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Can the inflammatory potencial of diet rather than the individual dietary components discriminates between calcium oxalate renal stone patients and healthy controls?

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Introduction:

- Many studies have investigated the relationship between individual food groups and the risk of urolithiasis focusing on how diet influences the urinary risk factors for CaOx supersaturation and crystallization.
- Diet also can play an important role in regulating chronic inflammation, which is one of several other processes by which stone formation can proceed.
- Since now there hasn't been used a quantitative measure for assessing the inflammatory potential of an individual's diet and whether such a measure is correlated with stone risk. The **Dietary Inflammatory Index (DII[®])** is an analytical tool which provides such a measure.
- **The aim of this study** is to test the hypothesis that the inflammatory potential of habitual diet is higher in renal stone formers than in normal controls.



Methods

- 160 subjects included prospectively:
 - 97 calcium oxalate stone formers (SFs) and 63 controls (Cs), matched on age and sex .
 - Patients:
 - Stone episode <3 months
 - Stone composition confirmed by optical crystallography and spectroscopy
 - Controls:
 - No history of stone disease
 - No stones confirmed by medical history and ultrasound
 - Exclusion criteria:
 - <18 y, pregnancy, history of serious illness, history of duodenal ulcer, osteoporosis or its treatment, morbid obesity (BMI >40kg/m²), bariatric surgery, previous urinary pathology and treatment with drugs having lithogenic potential.
- **Semi- quantitative food frequency questionnaire** from which nutrient composition was computed. These data were used to calculate the **Dietary Inflammatory Index (DII®)**
- To control the effect of energy intake, **energy-adjusted DII (E-DII)** scores were calculated.
- A single blood sample was obtained from each participant (n160), and two consecutive overnight (8h) urine samples were collected from a subset of these (n 59 SFs and n54 Cs) at the start of the study.
- Samples were analysed for stone risk factors
- Data were analysed using descriptive statistics and logistic and linear regression models



Results

Table 1. Clinical and demographic characteristics of patients and controls

	Total (160)	Controls (63)	Cases (97)	p
Age	47 (19-79)	43 (19-71)	48 (20-79)	0.22
Sex (male)	111 (69.3)	43 (68.2)	68 (70.1)	0.80
Family history of stones (n,%)	64 (40.2)	18 (9)	46 (47.4)	0.02
BMI (Kg/m ²)	26.4 (15.9-22.3)	26.7 (19.3-36.6)	26.1 (15.9-38.3)	0.81
HTA (n,%)	30 (18.7)	12 (19)	18 (18.5)	0.94
DLP (n,%)	31 (19.6)	11 (17.7)	20 (20.8)	0.63
Hiperuricemia (n,%)	4 (2.5)	2 (3.2)	2 (2)	0.65
Diabetes (n,%)	10 (6.4)	3 (4.9)	7 (7.3)	0.54
Metabolic syndrome (n,%)	14 (8.8)	6 (9.5)	8 (8.4)	0.78

Table 2. Dietary characteristics of patients and controls (median and range)

