Clinical Pharmacy

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Gastrointestinal Conditions

Constipation

Background

1-**Constipation**: is a condition characterized by the passage of **hard**, **dry** stools **less frequently** than the **person's normal pattern** [(1)].

2-The normal range may vary from three movements in 1 day to three in 1 week [(1)]. If it was stabilized at three daily for a patient, a reduction to one bowel movement daily might produce hard stools that lead to constipation. On the other hand, if a person's normal frequency is three weekly, two weekly might harden feces so that lead to constipation) [(2)].

3-**Women** are two to three times more likely to suffer from constipation than men and about 40% of women in late pregnancy experience constipation [(3)].

Etiology

1-Causes of constipation and their relative incidence are shown in (table 1-1) [(3)].

Table1-1: Causes of constipation and their relative incidence in community pharmacy [(3)]

Incidence	Cause
Most likely	Eating habits/lifestyle
Likely	Medication
Unlikely	Irritable bowel syndrome, pregnancy, depression, functional disorders (children)
Very unlikely	Colorectal cancer, hypothyroidism

2- Many drugs can induce constipation; some examples are listed in table1- 2 [(1)].

3-**Lifestyle factors**: like low-fiber diet, inadequate fluid intake, and chronic immobility can contribute to constipation [(4)].

4-**Examples of disease-induced constipation**: are diabetes mellitus, Hypothyroidism, IBS, bowel cancer, and painful anal conditions (such as anal fissures, and hemorrhoids) in which the patient tries to avoid defecation to avoid pain [(5)].

Table1 -2: Examples of drugs that may cause constipation [(1)]
Analgesics and opiates (Dihydrocodeine, codeine), **Antacids** (Aluminium salts), **Anticholinergics** (Hyoscine), **Anticonvulsants** (Phenytoin) **Antidepressants** (Tricyclics, selective serotonin reuptake inhibitors) **Antihistamines** (Chlorpheniramine, promethazine) **Antihypertensives** (Clonidine, methyldopa), **Anti-Parkinson** agents (Levodopa), **Beta-blockers** (Propranolol), **Diuretics** (Bendroflumethiazide)

Iron, **Laxative abuse , Antipsychotics** (Chlorpromazine)

5-Constipation is a common problem in **elderly,** and **pregnancy** (due to hormonal changes, reduced mobility, bowel compression by the uterus, and iron therapy commonly taken by pregnant) [1, 3].

Complications [6]

If untreated, constipation can lead to:

1-**Faecal impaction** (when a large mass of faeces cannot be passed) and **obstruction** (with potential to progress to bowel **perforation**)

2-**Rectal bleeding** 3-**Anal fissures** 4-**Hemorrhoids**

Patient assessment with constipation

A-Details of bowel habit:

1-Many people believe that a daily bowel movement is necessary for good health and laxatives are often taken and abused as a result. *In fact, the normal range may vary from three movements in 1 day to three in 1 week*. Therefore an important health education role for the pharmacist is in reassuring patients that their frequency of bowel movement is normal. ***Patients who are constipated will usually complain of hard stools which are difficult to pass and less frequent than usual*** [1].

2-The determination of any change in bowel habit is essential. A sudden change which has lasted for 2 weeks or longer [1] (**with no identifiable cause** [3]) should be referred for further investigations [1]. [Constipation continuing over several weeks to months is considered to be chronic [5]. If a patient suffers from longstanding constipation and has been previously seen by the physician then treatment could be given. However, cases of more than 14 days with no identifiable cause or previous investigation by the physician should be referred] [3].

B-Associated symptoms:

1-Intestinal obstruction:

Constipation is often associated with abdominal discomfort, bloating and nausea. In some cases constipation can be so severe as to **obstruct the bowel**. This obstruction or blockage usually becomes evident by causing ***colicky abdominal pain, abdominal distension and vomiting.***

When symptoms suggestive of obstruction are present, *urgent referral* is necessary as hospital admission is the usual course of action [1].

2-Blood in the stool:

The presence of blood in the stool can be associated with constipation. In such situations blood may arise from piles (**haemorrhoids**) or a small crack in the skin on the edge of the anus (**anal fissure**).

The bright red blood may be present on the surface of the stool (not mixed in with the stool). If piles are present, there is often discomfort on defaecation. The piles

may drop down (prolapse) and protrude through the anus. A fissure tends to cause less bleeding but much more severe pain on defecation [1].

