Dyspepsia - pregnancy-associated - Management

Scenario: Dyspepsia - pregnancy-associated

Definition

- Dyspepsia is upper abdominal discomfort or pain which may be described as a burning sensation, a heaviness, or an ache. It is often related to eating and may be accompanied by other symptoms such as nausea, fullness in the upper abdomen, or belching.
- The most common cause of dyspepsia in pregnancy is gastro-oesophageal reflux. It usually resolves after the birth of the child.

How should I assess a pregnant woman who has dyspepsia?

- Take a detailed history:
  - Rule out a serious cause by enquiring about atypical or alarm features, and previous history of gastro-oesophageal reflux disease or peptic ulcer disease.
  - Ask about symptoms and how they are affecting the woman's quality of life.
  - Ask about lifestyle (e.g. eating habits) and treatments already tried (e.g. over-the-counter antacids).
- Examination is usually normal, and investigations are generally not necessary.

In depth

What advice should I give to a pregnant woman with dyspepsia?

- Reassure the woman that dyspepsia symptoms rarely cause complications and will probably resolve after the birth.
- Give written lifestyle advice as first-line management, especially in the first trimester of pregnancy. Advise the woman to:
  - Adopt healthy eating habits, eat smaller meals more frequently, not eat within 3 hours of going to sleep, and avoid known irritants (e.g. alcohol, coffee, fruit juices, chocolate, and fatty and spicy foods).
  - Prop up the bed head when sleeping (lying flat may increase acid reflux).

- Avoid medications if appropriate (e.g. sedatives, calcium-channel antagonists, antidepressants, nonsteroidal anti-inflammatory drugs).
- Stop smoking (if applicable).

- Advise the woman to return if symptoms are not controlled with lifestyle changes, or if worsening or new symptoms develop.

In depth

What drug treatment should I prescribe?

- Antacids or alginates are recommended as first-line treatments if symptoms are relatively mild and are not controlled adequately by lifestyle changes.
  - Antacid products containing combinations of aluminium and magnesium are recommended on an 'as required' basis.
  - Calcium-containing products are recommended for short-term or occasional use.
  - Alginate products are particularly useful if symptoms of gastro-oesophageal reflux are dominant.
- If symptoms are severe, or persist despite treatment with an antacid or alginate, consider prescribing an acid-suppressing drug:
  - Ranitidine is an established drug but is not licensed for use in pregnancy.
  - Omeprazole is a more effective alternative. It is licensed for use in pregnancy, but there is less experience of its use in this context.

In depth

When should I refer a pregnant woman with dyspepsia?

- Refer *urgently* to a gastroenterologist if there are alarm features, such as: chronic gastrointestinal bleeding; progressive unintentional weight loss; progressive difficulty in swallowing (dysphagia); or persistent vomiting.
- Refer *non-urgently* to a gastroenterologist if:
  - Symptoms do not adequately respond to antacids, alginates, ranitidine, or omeprazole.
  - The woman is unable to eat sufficiently because of symptoms.

- The diagnosis is in doubt (e.g. biliary colic).
- There is a previous history of peptic ulcer disease; Barrett's oesophagus; or known dysplasia, atrophic gastritis, or intestinal metaplasia; and symptoms are inadequately controlled on usual medication.

- Refer to an obstetrician if symptoms suggest a pregnancy-related disorder other than dyspepsia (e.g. HELLP syndrome, pre-eclampsia).

In depth

Prescriptions

First line: antacids and alginates

Age from 12 to 60 years

Co-magaldrox 195/220mg suspension (sugar-free)

Co-magaldrox 195mg/220mg/5ml oral suspension sugar free
Take two to four 5ml spoonfuls 20-60 minutes after food and at bedtime, when required to relieve dyspepsia.
Supply 1000 ml.