	Total (n = 160)	Controls (n = 63)	Cases (n = 97)	p-value
Energy (Kcal)	2484.4(722-7189)	2425.7(788-4991)	2543 (722-7189)	0.41
Water_(g)	3341.7(996-8547)	3263.1(996-8547)	3420.3(1683-8441)	0.42
TotalProtein_(g)	129.2 (51-293)	125.9 (51-230)	132.5 (53-293)	0.30
Vegetal Protein_(g)	32.3 (3-86)	32.1(3-74)	32.6(10-86)	0.81
Animal Protein_(g)	96.2 (35-248)	93.9 (35-189)	99.9 (42-248)	0.24
Total Lipid_(g)	102.2 (24-308)	97.5 (28-207)	106.9 (24-308)	0.14
Saturated FattyAcids_(g)	36.8 (6-124)	34.8 (6-99)	38.7 (10-124)	0.15
Monounsaturated Fatty Acids(g)	40.4 (9-116)	38.8 (11-76)	42 (9-116)	0.23
Polyunsaturated Fatty Acids_(g)	15.5 (3-42)	14.7 (5-33)	16.4 (3-42)	0.09
Cholesterol_(mg)	438.4 (145-1111)	424.2 (154-1018)	452.7 (187-1111)	0.26
Glucides_(g)	248.4 (35-1068)	246 (35-655)	250.8 (74-1068)	0.79
DigestibleSugars_(g)	124.7 (11-834)	123.5 (19-368)	125.9 (11-834)	0.85
Polysaccharides_(g)	123.7 (10-384)	122.5 (10-384)	124.8 (40-257)	0.78
Fiber_(g)	29.6 (2-114)	29.2 (2-70)	29.8 (5-114)	0.78
Ethanol_(mg)	7.1 (0-51)	7.8 (0-51)	6.3 (0-29)	0.26
Sodium_(mg)	3249.2 (586-9724)	3203 (586-8049)	3295.5 (741-9724)	0.68
Potassium_(mg)	4361.2 (703-15306)	4303.1 (955-8793)	4419.4 (703-15306)	0.68
Calcium_(mg)	1130.9 (158-3389)	1108.7 (158-2156)	1153.2 (235-3389)	0.55
Magnesium_(mg)	419.4 (117-1225)	417.8 (125-908)	420.9 (117-1225)	0.90
Phosphore_(mg)	1831.3 (198-4152)	1799.9 (198-3633)	1862.7 (595-4152)	0.53
Iron_(mg)	16.5 (5-44)	16.2 (5-35)	16.8 (5-44)	0.54
Zinc_(mg)	13.4 (4-31)	16.1 (4-31)	13.7 (4-31)	0.42
VitaminA_(mcg_er)	1458.2 (101-5730)	1452.2 (327-5730)	1464.2 (101-4384)	0.93
Retinoid_(mcg)	644.6 (76-5670)	642.7 (76-5670)	646.5 (93-3222)	0.97
Carotenoid_(mcg)	4881.5 (48-16657)	4857.2 (294-13417)	4905.9 (48-16657)	0.92
VitaminD_(mcg)	7.9 (1-35)	7.8 (1-33)	8.1 (1-35)	0.75
VitaminE_(mg_et)	12.3 (1-42)	12.2 (4-34)	12.4b (1-42)	0.78
VitaminB1_(mg)	1.9 (0-5)	1.9 (0-4)	2 (0-5)	0.92
VitaminB2_(mg)	2.5 (0-6)	2.5 (0-5)	2.5 (1-6)	0.91
Niacin_(mg)	32 (11-73)	31.5 (13-63)	32.5 (11-73)	0.52
VitaminB6_(mg)	2.8 (1-9)	2.8 (1-6)	2.9 (1-9)	0.49
FolicAcid_(mcg)	418.2(39-1343)	416.7 (70-982)	419.8(39-1343)	0.87
VitaminB12_(mcg)	11.3(2-42)	11.4 (2-42)	11.2 (3-28)	0.76
VitaminC_(mg)	216.1 (8-940)	219.9 (8-712)	212.3(8-940)	0.72
DII	-1.7 (-4.5-3.73)	-2.6 (-4.5-2.7)	-0.7 (-4.2-3.7)	<0.0001
E-DII	-0.8 (-4.7-3.65)	-1.7 (-4.7-3.6)	-0.3 (-1.8-3.5)	<0.0001

Table 3. Blood concentrations and urinary parameters of patients and controls (median and range).