The presence of blood in the stool [1]***, or dark tarry stool*** [5] required referral for further investigations. (Medical referral is advisable as there are other more serious causes of bloody stools, especially where the blood is mixed in with the stool) [1].

3-Constipation with associated **weight gain**, **deepening of the voice**, **feeling of tiredness** and **coarse hair** (*may indicate* **hypothyroidism**) and required referral [4]

4-Constipation with associated **weight loss** (may indicate **carcinoma**) and required referral [4]

C-Diet and lifestyle [1, 6]:

Insufficient intake of dietary fibers (like fruit, vegetables,…..), inadequate fluid intake , eating different foods or at different times may cause constipation.

Also changes in lifestyle, for example: job changes, loss of work, retirement or travel may cause constipation.

D-Medication:

1-One or more laxatives may have already been taken in an attempt to treat the symptoms. Failure of such medication required referral [1].

2-Many drugs can induce constipation; some examples are listed in table 1-2 [1].

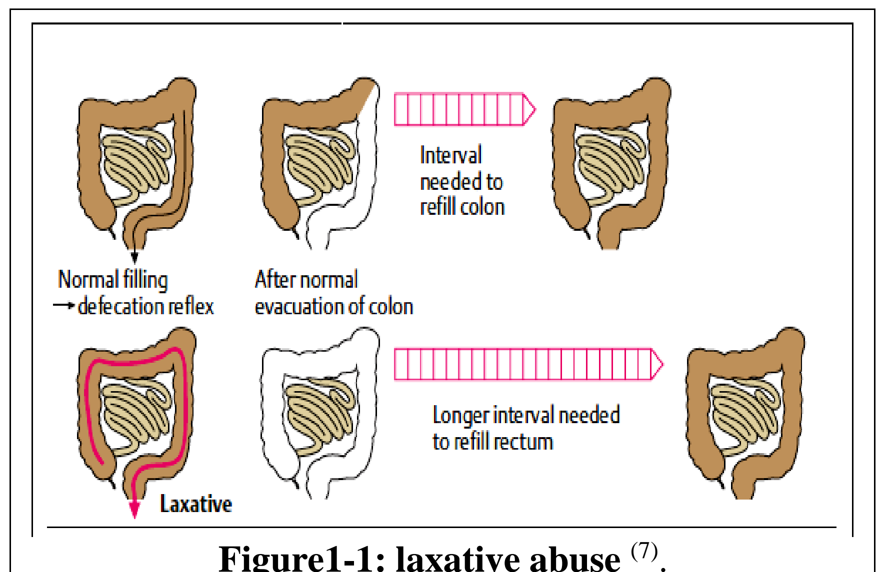

Figure1-1: laxative abuse [7].

3-**laxtive abuse**:

Continuous use, especially of stimulant laxatives, can result in a vicious circle where the contents of the gut are expelled, causing a subsequent cessation of bowel actions for 1 or 2 days. This then leads to the false conclusion that constipation has recurred and more laxatives are taken and so on [1]. (**See the figure1-1**) [7].

Chronic overuse of stimulant laxatives can result in loss of muscular activity in the bowel wall (an ***atonic colon***) and thus further constipation. Any patient who is ingesting large amounts of laxative agents should be referred to the doctor [1].

Note: well-designed recent clinical trials do not support an increased risk of colonic muscle or nerve damage with the use of these laxatives [5]. (many experts now believe that the risk of long-term use of stimulant laxatives use have been overestimated and they are safe for daily use) [8].

Treatment timescale [1]

A-If the pharmacist gives non-pharmacologic advice only, then the treatment timescale is 2 weeks.

B-If the pharmacist gives laxative drug, then the treatment timescale is 1week only.

When to refer [1, 3, 8]
-Change in bowel habit of 2 weeks or longer -Presence of abdominal pain, vomiting, bloating -Blood in stools -Pain on defecation, causing patient to suppress defecation reflex -Prescribed medication suspected of causing symptoms -Failure of OTC medication -Symptoms suggestive of anemia such as tiredness or lethargy. -Unexplained weight loss

Management

A-Non-pharmacologic advices:

For uncomplicated constipation, **nondrug treatment is advocated as first-line treatment for all patient groups** because simple dietary and lifestyle modifications (increasing exercise) will relieve most acute cases of constipation. Advice includes increasing fluid and fiber intake [3].

1-Eat a diet high in fiber, including wholegrains, fruits and vegetables [4].

