IBD management issues in Primary care

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Summary of UK IBD Audit 2012-
primary care questionnaire

survey of GPs caring for IBD patients recently admitted to hospital-key findings:

- < 10% GPs were ‘not confident’ to deal with flare-ups
- But a wide range of treatments given by GPs
- <10% of GPs took the chance to contact IBD nurse
- 50% of GPs said they didn’t know who to contact or lines of communication were slow
• Key findings continued:

• 33% of pts consulted GP in month prior to admission but Rx not initiated or specialist contact

• Differences between GP and hospital about speed/ease of access of urgent IBD OPAs

• There was a hunger for further IBD related education
Recommendations

- Promote the role of the IBD nurse in primary care
- PCSG to encourage educational activity
- Hospitals should provide timely correspondence
- Develop local care protocols and pathways
- Encourage GP related research re ‘lost patients’
- GPs require education re colon cancer surveillance
Miss LF, aged 24

- Recent diagnosis of distal colitis at FS and confirmed histologically
- Patient treated elsewhere with prednisolone
- Presented with BO x5/d with blood and hip pain
- Cause of hip pain?
Avascular necrosis of femoral head
BSG guideline bone protection in IBD

- All >65: consider bisphosphonate at start of steroid treatment
- <65 at high risk and steroids >3/12: DEXA and bisphosphonates if T score < 1.5
- Give Vit D and Calcium whilst on steroid
- DEXA scan for those at high risk of osteoporosis: (1) > 10kg wt loss (2) BMI <20 or (3) Age >70
UC disease extent

- Extensive or Pancolitis: 37%
- Left sided ulcerative colitis: 37%
- Distal UC: 36%
- Proctitis: 36%
Trends in steroid prescribing in IBD

Chhaya et al 2016
Topical 5-ASA treatment

• Proctitis: 5-ASA supps

• Distal colitis: 5-ASA foam enema

• L sided colitis: 5-ASA liquid enema

• Extensive/pancolitis: topical Rx PLUS oral Rx
Mild or moderate ulcerative proctitis or proctosigmoiditis

Colonoscopy to determine diagnosis, extent, and severity of disease

Choose either course of treatment

5-ASA or steroid suppository plus rectal enema or foam twice daily

No or partial response

Add oral 5-ASA medication (combined therapy)

Response

Continue medications needed to induce remission for long term maintenance; consider trial of gradually tapering either rectal or oral medications, but not both

Oral 5-ASA medication

No or partial response

If no response

Oral prednisone

Response

Continue medications needed to induce remission for long term maintenance; consider trial of gradually tapering either rectal or oral medications, but not both
Miss LF has an immediate relapse-what are the options?

- Further courses of steroids
- Further courses of topical treatment
- Add in a thiopurine (azathioprine or 6-mercaptopurine)
- infliximab
Azathioprine pathway
TPMT activity relative to genetic composition
298 unrelated adults

% of subjects per 0.5 units of activity

L/L
Low activity

L/H
Intermediate activity

H/H
High activity

TPMT activity (units/ml) RBC
Azathioprine induced neutropaenia

Colombel et al 2007
Azathioprine pathway

AZA → 6-MP → 6-TU → XO → 6-MMP → HPRT → TIMP → 6-TGN

TPMT → 6-MMP
# Drug monitoring for azathioprine

<table>
<thead>
<tr>
<th>6MMP</th>
<th>zero</th>
<th>low</th>
<th>high</th>
<th>High/norm</th>
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<tr>
<td>6TG</td>
<td>zero</td>
<td>low</td>
<td>Low/normal</td>
<td>high</td>
</tr>
<tr>
<td>Action</td>
<td>Non-compliant</td>
<td>Poor Compliance OR increase dose</td>
<td>Co-preserve alopurinol</td>
<td>Reduce dose</td>
</tr>
</tbody>
</table>
Case Miss JE

22yo female student
Pan UC
Refractory 2/52 oral pred

HR 88, T 37.2 C
   BO x 12/d bloody

Hb 13.4
WC 8.9
ESR 45
Alb 40
CRP 39

Stool MC&S NEG
AXR mucosal oedema

• Day 1
  • Hydrocortisone 100 qds
  • Mesalazine 1.2g bd
  • LMW Heparin
Day 3

- Poor clinical response
- CRP 33
- BO x 6/d

- Options?
Day 3

• Increase dose of steroids

• start ciclosporin 2 mg/kg

• Start infliximab 5mg/kg

• colectomy
Day 6

- Symptoms unchanged
- CRP 102
- Needs colectomy?
  Yes
  No

⇒ *Clostridium difficile* toxin +VE
Reports of *Clostridium difficile* isolated from faecal specimens under the voluntary reporting scheme: England, Wales, and Northern Ireland 1990-2004
C difficile and IBD

