Limited effect of refined carbohydrate dietary supplementation on colonization of the gastrointestinal tract of healthy subjects by Candida albicans

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ABSTRACT

Background: Infections due to Candida albicans occur readily in situations in which ample glucose is available. In mice, dietary refined carbohydrate supplementation leads to higher rates of Candida growth in the gastrointestinal tract and favors mucosal invasion.

Objective: The modulating properties of dietary carbohydrate supplementation on colonization of the human gastrointestinal tract by C. albicans were evaluated.

Design: A 2-step study was conducted in 28 healthy volunteers. First, we determined the subjects’ habitual uptake of refined carbohydrates and correlated these data with the C. albicans blastococid concentration in the mouth washes and feces of subjects with no intervention. Second, we compared C. albicans counts in the specimens before, during, and after a high-sugar diet.

Results: No correlation between C. albicans counts in the specimens and the habitual uptake of refined carbohydrates was observed. A high-sugar diet did not increase the frequency of C. albicans–positive samples, the number of subjects positive for C. albicans in the mouth washes, or the concentration of candidal blastococidin in the samples of the 28 subjects. However, in selected subjects with elevated counts of oral C. albicans, we observed an increase in fecal C. albicans counts in response to the diet.

Conclusions: The effect of adding a high amount of refined carbohydrates to the diet of healthy human subjects has a limited influence on Candida colonization. Follow-up studies should define whether selected patient groups might benefit from dietary restriction of refined carbohydrates.


KEY WORDS Candida albicans, refined carbohydrate, colonization, concentration, gastrointestinal tract, glucose, modulation, sugar, yeast, humans

INTRODUCTION

The ascomycetous yeast Candida albicans is found frequently on the mucosal surfaces of the gastrointestinal tract in healthy people. In severely immunocompromised hosts, local gastrointestinal candidiasis and disseminated invasive infection are thought to arise from gastrointestinal colonization and overgrowth of C. albicans (1–6). Factors that increase the frequency and magnitude of colonization with C. albicans may influence pathogenicity. Although a definitive threshold surface concentration has not been identified, invasion of the gastrointestinal mucosal wall depends largely on the number of organisms in the gastrointestinal tract (6, 7). According to Krause et al (6), invasion of the gut and fungemia occurred in a healthy volunteer after ingestion of $10^{12}$ C. albicans organisms. In addition, unbalanced C. albicans counts in the human gastrointestinal tract have been associated with a variety of clinical symptoms, such as diarrhea (8), relapsing vaginitis (9, 10), exacerbation of psoriasis and atop- and seborrheic dermatitis (11, 12), and the speculative candidiasis hypersensitivity syndrome (13, 14).

Interestingly, candidiasis occurs more often in situations in which ample glucose is available, as in patients receiving parenteral nutrition or suffering from diabetes (15). A high local glucose concentration leads to an increased incidence of Candida paronychia in sugar cane workers (15) and rinsing with sucrose leads to Candida-induced stomatitis in humans (16). A propagating role of a carbohydrate-rich diet in relapsing Candida vulvovaginitis was proposed in a study involving 240 women (17). Carbohydrate-rich diets favor the oral carriage of C. albicans in different animal models (18, 19). In a neutropenic mouse model, Vargas et al (7) showed that dietary glucose supplementation led to higher rates of Candida growth in the gastrointestinal tract of mice and favors mucosal invasion. To reduce the gastrointestinal C. albicans burden, the avoidance of refined carbohydrates, including dextrose and fructose, was proposed as an “antifungal diet” (7). The rationale for this diet is that restriction of glucose as a major substrate for C. albicans might suppress gastrointestinal candidal growth. This procedure is widely propagated by the lay press (13). However, little scientific information is available concerning a modulating effect of refined carbohydrates on the multiplication of C. albicans organisms inhabiting the human gastrointestinal tract.

To evaluate the effect of refined carbohydrate intake on gastrointestinal C. albicans colonization, a 2-step study was performed in...
healthy volunteers. In a first step, subjects were explored for their habitual uptake of refined carbohydrates with a food-frequency questionnaire. The data were correlated with the \( C. albicans \) blastoconidia concentration in the mouth washes and feces of subjects in whom there was no intervention. Subsequently, we compared the \( C. albicans \) counts in the mouth washes and feces of the subjects before, during, and after a high-sugar diet. During the diet period, the subjects ingested an excessive amount of refined carbohydrates.

