

# Prescribing for a patient with reduced intestinal length

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## SUMMARY

Surgical interventions involving the gut may result in either a temporary or, in some cases, permanent stoma. If a significant length of small intestine has been resected, there may be impaired drug absorption.

Many factors, including the underlying disease, influence drug absorption after bowel resection. The drug dose or formulation may need to be modified to improve bioavailability.

Pharmacists can advise on formulations. Specialist advice from a multidisciplinary intestinal rehabilitation unit may be needed in cases of short gut syndrome.

## Introduction

Surgical management of a range of intestinal disorders often results in a shorter intestine. In some cases patients are also left with permanent stomas (ileostomies or colostomies). Drug prescribing can be a concern for these patients and their doctors, especially when undissolved tablets are observed in a stoma bag. In most cases the presence of a stoma is not the predominant factor influencing drug absorption, but there is a correlation between drug absorption and the length of remaining small intestine.<sup>1</sup>

Reduced intestinal length can have profound effects on both the pharmacokinetics and the bioavailability of oral medications. There is minimal literature in the area and problems of drug absorption can easily be overlooked in day-to-day practice. A lack of efficacy should not automatically be seen as a failure of a drug, rather a realisation that other factors crucial for effective drug absorption, some of which may be modifiable, could be involved.

## Drug absorption in the gastrointestinal tract

Although drugs can be absorbed throughout the entire gastrointestinal tract, most absorption occurs in the upper small intestine where the long villi increase surface area. This part of the gut has a relatively high blood flow and an optimal pH for drug

absorption. The large intestine has a minimal role in drug absorption, primarily confined to slow-release drugs or drugs where the primary effect is in the large intestine (such as 5-aminosalicylates).

Plasma drug concentration is dependent on bioavailability which reflects the rate and extent of drug absorption into the systemic circulation. Many factors that are particularly relevant to patients following intestinal resections can have a profound influence on drug absorption (Box).<sup>2</sup>

## Intestinal length

The most significant influence on drug absorption in the gastrointestinal tract is the surface area of the lumen. This can be of particular concern, especially if repeated resections have reduced the length of remaining small intestine. It can be difficult to assess how much small intestine remains in some patients and radiology is known to be misleading. In most patients the length of the remaining small bowel can only be estimated by reviewing previous operative reports.

Key lengths of residual small intestine are listed in the Table. An intact ileocaecal valve and the presence of a colon improves function.<sup>3</sup> Patients with less than these lengths are at risk of short gut syndrome, which results in compromised absorption of not only drugs, but also fluids, macro- and micronutrients. These patients universally have altered drug absorption, but in most cases are co-managed with an experienced gastroenterologist or intestinal rehabilitation centre. Some will require parenteral nutrition to survive.

## Presence of a stoma

Patients with a colostomy are unlikely to suffer significant problems with drug absorption as most drugs are absorbed in the small intestine. Normal

## Box Factors influencing drug absorption

Residual intestinal length and presence of a stoma  
Mucosal integrity of the remaining bowel  
Gastric emptying, intestinal transit, motility and concomitant use of antimotility drugs  
pH of gastric and intestinal lumen  
Drug formulation  
Drug dose

doses and formulations can be used for most patients. In patients with small intestinal stomas (jejunostomy or ileostomy), the ability to use drugs normally is largely dependent on the residual length of small intestine.

**Mucosal integrity of the remaining bowel**

Even when the remaining small bowel is of sufficient length, function can be impaired, especially in the presence of underlying disease. Crohn’s disease in particular is one of the most common indications for multiple intestinal operations and a stoma. Uncontrolled disease leads to complications which impact on drug absorption. These include active inflammation (reduces villi contact and luminal permeability) and stricturing (holds up tablets proximally). Subsequent reductions in the bioavailability of oral drugs such as azathioprine and budesonide can result in worsening Crohn’s disease and create a vicious cycle that leads to more inflammation, operations and reduced intestinal length. The option of administering parenteral drugs such as methotrexate, or anti-tumour necrosis factor drugs such as infliximab or adalimumab, should be considered.

Coeliac disease is another common disease in the community which can coexist in patients with short gut syndrome or stomas. Villous atrophy reduces the available area for the absorption of drugs, even if there is a minimal reduction in bowel length.

**Gastric emptying, intestinal motility and transit**

Gastric emptying is variable and highly dependent on a multitude of factors, including the presence of food (or enteral feeds), underlying diseases and drugs. Initial rapid transit of gastric contents may reduce dissolution times, but also reduces the time the drug is exposed to an acid pH.

