Constipation

BEST Meeting

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Definition

- Defecation that is unsatisfactory because of:
    - Infrequent stool
    - Difficult stool passage
    - Hard or dry stool
    - Maybe abnormally large or abnormally small

Sub-classification

- Acute
- Functional (idiopathic)
- Secondary
- Opioid induced
- Faecal Loading / Impaction
- Chronic constipation can be further subdivided:
    - Obstructive
    - Colonic inertia
    - Constipation without obstruction or inertia

Diagnosis

- Constipation is a symptom
- Present if person continues to complain of constipation once clarity has been made over what is normal / abnormal
- Consider constipation in elderly with:
    - Confusion
    - Overflow diarrhoea
    - Abdominal pain
    - Urinary Retention
    - Nausea of loss of appetite
- Functional / Secondary Constipation are disorders
    - Differentiate by process of exclusion of secondary causes
- Careful history for obstructive symptoms / impaction
    - Faecal mass on examination (abdomen / PR)
    - Incontinence?
    - Manual measures of defecatory assistance?
        - Finger into vagina – rectocele?
        - Finger in rectum because of 'flap' – rectal ulcer
        - Pressure on perineum (behind anus) – levator muscle failure
        - Rectal evacuation – impaction / loading

Secondary Causes

- Drugs:
  - **Opioids**
  - Anti-depressants
  - Anti-epileptics
  - Sedating anti-histamines
  - Anti-psychotics
  - Anti-spasmodics
  - Calcium, aluminium preparations
  - Diuretics
  - Iron
- Other co-morbidities
  - DM; thyroid dysfunction; hypercalcaemia; hypokalaemia; uraemia
  - Myopathic (e.g. scleroderma, myotonic dystrophy)
  - Neurological disorders (e.g. Parkinson's, MS, autonomic neuropathy, spinal cord injury)
  - IBS

Other factors

Other factors

- Diet
    - Low fibre; Too little fluid;
- Social factors
    - Access to toilet
    - Privacy / Time
    - Lack of exercise / Limited mobility
- Psychological
    - Anxiety / Depression
    - Somatization
- Physical factors
    - Sitting position
- Past history of sexual abuse

Indications for urgent referral

- Persistent unexplained change in bowel habit?
- Palpable mass in the lower right abdomen or the pelvis?
- Persistent rectal bleeding without anal symptoms?
- Narrowing of stool calibre?
- Family history of colon cancer, or inflammatory bowel disease?
- Unexplained weight loss, iron deficiency anaemia, fever, or nocturnal symptoms?
- Severe, persistent constipation that is unresponsive to treatment?
- Other symptoms consistent with need for 2WW referral for colorectal cancer exclusion

Investigations

- No routine investigations needed for adult with constipation unless:
  - Concerned regarding possible secondary cause – investigate as necessary depending on other symptoms
  - Meets 2WW criteria or other concerns in history
  - Complex obstructive defecatory problems

Acute (Short Duration) Constipation

- Identify and adjust any contributory medication IF possible
- Lifestyle advice
    - Increase dietary fibre
    - Maintain adequate fluid intake (2L / day)
    - Increase exercise (Most effective measure)
- Short term laxatives
    - Bulk-forming (ensure adequate fluid intake; avoid in opioid induced and elderly; avoid late at night). Little value if adequate fibre in diet (increased side effects).
    - Osmotic laxative – if bulk forming contra-indicated OR ineffective
    - If soft stool but difficult to void add stimulant
- Stop once stools soft and easily passed

Chronic Constipation

- Relieve loading / impaction
    - Suppositories (glycerin / bisacodyl)
    - Enema (phosphate; arachis oil)
    - Macrogol (Laxido / Movicol)
- Set realistic targets / expectations
- Lifestyle adaptation (Diet, fluid, EXERCISE)
- Review and adjust medications

Chronic Constipation

- Laxatives
    - May be short term if waiting for instigation of lifestyle changes – review and STOP if possible
    - Secondary constipation (drug / co-morbidity)
  - Bulk forming (except opioid and elderly)
  - Osmotic (macrogols NOT lactulose – Cochrane review 2010)
  - Stimulant if soft and difficult to void
- Adjust / combine according to speed, tolerance and response to treatment.
- Titrate to achieve and maintain 1-2 soft formed stool /day
- Reduce down if this is achieved AND maintained
- Take away most recently added drug

