Article

Episodes of diverticulitis and hemorrhoidal proctitis and diets with selected plant foods: case-control study with a food frequency questionnaire

Juan Flich-Carbonell [1], Antoni Alegre-Martinez [2], Jose L Alfonso-Sanchez [3,4], Maria T Torres-Sanchez [1], Salvador Gomez-Abril S [1], Maria I Martínez-Martínez [5] and José M Martin-Moreno [4,6]

1.   Colorectal Surgery Section, General and Digestive Surgery Service, Dr. Peset University Hospital, Valencia (Spain)
2.   Department of Biomedical Sciences, Cardenal Herrera CEU University, Valencia (Spain)
3.   Head of Preventive Medicine Service. University General Hospital of Valencia, Valencia (Spain)
4.   Professor, Department of Preventive Medicine and Public Health. University of Valencia, Valencia (Spain)
5.   Department of Nursing, Faculty of Nursing and Podiatry, University of Valencia (Spain).
6.   INCLIVA and Clinical University Hospital, Valencia (Spain)

Prof Jose L Alfonso-Sanchez Email: jose.l.alfonso@uv.es, alfonso_jos@gva.es ORCID. 0000 0002 7075 9712

ABSTRACT :Background: The high incidence of diverticulitis and hemorrhoidal proctitis episodes in the population imposes an important healthcare and economic burden. **Aim:** To determine the association between intake of certain plant foods and diverticulitis and hemorrhoidal proctitis episodes. **Methods:** Case-control study with quantitative food frequency questionnaire focusing on selected plant foods and derived products. These were grouped by main chemical components into: ethanol, caffeine/theine/theobromine, capsaicin, alliin, acids, eugenol, and miscellaneous foods like curcumin. We quantified intake according to 24-h recall, either on a 1-4 scale (no intake, low, moderate, high intake) or as the number of units consumed (e.g. cups of tea/coffee, n of oranges or lemons); this value was multiplied by the number of reported intake days per week (1-7). Overall intake was expressed as a continuous variable obtained by successively multiplying the score for each food category, and the result was transformed into a common logarithm (range 0.3 to 27.7).Cases and controls were compared using the chi-squared test, student's t test, odds ratio (OR) and 95% confidence interval (CI), and predictive analysis (multiple logistic regression). **Results:** The sample included 410 cases and 401 controls, who were similar in mean age and gender distribution. The mean score for overall intake of included plant foods was 6.3 points (standard deviation [SD] 4.5), and this was significantly higher in cases (8.5 points, SD 5.3) than in controls (4.1 points, SD 1.2; p < 0.001). Overall intake was similar in cases presenting diverticulitis or hemorrhoidal proctitis. Cases had 13 times the odds of being in the upper quartile for overall intake (> 7 points) compared to controls (OR 13.2, 95% CI 8.3 to 20.8, p < 0.001). Predictive logistic regression models showed that the chemical food group most closely associated with diverticulitis and hemorrhoidal proctitis was capsaicin, followed by ethanol, eugenol, caffeine/theine/theobromine, and acids. The OR for age was near the null value. Neither alliin nor miscellaneous food groups showed any association. **Conclusions:** High, frequent consumption of some plant foods and derived products increases the risk of presenting symptoms of diverticulitis and hemorrhoidal proctitis.

1. Introduction

The high incidence of diverticulitis and hemorrhoidal proctitis episodes in the population imposes an important healthcare and economic burden. The etiology of these pathologies remains uncertain (1) (2). The most widely accepted theory points to low fiber intake in the population as a causal factor (1) (3), although other authors have proposed placing the blame on coffee and alcohol intake (4) (5), smoking (6) (7) (8) (9), pharmacological treatments (10) (11), obesity and lack of physical activity (6) (7) (12), constipation, diarrhea, inflammatory bowel disease and irritable bowel syndrome (1) (13) (14) (15) (16), genetic predisposition (4) (17), and geographic and ethnicity-related epidemiological factors (1) (13) (18). However, the level of evidence is of very low certainty.

