vegetables. In Japan and Britain, the main contributors to putrescine and spermidine were vegetables (1, 32). Meat was in general a minor contributor for spermidine and putrescine, but an important contributor to spermine overall intake.

The average daily intake for each polyamine was estimated for the adolescents as well as for SNO. A common finding is that putrescine has the highest and spermine the lowest levels of intake. This is clearly due to a relatively high consumption of fruits and fruit juices among the investigated group, even though the intake is far below the daily recommended level. This pattern was found to be consistent with other related studies (1, 32). The significantly higher intake of spermidine and spermine in males compared to females might be explained by the females' significantly lower intake of bread and meat products (p-values were 0.001 and 0.004, respectively).

Study limitations and general discussion

The current study included only adolescents and can therefore not be seen as representative for the Swedish population. Due to the low number of participants and the geographical distribution to only two schools, we cannot say that the results are representative for all Swedish adolescents. However, the 7-day dietary records were conducted with support by a trained nutritionist and according to the energy intake, underregistration occurred only in a few participants. With reasonably high confidence, we can therefore say that the results were representative for the groups that were investigated.

The aggregation that was made for each food group to give an average estimated value for each polyamine has some limitations. This is due to the fact that within the food groups there are wide variations in the polyamine contents; for instance, in the group of fruits, orange was reported to have about 20 times higher putrescine than apple (40). Moreover, green peas provide more than six times spermidine than the same amount of tomato does. Therefore, having one polyamine value for one food group was only an estimation and does not give any exact value for the average polyamine concentration in that specific food group. Nevertheless, the values of polyamine intake calculated from foods consumed compared to the values of polyamine intake that were estimated from the food groups showed some similarity, especially for putrescine intake among the male and female group.

The high standard deviation in the food group intakes was due to the large variation in the adolescents' intake of different foods, as seen in the females' intake to the group of fruits and fruit juice that ranged from only 11 g to almost 1,000 g. Together with the low number of adolescents, this variation has led to a polyamine intake with a high SD as well.

There is still a lack of data on polyamine contents in some Swedish food and food items, particularly manufactured products such as liver pate; different types of sour milk and bread; and different kinds of fish, cheeses, and sauces that are consumed by some of the study participants. Therefore, underestimation of polyamine intake is most likely the case in this study.

Animal studies have shown that bioavailability and recovery of putrescine (the highest contributor to the total polyamine intake) was lower than that for spermidine and spermine (1, 41). This difference in bioavailability makes it difficult to estimate the proper amount of polyamine that the body needs. Moreover, the higher bioavailability of spermine and spermidine could be an indication of the difference in nutritional and metabolic importance of these two polyamines in comparison to putrescine (1).

Even though several studies have shown the importance of polyamines as antioxidants (42), for wound healing processes (43) and for the maturation of the digestive tract during infancy and preventing from allergy in children (13, 14, 44), a recommended polyamine intake has not been established yet.

Dietary intake of foods high in polyamines might stimulate cancer cells (45). Several studies have focused on a polyamine-reduced diet and its role in cancer therapy (45–48). In mice, the effectiveness of the chemopreventive agents against colon cancer was partially reduced by dietary polyamines, particularly putrescine (46, 48). Thus, using a combination of low polyamine diet with polyamine antimetabolites and anticancer agent was an effective regimen in the treatment of gastrointestinal cancer (45, 47). In patients with prostate cancer, a polyamine-restricted diet was shown to be effective for maintaining their performance status and pain control (19). Therefore, limiting polyamine intake has been suggested as a strategy for cancer treatment and prevention. This makes it questionable whether the polyamine intake based on SNO is suitable for adults, especially for those who are at risk of carcinogenic diseases. However, since cancer is not a common disease among adolescents, a high intake of polyamines may not be of great concern especially because these are considered essential during physiological growth (5).

Furthermore, the needs may vary within the population, with higher needs in early infancy and possibly post-surgery, and lower polyamine requirements in other circumstances. For that reason, we cannot make any distinct conclusion regarding a possible recommended level of intake. Also before such recommendation can be set, a number of issues need to be further investigated such as the internal production, content of foods, and the bioavailability of polyamines from foods.

Conclusions

The average daily total polyamine intake was estimated to be similar to previous reports from Europe.

Fruits appeared to be the major dietary contributor to the total polyamine intake in a country like Sweden, where the intake of rich sources of polyamines such as soybeans, sauerkraut, and other fermented products is low.

Even though the estimated mean dietary polyamine intake can vary depending on the type of food consumed, the ratios of each polyamine (putrescine, spermidine, and spermine) to the total polyamine intake remained similar, even when compared with studies in other countries.

In an ideal diet, according to the Swedish Nutrition Recommendations Objectified, the total polyamine intake appears to be higher than the current estimated intake among adolescents. In addition, by following the SNO, the contribution to the total and individual polyamine intake seemed to be stemming mainly from foods of plant origin.

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