Age: from 12 years to 60 years
NHS cost: £3.42
OTC cost: £6.00
Licensed use: no - off-label indication

Gaviscon® Advance tablets (sugar-free): peppermint flavour

Gaviscon Advance chewable tablets
Chew one to two tablets (followed by water) after meals and at bedtime, when required to relieve dyspepsia.
Supply 120 tablets.

Age: from 12 years to 60 years
NHS cost: £6.48
OTC cost: £11.50
Licensed use: yes

Gaviscon® Advance liquid (sugar-free): aniseed flavour

Gaviscon Advance liquid original
Take one to two 5ml spoonfuls after meals and at bedtime, when required to relieve dyspepsia.
Supply 500 ml.

Age: from 12 years to 60 years
NHS cost: £5.40
OTC cost: £10.95
Licensed use: yes

Gaviscon® Advance liquid (sugar-free): peppermint flavour

Gaviscon Advance liquid peppermint
Take one to two 5ml spoonfuls after meals and at bedtime, when required to relieve dyspepsia.

Supply 500 ml.

Age: from 12 years to 60 years
NHS cost: £5.40
OTC cost: £10.95
Licensed use: yes

Peptac® liquid (sugar-free): aniseed flavour

Peptac liquid aniseed
Take two to four 5ml spoonfuls after meals and at bedtime, when required to relieve dyspepsia.
Supply 1000 ml.

Age: from 12 years to 60 years
NHS cost: £4.32
OTC cost: £7.50
Licensed use: no - off-label indication

Peptac® liquid (sugar-free): peppermint flavour

Peptac liquid peppermint
Take two to four 5ml spoonfuls after meals and at bedtime, when required to relieve dyspepsia.
Supply 1000 ml.

Age: from 12 years to 60 years
NHS cost: £4.32
OTC cost: £7.50
Licensed use: no - off-label indication

Rennie Duo suspension (sugar-free)

Rennie Duo oral suspension
Take two to four 5ml spoonfuls after meals and at bedtime, when required to relieve dyspepsia.
Supply 1000 ml.

Age: from 12 years to 60 years
NHS cost: £5.34
OTC cost: £9.41
Licensed use: yes

Second line: ranitidine

Age from 12 to 60 years

Ranitidine tablets: 150mg twice a day

Ranitidine 150mg tablets
Take one tablet twice a day.
Supply 60 tablets.

Age: from 12 years to 60 years
NHS cost: £1.05
Licensed use: no - off-label indication

Second line: omeprazole

Age from 12 to 60 years

Omeprazole capsules: 10mg once a day (usual dose)
Omeprazole 10mg gastro-resistant capsules Take one capsule once a day. Supply 28 capsules. **Age**: from 12 years to 60 years **NHS cost**: £1.96 **Licensed use**: yes

Omeprazole capsules: 20mg once a day (maximum dose)
Omeprazole 20mg gastro-resistant capsules Take one capsule once a day. Supply 28 capsules. **Age**: from 12 years to 60 years **NHS cost**: £2.02 **Licensed use**: yes

Dyspepsia - pregnancy-associated - Management

Detailed answers

safe practical clinical answers - *fast*

Overview of management

- Take a detailed history and assess the severity of symptoms and the impact on the woman's quality of life. Rule out serious causes for the symptoms.
- Give advice on lifestyle changes, such as eating and sleeping habits, stopping smoking, and avoiding aggravating risk factors, including the use of other drugs. For many women, advice alone is sufficient.
- If symptoms are severe, or if lifestyle changes are inadequate, consider drug treatment.
  - Antacids and alginates usually control symptoms effectively.
  - Consider treatment with a systemic acid-suppressing drug if symptoms are severe, or if antacids and alginates do not produce an adequate response. Ranitidine or omeprazole are appropriate choices.
- Consider referral to a specialist if symptoms fail to respond to drug treatment, or there is concern about the underlying disease.

How should I assess a pregnant woman who has dyspepsia?