This study aims to assess whether high and frequent intake of certain plant foods or derived food products is a risk factor for symptoms of diverticulitis and hemorrhoidal proctitis.

2. Material and Methods

2.1. Study design, setting and population

This epidemiological case-control study was based on food frequency questionnaires, focusing on consumption of certain foods (quantity consumed on intake days and number of intake days per week). It took place in the Dr. Peset University Hospital, a public healthcare center with a catchment population of 380,000 people.

The institutional Clinical Research Ethics Committee approved the research project (80/18). All patients signed informed consent and participated freely as volunteers.

Cases were defined as: patients attended in the surgery service for a diagnosis of diverticulitis, hemorrhoidal proctitis, and or symptomatic hemorrhoids from June 2018 to September 2019. Controls were drawn from patients seen during the same period in the orthopedic surgery and traumatology, ophthalmology, and dermatology services (considering patient history of colorectal conditions).

2.2. Interviews and variables

Three investigators undertook one-on-one interviews with participants, using the same interview protocol. Variables included were: age, gender, and intake patterns for seven groups of plant foods or derived food products, categorized by their chemical composition:

1. Ethanol: spirits with high alcohol content and burning or harsh taste. Wine and beer were excluded.

2. Caffeine/theine/theobromine: drinks, soft drinks (e.g. colas or tea beverages) and foods (e.g. chocolate) with these bitter-tasting alkaloids. Decaffeinated products were excluded.

3. Capsaicin/piperine: plant foods with acids and alkaloids (varieties of peppers chili peppers) used to season foods (e.g. cold cut meats) and sauces with a spicy flavor.

4. Alliin: sulfoxide in garlic, onion, and other plant varieties with a spicy flavor.

5. Acids: foods with an acidic flavor, such as vinegar, pickled vegetables, orange, lemon, strawberry, cilantro, juice, soft drinks (with orange or lemon juices), and sauces that contain these.

6. Eugenol: clove, ginger, curry, cinnamon, and mustard, which contain acids and aldehydes with a sour, spicy, and bitter flavor.

7. Miscellaneous: curcumin, ginseng, cuminaldehyde (cumin), fenugreek or trigonelline (alhova), cinnamaldehyde (cinnamon), nutmeg acids and alkaloids, menthol, and other plant-based chemical products.

2.3. Measures and scoring system

The scoring methodology used to quantify dietary intake patterns was designed as follows.

The food products or processed foods containing substances from different categories (sauces, soft drinks, sweets, and others) were counted a single time in the dominant group. All included plant food products consumed by the participants were recorded.

The daily intake (24 h) was recorded for each plant food or derivative in one of two ways, according to patients' responses: on a scale of 1-4 (no intake, low, moderate, or high intake) or as the number of units consumed (e.g. cups of tea/coffee/hot chocolate, ounces of chocolate, n soft drinks, n alcoholic drinks, n of oranges or lemons eaten or used to make juice, n of other food units). The frequency of intake was assessed as the number of days per week when the food product was consumed, and scored as follows: 1 point, occasional or no consumption, or as the number of intake-days per week (1-7). The value for 24 h intake was multiplied by the number of intake-days per week to obtain a single score for each included food group.

To assign an overall score considering the intake patterns across the diverse range of included plant food products, we calculated a continuous variable by successively multiplying the intake score for each category and transformed the result into a log with base 10 (range of values 0.03 to 27.7). For each participant, this composite score expressed the overall quantity and frequency of intake for all possible plant food risk factors included in the study.

2.4. Statistical analysis

The mean score for overall intake of included plant food categories was 6.3 points (standard deviation [SD] 4.5). We categorized participants by quartiles, establishing four intervals: ≤ 3.00 points, 3.01 to 5.00 points, 5.01 to 7.00 points, ≥ 7.01 points.

Groups were compared by means of Pearson's chi-squared test, the student's t test and Levene's test, and predictive analysis with multiple logistic regression and odds ratios (ORs) with 95% confidence intervals (CIs). Quantitative data were expressed as mean (SD) and qualitative data as percentages.

Analyses were undertaken with SPSS-25 software (IBM), with the level of significance established at $p < 0.05$.

