

Bariatric surgery patients and their medicines

There has been a steady increase in bariatric surgery¹ since the National Institute of Health and Care Excellence (NICE) published its clinical guideline (CG) on obesity in 2006.² As part of the medicines optimisation process post-surgery, it is important to consider how bariatric surgery can affect the medicines a patient is taking and also the effects of that particular medicine on the patient. Bariatric surgery can cause changes in the pharmacokinetics of medicines as they go through the altered digestive system. In addition, bariatric patients often have co-morbidities and associated complex polypharmacy that may be affected by weight loss. These changes need careful consideration as first-line choices of medication may no longer be suitable to meet the patient's needs.

Recommendations

The effects of bariatric surgery can vary between patients but some general recommendations for managing medication are as follows:

- Review patient's medication regularly.
- Monitor for decreased efficacy of medications.
- Monitor for side effects and signs of toxicity, a possible result of increased bioavailability.
- If efficacy is reduced consider change of formulation or route or alternative medications for the same indication with more favourable pharmacokinetics.
- Doses of medications for chronic conditions, e.g. antihypertensives and diabetic medication, may decrease as weight loss occurs so these medicines should be regularly evaluated.
- Staggering of doses, particularly of liquid formulations, may be necessary due to the reduced capacity of the stomach.
- Avoid effervescent, enteric coated and sustained or delayed release formulations.
- Avoid drugs that potentially damage gut mucosa, e.g. non-steroidal anti-inflammatory drugs (NSAIDs), bisphosphonates and aspirin.
- Be cautious with drugs with a narrow therapeutic index.
- Discuss any drug changes with the patient and communicate them to other health professionals involved in the patient's care including the community pharmacist dispensing the medicines.

Background

The NICE CG43 on obesity recommended bariatric surgery as a treatment option for adults and children with a BMI of 40kg/m² and as a first-line option for adults with a BMI > 50kg/m² in whom surgical intervention is considered appropriate.²

However, the NHS England policy for commissioning complex and specialised obesity surgery, published in April 2013, states that patients with a BMI of 50kg/m² will also need to fulfill the other criteria for eligibility for bariatric surgery. These criteria are outlined in the policy along with what should be considered when evaluating the risk:benefit ratio of the surgery for the individual.³

The proportion of adults that are morbidly obese with a BMI of 40kg/m² or more has risen. A CCG covering a population of 500,000, would be expected to have around 8,000 adults with morbid obesity.³

Clinical evidence

The three main types of bariatric surgery are gastric bypass, gastric band and gastric sleeve.

Gastric bypass surgery

Gastric bypass surgery is irreversible and involves creating a gastric pouch at the top of the stomach, either by stapling or vertical banding or by removing portions of the stomach. The gastric pouch is then connected to the ileum, bypassing the duodenum and the jejunum. Calorie and nutrient absorption is substantially reduced.^{4,5}

Impact on medicines:

- The dissolution and disintegration rate, as well as the absorption of drugs is affected by gastric bypass.
- Drugs in aqueous solution are more rapidly absorbed than those in oily solutions, suspensions or solid forms.
- The reduced size of the stomach results in much less hydrochloric acid (HCl) being produced. This increase in pH means increased solubility of more basic (higher pH) drugs and decreased solubility of acidic (lower pH) drugs. This in turn affects absorption. Higher pH can also reduce the disintegration of some solid formulations.^{6,7}
- The size of a tablet is usually only an issue if it is very big (generally a diameter larger than 10mm) as it can potentially get stuck and remain undissolved in the gastric pouch.
- The loss of so much of the upper small intestine and its associated villi and microvilli means that there is a lot less surface area over which absorption can occur. Drugs that are mainly absorbed in the upper intestine will have a reduced bioavailability in gastric bypass patients.^{6,7}
- Bypassing the upper small intestine reduces the mixing of drugs with bile salts thus lipophilic drugs will have decreased absorption.⁷

Gastric band surgery

During gastric band surgery an adjustable band is placed around the top part of the stomach to create a small pouch. This procedure is reversible. The band is attached via an access port to a thin tube that runs under the skin to sit, usually, below the breastbone. This tube can be filled with fluid to reduce the diameter of the stoma between the stomach and the pouch created by the band. The narrower the stoma, the longer it takes for the pouch to empty into the body of the stomach so patients feel fuller on smaller portions of food and for longer.