SUBJECTS AND METHODS

Subjects

Twenty-eight healthy subjects (19 women and 9 men) with an average age of 26.3 y (range: 17–48 y) were randomly selected. None of the subjects had received antifungal therapy in the 3 mo before the study. Body weight was determined for each participant. The study was conducted in accordance with the Helsinki Declaration.

Food-frequency questionnaire

The habitual mean daily frequency of sugar consumption (saccharose, glucose, and fructose) was evaluated with a food-frequency questionnaire. Subjects were asked what main sugar-containing foods and beverages they consumed, eg, baked goods, chocolate, candy, ice cream, fruit juice, or lemonade (20, 21). We asked the subjects to report their habitual diet rather than their diet during any specific period. We did not attempt to assess the role of total energy uptake or specific nutrients. Instead, we focused on the association of specific foods or food groups containing refined carbohydrates and colonization of the human gastrointestinal tract by \( C. albicans \).

Diet and experimental protocol

The subjects were examined for 11 wk over 3 periods. In period 1 (baseline), the subjects continued their habitual diet, and samples were obtained over 6 wk without intervention. In period 2 (during the high-sugar diet), we increased the total energy intake of the subjects by adding 110 g refined carbohydrates/d (10.8% glucose, 35.7% saccharose, 3.2% fructose, and 50.3% dextrin) to their habitual diet. We added the oral \( C. albicans \) counts to the multiple regression model. In this model we used the mean values of the logarithmic \( C. albicans \) counts in the specimens collected in period 1 (baseline) as the dependent variable. The habitual daily uptake of refined carbohydrates, age, sex, and body weight were used as independent variables. A Wilcoxon test for paired variables was performed to compare logarithmic yeast counts before, during, and after the high-sugar diet. STATISTICA for Windows (version 5.1; StatSoft Inc, Tulsa, OK) was used for the analyses.

RESULTS

Influence of habitual uptake of refined carbohydrates on \( C. albicans \) counts in the gastrointestinal tract

No significant correlation between the \( C. albicans \) counts in the mouth washes and the independent variables (habitual daily uptake of refined carbohydrates, age, sex, and body weight) of the multiple regression model were found. Likewise, the multiple regression analysis showed no correlation between the \( C. albicans \) counts in the feces and the independent variables.

Correlation of oral and fecal \( C. albicans \) blastoconidia concentrations

We added the oral \( C. albicans \) counts to the multiple regression model as an independent variable when evaluating \( C. albicans \) blastoconidia concentrations in the feces as the dependent variable. We found a highly significant correlation \((P < 0.001)\) between the \( C. albicans \) concentration in the feces and the independent variables \((C. albicans) \) counts in the mouth washes, habitual daily uptake of refined carbohydrates, sex, age, and body weight). However, on the basis of \( \beta \) coefficients, this correlation was significant only between the \( C. albicans \) concentration in the feces and one independent variable—the \( C. albicans \) counts in the mouth washes. Thus, in the multiple regression model the degree of oral colonization with \( C. albicans \) was the only index that influenced the fecal \( C. albicans \) blastoconidia concentration.

Influence of a high-sugar diet on the species isolated from the samples and the frequency of \( C. albicans \)-positive samples

No significant change in the spectrum of candidal species isolated from the oral and fecal samples was observed in response...
TABLE 1
Mean logarithmic values of Candida albicans in the mouth washes and feces of the subjects before, during, and after a high-sugar diet

<table>
<thead>
<tr>
<th></th>
<th>All subjects</th>
<th>Select subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mouth washes</td>
<td>Fecal samples</td>
</tr>
<tr>
<td></td>
<td>(n = 28)</td>
<td>(n = 28)</td>
</tr>
<tr>
<td></td>
<td>log_{10} CFU/L</td>
<td>log_{10} CFU/kg</td>
</tr>
<tr>
<td>Period 1, before</td>
<td>3.58</td>
<td>4.54</td>
</tr>
<tr>
<td>Period 2, during</td>
<td>3.66</td>
<td>4.71</td>
</tr>
<tr>
<td>Period 3, after</td>
<td>3.65</td>
<td>4.69</td>
</tr>
</tbody>
</table>

1 Subjects whose baseline C. albicans counts in mouth washes were > 1.0 \times 10^3 CFU/L.
2 Significantly different from period 1, P < 0.05 (Wilcoxon matched-pairs test).

