Comparison of traditional tools and fecal gluten immunogenic peptide detection to investigate gluten-free diet adherence in celiac disease.

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Background: Adherence to the gluten-free diet (GFD) for celiac disease (CeD) has traditionally relied on expert dietician assessment. A quantitative test was recently developed and shown to be sensitive and specific for the detection of gluten immunogenic peptides (GIP) in stool. **Aim:** We determine the performance of established dietary, laboratory and symptomatic parameters with stool GIP in CeD patients on GFD. **Methods**: A prospective and blinded study was conducted in adults with uncomplicated CeD on a GFD for more than two years. Patients collect stool samples once-a-week (on Friday or Saturday) for four weeks. At the end of the study, patients completed a ten-point scale self-assessment of adherence, a celiac symptom index (CSI), and a blind adherence analysis by an expert dietitian. Patients were categorized as having no evidence + trace or evident gluten exposure. CeD serology tests (IgA tTG and IgA DGP) were also determined. GIP was measured using an ELISA kit (iVYLISA GIP S®). We determined the weekly average GIP excretion. Based on previous studies investigating the threshold of gluten contamination needed for mucosal damage and a conversion formula, we estimated that an average stool GIP ≥0.32 µg/g/7 days represents gluten exposure >50 mg/day (50% association with mucosal damage), while ≥0.64 µg/g represents an average daily gluten intake >100 mg/day (100% association with mucosal damage). **Results:** 53 CeD patients on long-term GFD completed the study. Twenty-one (39.5%) had average stool GIP ≥0.32 µg/g/week. Compared with those with GIP ≤0.31 µg/g/week, patients with higher GIP reported lower self-estimated score of adherence (p=0.04), had higher IgA DGP antibodies (p=0.006), and higher frequency of serum concentrations above 20 AU/mL (p=0.02), but not difference in symptoms (CSI, p=0.47), mean IgA tTG (p=0.23) and cases with tests above the 20 AU/mL (p=0.87). The expert dietitian was not able to identify differences in dietary transgression (p=0.21) (Table1). Thirteen (24.5%) patients had an average GIP excretion ≥0.65 µg/g. Compared with those with GIP ≤0.64 µg/g/week, patients with higher stool GIP had lower self-assessed score (p=0.003), higher IgA DGP (p=0.0005) and antibody concentrations >20AU/mL (p<0.002), higher IgA tTG (p<0.02) but not cases with tTG IgA >20AU/mL and symptom intensity (CSI, p=0.9). The expert dietitian identified 69% of cases with GIP ≥0.64 (p=0.012) (Table 2). **Conclusions**: Weekly stool GIP monitoring in CeD patients on long-term GFD finds gluten contaminations that are not always detected by dietary assessment and other commonly used tools. The higher the level of GIP in the stool, the better the predictive value of serology and dietitian interview, and the patients' self-scoring of adherence.

Table 1 Demography and adherence information from 53 patients collecting stool samples once-a-week (Friday/Saturday). *P* values compare results categorized by the weekly average of GIP stool excretions ≥0.32 vs. ≤0.31 μg/g of stool.

	Overall population	**≥ 0.32 μg/g of GIP in stool**	**≤ 0.31 μg/g of GIP in stool**	***p* value=**
N of patients (%)	53 (100)	21/53 (39.6)	32/53 (60.4)	
Age. Median (IQR: 25-75)	46 (34-55)	41 (31-51)	51.5 (37-57.5)	0.08
Female gender. (%)	48 (90.6)	18 (85.7)	3 (14.3)	0.33
Average GIP excretion/week. Median (25% IQR) μg/g	0.11 (0.0-0.62)	0.81 (.53-2.21)	0 (0-0.11)	0.0000
Years from CD diagnosis. Median (25% IQR)	8 (5-12)	10 (5-14)	7 (4-11)	0.24
IgA DGP concentration. Median (25% IQR) AU/mL	18 (11-52)	44 (15-93)	13.5 (10-29.5)	0.006
> 20 AU/mL. N of cases (%)	25/53 (47.2)	14/21 (66.7)	11/32 (34.4)	0.021
IgA t-TG concentration. Median (25% IQR) AU/mL	16 (10-54)	17 (11-77)	14 (8-32)	0.23
> 20 AU/mL. N of cases (%)	22/53 (41.5)	9/21 (42.9)	13/32 (40.6)	0.87
CSI global score. Median (25% IQR)	34 (30-45)	37 (30-42)	33 (29-45.5)	0.47
N of cases with CSI >38 points (%)	18/53 (34.0)	8/21 (38.1)	10/32 (31.2)	0.61
Median self-estimation of adherence to the GFD (25% IQR)	9 (5-10)	6.5 (4.5-9.5)	9.5 (6.5-10.0)	0.04
Assessment by expert dietitian (No gluten + traces). N of patients (%)	21 (39.6)	11 (52.4)	10 (31.2)	0.12

Table 2: Demography and adherence information from 53 patients collecting stool samples once-a-week (Friday/Saturday). *P* values compare results categorized by the weekly average of GIP stool excretions ≥0.65 vs. ≤0.64 µg/g of stool.

	≥ 0.65 µg/g of GIP in stool	**≤ 0.64 µg/g of GIP in stool**	***p* value=**
N of patients (%)	13 (24.5)	40 (75.5)	
Age. Median (25% IQR)	40 (34-51)	47 (35.5-56.5)	0.2
Gender (F). (%)	11 (84.6)	37 (92.5)	0.4
Average GIP excretion/week. Median (25% IQR) µg/g	1.83 (0,82-2.56)	0.04 (0.00-0.24)	0.00001
Years from CD diagnosis. Median (25% IQR)	11 (6-15)	7.5 (4-11.5)	0.2
IgA DGP concentration. Median (25% IQR) AU/mL	69 (29-109)	14 (10.5-30)	0.0005
> 20 AU/mL. N of cases (%)	11/13 (84.6)	14/40 (35.0)	0.002
IgA t-TG concentration. Median (25% IQR) AU/mL	42 (14-201)	12 (8-32)	0.02
> 20 AU/mL. N of cases (%)	7/13 (53.8)	14/40 (37.5)	0.3
CSI global score. Median (25% IQR)	36 (31-41)	33.5 (30-46)	0.9
N of cases with CSI >38 points (%)	4/13 (30.8)	14/40 (35.0)	0.8
Median self-estimation of adherence to the GFD (25% IQR)	5 (4-9)	9 (7-10)	0.003
Assessment by expert dietitian (No gluten + traces). N of patients (%)	9 (69.2)	12 (30.0)	0.012