

New study:

Probiotic-Prebiotic combination may ease eczema in kids

Nah Li Ching, Executive Editor

New research from Taiwan suggested that combining probiotics and prebiotics as synbiotics can alleviate the severity of atopic dermatitis (AD) symptoms in young children<sup>21</sup>. The findings of this double-blind, randomized clinical trial were published in the recent January issue of the *British Journal of Dermatology*.

Sixty children aged 2-14 years with moderate to severe AD (SCORing AD (SCORAD) > 25) were randomly assigned to a treatment (synbiotic) or a control (prebiotic) group. They received one capsule twice daily for 8 weeks containing either *Lactobacillus salivarius* plus fructo-oligosaccharide (treatment group, n = 30) or fructo-oligosaccharide only (control group, n = 30). The content of each capsule is 475 mg of fructo-oligosaccharide and 25 mg of *L. salivarius* PM-A0006 (2 x 10<sup>9</sup> colony forming units) (treatment group) or 25 mg of corn starch (control group). SCORAD indices were monitored at weeks 0, 4, 8 and 10 (post-treatment). Laboratory results and AD medication use were also monitored.

Baseline demographic and clinical characteristics and SCORAD scores were similar between the two groups. The study results showed that at 8 weeks, the treatment group SCORAD scores (27.4 ± 12.7) were significantly lower than for the controls (36.3 ± 14.9) (P = 0.022); this difference remained at 10 weeks. The treatment group also has a significantly lower AD intensity at 8 weeks (P = 0.013); more children had mild AD in the treatment group (52%; 14/27) compared to the control group (30%; 8/27) (P = 0.024). Medication use frequency (P = 0.007) and eosinophil cationic protein levels (P = 0.002) were significantly reduced in the treatment group at 8 weeks compared with 4 weeks.

The study concluded that a synbiotic combination of a putative probiotic *L. salivarius* preparation with the prebiotic fructo-oligosaccharide was superior to the prebiotic alone for reducing the symptoms of AD in young

children with moderate to severe disease.

Alterations in the intestinal microflora, especially in early life, is said to be a predisposing factor to the susceptibility to atopic disorders. Overcoming these alterations in microflora, either by introducing non-infectious bacterial species (probiotics) or dietary components that selectively stimulate the growth and activities of certain bacteria (prebiotics) may reduce such susceptibility. The questions are which organisms or dietary components should be used and in what combinations.

Previous work with probiotics or prebiotics have demonstrated conflicting results in their role in allergic diseases. In this light, combinations of prebiotics, that selectively promote the growth of certain bacterial species and their activities, and probiotics, that elicit immune-modulating effects, may be a more effective strategy.

While a few studies have shown superiority of synbiotics compared to prebiotics alone or placebo for ameliorating AD, one or more showed no improvements in AD severity compared with the placebo. This is because results appear to be strain-specific for the particular probiotic used.

The present study demonstrated that *L. salivarius* PM-A0006 has therapeutic efficacy for treating children with moderate to severe AD when used in a synbiotic combination with a prebiotic, fructo-oligosaccharide. Considering that the incidence of AD among children has increased dramatically in recent decades, doctors may consider this option the next time they see these group of patients.



Quick Facts

*Lactobacillus plantarum* 299v is one of the most documented probiotic strains for irritable bowel syndrome. In studies on in vivo colonization of different *Lactobacillus* strains on human intestinal mucosa, the best results were achieved for *Lactobacillus plantarum* 299v and 299<sup>22</sup>.

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Medical Advisors

Dr Francis Seow-Choen  
MBBS, FRCSed, FAMS, FRES



Colorectal Surgeon  
Medical Director & Senior Consultant, Fortis Colorectal Hospital  
Director, Seow-Choen Colorectal Centre PLC  
President, Eurasian (European-Asian) Colorectal Technology Association (ECTA)  
Chairman, Guide Dogs Association of the Blind Singapore  
Chairman, Board of Directors City College Singapore  
Vice-President, Singapore-China Association for the Advancement of Science and Technology (SCAAST)  
Visiting Consultant, Department of Colorectal Surgery, Singapore General Hospital; Depts of General Surgery of Alexandra Hospital; Khoo Teck Puat Hospital & Tan Tock Seng Hospital  
Visiting Professor, Tianjin Police Hospital, Tianjin, PRC; Tianjin Union Medical College, Tianjin Colorectal Centre, Tianjin, PRC; National Ctr for Colorectal Disease, Nanjing TCM University, Nanjing, PRC; Wenzhou Medical College, Wenzhou, PRC; Dept of Colorectal Surgery, Guigang Renmin Hospital, Guangxi, PRC; Chengdu Colorectal Specialist Hospital  
Co-chairman Constipation Association China