Impact on medicines:

- The size of a tablet or capsule may be significant but a gastric band does not affect the absorption of drugs.
- If a tablet does get stuck in the pouch, the band can be loosened to allow passage into the stomach.^{4,5,8,9}

Gastric sleeve

A gastric sleeve is irreversible and involves the removal of up to 75% of the stomach. Appetite is reduced but the effect on absorption is far less than it is with gastric bypass surgery.^{4,5}

Impact on medicines:

The dissolution and disintegration of tablets and capsules might be affected by the smaller size of the stomach and the subsequent reduction in hydrochloric acid production.^{6,7}

Dealing with the impact of bariatric surgery on medicines

Solid dosage forms	Refer to 'PrescQIPP Bulletin 48: Liquid formulation requirements in bariatric surgery patients' http://www.prescqipp.info/bariatric-specials/viewcategory/177
Sugar containing medicines	To minimize dumping syndrome in gastric bypass patients, avoid products (including over-the-counter medicines) that contain a large amount of sucrose, corn syrup, lactose, maltose, fructose, honey and mannitol. ^{8,10}
Effervescent tablets	Effervescent formulations should be avoided in bariatric patients as the build-up of gas trapped in the pouch can be uncomfortable for the patient. The excess sodium in these formulations is also not appropriate for bariatric patients with hypertension. ¹⁰
Big volumes	The reduction in the capacity of the stomach can mean that doses need to be staggered, particularly of liquid formulations. Consider licensed higher strength liquid formulations to reduce the volume of each dose.
Acidic formulations	<p>Disintegration and dissolution usually occur in the stomach and are rate-limiting steps of drug absorption and bioavailability. Gastric mixing is reduced in the smaller pouch. Tablets are usually formulated to dissolve in an acidic environment but the increased pH of the pouch alters this process so the drug behaves differently than predicted. The solubility of more basic drugs is increased while that of acidic drugs is decreased. The disintegration of solid dosages forms is also decreased. Examples of drugs affected are rifampicin, digoxin, simvastatin, ketoconazole and iron supplements.^{6,7}</p> <p>With iron supplements co-administering ascorbic acid converts the iron into an absorbable ferrous form. Another solution is to use an alternative salt, e.g. calcium citrate, will be better absorbed than calcium carbonate.^{6,7}</p>
Sustained/delayed release or enteric-coated preparations	<p>Formulations with prolonged dissolution times (e.g. sustained release, long-acting, modified release, extended release, enteric coated) should be avoided as they can pass through the altered gastrointestinal (GI) tract of gastric bypass patients before absorption is complete. They will have a reduced bioavailability so should be replaced with immediate release formulations.^{6,7}</p> <p>These preparations should not be crushed or split.</p>
Lipophilic drugs	The reduction in mixing with bile salts will result in changes in volume of distribution of highly lipid-soluble drugs. Lipophilic drugs, for example ciclosporin, phenytoin, rifampicin, and levothyroxine, will have decreased absorption. ⁷ These drugs will require close monitoring and possibly dose adjustments.

<p>Drugs damaging to gut mucosa</p>	<p>Increased potential of GI perforation by bisphosphonates (drugs that are usually taken with a full glass of water) due to reduced stomach size. However, bariatric surgery patients are at risk of osteoporosis due to reduced calcium absorption. Possible alternatives to oral bisphosphonates are raloxifene, denosumab, or teriparatide and local commissioning arrangements should take this group of patients into consideration.^{6,10}</p> <p>Avoid NSAIDs or aspirin as the risk for GI bleeds, ulcers or perforations is increased.^{6,10}</p> <p>Avoid diuretics as they can precipitate potential complications in patients who are dehydrated or have prolonged nausea or vomiting.</p>
<p>Malabsorption</p>	<p>In gastric bypass the sites of absorption for some vitamins and minerals is bypassed, for example calcium is absorbed in the duodenum. The result is deficiency of the vitamin or mineral. Substituting calcium carbonate with calcium citrate can increase calcium absorption in these patients.^{10,11}</p> <p>Deficiencies in fat soluble vitamins, i.e. vitamins A, D, E, K, occur due to fat malabsorption in gastric bypass patients. These patients will need life-long supplementation of these vitamins.^{10,11}</p> <p>The level of parietal cells in gastric bypass and gastric sleeve patients is reduced due to the loss of stomach. This means that less intrinsic factor is secreted so absorption of vitamin B12 is reduced. Monthly vitamin B12 injections can be an effective alternative route of administration.^{10,11}</p> <p>Deficiencies are less likely in gastric band patients.</p>

Implementation aids

The effects of bariatric surgery on the absorption of some commonly prescribed medicines are listed in the table in Appendix 1.⁶

Practice pharmacists are well placed to review medications of bariatric surgery patients regularly as they have access to patient records, including blood results. Appendix 2 includes points to consider in these reviews. Attachment 1 (Word template) is a useful tool to complete during reviews and give to patients to share with other healthcare professionals and re-enforce key messages discussed.

