

indices underestimate biologic activity and cannot detect transmural disease. We aimed to assess the role of CT enterography (CTE) in assessing Crohn's disease (CD).

Methods A retrospective review of 406 consecutive CTE studies was performed between January 2009 and December 2012 at our institution. Clinical data including demographics, disease characteristics and therapy were obtained from electronic patient record review. Inflammatory markers, radiological investigations and ileo-colonoscopy when performed within 90 days of CTE were recorded. CTE reports were recorded using accepted activity criteria- small bowel dilatation, stenosis, wall thickening, enhancement, mucosal irregularity, mesenteric inflammation, hypervascularity, lymph node enlargement, abscesses, fistulation and extraintestinal features.

Results Of 175 patients with IBD at time of CTE, 154 had CD. Ninety-four of 154 patients were female, mean age 52 (range 16–87) and median term of follow up of 5 years (range 0–35).

Abnormalities were noted in 100 scans; 56 had active non-stricturing, 42 active stricturing and 2 fibrostenotic disease. Within active groups, there were 10 fistulae and 3 abscesses in 11 patients. Ileo-colonoscopy was performed in 42 patients with 27 showing active inflammation and raised CRP in 38/96. Treatment was increased in 52% of the active non-stricturing group, 6/29 to azathioprine, 4/29 to biologics, 4/29 to methotrexate, 7/29 to steroids, 5/29 to surgery with no change in the remaining 48%, of whom 8/12 had inactive disease at ileo-colonoscopy and 16/24 normal CRP.

In 57% of active stricturing patient treatment was increased in 1 to azathioprine, 11 to biologics, 5 to surgery. Twelve of 26 patients in this group had an elevated CRP and 10/13 had active colitis at ileo-colonoscopy.

Of 53 normal CTE, treatment was escalated in 3 to methotrexate or azathioprine with colitis at colonoscopy and unchanged in 92%. **Conclusion** Concerns regarding potential cumulative effects of ionising radiation are valid but likely to be offset by changing technology and reduction in average doses of radiation.

CTE has a role in well-selected patients with CD (e.g. age > 50, very sick patients) identifying active disease and influencing meaningful therapeutic decisions.

Disclosure of Interest None Declared.

PWE-086 THE ROLE OF HUMAN NEUTROPHIL ELASTASE AND ITS INHIBITOR ELAFIN IN ULCERATIVE COLITIS

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Introduction Mucosal inflammation in ulcerative colitis (UC) is characterised by an influx of neutrophils which secrete large amounts of human neutrophil elastase (HNE), causing matrix degradation. They also produce the elastase-specific inhibitor, elafin. The aim of this study is to evaluate the relative production of elastase and elafin in active UC, and to investigate the modulatory effect of elafin on mucosal proteolytic activity *ex vivo*.

Methods We utilised intestinal biopsies from 18 patients with active UC and 12 non-UC healthy controls. Biopsies were homogenised and lysed to extract mucosal proteins. Proteolytic activity, using elastin as a substrate, was determined. Concentrations of elafin were measured using ELISA. The effect of protease inhibitors on proteolytic activity were determined *in vitro* using elafin, marimastat (matrix metalloproteinase inhibitor) and the synthetic elastase inhibitor, AAPV [N-(Methoxysuccinyl)-Ala-Ala-Pro-Val Chloromethyl Ketone]. The effect of elafin on proteolytic activity *ex vivo* was assessed by 24 hour organ culture in the presence and absence of elafin. Unpaired Student's t-test was used for statistical analyses.

Results Mucosal protein homogenates from patients with active UC displayed higher proteolytic activity in comparison to healthy controls ($p = 0.002$). Elafin levels were increased in mucosal homogenates from active UC ($p = 0.007$). The addition of elafin, marimastat or AAPV, *in vitro*, each diminished proteolytic activity. Organ culture of UC biopsies in the presence of elafin reduces the proteolytic activity of active UC *ex vivo* (n.s.).

Conclusion Colonic mucosal tissue from UC patients displays significantly higher elastinolytic activity in comparison to healthy controls. The addition of elafin has a restorative effect on the elastinolytic activity of UC mucosal homogenates, with the most notable effect in those tissues that had highest proteolytic activity. This occurs in the presence of significantly higher quantities of elafin in active UC mucosa. These data also show a beneficial modulatory effect of elafin on human gut tissue, suggesting a possible role for supplementary elafin in the treatment of UC.