Chronic Constipation

- Refer to secondary (specialist) care:
    - No / inadequate response to:
    - AT LEAST 2 different laxatives (**different classes**)
    - At MAXIMUM dose
    - For AT LEAST 6 months

Chronic Constipation

- Secondary Care Interventions
  - **Prucalopride**:
    - Selective high-affinity serotonin (5HT4) receptor agonist
    - Prokinetic effect – enhanced intestinal mobility
    - NICE TA211 – only licensed in female patients (due to study limitations – insufficient data in male cohort)
    - Amber light – can be passed through to primary care after 4 weeks if adequate response
    - Discontinue if no effect at 4 weeks.
    - Side effects – headache, abdominal pain, nausea and diarrhoea
  - **Lubiprostone:**
    - Chloride Channel activator – promotes chloride secretion into colonic lumen hence sodium and thus water excretion
    - Increase in fluid secretion – increased motility
    - NICE TA318 – available to both **male** and **female** patients
    - Effective within 2 weeks – discontinue if no benefit
    - Side effects – diarrhoea, abdominal pain.

Obstructive defecation

- Manage constipation by lifestyle / simple laxatives where possible.
- Diagnosis often made by good history and examination
- Consider ano-rectal physiology / defecting (MRI) proctogram in complex cases
- Referral to bowel dysfunction service (ARU – Lindsey Reynolds)
    - Biofeedback, pelvic floor exercises, ano-rectal irrigation.
- Referral to Sheffield when all local interventions have failed
    - Rectopexy; defunction (very poor outcomes)

Opioid Induced Constipation

- Now recognised in own right
    - ROME IV criteria – C6: Diagnostic Criteria for Opioid-Induced Constipation
- Beware narcotic bowel syndrome
    - Opioid sensitisation of nerve fibres
    - 5-10% of acute high dose / chronic users of opioid narcotics
    - Pain increasing / not recovered by increasing doses of medication
    - Direct effect on intestinal muscle function through targeted effect on Mu receptors; associated effect on acetyl-choline, 5HT, VIP and other intestinal neurotransmitters

Opioid Induced Constipation

- Often multi-factorial
    - Present in 41% of opioid users
    - Not specific to brand or type of opioid
    - Maybe slightly less common in patch over oral preparation (meta-analysis data) but not shown in comparative studies
    - No association with dose or gender
    - Bristol Stool Chart
        - Correlation with transit / secretion, but NOT perceived symptoms OR QOL.
    - Associated with significant financial impact (109% increase in cost vs analgesia alone)
- Establish if constipated BEFORE starting opiates (if so continue previous regime – if helped)

Opioid Induced Constipation

- Treatment
  - Lifestyle – AVOID increased fibre; exercise in older population (combined approach). No clear benefit in younger population
  - Laxatives – Osmotic +/- softener +/- stimulant; No trial data indicating benefit!
  - Anticipate and intervene early - ?better outcomes

Opioid Induced Constipation

- Lubiprostone – 12% improvement vs placebo (Cryer et al Pain Med 2014) – not NICE approved
- Prucalopride – 20% improvement vs placebo – not licensed
- Opioid Antagonists
    - Targinact – Improvement in Bowel function assessment at 12 weeks; open label follow up – both groups meet same primary end-point
    - Naloxegel – complex trial end-points, 20% improvement vs placebo
    - Expensive vs laxatives

Opioid Induced Constipation

- Suggested pathway
    - Previous problem? – Yes – Restart / Continue regime if successful
    - No – OIC
    - Try simple laxatives (not fibre based) as per other constipation management
    - Consider opiate-antagonists (targinact / naloxegol)
    - Trial lubiprostone / prucalopride (off license / NICE).
- Role of Peripheral Mu-opioid receptor antagonists (PAMORAs) – alvimopan, methylnaltrexone. Naldemedine (FDA approval, Japanese license)?

Summary

- Be clear with history and goals / expectations
- Consider obstructive defecation
- Elicit relevant lifestyle / psychological factors
- Drug History and review; secondary conditions
- Lifestyle changes (exercise especially in the elderly)
- Fibre except in OIC and Elderly
- Step wise approach
- Refer if ‘alarm symptoms’ ; 2WW criteria; failed maximal intervention (2 different laxatives of different classes at maximal doses for 6 months)
- New drugs have novel action, but limited data
- OIC – new ROME IV definition. Combination antagonist drugs.