Changes in gastric emptying may directly influence the rate of absorption of a given drug, but the effect is not always uniform. For example, when metoclopramide (which promotes gastric emptying) is administered concurrently, the absorption of digoxin is

reduced while the absorption of paracetamol, aspirin and tetracycline is increased. Other prokinetic drugs such as domperidone and erythromycin may have similar effects and are therefore best avoided.<sup>2</sup>

Drugs such as codeine and loperamide are often used to reduce intestinal motility and increase transit time in patients with a stoma. This strategy may be trialed in patients who experience impaired absorption of other drugs. The use of loperamide for this indication will often require higher doses than those usually prescribed.

**pH**

Proton pump inhibitors are often used in patients with a short gut to reduce the volume of upper gastrointestinal secretions. These drugs affect the gastric pH which can pose a problem for drugs dependent on an acidic environment for absorption or dissolution, such as ketoconazole.<sup>2</sup>

**Drug formulation**

In the absence of evidence, recommendations often need to be made based on first principles. If tablets or capsules emerge unchanged in the stoma output or stool, or if poor absorption is suspected, investigate if the drug can be crushed, opened or mixed with water or if there is an alternative formulation. Preference should be given to dispersible formulations if they are available. Formulations such as liquids, capsules and uncoated tablets are likely to be better absorbed. It may be necessary to avoid modified-release formulations (slow-release, controlled-release or sustained-release) or those with an enteric coating.

If a solid dose form is to be altered, there is a potential for its tolerability or efficacy to change. Consulting the product information or seeking advice from a pharmacist or medicines information service is recommended.

Before prescribing liquid preparations, consideration should be given to the osmolarity, excipient content and volume required. Some liquids have high osmolarities compared with gastrointestinal secretions. Giving hyperosmolar products can cause

Table Anatomical predictors of short gut syndrome

Resection	Residual small bowel length
End jejunostomy (no colon)	<100 cm
Jejunocolic anastomosis (partial colon)	<65 cm
Jejunioileocolic anastomosis (complete colon and ileocaecal valve)	<30 cm

Normal length of small bowel approximately 4.5 metres, large bowel 1.5 metres

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dose-related osmotic diarrhoea, abdominal cramps and vomiting. This can be particularly dangerous in patients whose electrolyte and fluid absorption may already be compromised by a shortened gut. Likewise, products containing sorbitol such as sodium valproate oral liquid can in theory cause diarrhoea. Diarrhoea is more likely to occur if these drugs are delivered directly into the duodenum or jejunum, such as via an enteral feeding tube. Adults often require large volumes of liquid if they are prescribed paediatric formulations. Although liquid preparations may enhance absorption, their use should be discontinued if significant symptoms develop.

In some situations an alternative route of administration such as transdermal, sublingual, buccal or parenteral may be preferred. For example, there are effective alternatives to the oral contraceptive pill, and transdermal opioids such as fentanyl patches can be used instead of sustained-release oxycodone or morphine.

**Drug dose**

A common strategy to improve drug bioavailability is to increase the prescribed dose – even beyond

that 'recommended'. This strategy is best used for drugs with an end result that can be monitored or are suitable for therapeutic drug monitoring. For example digoxin and lithium drug concentrations are measurable, while warfarin and beta blockers have effects which can be monitored (INR, heart rate).<sup>4</sup>

**Conclusion**

There is a potential for impaired drug absorption in patients with a shortened gastrointestinal tract. Most patients can be managed with simple measures such as selecting the appropriate formulation and dose of a drug and monitoring the outcomes of therapy. If doubt remains regarding the best way to use a drug, seek advice from a pharmacist or medicines information service. In patients who also have a short gut syndrome there is often a need for co-management with an experienced gastroenterologist, preferably in the multidisciplinary environment of an intestinal rehabilitation centre. <

*Conflict of interest: none declared*

**SELF-TEST QUESTIONS***True or false?*

7. Liquid formulations may cause osmotic diarrhoea in a patient with a stoma.

8. All patients with a stoma have short bowel syndrome.

*Answers on page 143*

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**Australian Council of Stoma Associations**

The Australian Council of Stoma Associations (ACSA) coordinates support services for people who have had ostomy surgery. In conjunction with the Australian Department of Health and Ageing, it manages the Stoma Appliance Scheme which supplies ostomy products to members.

ACSA collaborates with appliance suppliers and ostomy associations, advocates for those with inflammatory bowel disease, and produces a journal 'Ostomy Australia' which provides information on ostomy products and practice.

The state and territory associations offer assistance with appliances and supplies, through stoma therapy nurses. There are support groups in New South Wales, Victoria, Queensland, Western Australia and Tasmania.

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