- Majority community acquired
- Higher rates of carriage in IBD ~8-10%
- Usually **not** associated with antibiotic use
- Associated with steroids and colonic disease
- Co-infection associated with poorer outcomes
- Always test on admission
- Pseudo-membranes uncommon
Faecal transplant-RCT

- Vanc 500mg qds 5/7 followed by gut lavage then donor faeces duodenal infusion, n=16
- Vanc 500mg qds 14/7, n=13
- Vanc 500mg qds 14/7 followed by gut lavage, n=13

Van Nood 2013
Figure 2. Rates of Cure without Relapse for Recurrent *Clostridium difficile* Infection.
A midwife with watery diarrhoea

- 58 yo midwife presented with intermittent watery diarrhoea for 6 months
- She opens her bowels 3-6/d has had diarrhoea at night. she has lost 3kg.
- No abnormality was seen at a recent colonoscopy performed elsewhere
- Options?

Colonoscopy with colonic biopsies
Collagenous Colitis
Microscopic colitis

- Collagenous colitis
- Lymphocytic colitis
Treating microscopic colitis

PATIENT PRESENTATION:
Persistent watery diarrhoea lasting more than 3 weeks

Investigate chronic diarrhoea as per BSG guidelines
■ include colonoscopy and colonic biopsies
(ensure right and left biopsies are taken to increase accuracy)

Consider drug-induced diarrhoea
■ review PPI, NSAID, H2-antagonist, acarbose, aspirin, clozapine, SSRI and ticlopidine usage
■ consider smoking cessation

DIAGNOSIS:
Collagenous colitis

Treat with budesonide
9 mg/day for 6-8 weeks

Non-responsive/ intolerant:
reconfirm MC diagnosis

Relapse

Retreat with budesonide
9 mg/day followed by low dose budesonide up to 6mg/day + calcium / vitamin D

Alternative treatments to consider
■ bismuth
■ +/- anti-diarrhoeals
■ mesalazine

Continued refractory symptoms
■ consider immunomodulators eg. azathioprine methotrexate, biologics
■ consider surgery

Adapted from Münch A et al. J Crohn's Colitis 2012; doi:10.1016/j.crohns.2012.05.014.

The views expressed in this algorithm represent the author's intention to highlight both the evidence base of the treatment options in the management of collagenous colitis, along with treatment options that are non-evidence-based which may also be considered.
Mrs SC Aged 72

- History of ulcerative colitis > 20 years
- BO>6/d c nocturnal symptoms
- Intolerant to AZA, 6MP and methotrexate
- Maintained on prednisolone long term >18mo by prior Gastroenterologist
- No recent investigation
- Options?
Colonoscopy #1

- Pan colitis with features of chronic inflammation including inflammatory polyps and a villiform appearance to the mucosa

- Biopsies confirm above, and x1 biopsy: “..indeterminate for dysplasia…”

- Treated with IFX x 3 induction infusions and repeat colonoscopy
Repeat Colonoscopy

- Repeat biopsies from flat mucosa reveal changes consistent with

- “high grade dysplasia”

Options?
Dysplasia in UC

- **High grade dysplasia**
  - Colectomy recommended, up to 40% may have occult CRC

- **Low grade dysplasia**
  - Controversial need 2 specialist pathologists
  - 10-30% may develop CRC within 1 year
  - Consider colectomy or 3-6 monthly colonoscopy
COLITIS SURVEILLANCE

SCREENING COLONOSCOPY AT 10 YEARS
(preferably in remission, pancolonic dye-spray)

LOWER RISK
Extensive colitis with NO ACTIVE endoscopic/histological inflammation
OR left-sided colitis
OR Crohn's colitis of <50% colon

INTERMEDIATE RISK
Extensive colitis with MILD ACTIVE endoscopic/histological inflammation
OR post-inflammatory polyps
OR family history CRC in FDR aged 50+

HIGHER RISK
Extensive colitis with MODERATE/SEVERE ACTIVE endoscopic/histological inflammation
OR stricture in past 5 years
OR dysplasia in past 5 years declining surgery
OR PSC / transplant for PSC
OR family history CRC in FDR aged <50

5 Years

3 Years

1 Year

BIOPSY PROTOCOL
Pancolonic dye spraying with targeted biopsy of abnormal areas is recommended, otherwise 2-4 random biopsies from every 10 cm of the colorectum should be taken.