Dr Steven J. Mesenas  
MBBS (S'pore), MRCP (UK),  
FAMS (Gastroenterology)



Senior Consultant,  
Dept of Gastroenterology & Hepatology (SGH)  
Director, SGH Endoscopy Centre  
Clinical Lecturer, National University of Singapore

Dr Reuben Wong Kong Min  
MBBS (S'pore), MRCP (UK),  
FAMS (Gastroenterology)



Consultant, Dept of Gastroenterology & Hepatology, National University Health System SINGAPORE  
Clinical Director, Gastrointestinal Motility Lab, National University Health System SINGAPORE  
Assistant Professor, Yong Loo Lin School of Medicine SINGAPORE  
Adjunct Assistant Professor of Medicine, University of North Carolina USA

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For enquiries, comments, suggestions or article contribution, please write to:

The Editor (The Probiotics News)  
MD Pharmaceuticals Pte Ltd  
896 Dunearn Road #02-01A  
Sime Darby Centre Singapore 589472

Tel: (65) 6465 4321  
Fax: (65) 6469 8979

Website: <http://www.mdpharm.com>  
Email: [liching.nah@mdpharm.com](mailto:liching.nah@mdpharm.com) or  
[waisin.leong@mdpharm.com](mailto:waisin.leong@mdpharm.com)

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Message from the Editor

As probiotics receives greater attention and recognition worldwide, it is timely to reiterate and remember that not all probiotics are the same.

With probiotics, there is the genus (family), species (type) and strain (specific). For example, *Lactobacillus* represents the family, *Acidophilus* the type and *Lactobacillus Acidophilus* LA-5 the specific strain.

Different strains of even the same genus and species may have different physiological effects. However, the observation that several strains have been proven effective for one particular indication should not be interpreted to mean that any possible probiotic strain will be effective. Thus, understanding the genus, species and strain will assist you to make an informed decision in choosing a probiotic. This will avoid repetition of similar probiotics for the same indication in your inventory.

In this issue, we welcome Dr Reuben Wong, a consultant gastroenterologist from NUH to be one of our Medical Advisors, and would like to thank Dr CK Ng, a consultant urologist from Mount Elizabeth for his informative contribution on recurrent urinary tract infection in women.

God bless!

Melvin Wong  
Editor-in-chief

Probiotics and IBS: An Update

Eamonn MM Quigley  
MD, FRCP, FACP, FACG, FRCPI  
Cork, Ireland

Why use Probiotics in Irritable Bowel Syndrome?

Irritable bowel syndrome (IBS) is a very common disorder worldwide; despite this high prevalence we still lack a diagnostic biomarker and effective therapies. It should therefore come as no surprise that those afflicted with IBS commonly turned to complementary and alternative medical remedies and practices<sup>1</sup>. As food intake is one of the most common precipitants of symptoms in IBS, foremost among such approaches have been various dietary manipulations, including exclusion diets, and a variety of dietary supplements<sup>2</sup>. In Europe, in particular, where dietary supplements are advertised widely for their general 'immune-boosting' and 'health-enhancing' properties, probiotics have been widely used by patients with IBS. Recently, based on data from the experimental laboratory, as well as some evidence from clinical trials, the concept of probiotic use in IBS has begun to wend its way into the realm of conventional medicine; indeed, several recent developments provide a more logical basis for their use in this context<sup>3,4</sup>. These include the clear recognition that IBS is, in some instances, induced by bacterial gastroenteritis (post-infectious IBS) and that qualitative changes in the microbiota, as well as immune dysfunction, might be prevalent in IBS, in general<sup>5</sup>. Accordingly, the anti-pathogenic activity of some commensal/probiotic organisms and the anti-inflammatory properties of other organisms may be of particular relevance to the use of probiotics in IBS<sup>6</sup>. Other factors, including a reduction in gas production, changes in bile salt conjugation, antiviral effect, the promotion of motility, and effects on mucus secretion could also be relevant to the benefits of specific probiotic strains in IBS.



Evidence for Probiotics in IBS

However, up until 2000, only a few studies had evaluated the response of IBS to probiotic preparations and, although results between studies were difficult to compare because of differences in study design, probiotic dose and strain, there was some, but by no means consistent, evidence of symptom improvement. Since then, further studies have assessed the response to several well-characterized organisms and have produced discernible trends. While meta-analyses have indicated that, as a category, probiotics are effective in IBS<sup>7-10</sup>, the interpretation of such aggregate assessments needs to be cautious given the tremendous differences in biological and clinical activities between individual strains.