Disclosure of Interest None Declared.

PWE-087 A CRITICAL REVIEW OF GROUNDED THEORY USE IN INFLAMMATORY BOWEL DISEASE STUDIES

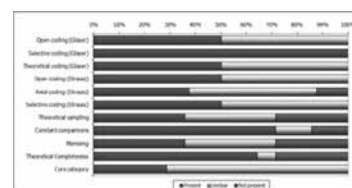
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Introduction Grounded Theory (GT) is a research methodology predominantly used with qualitative data. The purpose of the present study is to critically evaluate the use of GT in inflammatory bowel disease (IBD) studies and to examine the clinical implications this entails.

Methods A systematic literature review was performed using keywords *Grounded Theory* and *IBD* in Pubmed, EMBASE and Scopus with no time limits. Assessment of GT was performed using standard criteria suggested by Glaser (1998). The application of the following basic principles was examined: simultaneous data collection and analysis; construction of analytic codes and categories from data, not from preconceived logically deduced hypotheses; use of constant comparative method; advancement of theory development during each step of data collection and analysis; memo-writing; sampling aimed toward theory construction (theoretical); Literature review after the core category emergence.

Results Fifteen studies have used GT investigating patient education, quality of life, experiences with therapeutic strategies or coping mechanisms in IBD, providing theories based on emerging categories. About half of all studies have applied the basic principles of GT, with the remaining studies being unclear or having not applied them. The most reported principle was Glaserian selective coding and least reported were memoing, theoretical sampling and the achievement of theoretical completeness, while the identification of the core category was unclear in many instances (Figure 1). These weaknesses are attributed predominantly to methodological, verification and reporting bias. These biases affect the applicability of these results in clinical practise. Hence, results concerning quality of life or experiences of IBD patients should be treated with caution, as they could represent authors' predisposition from their experience (empirical or from literature reviews).



Abstract PWE-087 Figure 1

Conclusion The main advantage of GT studies remains the generation of theory that can be applied in practise, reinforced by the presentation of conceptual prospects for testing new variables in quantitative studies. Overall, the contribution of Grounded Theory studies to IBD should be based on more rigorous methodology and aim to challenge rather than confirm existing conceptions with the purpose of advancing knowledge in the field.

Disclosure of Interest None Declared.

REFERENCES

Glaser BG, (1998), Doing Grounded Theory: Issues and Discussions, Sociology Press, Mill Valley, CA.

PWE-088 ABNORMAL LIVER FUNCTION TESTS FOLLOWING USE OF THIOPURINES IN A LARGE COHORT OF INFLAMMATORY BOWEL DISEASE PATIENTS-DO TPMT LEVELS MATTER?

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Introduction Thiopurine (azathioprine and 6-Mercaptopurine (6MP)) use is one of the aetiologies for abnormal liver function tests in patients with inflammatory bowel disease. Some studies report hepatotoxicity is associated with high levels of the 6-MP metabolite, 6-methylmercaptopurine ribonucleotide (6-MMPR). This may indicate that hepatotoxicity correlates with the level of thiopurine methyl transferase enzyme (TPMT) activity. The aim of this study was to assess the prevalence of 6-MP/Azathioprine hepatotoxicity in a large cohort of IBD patients and to determine its correlation with serum TPMT levels in adult IBD patients.

Methods Patients with IBD initiated on thiopurines following TPMT assay were included and follow up data collected on development of abnormal liver function tests. We excluded patients who had abnormal LTs before initiation of AZT. We used Council for International Organizations of Medical Sciences (CIOMS) definitions to determine the grade of hepatic alterations: "Abnormality of LTs" defined as an increase in AST, ALT, AP, GGT, or total bilirubin between N (upper limit of the normal range) and 2 N. "Liver injury" (or "hepatotoxicity") defined as an increase of over 2 N in the aforementioned LTs. Data was collected on demographic factors, concomitant medication use and additional factors favouring liver injury. TPMT levels were categorised as low, normal and high based on local laboratory reference standards.

