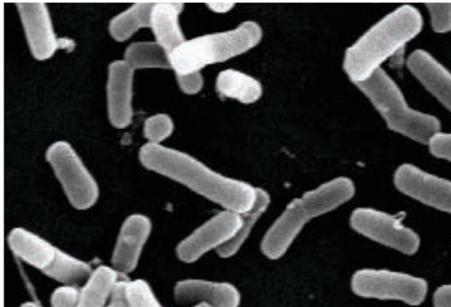


Practical Insights: Probiotics & Diarrhoea



Infectious gastroenteritis is still the leading cause of mortality and morbidity in children among many nations. Diarrhoea, its common symptom, is a terrible experience that we can all identify with. In our developed society, the discomfort and inconvenience from diarrhoea result in the loss of productive work days and quality of life. Other than the usual oral rehydration salts and anti-motility drugs, probiotics have gradually been introduced as a treatment for diarrhoea. As probiotics enter into the mainstream medical practice, let us explore further into the recent clinical reports on how these friendly microorganisms work.

With more research ventures into investigating the uses of probiotics, the entire healthcare community are now more aware and actively prescribing them. Based on a 2006 article in the Expert Review Anti-Infective Therapy, **the significant clinical effectiveness of probiotics are in their usage on the prevention of lactose-intolerance, treatment of acute diarrhoea, reducing antibiotic-associated gastrointestinal side effects, and the prevention and treatment of allergy manifestations.** As we focus on acute diarrhoea among children and adults in this issue, let us first look into some of the recent clinical evidences of probiotics in common acute diarrhoea and thereafter the possible mechanisms of action of probiotics.

Clinical evidences

In 2006, a meta-analysis on the efficacy of probiotics in the prevention of acute diarrhoea was published in the Lancet Infectious Diseases. It comprehensively examined the effectiveness of probiotics by different age groups, setting, causes of diarrhoea, probiotic strains and formulations. The overall analysis suggested

that probiotics are effective in the prevention of diarrhoea. In particular, **results showed that probiotics reduced acute diarrhoea of diverse causes by 34%. Furthermore, the decrease in antibiotic-associated diarrhoea emerged significantly at 52%.**

Several other studies have revealed relatively more promising results of probiotics in acute diarrhoea in children than adults. In fact, the best clinical use of probiotics in children is for acute watery diarrhoea of viral origin. Its support on viral gastroenteritis is more significant than infections caused by bacteria and parasites.

More clinical support in children than adults' diarrhoea may be due to a large number of factors such as the difference in the nature and composition of native flora, adhesion rates of probiotics strains, etc. The underlying reason for the better documentation in viral infection may not be entirely known at this moment. Our current understanding on the documented modes of action of probiotics may shed more light into the intrigue and diverse actions of probiotics.

Mechanisms of action

Warzone! That is probably the one word we can use to describe the situation among our intestinal flora. The knowledge on the consumption of health beneficial bacteria to outnumber the pathogenic ones is a widely accepted and known fact. What is more? In an article published in June 2007, the following mechanisms were cited: 1. Modification of the environmental conditions, 2. Competition for nutrients and adhesion sites. 3. Production of antimicrobial metabolites and 4. Modulation of the immune and non-immune defense mechanisms of the host. This also clearly coincides with the ones mentioned in the 2001 paper released from the Joint FAO/WHO expert consultation on probiotics.

Among the probiotic formulations readily available in Singapore, they consist of either live or killed microorganisms. Theoretically, the live ones will be able to do more in terms of producing antimicrobial substances and competing with the pathogenic microbes for nutrients. For instance, *Saccharomyces boulardii*, a well-studied non-pathogenic yeast, produces a 54-KDa protease that can neutralise certain bacterial toxins. It is also noteworthy that mechanisms of actions are specific to the strains that are being used. **The way each strain works is different from another, and thus varies in their effectiveness on various indications.**

One thing that we are sure...

The exact way on how different strain transits, survives, acts and exits may still remain unclear. However, we can all be confident that the efficacy of probiotics in the treatment of diarrhoea is not one that is without proper clinical support. As more is being done in the scientific venture, maybe one should not avoid but be part of this next big thing.

Quick Facts

There are ten times as many bacteria as human cells in our body. So you can think of our body as a "super-organism" – a partnership in which the human part is a minority. So for the overall health of this living system, the importance of the bacterial part cannot be under-estimated.

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Getting to know the friendly bacteria

I would like to congratulate the entire editorial board for this pilot issue of "The Probiotics News". Over the last 30 years, there have been an emerging numbers of scientific and clinical evidence to support the use of probiotics in human health and disease.