OTHER CONSIDERATIONS
Patient preference, multiple post-inflammatory polyps, age & comorbidity, accuracy & completeness of examination

CRC = colorectal cancer
FDR = first degree relative
PSC = primary sclerosing cholangitis
Miss EW, aged 34

• Crohn’s disease 5 years in stable remission for 3 years on azathioprine
• Plans to visit S America
• Attends IBD clinic prior to departure, mentions incidentally she’d had yellow fever vaccination that morning at her GP practice
• Options?
**Vaccinations in IBD**

1. **VZV serology**
   - History of chickenpox
   - If negative: Varicella vaccination
   - Wait min 3 wks
   - Start immunomodulator/anti-TNF

2. **HBV serology**
   - If negative: vaccination
   - If HBsAg+: Start nucleotide/nucleoside analogues
   - Wait min 2 wks
   - Start immunomodulator/anti-TNF (continue antiviral therapy for 6 mths)

3. **Influenza virus**
   - Vaccination yearly

4. **Pneumococcus**
   - Vaccination every 3-5 years

5. **Human papilloma virus (young females)**
   - Vaccination

ECCO guidelines 2010
Miss JE

- 26 yo IT specialist with a history of distal colitis
- Repeated ‘flare-ups’ with bloating, loose stool and occasional fresh blood on paper
- Receives several course of prednisolone with short-lived benefit
- FS is normal, Proctoscopy-haemorrhoids only
- Q. what is your diagnosis and how do you approach the problem
Prevalence of IBS-like symptoms in IBD

- Simrén et al. (2002)

57% (23/40) of CD had IBS-like symptoms
33% (14/43) of UC in remission

This is 2-3 times higher than in the general population (IBS prevalence = ~15-20%).

Assoc. with depression and ↑ visits to GP & Gastroenterologist.
low FODMAP diet

**F**ermentable
**O**ligosaccharides
**D**isaccharides
**M**onosaccharides
And
**A**nd
**P**olyols
<table>
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<tr>
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<th>Fructans &amp; Galactans</th>
<th>Polyols</th>
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<tr>
<td>Apple</td>
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<td>Bread</td>
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<tr>
<td>Pear</td>
<td>(cow, goat &amp; sheep)</td>
<td>Pasta</td>
<td>Cherries</td>
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<td>Biscuits Cereals</td>
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<td>Chickpeas</td>
<td>Prunes</td>
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<tr>
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<td>Lentils</td>
<td>Pears</td>
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<tr>
<td>High fructose corn syrup</td>
<td></td>
<td>Kidney beans</td>
<td>Cauliflower</td>
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<tr>
<td>Large serves of:</td>
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<td>Baked beans</td>
<td>Mushrooms</td>
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<tr>
<td>Dried fruit</td>
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<td>Broccolli</td>
<td>Avocado</td>
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<td>Cabbage</td>
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<tr>
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<td>Brussel sprouts</td>
<td>Xylitol</td>
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<tr>
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<td>Onion / garlic</td>
<td>Sorbitol</td>
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The FODMAP Hypothesis

Loose stools

Pain

Bloating

Small intestine

Colon

Flatulence
FODMAP summary

- A low FODMAP diet is useful in patients with functional symptoms
- It is supported by high quality studies that show efficacy and mechanisms
- Recent trial support its use in IBD patients with functional symptoms
Faecal calprotectin

- To help distinguish between IBD and IBS
- To assess laboratory disease activity in IBD
- To assess responses to treatment
- To assess disease prognosis
- Research uses
In a population with suspected IBD, n=100 (an overall prevalence of IBD 32%)

<table>
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<td>9</td>
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<tr>
<td>false negative</td>
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Meta analysis BMJ, 2010
Calprotectin pathway

Patients with suspected inflammatory bowel disease

Screen with faecal calprotectin

- +
  - +
  - +

Urgent endoscopy

Start treatment for inflammatory bowel disease

Plan other investigations
Mr KI

- 25yo male refractory L sided UC 7yr Hx
- Embolic MI shortly after starting Aza
- Methotrexate intolerant
- 6-mercaptopurine abnormal LFTs
- 6MP and alopurinol co-rescribed poor response
- Recruited to GO-COLITIS-golimumab trial
- Infliximab non-response, IFX level low
- IFX dose escalation-non-response
- Options?
Available new therapies

• Vedolizumab (NICE aproved)

• Ustekinumab (licenced)
Response to Vedolizumab

- Sept
- Oct
- Nov
- Jan

FCP
Summary

- Use topical Rx in UC
- How to use azathioprine in IBD
- C difficile
- Microscopic colitis
- Cancer risk in colitis
- Vaccination in IBD
- Using a low FODMAPs diet for IBS
- Calprotectin
- New treatments
Contacts at SGH and QMH

IBD CNS Ciara Price 0208 725 2996

OR

Gastro secs 0208 725 1206/3811/3429 (SGH)
0208 487 6797 (QMH)

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