- Take a detailed history. Ask about:
  - Symptoms and how they are affecting the woman's quality of life: heartburn and acid reflux are common, but people may also describe upper abdominal discomfort, retrosternal pain, anorexia, bloating, fullness, or early satiety.
  - Previous history of gastro-oesophageal reflux disease or peptic ulcer disease.
  - Features suggesting a serious cause (alarm features) or an illness unrelated to pregnancy (e.g. symptoms of fever, rigours, vomiting, and malaise).
  - Lifestyle (e.g. diet and medication) that may worsen dyspepsia.
  - Treatments already tried, especially over-the-counter medication (antacids).
- Examination is usually normal, and investigations are generally not necessary.

Clarification / Additional information

- **Signs:** epigastric tenderness may be present, but is a poor discriminating sign [NICE, 2005].
- **Investigations:** are usually carried out in secondary care and may include:
  - An endoscopy.
  - Testing for *Helicobacter pylori*, which may be delayed until after delivery, since eradication therapy is contraindicated during pregnancy [Mahadevan and Kane, 2006].

Basis for recommendation

These recommendations are largely based on expert opinion [Ali and Egan, 2007], and pragmatic advice:

- Knowing the individual's diet and lifestyle, the symptom severity, and previously tried treatments will allow the healthcare professional to judge the next step in dyspepsia management.

What advice should I give to a pregnant woman with dyspepsia?

- Reassure the woman that dyspepsia symptoms are common in pregnancy and will likely resolve after birth, and that complications are rare.
- Give written lifestyle and dietary advice as first-line management, especially in the first trimester. Advise the woman to:
  - Adopt healthy eating habits, eat smaller meals more frequently, not eat within 3 hours of going to sleep, and avoid known irritants (e.g. alcohol, coffee, fruit juices, chocolate, and fatty and spicy foods).
  - Prop up the bed head when sleeping (lying flat may increase acid reflux).
  - Avoid medications if appropriate (e.g. sedatives, calcium-channel antagonists, antidepressants, nonsteroidal anti-inflammatory drugs).
  - Stop smoking (if applicable).
- Advise the woman to return if symptoms are not controlled with lifestyle changes, or if worsening or new symptoms develop.

Clarification / Additional information

- See the CKS topic on Smoking cessation if the woman is having difficulty stopping smoking.

Basis for recommendation

- CKS could find no trial evidence of lifestyle modifications for managing dyspepsia in pregnancy. These recommendations are largely based on expert opinion [Madanick and Katz, 2006; Mahadevan and Kane, 2006; Ali and Egan, 2007], and extrapolated from the National Institute for Health and Clinical Excellence guidance *Dyspepsia: Management of dyspepsia in adults in primary care* [NICE, 2005]:
  - Lifestyle modifications are safe and inexpensive, and encourage individual participation. Although there is no evidence that lifestyle changes help symptoms of dyspepsia in pregnancy, more important general health benefits can be gained [MeReC, 1998; NICE, 2005].

- Lifestyle modifications are thought to resolve symptoms in up to 25% of non-pregnant people with uncomplicated gastro-oesophageal reflux disease [Madanick and Katz, 2006], but this evidence is based on small and inconclusive epidemiological studies [NICE, 2005].

What drug treatment should I prescribe?

- Antacids or alginates are recommended as first-line treatments if symptoms are relatively mild or are not controlled adequately by lifestyle changes.
  - Antacid products containing combinations of aluminium and magnesium are recommended on an 'as required' basis.
  - Calcium-containing products are recommended for short-term or occasional use.
  - Alginate products are particularly useful if symptoms of gastro-oesophageal reflux are dominant.
- If symptoms are severe, or persist despite treatment with an antacid or alginate, consider prescribing an acid-suppressing drug:
  - Ranitidine is an established drug but is not licensed for use in pregnancy.
  - Omeprazole is a more effective alternative. It is licensed for use in pregnancy, but there is less experience of its use in this context.

Clarification / Additional information

Further information on specific drugs and their use in pregnancy is provided by the UK Teratology Information Service (UKTIS), formerly the National Teratology Information Service (NTIS), (part of the Regional Drug & Therapeutics Centre — www.nyrdtc.nhs.uk, telephone: 0844 892 0909).

