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Clinical Pharmacology
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Absorption of medicines following bariatric surgery

In Aotearoa New Zealand 1 in 3 adults (≥ 15 years) are obese (BMI ≥ 30 kg/m^2).[1] Around 2000 bariatric procedures are performed each year; approximately half are restrictive, and half are restrictive-malabsorptive.[2] Restrictive procedures e.g. gastric sleeve (GS), reduce the size of the stomach. Restrictive-malabsorptive procedures e.g. Roux-en-Y gastric bypass (RYGB), reduce the size of the stomach and bypass areas of the gastrointestinal tract such as the duodenum, jejunum, and some of the small intestine.

Following bariatric surgery physiologic and pharmacokinetic changes may affect medicines use and absorption. Most oral medicines will be adequately absorbed even when sections of the small intestine are bypassed. In some cases, switching formulations from solid to liquid or from sustained to immediate release may improve absorption or using non-oral routes of administration may be necessary e.g. sublingual, buccal, rectal. Clinical symptoms, biomarkers and drug concentrations can be monitored to assess effects of medicines. Reduced absorption post-surgery may recover over time.

Recommendations for some medicines to help guide oral dosing [3–7]

Medicines	Recommendations
Anticoagulants **Antiplatelets**	Increase anticoagulant monitoring to guide dosing post-surgery. • *Dabigatran etexilate:* low oral bioavailability (<10%) and acidic environment required for absorption. Monitor trough concentrations or thrombin clotting time (TCT). • *Rivaroxaban:* limited evidence suggests no dose adjustment required after bariatric surgery. Monitor trough concentrations or INR. • *Warfarin:* dose requirements may decrease immediately after bariatric surgery and then normalise to pre-surgery dose over following months. Monitor INR. • *Aspirin, clopidogrel:* no dose adjustment is required for antiplatelet agents.
Antidepressants	Routine dose adjustment is not recommended but some pharmacokinetic studies report lower concentrations and relapse after RYGB. • Decreased AUC (54%) 1 month post-RYGB for venlafaxine (n = 5), citalopram (n = 2), escitalopram (n = 2), sertraline (n = 2) and duloxetine (n = 1). AUC generally returned to baseline at 6 months.[8] • Similar AUC (±20%) for escitalopram 1, 6 and 12 months post-GS (n = 5) or RYGB (n = 4).[9] • Similar AUC (±21%) for venlafaxine (and active metabolite) (n = 10) from sustained-release capsules pre- and post-RYGB (3-4 months).[10]
Antihypertensives	Blood pressure treatment requirements can change after bariatric surgery. Monitor blood pressure and adjust dose accordingly. Be aware of diuretics and dehydration.
Blood-glucose lowering therapy	Diabetes treatment requirements usually decrease after bariatric surgery. Monitor blood glucose and adjust dose accordingly.
Bisphosphonates	IV route preferred (e.g. zoledronic acid). Oral alendronic acid has increased risk of adverse gastrointestinal effects and low oral bioavailability (<1%).
Digoxin	Monitor concentrations. Unchanged AUC and C_{max} for digoxin (n = 12) pre- and post-RYGB (3 and 12 months).[11]
Immunosuppressants	Monitor concentrations. • *Post-RYGB*: limited evidence suggests decreased AUC for tacrolimus, sirolimus and mycophenolate.(3) • *Post-GS*: increased AUC (46%-77%) for tacrolimus and mycophenolate (n= 12) after 1 year.[12]
Levothyroxine	Monitor thyroid function tests (TFTs) and adjust dose accordingly. Observational studies suggest most patients will need either no change or a reduction in levothyroxine doses.[4]
Lithium	Monitor concentrations.
NSAIDs	Avoid due to increased risk of adverse gastrointestinal effects.
Omeprazole	No dose adjustment required. Unchanged AUC for omeprazole (n = 36) in patients with prior RYGB (≥ 1 year) compared to healthy controls. The T_{max} was shorter (1 versus 4 hours).[13]
Oral Contraceptives	Oral contraceptives may not be reliable after bariatric surgery. Chronic diarrhoea may be present. Consider using non-oral options e.g. depot medroxyprogesterone.[14]
Statins	No dose adjustment. Monitor lipids, absolute cardiovascular risk, adverse effects e.g. muscle weakness/pain.
Tamoxifen **Aromatase inhibitors**	Post-RYGB an aromatase inhibitor or tamoxifen 40 mg daily (double dose) is recommended. Subtherapeutic concentrations with tamoxifen 20 mg daily (5 out of 6 cases) and therapeutic concentrations with 40 mg daily (4 out of 6 cases) post-RYGB. Anastrozole and letrozole (n = 4) adequately absorbed post-RYGB.[15]

AUC = area under the curve, C_{max} = maximum concentration, T_{max} = time to maximum concentration.

Key points

1. Manage each patient on a case-by-case basis. There is large inter- and intraindividual variability.
2. Monitor all patients for signs of efficacy and toxicity to help detect altered absorption. GS is less likely to affect absorption than RYGB.
3. Monitor all narrow therapeutic index medicines before and after surgery e.g. anticoagulants, immunosuppressants, lithium and digoxin.

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