2- Drink plenty of fluids, the equivalent of at least 8–10 glasses of water a day[4]. However, it should be noted that fluid increase is contraindicated in some people (e.g. in heart or renal failure) [6].

3-**Develop and maintain a routine exercise program.** Walking can be helpful if the cardiovascular system is healthy [5] .

4-Patients should also be encouraged to **respond immediately to any urge to defecate**. Failure to do so can result in a build-up of faeces that continue to have water absorbed from them, making them more difficult to pass [6].

B-Laxatives:

1-Laxatives can be classified into groups depending on their mode of action [9] (table1-3).

Table1-3: types of laxatives

Type of laxative	Example(s)	Approximate onset of action
1-Stimulant laxative	Senna, Bisacodyl, Sodium picosulfate, and Glycerin (supp.)	Oral:6-12hours [1] Rectal: within 1 hour [1]
2-Bulk-forming laxative	Methylcellulose, Bran , Sterculia and Ispaghula (Metamucil®)	12 -24 hours, but onset may be delayed as long as 72 hours [5]
3-Lubricant (faecal softeners)	Liquid paraffin	6-8 hours [5]
4-Osmotic laxative	Lactulose	1-2 days [1]

2-The drug selection should be based on: Patients characteristics (age, pregnancy…), patient preference, how quickly an effect is needed, side effects, and cost [6] (table1-4).
Where constipation is not induced by necessary drug therapy or chronic illness, the laxative should be used for a short time until dietary and lifestyle changes become effective [6].

Table1-4:Product selection guidelines	
Patient	**Preferred laxative**
Pregnant women	Bulk-forming laxative. Lactulose may be used [1, 9, 10]
Breast-feeding mother	Bulk-forming laxative, Lactulose [3]
Children	Glycerin(supp.) [1], Lactulose [9]
Advanced age(elderly)	Bulk-forming laxative, Also Lactulose and Glycerin (supp.) are safe [5].

A-Stimulant laxatives:

1-Stimulant laxatives are thought to act mainly by stimulating the intestinal mucosa to secrete water and electrolytes [4].
2-The main **adverse effects of stimulant laxatives** are griping and intestinal cramps. Prolonged use may result in loss of colonic smooth muscle tone (see laxative abuse) [9].
Stimulant laxatives should therefore be used for only short periods of a few days at most, to reestablish bowel habit [4].
3-Bisacodyl tablet is **enteric-coated**; therefore, it should be swallowed whole and should not be taken within one hour of antacid or milk as this will lead to dissolution of the coating and release of the drug into the stomach and cause gastric irritation [9].
4-Senna is excreted via the kidney and may **color the urine** a yellowish-brown to red color depending on its PH [4].
5-Senna is secreted in breast milk, and large dosages may cause increased gastric motility and diarrhea in breastfed infants. Breastfeeding mothers should, therefore, avoid this laxative [4]. (However BNF-74 states that specialist sources indicate suitable for use in breast-feeding in infants over 1 month [10] and other reference states that its use in breastfeeding is OK but other safer laxatives are preferred [3]).

6-**Usual Doses:**
Bisacodyl 5 mg tab. Adult dose: usually 1-2 tablets (usually take at night to produce the effect next morning).
While the dose of supp. Is one supp. (usually in the morning) [9, 10].
Senna tab. Adult dose: usually 2 tablets (usually take at night to produce the effect next morning) [3, 9].
Glycerin suppositories: The patient should expect to have bowel movement quickly (within one hour). Varying sizes are made: the 1 gm suppositories are designed for infants, 2 gm for children and the 4 gm for adults (3).

B-Bulk-forming laxative:
1-Bulk laxatives are those that most closely resemble the normal physiological mechanisms involved in bowel evacuation. Bulk laxatives work by swelling in the gut and increasing faecal mass so that peristalsis is stimulated [1].

2-The laxative effect can ***take several days to develop*** [1].
3-***None of the above preparations should be taken immediately before going to bed***, because there may be a risk of oesophageal blockage if the patient lies down directly after taking them [9].
4-When recommending the use of a bulk laxative, the pharmacist should advise that ***an increase in fluid intake would be necessary*** [1].
5-***Adverse effects*** and disadvantages are relatively minor. They include:
- –Risk of oesophageal and intestinal ***obstruction*** if preparations are not taken with sufficient water
- – Abdominal ***distension*** and ***flatulence***.
- – They may not be suitable for patients who must restrict their fluid intake severely [4].