Antacids and alginates:

- A variety of antacids are available on prescription or over-the-counter. The choice of product should be made according to the woman's preference. However, products containing sodium bicarbonate and magnesium trisilicate are not recommended.
- For more information on the antacids available, and their contraindications and adverse effects, see section on Antacids and alginates in Prescribing information.

Acid-suppressing drugs:

- For information on the dosing regimens, contraindications, and adverse effects of ranitidine and omeprazole, see Prescribing information.
- Only ranitidine and omeprazole are recommended for the treatment of dyspepsia in pregnant women. Other histamine antagonists (cimetidine, famotidine, and nizatidine) and proton pump inhibitors (esomeprazole, lansoprazole, pantoprazole, and rabeprazole) should be avoided.

Basis for recommendation

Antacids and alginates:

- Antacids relieve symptoms of dyspepsia by neutralizing stomach acid, and alginates protect the oesophagus by forming a protective 'raft' when they come into contact with stomach acid. Most evidence for their safety and effectiveness in pregnancy is derived from historical use, as there is a lack of evidence from controlled trials.
- **Antacids** are often not licensed specifically for use in pregnant women, but most are considered to be safe. The choice of antacid should be made according to individual preference, although some products should be avoided:
  - Products containing magnesium or aluminium are generally preferred. They have limited absorption and have caused no teratogenic effects in animal studies [Schaefer, 2001]. However, aluminium products have a tendency to cause constipation, and magnesium products may have a laxative effect [BNF 54, 2007].
  - Products whose principal ingredient is a calcium salt are widely available over-the-counter, but are only recommended by CKS for short-term or occasional use. Calcium products have a limited duration of action, and have been reported to cause acid rebound reflux on discontinuation [Sweetman, 2005], although this has been refuted as being a calcium-specific effect [Texter, 1989]. At very high doses, calcium can cause milk-alkali syndrome [American Gastroenterological Association, 2006].
  - Products containing sodium bicarbonate or magnesium trisilicate (a common constituent of magnesium-only products) should be avoided as they can precipitate metabolic alkalosis and fluid overload [Ali and Egan, 2007] or cause serious adverse effects in the fetus [Madanick and Katz, 2006].

- **Alginates** are particularly useful where reflux symptoms predominate, as they physically block acid from entering the oesophagus. Some alginate products, such as Gaviscon®, are preferred as they are specifically licensed for use in pregnancy [ABPI Medicines Compendium, 2005; ABPI Medicines Compendium, 2007].

Acid suppressing drugs:

- **Ranitidine** is an H_2-receptor antagonist, and indirectly prevents the secretion of acid into the stomach. Most evidence for the safety of ranitidine comes from observational studies, although ranitidine has been an established choice in pregnancy for many years with no reports of harm to the fetus. There is only limited direct evidence for the effectiveness of ranitidine in pregnancy; however its efficacy can reasonably be extrapolated from studies conducted in the general population.
- **Omeprazole** is a proton pump inhibitor (PPI) and directly prevents the production of acid in the stomach. There are no controlled trials addressing the safety of omeprazole in pregnancy; the best available evidence comes from numerous observational studies. Likewise, evidence for the effectiveness of omeprazole in treating dyspepsia in pregnancy is extrapolated from studies in the general population, where it is known to be more effective than ranitidine [Christopher, 2005].
- **CKS does not recommend a preference of ranitidine or omeprazole** in the treatment of dyspepsia in pregnancy; both are reasonable choices.
  - Ranitidine is recommended first-line by most experts [Madanick and Katz, 2006; Ali and Egan, 2007]. This is because it is more established than omeprazole, with more overall confidence in its safety during pregnancy. However, it is not specifically licensed for this purpose [ABPI Medicines Compendium, 2009].
  - Omeprazole is a newer drug and therefore there is less experience with it. However, some experts believe it is a suitable choice, arguing that if the drug is safe to use second-line, then it should be safe to use first-line [Christopher, 2005]. In a review of the use of proton pump inhibitors (PPIs) in pregnancy, UK Medicines Information concluded that 'PPIs are a reasonable therapeutic option in pregnancy' [UKMi, 2007]. In addition, omeprazole is specifically licensed for use in pregnancy [ABPI Medicines Compendium, 2008].