3. Results

A total of 872 patients (410 cases and 462 controls) were initially included and interviewed; however, 61 controls were excluded from the analysis because they had a history of the pathologies under study. Thus, the final sample consisted of 811 patients: 410 cases and 401 controls (table 1). The two groups were similar with regard to gender

distribution and age, although the score for overall intake of the studied plant foods was higher among cases.

Table 1. Participant characteristics and overall intake of plant-based foods.

	Cases (N = 410)	Controls (N = 401)	Total (N = 811)	*P* value
Age in years, mean (SD)	55 (14)	55 (19)	55 (16)	0.98*
Age groups, n (%)				
18-50 years	154 (37.6)	141 (35.2)	295 (36.4)	0.05†
51-65 years	153 (37.3)	129 (32.2)	282 (34.8)	
66-94 years	103 (25.1)	131 (32.7)	234 (28.9)	
Gender, n (%)				
Men	239 (58.3)	217 (54.1)	456 (56.2)	0.23†
Women	171 (41.7)	184 (45.9)	355 (43.8)	
Overall intake, mean (SD)	8.45 (5.33)	4.12 (1.64)	6.31 (4.51)	0.001*

*t-test, †χ^2.

Table 2 shows the distribution of pathologies among the cases. There were 24% more cases of hemorrhoids compared to diverticulitis. In addition, among patients with hemorrhoids, 67 colonoscopies were performed, revealing 39 patients (15.6%) who also had diverticulosis. Similarly, 96 (59.6%) patients with diverticulitis had presented episodes of acute hemorrhoids, and 17 of these were treated surgically. Participants with hemorrhoids were more frequently men and, on average, 6 years younger than the patients with diverticulitis, although these groups were similar in terms of the overall intake score for the included plant foods.

Table 2. Demographic, clinical, and dietary characteristics of cases.

	Diverticulitis (N = 161)	Hemorrhoids (N = 249)	*P* value
Age, mean (SD)	59 (14)	53 (13)	0.001*
Gender, n (%)			
Men	83 (51.6)	156 (62.7)	0.026†
Women	78 (48.4)	93 (37.3)	
Symptom severity, n (%)			
Simple	115 (71.4)	183 (73.5)	0.64†
Complicated‡	46 (28.6)	66 (26.5)	
Overall intake, mean (SD)	8.98 (5.25)	8.10 (5.36)	0.10*

*t-test, †χ^2 , ‡Perforation, abscess, fistula.

Mean intake scores for some individual plant foods and their most common derivatives were compared between cases and controls (table 3), showing higher intake for most of these foods in cases. When the foods were categorized by chemical composition, there were significant differences between groups for all of them.

Table 3. Mean intake and frequency for individual food products and plant food categories, by study group.

Plant foods	Cases (N = 410)		Controls (N = 401)		2-tailed p value*	Mean difference	95% CI	
	N	Mean	N	Mean				
Individual products								
Chocolate	300	14.27	210	6.94	< 0.001	7.33	5.64	9.02
Tea	82	11.92	53	6.25	< 0.001	5.68	2.67	8.69
Lemon	133	11.63	65	7.95	< 0.001	3.67	1.67	5.67
Soft drinks	82	12.52	50	8.92	0.045	3.60	0.08	7.12
Pepper	219	7.60	113	4.10	< 0.001	3.50	2.34	4.65
Strawberry	44	6.98	8	3.75	0.034	3.23	0.26	6.20
Vinegar	223	9.37	170	6.32	< 0.001	3.06	2.00	4.11
Cold cut meats†	329	6.24	108	3.22	< 0.001	3.02	2.09	3.96
Coffee	337	16.20	241	13.68	0.003	2.52	0.85	4.19
Pickled vegetables	301	8.48	211	6.44	< 0.001	2.04	1.01	3.07
Raw onion	305	4.52	204	3.54	< 0.001	0.98	0.60	1.36
Cooked onion	349	3.88	334	3.14	< 0.001	0.74	0.50	0.98
Cooked garlic	296	3.72	295	3.05	< 0.001	0.67	0.37	0.97
Curcumin	35	6.39	11	3.91	0.136	2.28	−0.75	5.30
Ginger	39	7.96	10	6.40	0.358	1.56	−1.82	4.95
Curry	41	4.48	10	3.00	0.135	1.48	−0.47	3.42
Orange	282	11.56	279	10.59	0.084	0.97	−0.13	2.08
Chili pepper	83	5.13	15	4.27	0.467	0.87	−1.49	3.22
Raw garlic	166	3.78	114	3.27	0.175	0.51	−0.23	1.25
Clove	30	4.28	0	—	—	—	—	—
Plant foods grouped by chemical component								
Ethanol	130	7.71	51	2.59	< 0.001	5.12	3.11	7.13
Caffeine‡	404	14.97	338	10.21	< 0.001	4.76	3.61	5.90
Capsaicin	371	6.44	187	3.74	< 0.001	2.70	2.05	3.36
Alliin	381	3.94	379	3.09	< 0.001	0.84	0.11	0.63
Acids	391	10.09	363	8.13	< 0.001	1.96	1.22	2.71
Eugenol	64	6.38	25	4.32	0.026	2.07	0.26	3.88
Miscellaneous	108	5.09	34	3.85	0.042	1.24	0.60	0.04