DISCUSSION

Our study was the first to evaluate the influence of a high-sugar diet on C. albicans counts in the human gastrointestinal tract. Mouth washes and homogenized fecal samples were chosen as representatives of colonization of the gastrointestinal tract by C. albicans. We were able to confirm a correlation between C. albicans blastoconidia concentrations in the mouth washes and the stool samples of healthy subjects, indicating that both specimens may reflect the degree of candidal colonization in the gastrointestinal ecosystem. In contrast with our results, Kusne et al (23) found no correlation between the presence or absence of Candida spp. in either oral or rectal swabs and colonization at other anatomic sites in 30 randomly selected patients with advanced liver disease. This finding indicates that sampling plays a pivotal role in the assessment of Candida colonization.

Our data showed no correlation between oral or fecal C. albicans counts and habitual carbohydrate uptake in our subjects, as estimated with a food-frequency questionnaire. Frequent consumption of refined carbohydrates did not promote increased candidal colonization or infection in the gastrointestinal tract of healthy individuals. Age, sex, and body weight did not influence yeast counts in the gastrointestinal tract.

To evaluate the modulatory effect of excessive carbohydrate intakes on C. albicans growth in the human gastrointestinal tract, we dramatically increased the amount of refined carbohydrates consumed by healthy subjects over 7 consecutive days. Glucose is well metabolized by C. albicans and a dietary glucose-dependent effect has been shown in various animal models (7, 19). We supplemented the diet with refined carbohydrates, consisting predominantly of glucose and its short-branched oligomers. According to the National Food Consumption Survey (Nationale Verzehrsstudie), a study initiated by the German Federal Ministry of Research and Technology (Bundesministerium für Forschung und Technologie), which enrolled 24632 persons from 11141 randomly selected households (24), the average German citizen aged > 14 y consumes 37 g monosaccharides and 51 g disaccharides daily. On the basis of these data, we increased the subjects’ daily intakes of refined carbohydrates to 225% of their average intake.

There was no striking change in the ratio of candidal species isolated from the feces or from the mouth washes in response to the high-sugar diet. In an earlier study, Larmas et al (25) examined the effect of diets high in sucrose, fructose, and xylitol on human salivary yeast counts. They noticed increased salivary candidal concentrations in the fructose and sucrose groups, but the study failed to differentiate the yeasts by species. Because numerous yeast species contribute to the human orointestinal yeast flora, it is not clear whether Larmas et al’s results reflect an effect on C. albicans counts or whether multiplication of a species other than C. albicans occurred. A major strength of our study was that all yeasts were differentiated by species and that the dependent variable (C. albicans concentration in the human gastrointestinal tract) did not rely on recall or accuracy of a diagnosis, as in the case of Candida vulvovaginitis (17).

We observed no significant modulation in the frequency of C. albicans-positive fecal and oral samples and no alteration in the number of subjects positive for C. albicans in the mouth washes during or after the high-sugar diet. Furthermore, no significant change in the C. albicans germ cell concentration in the mouth washes and stool samples for the 28 subjects during or shortly after the diet were detected. These results suggest little modulating effect of dietary carbohydrates on colonization of the gastrointestinal tract. 

Influence of a high-sugar diet on the number of subjects positive for C. albicans

During period 1, 78.6% of the subjects (22/28) had detectable amounts of C. albicans blastoconidia in the mouth washes and 71.4 % of the subjects (20/28) had C. albicans in the fecal samples examined during this period. No increase in the number of persons with positive mouth washes was observed during periods 2 and 3. However, 78.6% of the subjects (22/28) had C. albicans in the feces during and shortly after the high-sugar diet ended.