When should I refer a pregnant woman with dyspepsia?

- Refer *urgently* to a gastroenterologist if there are alarm features, such as: chronic gastrointestinal bleeding; progressive unintentional weight loss; progressive difficulty swallowing (dysphagia); or persistent vomiting.
- Refer *non-urgently* to a gastroenterologist if:
  - Symptoms do not adequately respond to antacids, alginates, ranitidine, or omeprazole.
  - The woman is unable to eat sufficiently because of symptoms.
  - The diagnosis is in doubt (e.g. biliary colic).
  - There is a previous history of peptic ulcer disease; Barrett's oesophagus; or known dysplasia, atrophic gastritis, or intestinal metaplasia; and symptoms are inadequately controlled on usual medication.
- Refer to an obstetrician if symptoms suggest a pregnancy-related disorder other than dyspepsia (e.g. HELLP syndrome [haemolysis, elevated liver enzymes, and low platelets], pre-eclampsia).

Clarification / Additional information

- The classical alarm features of weight loss, an epigastric mass, or iron deficiency anaemia may be difficult to interpret in pregnancy.
- An endoscopy can be safely undertaken in pregnancy, but is generally avoided unless symptoms are severe, there is diagnostic uncertainty, or there are alarm features suggesting gastrointestinal bleeding.

Basis for recommendation

- CKS could find no UK guidelines on referral criteria for dyspepsia in pregnancy. These recommendations are based on expert opinion [Ali and Egan, 2007], and extrapolated from the National Institute for Health and Clinical Excellence guidance *Dyspepsia: Management of dyspepsia in adults in primary care* [NICE, 2005].

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Prescribing information

Important aspects of prescribing information relevant to primary healthcare are covered in this section specifically for the drugs recommended in this CKS topic. For further information on contraindications, cautions, drug interactions, and adverse effects, see the electronic Medicines Compendium (eMC) (http://emc.medicines.org.uk), or the British National Formulary (BNF) (www.bnf.org).

Antacids and alginates

What should issues should I consider before prescribing antacids or alginates?

- Antacids and alginates are considered safe in pregnancy when used at the correct dosage, despite a lack of evidence from controlled or observational studies. They are considered to be an unclassified risk in pregnancy by the United States Food and Drug Administration [American Gastroenterological Association, 2006], and pregnancy is not listed as a contraindication or caution to antacid use in the British National Formulary (BNF) [BNF 54, 2007]. Some products, such as Gaviscon®, are licensed for use in pregnancy [ABPI Medicines Compendium, 2005; ABPI Medicines Compendium, 2007].
- The recommended antacids and alginates are listed in Table 1. Liquids are generally preferred as they are considered more effective [BNF 54, 2007], and tablets are not as widely available on the NHS.
- Antacids and alginates are usually used as required or just before symptoms are expected (e.g. before meals and sleep).
  - Taking antacids with food may prolong their duration of action.
  - Antacids may impair the absorption of some drugs, and they can prevent the absorption of iron supplements. If an interaction is anticipated, the drug should ideally be taken at least 2 hours after the antacid is used.
- Antacids and alginates are well tolerated with few adverse effects when used at the correct dosage:

- Magnesium products tend to cause diarrhoea, whereas aluminium products cause constipation [BNF 54, 2007]. Taking a product with both minerals may alleviate these symptoms, although CKS found no evidence to support this.
- Some alginate products have a high sodium content. If hypertension or pre-eclampsia is likely to be problematic, it may be better to avoid these, although there is a lack of evidence to support this [Duley, 2004].