*Student t test. CI: confidence interval. †Seasoned with pepper and other spices in the capsaicin/piperine category, ‡Caffeine, theine and theobromine.

Note: The most frequently consumed individual foods are presented, excluding some with minimal use among both cases and controls (included under the chemical food group "Miscellaneous").

A comparison of the mean intake scores by quartiles (table 4) shows that the progressively higher scores result in an increased OR, which reaches a value of 13.16 in the highest quartile. A predictive analysis using multiple regression (table 5) was performed to assess the association between plant food categories and presentation of symptoms. The final model indicated that capsaicin was the strongest predictor of the pathologies under study (OR 1.45), followed by ethanol (1.30), eugenol (OR 1.19), caffeine/theine/theobromine (OR 1.11), and acids (OR 1.08). The OR for age was near the null value. Neither alliin nor miscellaneous food groups showed any association.

Table 4. Comparison by quartiles of overall intake in cases versus controls

Quartiles by overall intake score, n (%)	Cases (N = 410)	Controls (N = 401)	Total (N=811)	$P*$ value	Odds ratio (95% CI)
	n (%)	n (%)	n (%)		
Q1: 0.30-3.00	**8 (2.0)**	112 (27.9)	120 (14.8)	< 0.001	0.05 (0.02 0.11)
Q2: 3.01-5.00	77 (18.8)	174 (43.4)	251 (30.9)	< 0.001	0.30 (0.22 0.41)
Q3: 5.01-7.00	138 (33.7)	91 (22.7)	229 (28.2)	0.001	1.73 (1.23 2.36)
Q4: 7.01-27.7	187 (45.6)	24 (6.0)	211 (26.0)	< 0.001	13.16 (8.33 20.83)

*χ^2.

Table 5. Final model and interactions in predictive analysis of the influence of age and intake of plant food categories on the appearance of symptoms.

Predictor variables: Case over control	β coefficient	β standard error	P value	OR	(95% CI)	
Age	0.014	0.006	0.018	1.01	1.00	1.03
Ethanol	0.263	0.062	< 0.001	1.30	1.15	1.47
Caffeine*	0.101	0.018	< 0.001	1.11	1.07	1.15
Capsaicin	0.370	0.067	< 0.001	1.45	1.27	1.65
Alliin	0.099	0.115	0.39	1.10	0.88	1.38
Acids	0.075	0.038	0.048	1.08	1.00	1.16
Eugenol	0.172	0.058	0.003	1.19	1.06	1.33
Miscellaneous	0.019	0.068	0.78	1.02	0.89	1.16
Capsaicin-caffeine*	0.003	0.005	0.55	1.00	0.99	1.01
Acid-alliin	0.000	0.011	0.97	1.00	0.98	1.02

CI: confidence interval; OR: odds ratio, *Caffeine, theine and theobromine.

