EFFICACY OF FAECAL LACTOFERRIN IN IBS & IBD: A COMPARATIVE STUDY

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Abstract:

Faecal lactoferrin (FL) has been proposed as a non-invasive diagnostic tool in Inflammatory bowel disease (IBD)[1]. This is the first study conducted in a UK outpatient setting comparing simple colitis index (SCI) for ulcerative colitis and Harvey Bradshaw index (HBI) for Crohn's disease against FL concentration in IBD and IBS patients. From an IBD outpatient clinic, stool samples were collected and concurrent disease activity recorded for Ulcerative colitis (UC), Crohn's disease (CD) and irritable bowel syndrome (IBS) patients along with samples from healthy volunteers. Using IBD-SCAN®, a quantitative ELISA, FL concentration was measured. Each participant's recorded clinical index at time of collection was compared against measured FL concentration to assess clinical efficacy of FL in determining disease status in IBD and in differentiating IBD from IBS.

FL is useful in staging of IBD and in differentiating IBD from IBS.

Introduction:

Lactoferrin is an iron binding glycoprotein within the neutrophil granulocyte. High concentrations of lactoferrin are released by the gut mucosa during intestinal inflammation. Presence of lactoferrin in faeces can therefore be quantified using quantitative ELISA. Lactoferrin is remarkably stable in faeces as it resists proteolysis within gut lumen and can be kept at room temperature for up to 14 days. If frozen it can be stored long term for delayed analysis. Only a small sample of 0.05-0.1g is required for ELISA measurements. Its proposed uses are[2]

1) Diagnostic marker and helpful in predicting clinical course of IBD
2) Help differentiate IBS from IBD
3) Longitudinal monitoring of medical treatment and post surgery
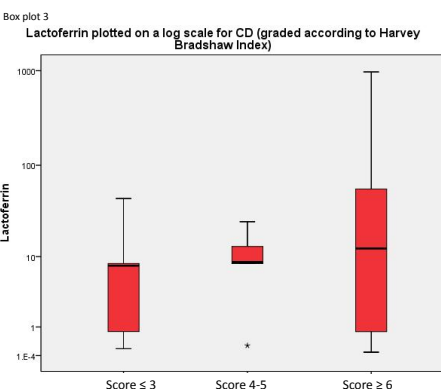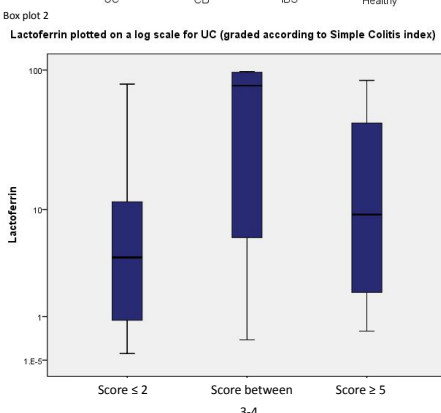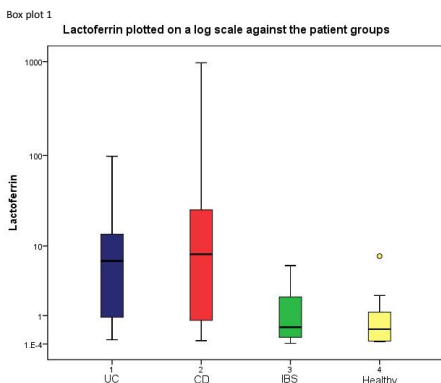
Method:

A total of 167 patients were recruited from an IBD out patient clinic. Stool samples were collected and concurrent disease activity at time of sample collection were recorded using Harvey Bradshaw index (HBI) and the simple colitis index (SCI) for CD and UC respectively. We also collected stool samples from patients with IBS (diagnosed according to ROME II criteria) and healthy volunteers.