MD Pharmaceuticals plans to produce two issues annually. It is our objective to ensure that each newsletter is informative, non-bias and beneficial to the medical community. This is MD's modest CME contribution to the health care industry.

We value feedback, both positive and negative. In so doing, we hope to meet your needs and expectations for every subsequent issue of The Probiotics News.

In conclusion, we wish to express our sincere thanks and appreciation to Dr. Charles Vu, Dr. Francis Seow-Choen and Dr. Steven J. Mesenas for being our medical advisors.

Thank you & God Bless!

Melvin Wong
CEO

IBS & Probiotics

by Dr. Steven J. Mesenas

IBS & its Epidemiology

Irritable bowel syndrome (IBS) is a common gastrointestinal problem characterised by abdominal discomfort and altered bowel function. These symptoms occur in the absence of structural and serum biochemical abnormalities. Abdominal pain or discomfort is sine qua non of IBS. It usually occurs in the left lower quadrant but can occur anywhere in the abdomen. Isolated pain above the umbilicus is rare in pure IBS.

The point prevalence worldwide is 10 to 20%. A 1998 study of 696 Asians in Singapore reported a prevalence of 2.7%. Another local study reported that 50.4% of 2,364 people consulting a gastroenterologist had a functional rather than an organic disorder. A 2004 study of a random sample of 3,000 households in Singapore found a 8.6% prevalence of IBS using Rome II criteria. This study showed a higher prevalence of IBS in those less than 50 years of age with more than 6 years of education and living in a landed property (and presumably higher social status). There were no significant differences in prevalence seen in terms of racial groups, marital status and gender in this particular study.

However, in many other studies, IBS does seem more prevalent in women, with 2:1 female predominance. Interestingly, when individuals who chose to seek medical care for IBS were reviewed, this ratio increased to 4:1 (female:male). The prevalence of IBS also varies with age. Patients below 45 years of age were more likely to be diagnosed with IBS than those above 45 years (13.5% vs 9.4%).

IBS can occur in children. In children less than 3 years old, the predominant symptom is diarrhoea; pain-predominant IBS is more common in children over the age of 5. Weight loss may occur in these children as they avoid food to try to prevent the pain. A stressful event like teething, a bout of flu, problems at school or at home can trigger symptoms of IBS.

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Social & Economic Impact

IBS is usually associated with emotional distress, impaired health-related quality of life (QOL), disability and high health care costs. Although patients with IBS have no increased mortality, significant morbidity exists. These patients have rates of absenteeism from work 3 times that of non-IBS individuals. Absence from school, inability to participate in activities of daily living, modifying one's working hours or even giving up one's occupation are not uncommon. In two studies using a standard QOL instrument comparing IBS patients and patients with other chronic medical conditions, **IBS patients had significantly lower QOL than normal individuals, and poorer scores when compared to patients with rheumatoid arthritis, diabetes, asthma and gastroesophageal reflux disease.**

It is impossible to fully comprehend a chronic illness without capturing the true cost of IBS on society. There is no available local data, but if one explores the US model, the financial impact is between US\$20 billion to US\$30 billion per year (US\$8 billion direct and US\$20 billion indirect costs). Patients with IBS are 3 times more likely to receive a hysterectomy, and have more surgical procedures such as appendectomies.

Pathophysiology, Diagnosis and Treatment of IBS

The pathophysiology of IBS, diagnosis and treatment of IBS is constantly evolving. The question for the clinician is often how extensively these patients should be investigated and what treatment modalities exist for the treatment of IBS, as such patients can present in a myriad of ways, occasionally in a bewildering manner. Better understanding of the pathophysiology of IBS has led to a more concise and cost-effective diagnostic approach. Newer and novel therapeutic regimes address the fact that IBS is a biopsychosocial disorder. These include psychological treatment, psychotropic medications and newer drugs that target specific serotonin receptors. There is no diagnostic test that is

specific for IBS. Neither is there a "cure" for IBS, which remains a chronic and recurring condition. Treatment for IBS may require multiple modalities and even multiple specialities in the management of patients with severe IBS. However, IBS is far from being an "untreatable" disease, and most patients can return to a satisfactory functional level with proper therapy.

Recent years have seen an emerging trend towards the use of alternative therapies for the management of IBS. This includes the consumption of probiotics which have been shown to alter gut flora and improve symptoms of IBS.



Microflora and IBS

Disruption of the intestinal microbiota is one of the many suggested aetiologies of IBS. There are links between the disruption of intestinal microflora and the onset of IBS. In a retrospective study, occasions such as a course of antibiotics and abdominal or pelvic surgery, are responsible for the onset of IBS among 40% of the patients.