C-Liquid paraffin:

Liquid paraffin is considered to have a limited usefulness as an occasional laxative in situations where straining at stool must be avoided (for example, following an operation or a myocardial infarction), but it ***has several drawbacks*** that make it unsuitable for regular use [4] (it should never be recommended because other, safer and more effective medications are available) [3].:
-It can ***seep*** from the anus and cause irritation.
-It may ***interfere with the absorption of fat soluble vitamins***.
-It is slightly absorbed into the intestinal wall, where it may set up foreign-body ***granulomatous reactions***.
-It may enter the lung through aspiration and cause ***lipoid pneumonia*** [4].

D-Lactulose:

It can be taken by all age group, have no drug interactions and can be safely used in pregnancy [3]. However, there are some factors that may deter patients from using Lactulose: It may take 72 hours of regular dosing to produce an effect. **It is intensely sweet in taste** which makes it more palatable for children, to whom it can be given safely [9].
Adult laxative dose [10]: 15 ml twice daily.
Serious adverse effects with lactulose are rare. Relatively minor side-effects occur in about 20% of patients taking full doses and include flatulence, cramp and abdominal discomfort, particularly at the start of treatment [4].

Note: Lactulose syrup should be used with caution in diabetic patients because it contains lactose and galactose [11].

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Hemorrhoids:

Hemorrhoids (also known as piles): are abnormally dilated, swollen, bulging of hemorrhoidal vessels and the overlying skin in the anorectal region [(1)].

Prevalence and epidemiology

Hemorrhoids can occurs at any age but are rare in children and adults under the age of 20. Prevalence appears to be increased with increasing age and is most common in patients between the ages of 45-65 years. In addition, there is a high incidence of hemorrhoids in pregnant women [(2)].

Etiology:

The cause of hemorrhoid is probably multifactorial with **anatomical** (degeneration of elastic tissue), **physiological** (increased anal canal pressure), and **mechanical** (straining at defecation) processes implicated [(2)].

In addition hemorrhoid is often exacerbated by inadequate dietary fiber or fluid intake [(3)]. **Pregnancy** is believed to **precipitate** hemorrhoids in **susceptible women** [(4)].

Types of hemorrhoids:

1-Superior to the anal sphincter there is an area known as the dentate line (see the figure1-2). Hemorrhoids above the dentate line are classified as **internal**, while hemorrhoids below the dentate line are classified as **external** [(2)]. The term **mixed hemorrhoids** is used when internal and external hemorrhoids coexist [(4)].

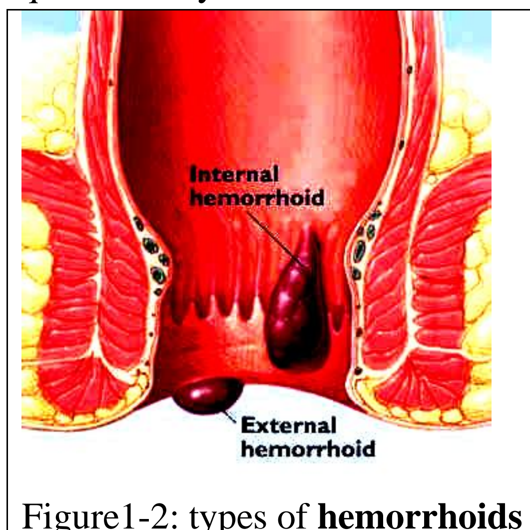

Figure1-2: types of **hemorrhoids**

2-**Internal** hemorrhoids should **not cause pain** unless complications develop, since this area has **no nerve fibers** [(4)].

3-Furthermore ***internal*** haemorrhoids are graded according to severity: **grade I**, do not prolapse out of the anal canal; **grade II**, prolapse on defecation but reduce spontaneously; **grade III**, require manual reduction; and **grade IV**, cannot be reduced [(2)].

Patient Assessment (Specific questions to ask)

A-Duration:

Patient with symptoms that have been constantly present for **more than 3 weeks** required referral for further investigations [(2)].

B-Severity:

Medication is unlikely to help patient who has to **manually reduce hemorrhoids** or of **3rd or 4th degree** required referral [2] (fourth degree hemorrhoids are at risk of **thrombosis** and **gangrene** [4].

C-Pain:

Pain is not always present [3] pain associated with hemorrhoids tend to occurs on defecation and at other time for example when sitting. It is usually described as a dull ache. **Sharp** or **stabbing pain** at the **time of defecation** can suggest an **anal fissure** [2] and required referral [3].