Indeed, the specificity of strains in relation to a given property, activity or therapeutic effect is an important but often overlooked issue in the area of probiotics. No two strains are alike; the deletion or substitution of just one gene can dramatically affect the immunological or metabolic activity of a bacterium; making sweeping statements about all probiotics or even all members of a given species cannot be supported. Similarly, claims associated with a given strain cannot be extrapolated to other strains no matter how closely related. A similar issue arises when attempting to analyze the mechanism of action of a probiotic cocktail as it will be very difficult to determine whether the beneficial effect is due to one of the component strains, or is reliant on the presence of all included strains.

When one attempts to analyze the efficacy of individual probiotic products, several strains, such as *Lactobacillus plantarum*, *Lactobacillus GG*, *Lactobacillus acidophilus*, *Lactobacillus casei*, the probiotic 'cocktail' VSL#3 and *Bifidobacterium lactis* DN-173 010, have been shown to alleviate individual IBS symptoms, such as bloating, flatulence and constipation. The latter organism, *Bifidobacterium lactis* DN-173 010 has also been shown to produce objective reductions in abdominal girth in IBS, in association with improvements in bloating and distension<sup>11</sup>. However, only a few products have been shown to affect pain and global symptoms in IBS<sup>12</sup>. For example, *Bifidobacterium infantis* 35624 has shown, in a pilot study, superiority over both a Lactobacillus and placebo for each of the cardinal symptoms of IBS<sup>13</sup> and a larger, four-week duration, dose-ranging study confirmed efficacy for this organism at a dose of 10<sup>9</sup> - again, all of the primary symptoms of IBS were significantly improved and a global assessment of IBS symptoms at the end of the therapy revealed a >20 % therapeutic gain for the effective dose the probiotic had over placebo<sup>14</sup>.

The Future

These studies are encouraging but the numbers of IBS subjected to high-quality clinical trials involving probiotics remain small and most studies have been of relatively short duration; further large, long-term, randomized controlled trials of these strains are warranted in IBS and detailed explorations of their mechanism(s) of action are indicated. This field must move forward from an era where extrapolations were made from the outcome of studies on a single strain to well-designed, appropriately powered studies which focus on single strains and define optimal dose, formulation and duration of therapy. In the meantime, the consumer has a dilemma: how to choose a truly effective product from a vast range of strains and formulations that purport to offer a range of often unsupported benefits? Pending regulatory reform, the consumer should tread carefully; one reassuring element is the very good safety record of probiotics, especially in a healthy population<sup>15</sup>.



Eamonn Quigley is a Professor of Medicine and Human Physiology and a Principal Investigator at the Alimentary Pharmabiotic Centre at the National University of Ireland, Cork, Ireland. He is the immediate past president of the World Gastroenterology Organization (WGO-OMGE) and has also served as president of the American College of Gastroenterology. He is a past Editor-in-Chief of the American College of Gastroenterology. His major research interests include motility, functional gastrointestinal disease, neurogastroenterology, gastroesophageal reflux disease and probiotics in health and disease. He has published over 600 original papers, reviews, editorials, book chapters, and media educational items and has received numerous awards worldwide.

email: e.quigley@ucc.ie

Recurrent Urinary Tract Infections (UTIs) In Women - Management and the Role of Probiotics

Dr Ng Chee Kwan  
MBBS (Singapore), FRCS (Edin), FRCS (Glasg), FAMS (Urology)  
CK Ng Urology & Minimally Invasive Surgery, Mount Elizabeth Medical Centre  
United Specialist Centre, Novena Medical Centre

Introduction

Worldwide, it is estimated that several hundred million women suffer from UTIs annually. Risk factors for UTI include:

- 1. Sexual intercourse, likely due to bacteria entering the urethra during sex.
- 2. Exposure to spermicidal agents, which affect the vaginal flora, causing loss of lactobacilli and increase in pH.
- 3. Menopause, in which the loss of oestrogen results in increase in vaginal pH.
- 4. Inadequately treated UTI. Sometimes the infections recur because the bacteria have not been totally eradicated.
- 5. Other urinary tract problems e.g. urinary stones.

Investigations for Recurrent UTI

A healthy young woman who had a single episode of UTI after sexual intercourse, may not need to be investigated before she starts on treatment. However, further evaluation is recommended if the infection is serious (e.g. pyelonephritis), or the UTI becomes recurrent.