Influence of a high-sugar diet on the C. albicans blastoconidia concentration in the gastrointestinal tract

Mean logarithmic C. albicans counts in the mouth washes and the feces of the 28 subjects were compared before, during, and after the high-sugar diet and are shown in Table 1. Mean counts in the mouth washes were as follows: 3.8 \times 10^3 colony-forming units (CFU/L) (3.58 log_{10} CFU/L), 4.6 \times 10^3 CFU/L (3.66 log_{10} CFU/L), and 4.5 \times 10^3 CFU/L (3.65 log_{10} CFU/L) before, during, and after the high-sugar diet, respectively. Mean counts in the feces were as follows: 3.5 \times 10^4 CFU/kg (4.54 log_{10} CFU/kg), 5.1 \times 10^4 CFU/kg (4.71 log_{10} CFU/kg), and 4.9 \times 10^3 CFU/kg (4.69 log_{10} CFU/kg) before, during, and after the high-sugar diet, respectively. There were no significant differences between periods (Wilcoxon matched-pairs test).

In a subgroup of subjects (n = 12) with > 1.0 \times 10^4 CFU C. albicans germ cells/L in the mouth washes collected in period 1, mean counts in the feces during and after the high-sugar diet were 8.9 \times 10^5 CFU/kg (5.95 log_{10} CFU/kg), 2.6 \times 10^5 CFU/kg (6.42 log_{10} CFU/kg), and 1.3 \times 10^5 CFU/kg (6.12 log_{10} CFU/kg) before, during, and after the high-sugar diet, respectively. Mean logarithmic values are shown in Table 1. The mean fecal C. albicans count in this subgroup during the diet (period 2) was significantly greater than that at baseline (period 1). In contrast, there was no significant difference in C. albicans counts in the mouth washes as a result of the high-sugar diet.

to the diet. C. albicans was the fungal organism most frequently identified in the specimen, detectable in 59.5% (100/168) of the fecal samples in period 1 and in 60.7% (102/168) of the fecal samples in periods 2 and 3. Geotrichum candidum was detectable in 13.7% (23/168), Rhodotorula spp. in 7.7% (13/168), Saccharomyces cerevisiae in 4.8% (8/168), and other non–C. albicans species in <4% of the fecal samples examined during period 1. No significant increase in the isolation frequency of these organisms occurred during periods 2 and 3.

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human gastrointestinal tract by \textit{C. albicans}. Therefore, we conclude that healthy individuals do not develop increased \textit{Candida} counts as a result of consuming high-sugar diets. Although glucose is a substrate for \textit{C. albicans}, the complex interplay of the yeast germs with the host and the indigenous bacterial microflora might explain these results. In the gastrointestinal ecosystem, various mucosal defense mechanisms control \textit{C. albicans} germ cell concentrations (26), and numerous bacterial properties and products are known to modulate candidal growth (27, 28).

Monosaccharides such as glucose and degradable oligo- and polysaccharides are absorbed in the small intestine. Therefore, it might be expected that dietary glucose does not affect yeast growth distal to this region. Hypothesizing that an effect of dietary glucose is restricted to yeasts inhabiting the proximal gastrointestinal tract, we speculated that the modulating effect of glucose is more likely to be observed in persons with an elevated candidal colonization of the upper gastrointestinal tract. Indeed, we did observe a significant, although moderate, increase in fecal \textit{C. albicans} counts during the high-sugar-diet period in those subjects whose baseline mouth wash counts were $> 1.0 \times 10^4$ CFU/L. Furthermore, we observed an increased number of subjects with \textit{C. albicans}–positive fecal samples in response to the high-sugar diet. Taken together, these data support the hypothesis that excessive dietary glucose leads to a multiplication of \textit{C. albicans} proximal to the small intestine and that replicated yeasts reach the large intestine with the feces. However, it should be emphasized that the limited effects observed in our study apply to healthy individuals with intact control mechanisms to keep \textit{Candida} counts low. The role of refined carbohydrates in patients with compromised defense mechanisms is still speculative.

Clinical follow-up studies should address the question of whether restriction of refined carbohydrates might decrease the number of \textit{C. albicans} organisms colonizing the human gastrointestinal tract in specific patient groups, eg, in persons receiving broad-spectrum antibiotics or in heavily colonized, immunosuppressed patients with a high risk of disseminated candidiasis. Because long-term restriction of food groups containing mono- and oligosaccharides seems nutritionally unbalanced, a clear definition of those patients who would benefit from such a diet is necessary.

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REFERENCES