4. Discussion

This study was conceived to investigate dietary patterns in patients with diverticulitis and hemorrhoidal proctitis, specifically the intake patterns for certain plant foods and derived products (some of which have been studied by other authors (4) (5)) with a sour, spicy, or bitter flavor. These products can be consumed directly or added to other foods like meat, preserves, sauces, or processed foods and consumed in the form of sweets, tea, soft drinks, or other industrialized foodstuffs. The potential biological health benefits for some of these substances are under study (19) (20) (21) (22). However, a high concentration or quantity of certain chemical components can, in contact with conjunctiva (23) (24) or mucous (25) (26) (27), provoke irritation, with varying degrees of secretion; connective edema; increased vascularization; and other effects like cytotoxicity, necrosis, and ulceration of skin cells (28). These effects support the hypothesis that concentrations of these chemical products in the residues of the colon and rectum may facilitate the pathophysiology (1) (29) of the acute symptomatic period of diverticulitis and hemorrhoidal proctitis, which is characterized by edema in the connective tissue and vascular ecstasy. These processes lead to the appearance of symptoms (pain and/or hemorrhage) of varying intensity; persistence; and propensity for recurrence or complications like ulceration, fissure, perforation, abscess, or fistula.

The development of the research methodology was based on other studies that used standardized food frequency questionnaires with 24 h recall to identify differences in the dietary patterns between populations and over time (30) (31) . Taking into account the potential challenges of these studies (32) (33) , we developed a questionnaire tailored to our case-control design, extending the data collection period to 7 days and analyzing the data in the same form as they were collected (without transforming them to g or mg). We created a continuous variable using a numerical formula that considers overall intake of different plant foods according to 24 h self-reported intake and its frequency (intake days/week) for each food category. Possible biases in data collection and analysis would have been the same for both cases and controls.

The intensely and harshly flavored plant foods included in the present study were more prominent in the diets of cases compared to controls, both overall and in most cases at an individual level. Similarly, when the foods were grouped by chemical composition, patients with symptoms of diverticulitis and hemorrhoidal proctitis showed higher intake patterns. On considering the length of time over which the foods were consumed, we observed that few patients presented an acute symptomatic episode following several weeks of abundant, daily intake of the plant foods in question (for example, after vacationing in countries or regions where these foods formed an integral part of the local diet). Rather, the vast majority of cases reported moderate, regular intake of these products and few to no symptoms for months or years prior to the episode prompting the medical consultation. Age was included as a variable in the logistic regression model, showing that this was not a factor.

One limitation of the study was not physically examining participants in the control group to understand how many presented diverticulitis and hemorrhoids, as these pathologies frequently manifest with few symptoms. However, we did exclude the 13.2% of the control sample with a history of seeking medical care for such causes. We also observed that that subgroup presented similar overall intake scores to cases, so on exclusion from the comparative analysis, the OR increased for the quartiles with higher intake scores.

Despite the difficulties and limitations mentioned and other possible reservations that may exist, our results suggest that people who rarely consume the plant foods studied are less likely to present symptoms of diverticulitis or hemorrhoidal proctitis. As intake of different products rises in quantity and frequency, so does people's risk for these pathologies. This conclusion would explain why young patients with high intake patterns present symptoms, while older ones with low lifetime intake do not and show no evidence of alterations in their colon, rectum, or anus on physical examination. Our results also suggest a shared pathophysiology and etiology between diverticulitis in the colon and hemorrhoids in the rectum and anus. The different alterations subsequently found in the mucosa and connective tissue of these organs depend on the anatomical differences in the vascular supply and distribution of the muscular layers on the gastrointestinal wall.

5. Conclusions

Abundant, frequent intake of certain plant foods and derived products appears to increase the risk of presenting symptoms of

diverticulitis and hemorrhoids. Moderating the amount and frequency of intake in the population could help people decrease their risk for these symptoms.

Additional studies investigating these and other proposed risk factors and their interaction with the mucosa and connective vascular tissue of the colon, rectum, and anus could add to the evidence base supporting these observations.

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