D-Itching:

The most troublesome symptom for many patients is itching and irritation of the perianal area rather than pain [3].

E-Bleeding:

1-**Bright blood** does not normally have a sinister significance, but patients experiencing this for the **first time** should be referred [5].
2-**Blood mixed** in the stools, giving them a tarry red or black appearance. This indicates bleeding within the gastrointestinal system and must be investigated [5].
3-**Large volumes of blood** not associated with defecation; this may indicate carcinoma and must be investigated [5] (patient with hemorrhoids does not usually bleed at time other than defecation) [4].

F-Constipation:

Constipation is a common causatory or exacerbatory factor in hemorrhoids. In addition if piles are painful, patient try to avoid defecation which makes the constipation worse [3].

G-Bowel habit:

A persisting change in bowel habit (persisting alteration from normal habit) required referral (may be due to tumor) [3].

When to refer [2, 3]
-Duration of longer than 3 weeks -Presence of blood in the stools -Change in bowel habit (persisting (alteration from normal bowel habit -Suspected drug-induced constipation -Associated abdominal pain/vomiting -Fever -Severe pain associated with defecation

H-Associated symptoms:

Symptoms of hemorrhoids are usually local (pain, itching…). Other symptoms such as abdominal pain, **vomiting**, loss of appetite, **tenesmus** (desire to defecate when there is no stool), **seepage** (involuntary passage of fecal material) required referral [2, 3].

I-Medication

To know [3]:
1- Products already used to treat hemorrhoids.
1- Drug-induced constipation which exacerbate the condition.

Treatment timescale:

Patient should see the Dr. If the symptoms have not **improved after 1 week** [3].

Management

A-Non-drug measures :

1-**Increase** the amount of **fiber and fluid** in the diet [1].
2-**Avoid lifting heavy objects** [1].
3-**Avoid delaying the urge** to defecate [1].
4-Avoid **prolonged sitting** in the toilet to reduce straining and pressure on the hemorrhoids vessels [1].
5-**Wash the perianal area with warm water** after each bowel movement. In addition many patients find that warm bath soothes their discomfort [3].

B-pharmacological therapy:

1-The OTC products for hemorrhoids include the followings (alone or commonly in combined products) (table1-8) [1-3]:

Table 1-8: ingredients included in products for hemorrhoids [1-3]		
Type	**Example(s)**	**Purpose(and mechanism)**
Anesthetics	Lidocaine, benzocaine	Reduce pain and itching
Astringents	Bismuth, zinc, Peru balsam	Precipitate the surface protein producing coat over hemorrhoids to reduce itching, irritation, ….
Anti-inflammatory	Hydrocortisone (the only OTC)	Reduce inflammation and swelling to relief Pain and itching.
Protectants	Zinc oxide, AL-hydroxide, calamine, shark liver oil	Form a barrier on skin to prevent irritation , itching, and loss of moisture
Antiseptics	resorcinol	antiseptic
Counter-irritants	menthol	Give tingling sensation to overcome pain and itching.
Vasoconstrictor	Phenylphrine, ephedrine…	Reduce swelling to relief pain and itching.

2-Laxatives: The short-term use (1-2 days) of a stimulant laxative to relieve constipation while dietary fiber and fluid are being increased.
For patients who cannot adapt their diet, bulk-forming laxative may be used long term [3].

How to use OTC products

1-Ointments and creams can be used for internal and external hemorrhoids while **suppositories are used for internal hemorrhoids**. However both are used twice daily (morning and evening) and after each bowel movement [3].

2-Many people prefer **suppositories**, but these products are often **not effective** because they **tend to slip into the rectum and melt, thus bypass the anal canal where the**

medication is needed. In general Ointments and creams are preferred over **suppositories** (4).

3-When used intrarectally, the ointment may be inserted using an applicator or finger but the **applicator is preferred** because it can reach an area where the finger cannot reach. The applicator should be **lubricated** by the ointment before insertion (1).

4-Products that contain hydrocortisone are restricted to those aged above 18 years and for no longer than of 7 days of continuous treatment (3).

References:

1-American pharmacists association. Handbook of Non-prescription drugs: An Interactive Approach to Self-Care. 18th edition. 2016.
2-Paul Rutter. Community Pharmacy. Symptoms, Diagnosis and Treatment. 4th edition. 2017.
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