The investigations may include:

- 1. Urinalysis and urine culture. In recurrent UTIs, it is best to obtain definitive assessment of the urine and to document the sensitivities of the bacteria causing the infection.
- 2. Ultrasound of the kidneys and bladder. The advantage of ultrasound is that there is no radiation exposure or need for intravenous contrast. The disadvantage is that it is operator-dependent, and the ureters cannot be imaged.
- 3. CT urogram or intravenous urogram. Both investigations allow further evaluation of the lining of the urinary tract including the ureters. In addition, CT scan shows the kidneys in further detail. The disadvantage is the need for intravenous contrast and radiation exposure.
- 4. Flexible cystoscopy. This is not always necessary but is performed by the urologist if there is a suspicion of bladder cancer, which can occasionally also cause symptoms similar to that of UTI.

Treatment of UTI

Once the diagnosis of UTI is made, the patient will be prescribed a course of antibiotics. A three day course of antibiotics may be enough for an uncomplicated case of cystitis, but if the infection is more serious, e.g. pyelonephritis, a longer course of up to 3 weeks may be necessary.

Prevention of UTI

Recurrent UTIs are a significant cause of morbidity among women. Antibiotics may have side-effects. In addition, the frequent use of antibiotics may encourage the development of drug-resistant bacteria, as well as vaginal candidiasis.

There are some general measures that are useful in preventing UTIs:

- 1. Empty the bladder after sexual intercourse; this will reduce the risk of infection from bacteria that entered the bladder during intercourse.
- 2. Keep the body hydrated by drinking at least 1.5 to 2 litres of water a day.
- 3. Empty the bladder regularly e.g. every 2 to 3 hours. Avoid holding urine for prolonged periods.
- 4. When washing or wiping the private areas, wipe the genital areas first before the anus.
- 5. Cranberry juice or supplements that contain proanthocyanidins prevent harmful bacteria from attaching themselves to the lining of the urinary tract. Meta-analyses have shown that cranberry juice and derivatives are effective in prevention of recurrent UTIs.



Probiotics in Prevention of UTI

Probiotics are live bacteria similar to those occurring naturally in the human body, and may be beneficial to health. Lactobacilli are commensals that are normally found in the vagina. Low lactobacilli counts have been found in the vagina and urethra in women suffering from recurrent UTI<sup>16</sup>. Certain lactobacillus strains have been found to be effective in inhibiting the growth of pathogenic bacteria in the vagina. In an in-vitro study, *Lactobacillus casei* GR-1 was found to have much better inhibitory effect against uropathogens compared to commercial strains such as *Lactobacillus acidophilus* (found in yogurt preparations)<sup>17</sup>. *Lactobacillus fermentum* RC-14 produces H<sub>2</sub>O<sub>2</sub>; it has been shown that females colonized by H<sub>2</sub>O<sub>2</sub> producing lactobacilli, vaginally and rectally, had a reduced risk of vaginal infection<sup>18</sup>.

Treatment with probiotics, either via the per-vaginal or oral route, can be considered as part of the overall preventive strategy for recurrent UTI. A randomized controlled trial of vaginal suppository of *Lactobacillus crispatus* CTV-05 showed reduction in the rate of recurrent UTI by approximately 1/2, which compares favourably with historical data on antimicrobial prophylaxis<sup>19</sup>. In a randomized controlled trial involving oral administration of capsules containing *Lactobacillus rhamnosus* GR-1 and *L. fermentum* RC-14, patients in the active arm showed significant increase in vaginal lactobacilli, and a significant reduction in coliforms<sup>20</sup>.

Generally, probiotics have minimal side effects. However as they are live bacteria, they should not be taken if the patient is very ill or has a weakened immunity.

Conclusion

Recurrent urinary tract infections in women are common. It is not ideal to subject patients to repeated courses of antibiotics, due to potential side-effects of antibiotics and development of drug-resistant bacteria. Patients should be counselled on general preventive measures against UTI. While data from large-scale randomized trials is lacking, it is reasonable to consider judicious use of probiotics as a preventive measure.



Dr Ng is a Consultant Urologist at CK Ng Urology & Minimally Invasive Surgery and United Specialist Centre, and a Visiting Consultant Urologist at Tan Tock Seng Hospital. He has extensive experience in minimally invasive urological procedures. His subspecialty interests include surgery for urological cancers, laparoscopic (keyhole) surgery including robotic surgery and single port surgery, and treatment of prostate problems and overactive bladder. His research interests include the epidemiology and detection of prostate cancer in Singapore, and novel treatments for advanced prostate cancer.

email: drckng@urospecialist.com.sg