UC 29%, CD 25%, IBS 18%, Healthy 28%

Table 1
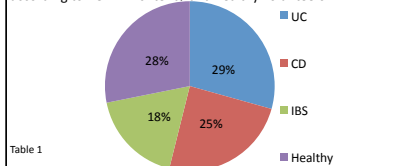
Group	UC (Using SCI)			CD (Using HBI)			IBS	Healthy
	≤2	Between 3-4	≥5	≤3	Between 4-5	≥6		
No: of patients	35	6	8	19	5	17	30	47

Faecal samples (1g) were collected in air-tight containers and frozen at -20°C at the time of sample collection. Dilutions of 1:10, 1:100 and 1:1000 were prepared for each sample and vortexed. Then using IBD-SCAN®, an ELISA for quantitative analysis, lactoferrin concentration was measured (as absorbance measured is directly proportional to concentration of lactoferrin present). Lactoferrin standards ranging from 6.25 to 100 ng/mL were used to generate a standard curve. By plotting absorbance values versus lactoferrin concentrations, the lactoferrin concentration within the faecal sample was determined. For each participant, plasma viscosity (PV), white blood cell count (WBC) and C-reactive protein (CRP) measurements at time of faecal sample collection were also recorded.

Box plot 1

Lactoferrin plotted on a log scale against the patient groups

Box plot 2

Lactoferrin plotted on a log scale for UC (graded according to Simple Colitis index)

Box plot 3

Lactoferrin plotted on a log scale for CD (graded according to Harvey Bradshaw index)

Table 2

	UC (Using simple colitis index)			CD (Using Harvey Bradshaw index)			IBS	Healthy
	≤2	3 - 4	≥5	≤3	4-5	≥6		
Mean & standard deviation (mcg/ml)	13 +/- 22.1	59.5 +/- 44.8	24.5 +/- 31.1	9 +/- 12.7	11 +/- 8.9	117 +/- 266	1.4+/-1.8	0.8+/-1.2
Median (mcg/ml)	4.1	78.2	9.3	7.8	8.6	12.4	0.5	0.44

Table 3

			LF concentration	PV
Spearman's rho	LF concentration	Correlation Coefficient	1	0.219
		Sig. (2-tailed)		0.104
		N	167	56
	PV	Correlation Coefficient	0.219	1
		Sig. (2-tailed)	0.104	.
		N	56	56
	WBC	Correlation Coefficient	0.1	.374**
		Sig. (2-tailed)	0.367	0.005
		N	83	55
	CRP	Correlation Coefficient	.257*	.311*
		Sig. (2-tailed)	0.04	0.026
		N	64	51

Results:

A lactoferrin concentration of <7.25mcgmL is considered to be normal. Lactoferrin concentrations were notably much higher in those with active IBD than IBS (P<0.001) and healthy volunteers (P<0.001). When clinical scoring indexes were used to grade disease severity in IBD, we found that there were lower lactoferrin concentrations recorded in both inactive UC and CD patient groups when compared to active UC and CD groups (P= 0.013). Within the UC group, we found lactoferrin concentrations were significantly lower in patients with inactive disease (SCI score ≤ 2) compared to active disease (SCI score ≥ 3) (P = 0.032). However, we did not find a statistically significant difference in lactoferrin concentrations between inactive (HBI score ≤ 3) and active (HBI score ≥ 4) CD patient groups (P =0.089). When lactoferrin concentrations were compared against blood results available at the time of sample collection for each patient, a significant correlation using Spearman's correlation (P <0.05) was noted between CRP measurement and lactoferrin concentration and less so for use of PV and WBC.

Discussion and Conclusions:

Lactoferrin is a useful biomarker in identifying bowel inflammation. Low levels of lactoferrin were recorded in IBS and healthy volunteers when compared with active IBD patients. Therefore we believe that lactoferrin is a useful biomarker in differentiating those with from those without true bowel wall inflammation. We also believe that when used in conjunction with clinical scoring indexes and blood tests, lactoferrin may be helpful in predicting and staging patients with IBD.

Longitudinal studies are required to assess the efficacy of lactoferrin in monitoring medical treatment and post surgical recovery in IBD patients.

References:

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