Attachment 1 is available for download here:

<http://www.prescgipp.info/resources/viewcategory/226-bariatric-patients-and-their-medicines>

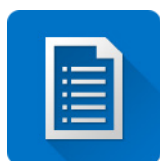
Summary

Medicines should be tailored to the individual bariatric surgery patient and their efficacy should be assessed on a regular basis. Practice pharmacists are well placed to perform this role. Any drug changes must be communicated to the patient and the health professionals involved in their care.

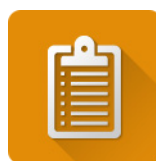
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Additional PrescQIPP resources



Briefing



Patient review aid

Available for download here:

<http://www.prescqipp.info/resources/viewcategory/226-bariatric-patients-and-their-medicines>

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Appendix 1: Commonly prescribed drugs that have the potential for decreased absorption in patients who have undergone bariatric surgery⁶

Drug	Possible site(s) of absorption	Management
Enalapril	Hydrolyzed to active form, enalaprilat, in stomach; absorbed in small intestine	May exhibit decreased activity; consider other angiotensin-converting-enzyme inhibitors (except ramipril – see below)
Ketoconazole	Likely absorbed in stomach because acidic medium required for absorption	Absorption likely to be negligible; consider alternative agents
Lamotrigine	Likely stomach and proximal small intestine due to rapid and complete absorption	Monitor for and advise patients of decreased efficacy
Metformin	Slowly and incompletely absorbed in duodenum	Increased monitoring of blood glucose; drug requirements can decrease as weight loss occurs
Metoprolol tartrate	Absorbed rapidly and completely, indicating stomach and duodenum	Monitor blood pressure; medication requirements may decrease as weight loss occurs
Niacin	Primarily absorbed in duodenum	Administer with low-fat snack to maximize absorption
Olanzapine	Stomach	Ensure that patient is being monitored by the mental health team for decreased efficacy; switching to orally disintegrating tablet will not increase absorption (still absorbed in stomach)
Quetiapine fumarate	Exact location unknown, but likely stomach and duodenum due to rapid absorption	Ensure patient is being monitored by the mental health team for decreased efficacy
Ramipril	Unknown; decreased absorption documented in patients with steatorrhea and malabsorption	Consider other agents; monitor blood pressure in the postoperative period; need for antihypertensives may decrease as weight loss occurs
Simvastatin	Absorption site unknown, but must be hydrolysed to the active form in stomach	Consider alternative statin; monitor serum lipids
Zolpidem	Absorbed rapidly and completely; absorption affected by food	Absorption time may increase, resulting in delay to effect; take on an empty stomach. Review for continued need of hypnotic- should be short term use only.

Appendix 2: Medication review of bariatric patients – Things to consider

Consider	Note	Actions that can be performed by the pharmacist
Medications that were stopped before surgery	<ul style="list-style-type: none"> Do they need to be restarted? What are the restart dates? 	<ul style="list-style-type: none"> » When the patient first comes in after surgery do a medicines reconciliation of what they were prescribed and taking before the surgery and their current medications. » Speak to the patient about whether they are aware of when medicines need to be restarted. » Consider a medicines use review (MUR) in appropriate patients.
Solid medications that were converted to liquid formulations	<ul style="list-style-type: none"> Can they be reverted to solid preparations? If not after this review, what date should they revert back? Do the doses need to be staggered due to the reduced capacity of the gastric pouch? 	<ul style="list-style-type: none"> » Ask if the patient is taking any other tablets and whether they feel able to take any small tablets (particularly where liquid medicines being used are specials). » If the dose needs to be staggered check if there is an alternative licensed liquid formulation where a lower dose could be taken.
Medications that are being crushed	<ul style="list-style-type: none"> Can they be taken whole again? If not after this review, what date should they revert back? 	<ul style="list-style-type: none"> » Ask the patient if they are able to swallow tablets without any difficulty. » When they are ready, inform the GP that tablet formulations will be appropriate to prescribe again.
Efficacy of medications since surgery	<ul style="list-style-type: none"> Are any of the medicines less effective? Are there more side-effects or signs of toxicity (possible increased efficacy)? Does there need to be any dose adjustments? 	<ul style="list-style-type: none"> » Ask patient how they are feeling. If appropriate, take physical measurements such as blood glucose testing or blood pressure (BP). » Discuss and agree with patient whether side effects are a problem. » Ask patient if all healthcare professionals involved in their care, e.g. GP, mental health team, are aware of the surgery and whether they would be happy for you to liaise with them to discuss possible problems with medication.
Effect of weight loss	<ul style="list-style-type: none"> Are there any medications that are no longer needed? Do any doses need to be reduced? 	<ul style="list-style-type: none"> » Physical measurements such as BP and blood glucose testing will help assess this.
Discuss with patient	<ul style="list-style-type: none"> Medications stopped/started. Dose adjustments. Any other useful information e.g. over-the-counter (OTC) preparations that should be avoided. 	<ul style="list-style-type: none"> » MUR may be appropriate.