Table 1. Antacid and alginate products recommended for prescription by CKS.

Product type	Active ingredients and form	Proprietary names
Combined magnesium and aluminium (co-magaldrox)	Magnesium hydroxide, dried aluminium hydroxide suspension	Maalox® Mucogel®
Combined alginate products	Sodium alginate combined with various ingredients, including calcium carbonate, potassium bicarbonate, magnesium carbonate	Gaviscon® Advance* Peptac® Rennie® Duo*

* Licensed for use in pregnancy.

Ranitidine

What issues should I consider before prescribing ranitidine?

- Ranitidine is not licensed for use in pregnant women, but is considered safe on the basis of several years of use without incident, and supporting evidence from observational studies.
  - The British National Formulary (BNF) states 'Manufacturer advises avoid unless essential, but not known to be harmful' [BNF 54, 2007]. This is in accordance with the product license stated in the Summary of Product Characteristics [ABPI Medicines Compendium, 2009].
  - It is classed as a group B drug in terms of risk to pregnancy by the United States Food and Drug Administration (i.e. 'animal studies shown no risk but human studies inadequate or animal studies show some risk not supported by human studies') [Ali and Egan, 2007].
- CKS recommends the usual dosage of ranitidine; 150 mg, twice a day [Schaefer et al, 2007]. This is consistent with an RCT which found a lower dosage (150 mg, once a day) to be ineffective

[Larson et al, 1997]. If this dosage provides insufficient protection, consider switching to omeprazole or seeking specialist advice.

- Ranitidine is well tolerated by most women. Some adverse effects were reported following post-marketing surveillance (rather than data from controlled trials, so they were not necessarily causal associations) and are estimated to occur rarely (affecting less than one person in 1000) [ABPI Medicines Compendium, 2009].

Omeprazole

What issues should I consider before prescribing omeprazole?

- Omeprazole is licensed for use in pregnancy [ABPI Medicines Compendium, 2008] and is likely to be safe for use in all trimesters:
  - The British National Formulary states it is 'not known to be harmful (in pregnancy)' [BNF 54, 2007].
  - It is considered to be a class C drug in pregnancy by the United States Food and Drug Administration (i.e. 'Animal studies show risk but human studies are inadequate or no studies in humans or animals'). This is in contrast to the other proton pump inhibitors (namely esomeprazole, lansoprazole, pantoprazole, and rabeprazole), which are all class B [Madanick and Katz, 2006]. However, this classification is based on animal studies where very high doses were found to be teratogenic; recent evidence from observational studies in humans show that the drug is unlikely to be harmful to the fetus.
- CKS recommends the use of standard doses of omeprazole as used for other people with acid reflux disease, as there is an absence of evidence on dosage in pregnancy from controlled trials [ABPI Medicines Compendium, 2008]. This is a relatively conservative regimen, using low doses. The maximal effect develops after 5 days [Christopher, 2005].
  - The starting dose is 10 mg, once a day [Christopher, 2005].
  - This can be increased to 20 mg, once a day, if symptoms are not fully improved after 5 days or if they return.
  - If symptoms persist, seek specialist advice.

- Omeprazole is well tolerated. The most common adverse effects are headache or gastrointestinal effects (e.g. diarrhoea), including symptoms often seen in pregnancy (e.g. nausea and vomiting). It therefore may not be clear if it is the drug that is causing these adverse effects [ABPI Medicines Compendium, 2008]. If in doubt, stop the drug, and seek specialist advice if symptoms are severe or persistent.

- Advise that:

  - The best available evidence suggests that omeprazole is a safe treatment in pregnancy, and the baby will not be harmed by its use.
  - If symptoms are severe, treating symptoms will lead to a more fulfilling and pleasant pregnancy.
  - Treatment can usually be discontinued after delivery as the condition resolves spontaneously.

- Adverse effects are unusual with omeprazole and rarely serious. If severe gastrointestinal symptoms or headache begin shortly after starting the drug, advise the woman to return for advice.