Based on samples gathered from the gastrointestinal tract, the composition of gut microflora among healthy subjects is consistent. When compared with IBS patients, the latter is found to contain higher numbers of facultative organisms such as *Klebsiella* spp. and *enterococci*, and low in the amount of *lactobacilli* and *bifidobacteria*. While their qualitative difference in microflora is not significant, the quantitative difference in microbiota may be of aetiological importance.



Effects of Probiotics on IBS patients

IBS patients are a diverse group. Their symptoms and triggers vary from one to the other. Therefore, few studies have been done on probiotics in this disease. Some trials have used symptomatic differences as a gauge for the improvements brought about by probiotics.

Among many trials done using single or multi-strain probiotic products, their effect on the treatment of IBS symptoms such as diarrhoea, abdominal pain/discomfort, distension/bloating and difficult defecation had shown to be effective. In a study done on 75 IBS subjects, *Bifidobacterium infantis* 35624 was shown to be better than *Lactobacillus* and placebo on IBS symptoms such as abdominal pain, bloating and difficult defecation. This study was further confirmed in a later study done on 360 IBS patients where *B. infantis* proved to have significant improvements in all symptoms.

In addition, a study using a synbiotic (probiotics + prebiotics) had shown to be effective in the treatment of the symptoms of constipation-type IBS patients. In the trial involving 636 patients diagnosed with constipation-type IBS by Roma II criteria, a combination of *Bifidobacterium longum* and fructo-oligosaccharides (FOS) increased their stool frequency and reduced abdominal pain and bloating.

Given the safety profile and positive results, probiotics warrant more attention. The available studies show likelihood that probiotics may help in the prevention of IBS and the treatment of its symptoms. While more are now using these live bacteria, more work should be done using specific probiotics formula on particular types of IBS patients.

Probiotics affect metabolism, says new study

Probiotics found in dietary supplements, yogurt and other dairy products as well as various soy products, have a tangible effect on the metabolism, according to the results of a new study published on 15 January 2008 in the journal *Molecular Systems Biology*.

The research is the first to look in detail at how probiotics modulate the gut microbiome and exert a significant effect on the host metabolic phenotypes. In essence, the microbiome is the entire set of microbial species living in the human body. The human microbiome has become an important research field because the microbes that live in and among us play critical roles in human health and disease. The gastrointestinal tract has the most abundant, diverse population of bacteria in the human body. A shift within this population, leading to the absence or deficiency of beneficial microbes, can trigger defects in metabolism. In susceptible individuals, this may even lead to the development of diseases such as inflammatory bowel disease, diabetes and obesity. Probiotics contain so-called 'friendly' bacteria and there is evidence to suggest that adding 'friendly' bacteria to the gut can help the digestive system.

For the study, researchers from Imperial College London and Nestlé Research Center, Lausanne, Switzerland, fed two groups of mice that had been transplanted with human gut microbes, with either a daily probiotic beverage (treatment group) or saline drink (control group). The treatment group was further divided into two groups, one group received *Lactobacillus paracasei* supplement and the other group *Lactobacillus rhamnosus* supplement. The researchers then compared the levels of different metabolites in the liver, blood, urine, and faeces, between the treatment and control groups.

They found that supplementation with probiotics exhibited a whole range of biochemical effects and that these effects differed markedly between the two *Lactobacillus* strains. **Adding 'friendly' bacteria exerted a modification over the microbiome in the gut, not only through an increase in the number of such bacteria, but also through synergism with other gut bacteria.**



Probiotic exposure resulted in different hepatic influx and efflux of fatty acids in the liver with increased enterohepatic recycling of bile acids and dietary fats, coupled with lowered plasma lipoprotein levels and stimulated glycolysis. In addition, probiotics also induced a different microbial proteolytic activity as well as modulation of bacterial metabolism of amino acids, methylamines and short-chain fatty acids.

Among them, one important biochemical change observed by the researchers was a change in how mice treated with probiotics metabolised bile acids. *Lactobacillus* supplementation resulted in decreased faecal excretion of bile acids, as well as different bile acid composition and enterohepatic recirculation compared to the control. This is significant because, **if probiotics can influence the way in which bile acids are metabolised, this means they could change how much fat the body is able to absorb.**

The study demonstrated that probiotics can have an effect on the gut microbiome by changing the dynamics of the whole population of microbes in the gut, and that different probiotic strain exerts different metabolic effects in the host. The researchers hope that that their new insights about how probiotics and gut microbes interact will ultimately enable the development of new probiotic therapies, which can be tailored for people with different metabolic profiles and different medical conditions. Through a better understanding of the molecular changes triggered in the host metabolism, dietary supplementation of probiotics can impact on the overall health of human beings.