Results

Abstract PWE-088 Table

	TPMT levels			Total
	Low	Normal	High	
Normal liver function	27 (8.7%)	184 (59.2%)	5 (1.6%)	216 (69.5%)
Abnormal liver function	11 (3.5%)	55 (17.7%)	0	66 (21.2%)
Liver toxicity	2 (0.6%)	27 (8.7%)	0	29 (9.3%)
Total	40 (12.9%)	266(85.5%)	5 (1.6%)	

311 IBD patients (249 Crohn's disease, 53 ulcerative colitis and 9 undifferentiated) were included. The median age was 35 years (range, 14–86 years). Abnormal LTs developed in 66 (21.2%) of patients. Hepatotoxicity was noted in 29 (9.3%) of patients with 18 of these patients (6%) needing to stop thiopurines. None of the patients with high TPMT developed abnormal LTs or hepatotoxicity. 27 of the 29 patients with hepatotoxicity had normal TPMT levels and remaining 2 had low TPMT levels.

Conclusion Abnormal liver tests following initiation of thiopurines occur in a relatively high proportion of patients, but the development of hepatotoxicity necessitating treatment cessation occurs only in 6% of cases even in the era of concomitant anti-TNF therapy. Pre treatment TPMT levels do not appear to have an impact on the probability of development of hepatotoxicity.

Disclosure of Interest None Declared.

PWE-089 OUTCOMES OF PATIENTS WITH CROHN'S DISEASE: AZATHIOPRINE TOLERANT AND AZATHIOPRINE INTOLERANT

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Introduction Azathioprine is well established for the maintenance of remission in patients with Crohn's disease and 87% patients on maintenance therapy are able to reduce steroid consumption. However, azathioprine is less effective at treating disease recurrence and seven patients need to be treated to prevent one recurrence (1). Intolerance to azathioprine occurs in almost a third of patients and it has been proposed that the intolerance to azathioprine is a poor prognostic marker that may predispose patients to a more aggressive disease course.

Methods A cross sectional study was performed using the Milton Keynes Hospital IBD database to compare outcomes of patients that were azathioprine intolerant and those that were azathioprine tolerant. A descriptive analysis of clinical features and outcomes of these two groups was performed.

Results 141 patients were included for analysis of which 24.8% were intolerant to azathioprine. The median age of azathioprine intolerant patients was 47 and 31.4% were male. In the azathioprine tolerant cohort, the median age was 36 and 41.5% were male. Azathioprine was not tolerated due to gastrointestinal side effects in 53.6%, neurological effects (depression/headaches/vertigo) in 17.9%, deranged LFTs in 17.9% and the arthralgia/neutropenia and cutaneous side effects making up the remaining cases.

Abstract PWE-089 Table

	Azathioprine intolerant (n = 35)	Azathioprine tolerant (n = 106)
Requiring surgery (%)	13 (37.1)	55 (51.8)
% stricture/fistula	17 (48.6)	63 (59.4)
Extensive disease	3/30 (10)	11/92 (12.0)
Disease activity:-	19/34 (55.9)	76/96 (79.2)
- Remission (HBI < 5)	7/34 (20.6)	17/96 (17.7)
- Mild disease (HBI 5–7)	8/34 (23.5)	3/96 (3.1)
- Moderate disease (HBI 8–16)	0/34 (0)	0/96 (0)
- Severe disease (HBI > 16)	7 (20.0)	2 (1.9)
Steroid dependent	9 (25.7)	13 (12.3)
Monoclonal antibody		

Conclusion Azathioprine is a drug that is not tolerated in nearly a quarter of Crohn's disease patients and this effect demonstrated a sex bias towards females. Patients who were intolerant to azathioprine were not more likely to undergo surgery or to have more strictures or fistulas. However, azathioprine-intolerant patients were considerably more likely to have more active disease, to require monoclonal antibody therapy and steroids. Compared to patients who are able to use azathioprine, for every 100 patients who are intolerant, 24 less will be in remission and 20 more will have moderate to severe disease. We conclude that patients with azathioprine intolerance will have poorer symptom control, but does not predispose to a more aggressive disease course.

Disclosure of Interest None Declared.