GUT FEELING GASTROLAB NEWS FOR GPs

SPRING 2015

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Lactose Intolerance

The contribution of specific foods to the genesis of symptoms in irritable bowel syndrome (IBS) has been increasingly recognised in recent years. Specifically, the identification of highly fermentable, poorly absorbed short-chain carbohydrates called FODMAPs as a dietary trigger for functional gastrointestinal symptoms has significantly improved symptom management for many IBS sufferers.[1]

Lactose, a disaccharide found in mammalian milk, was the first carbohydrate to be recognised as important in IBS.[2] The enzyme lactase is required in the microvilli of the small bowel mucosa to split lactose into its component monosaccharides, glucose and galactose, for transport across the cell membrane. If lactase is absent or deficient (hypolactasia), unabsorbed lactose osmotically attracts fluid into the bowel lumen, and fermentation by colonic bacteria produces gas leading to luminal distention. The symptoms patients experience vary according to the quantity of lactose ingested and patients' ability to digest lactose, however symptoms of lactose intolerance include those typical of IBS such as abdominal pain, bloating, wind and diarrhoea.

Up to 70% of the world population has primary hypolactasia, the most common type of lactase deficiency (hypolactasia secondary to certain gastrointestinal illnesses and congenital alactasia being the other two).[3] Ethnic origin affects the frequency of lactase deficiency. In adults, lactase deficiency occurs in approximately 2% of Northern Europeans, 6% of Caucasian Australians, and is particularly prevalent in those of Asian or African background (60-95%), and to a lesser extent, those from a Middle Eastern, South American and Southern European background (>50%).[4]

Despite the prevalence of hypolactasia, it often remains undiagnosed and has the potential to cause some morbidity. Symptoms of lactose intolerance may present some time after the ingestion of lactose, and lactose is hidden in many common foods and pharmaceuticals; therefore the patient may not connect the symptoms to dietary factors. Self-diagnosis has been shown to have a poor positive predictive value: one study showed that one-third of self-reported milk intolerants did not actually have lactose malabsorption when assessed by hydrogen breath testing.[5] Patients may also confuse lactose malabsorption with milk allergy (due to development of IgE antibodies against the milk proteins casein, alpha lactalbumin and/or beta-lactoglobulin), a much rarer condition than lactose malabsorption in adults. Patients who describe themselves as lactose intolerant may self-initiate elimination diets that exclude all milk and dairy products to control their symptoms. To avoid unnecessary exclusion and potential dietary deficiencies a diagnosis of lactose malabsorption should always be substantiated with objective evidence where possible.

Various clinical tests are available to investigate lactase deficiency. The lactose hydrogen/methane breath test is currently considered to be the most cost-effective, non-invasive and reliable test to diagnose lactose malabsorption, with superior diagnostic properties compared to other modalities such as faecal reducing substances, lactose blood tolerance test, and jejunal biopsy.[6] Testing usually involves taking 25g lactose orally (equivalent to that found in 500 mL of milk) and measuring breath hydrogen/methane levels over the following 3 hr. With the development of breath test kits that allow convenient self-collection (at home or work), and which are just as reliable as testing in clinic, a diagnosis of lactose malabsorption is now even easier.

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Hepatitis C Treatment Revolution

The treatment of hepatitis C is currently undergoing a dramatic change. Within the next few months, many of the estimated 230,000 people living in Australia with chronic hepatitis C virus (HCV) may be able to access new treatment regimens. These new combination therapies involve tablets only, have few side effects, last between 8 and 24 weeks and lead to cure rates approaching 100%. Sustained virological response (SVR) or cure is defined as the absence of HCV RNA by sensitive polymerase chain reaction (PCR) six months after therapy is completed. Although such high SVR rates and favourable side effect profiles may sound too good to be true, these direct-acting antivirals (DAAs) have been available in USA, UK, Europe and parts of Asia for almost two years and are expected to be available on the Pharmaceutical Benefits Schedule (PBS) in the coming months.

Many patients (and clinicians) will be familiar with the standard therapy for chronic HCV infection available since 2003, which involves 48 weekly injections of pegylated interferon (pegIFN) and twice daily tablets of ribavirin. The treatment is legendary for its side effects of fatigue, fever, rigors, depression, anxiety, exhaustion and many other unpleasant experiences. Clinicians and patients have been prepared to endure these difficulties in pursuit of the chance of SVR, which could be achieved in up to 70% of people completing therapy.[1] However, the unfavourable side effects meant that treatment was intolerable for many people and treatment uptake was low. Many others were excluded from pegIFN treatment due to medical or psychiatric comorbidities such as severe liver disease, auto-immune diseases or severe depression. Increasing treatment uptake is vital to improve lives and reduce the risk of decompensated cirrhosis and liver cancer.[1]

Over the past few years we have seen the development and successful introduction into clinical practice of a number of new therapies to cure HCV. Initially these have been added to pegIFN and ribavirin, leading to increased cure rates and shorter treatment duration. However, the need for pegIFN and ribavirin excluded many people from therapy.

Telaprevir and Boceprevir and subsequently Simeprevir were approved only for genotype 1, caused additional side effects and introduced new complexities to treatment. Genotype 1 HCV is the most common genotype in Australia (approximately 55%) and can be sub-divided into 1a and 1b. Genotype 3a is also common (35%) with the balance made up of genotype 2, genotype 4 and rarely genotypes 5 and 6.

Earlier this year, the Pharmaceutical Benefits Advisory Committee (PBAC) recommended PBS listing of several new DAAs for HCV which treat all the recognised genotypes.[2,3] Sofosbuvir (Sovaldi®), Daclatasvir, Ledipasvir (co-formulated with Sofosbuvir as Harvoni®) and another combination of medications known as AbbVie 3D regimen (Viekira Pak®) all await PBS listing. These regimens have achieved cure rates of 97-100%, including people with cirrhosis, although slightly different regimens are used according to genotype (even subtype 1a versus 1b).[4-6]

These exciting new developments offer a chance of cure to people with medical and psychiatric comorbidities, a range of HCV genotypes, underlying cirrhosis or previous unsuccessful treatment experience. New DAA therapy is not yet available via the PBS in Australia, but is anticipated in the next few months. In the meantime, HCV genotype and viral load are useful tests that may help guide decisions around HCV therapy. It is now time to encourage all our patients living with HCV to consider treatment.

In summary

1. New all-oral, interferon-free medicines for HCV are imminent, with high cure rates, shorter treatment duration and fewer side-effects than existing therapies
2. Almost everyone will be treatable, and chance of cure is high (~95%) even in cirrhosis or prior treatment failure
3. It will be important to know HCV genotype, viral load (if genotype 1) and subtype (i.e. genotype 1a vs 1b) as this may affect choice and duration of therapy. GPs may need to retest or test genotype for first time.

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