Chronic Diarrhoea in IBS

Management of Chronic Diarrhoea
Chronic diarrhoea is a common symptomatic complaint of patients with functional gastrointestinal disorders. Patients may define chronic diarrhoea as loose stools, increased stool frequency and/or urgency, hence it is important to take a history to clarify what the patient means by “diarrhoea”. Functional causes of chronic diarrhoea include irritable bowel syndrome (IBS) and functional diarrhoea. IBS is characterised by the presence of abdominal pain, which is often relieved by defaecation. When abdominal pain is absent, the patient is considered to have functional diarrhoea.

Drugs Acting on Opioid Receptors
The opioid analogues, loperamide, diphenoxylate and codeine, are often used for treatment of chronic diarrhoea. These agents stimulate inhibitory receptors in the enteric nervous system, hence reducing secretions and peristalsis. A few randomised control trials have been conducted with loperamide in diarrhoea-predominant IBS (IBS-D) and Mixed IBS (IBS-M), albeit with small numbers. Loperamide was effective in improving stool frequency, consistency and urgency, but did not improve global symptoms of IBS. Other older studies have explored the role for diphenoxylate and codeine, showing efficacy in reduction of stool frequency and improving stool consistency. Overall, loperamide is preferred, due to potential anticholinergic sides effects with diphenoxylate and central narcotic effects of codeine.

Dietary Modification
Dietary therapy for functional gastrointestinal disorders is often an area of intense interest for patients. Patients often generate their own correlations between foods and symptoms, leading many to seek, usually unsupported, dietary remedies.

Of the myriad of diets available, the low FODMAP diet (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) has received the most scrutiny and rigorous scientific evaluation in recent years. In a randomised cross-over trial, IBS patients were provided a typical Australian diet or a low FODMAP diet in random order for 21 days. Patients receiving the low FODMAP diet had reduced overall gastrointestinal symptoms. In particular, patients of all IBS subtypes had greater satisfaction with stool consistency. Similarly, in a US study involving IBS-D patients, comparing the low FODMAP diet and a diet based upon modified National Institute for Health and Care Excellence guidelines (NICE), the low FODMAP diet led to reduced bowel frequency and urgency compared to baseline symptoms. Due to the complexities of the low FODMAP diet, dietitian guidance is highly recommended.

Probiotics
The role of probiotics in the management of IBS remains poorly defined. This is due to significant variability in probiotics strains and study design heterogeneity. A recently updated meta-analysis concluded that some specific probiotics may relieve symptoms of IBS although the evidence for their efficacy is weak.
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**Bile Salt Binders**
A systematic review has suggested that bile acid malabsorption may be present in up to one third of patients with IBS-D. Definitive diagnostic testing is often poorly accessible or costly, although an empiric trial of bile salt sequestrant, such as cholestyramine, may be helpful.

**Antibiotics**
There is increasing interest in the role of the gut microbiota in IBS. Manipulation of the microbiota in the treatment of IBS is also a current area of intense research. Rifaximin is a minimally absorbed antibiotic which has shown benefit in IBS without constipation in two large phase 3 randomised trials involving a total of 1260 patients. Patients treated with 2 weeks of rifaximin had significantly less global IBS symptoms, bloating and loose watery stools compared with placebo. Unfortunately, relapse of symptoms despite an initial response is common. Recent studies have shown that repeated treatment with rifaximin after initial relapse is safe and effective. The exact mechanism of action of rifaximin is poorly understood but may be related to underlying small intestinal bacterial overgrowth which has been linked with IBS.

**Gut Directed Hypnotherapy**
The brain-gut axis is increasingly recognised as a potential therapeutic target in functional gastrointestinal disorders. Gut directed hypnotherapy aims to control and normalise gastrointestinal function via suggestions to the subconscious mind. A recent randomised clinical study assessed the efficacy of gut directed hypnotherapy compared to the low FODMAP diet for the treatment of IBS. Although this study included all subtypes of IBS, patients who received gut directed hypnotherapy demonstrated significant improvement in stool consistency at 6 weeks. The response was on par with the low FODMAP diet and efficacy was maintained up to 6 months post treatment. Other clinical studies involving gut directed hypnotherapy have shown variable results for the specific control of diarrhoea in IBS. In the right hands, gut directed hypnotherapy remains an exceedingly safe, efficacious and durable treatment option for IBS-D.

**Antidepressants**
The brain-gut axis and abnormal central pain processing are important components of the pathophysiology of IBS, often with comorbid anxiety and depression. The use of low dose antidepressants aims to modulate these factors. There is high quality evidence that tricyclic antidepressants and serotonin reuptake inhibitors (SSRIs) are efficacious when treating IBS. Side effects of the anti-depressants can be harnessed to improve symptoms. For example, constipation is a common side effect for amitriptyline, a tricyclic antidepressant. Amitriptyline is therefore preferentially used in IBS-D for the added benefit of reducing diarrhoea.
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Serotonin Receptor Agonists/Antagonists
Serotonin (5-HT) is an important neurotransmitter in gastrointestinal motility, secretion and sensitivity. Ondansetron, a 5 HT3 antagonist, is widely used as an antiemetic with a well-established safety profile. There is emerging evidence for its use in IBS-D with improvement in stool consistency, frequency, urgency and bloating demonstrated in a recent randomised trial. Other 5-HT3 antagonists are not yet available in Australia.

References