Blood (mg/dl)	Concentrations		
	Controls (63)	Cases (97)	p-value
Creatinine	0.92 (0.6-1.8)	0.91(0.5-1.3)	0.25
Uric acid	5.1 (0.7-9.4)	5.4 (2.6-7.6)	0.95
Calcium	9.4 (8.8-10.1)	9.4 (8.3-10.8)	0.90
Phosphate	3.6 (2.5-5.4)	3.2 (2.2-4.8)	<0.001
Magnesium	2.1 (1.7-2.5)	2.1(1.6-2.9)	0.19
Total Cholesterol	190 (116-290)	194 (122-298)	0.74
HDL Cholesterol	52.4 (25.2-145)	51.1 (29-80.1)	0.06
LDL Cholesterol	110 (34.8-200)	111 (44-192)	0.66
Triglycerides	96 (36-483)	108(33-966)	0.56
Glucose	92 (70-150)	94 (65-213)	0.08
Parathormone (pg/ml)	35.9 (12.3-89.8)	46.9 (5.3-138)	<0.001
Urinary parameters			
	Controls	Patients	p-value
Calcium concentration (mmol/L)	3.3 (0.2-10.3)	4.4 (0.8-14.6)	0.008
Phosphate concentration (mmol/L)	25 (4.6-68.2)	27.3 (6.6-64.1)	0.43
Magnesium concentration (mmol/L)	3.3 (0.3-9.2)	3.1 (0.5-10.6)	0.81
Citrate concentration (mmol/L)	1.7 (0.2-4.2)	1.5 (0.2-3.3)	0.27
Oxalate concentration (mg/L)	21.3 (5.1-76.8)	20.7 (3-50.4)	0.29
Uric acid concentration (mmol/L)	1.9 (0.2-5.5)	2.2 (0-6.3)	0.84
pH	6 (5-7.5)	6 (5-7)	0.70
Volume (ml)	425 (50-1900)	450 (50-1700)	0.81
SS (CaOx)	4.7 (0.5-20.4)	5.8 (0.4-15.5)	0.83
SS (Bru)	1.8 (0.06-28.18)	3.6 (0.18-19.05)	0.16
SS (UA)	1.8 (0.03-9.3)	1.7 (0.01-10.9)	0.10

SS:supersaturation; CaOx: calcium oxalate; Bru: brushite (calcium hydrogen phosphate); UA: uric acid

Table 4. Correlations between blood and 24h urine concentrations and excretions and E-DII.

	Correlation coefficient	p-value
Blood concentrations		
Creatinine (mg/dl)	0.01	0.20
Uric acid (mg/dl)	-0.006	0.64
Calcium (mg/dl)	0.0009	0.54
Phosphate (mg/dl)	-0.012	0.07
Magnesium (mg/dl)	-0.0013	0.71
Total Cholesterol (mg/dl)	-0.006	0.36
HDL Cholesterol (mg/dl)	-0.02	0.03
LDL cholesterol (mg/dl)	0.01	0.30
Triglycerides (mg/dl)	-0.003	0.87
Glucose (mg/dl)	-0.01	0.09
Parathormone (pg/ml)	0.02	0.18
Urine parameters		
Calcium concentration	0.25	0.02
Phosphate concentration	0.48	<0.0001
Magnesium concentration	0.33	<0.0001
Citrate concentration	0.04	0.34
Oxalate concentration (mg/L)	0.11	0.21
Uric acid concentration	0.27	0.004
pH	-0.08	0.16
Volume (ml)	-0.25	0.003
SS (CaOx)	-0.09	0.23
SS (BRU)	-0.02	0.38
SS (UA)	0.16	0.21

SS:supersaturation; CaOx: calcium oxalate; Bru: brushite (calcium hydrogen phosphate); UA: uric acid



Results

- DII and E-DII values were significantly more positive (i.e., more pro-inflammatory) in cases (-0.7 and -0.3) than in controls (-2.6 and -1.7), $p < 0.0001$ and $p < 0.0001$ respectively.
- In blood, a significant negative correlation was seen between E-DII and HDL cholesterol ($p = 0.03$).
- In urine, significant positive correlations were seen between E-DII and each of calcium ($p = 0.02$), phosphate ($p < 0.0001$), magnesium ($p < 0.0001$) and uric acid ($p = 0.004$) concentrations.
- A significant negative correlation was seen between E-DII and volume ($p = 0.003$).

Conclusions

Our results show that, the **evaluation of the inflammatory potential of the whole diet** rather than that of individual dietary components, **can differentiate between SFs and Cs**, thereby demonstrating the importance of pro-inflammatory diets in stone pathogenesis.

Thus, our study provides a compelling argument for **determining DII/ E-DII scores in lithogenic patients** on presentation and after dietary intervention, as part of their **routine work-up**.

