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Home > Colitis ulcerosa and pouchitis

**Ulcerative Colitis and Pouchitis** [1]

**Ulcerative colitis and pouchitis**

In Europe, an estimated 2.5 to 3 million people suffer from chronic inflammatory bowel disease (IBD). Just over half of these patients have ulcerative colitis (UC). The others have Crohn’s disease (CD). In people with CD the entire gastrointestinal tract can be affected, while UC is limited to the large intestine and the rectum. Pouchitis refers to inflammation of the so-called ileal pouch. This is a surgically constructed stools reservoir, made from the small intestine in people who have had their large intestine surgically removed. UC and pouchitis are characterized by alternating periods of exacerbation (referred to as flare-ups) and periods without inflammation (referred to as remission). Around 75% of all UC patients have a flare-up at least once a year. 10-15% of pouchitis patients suffer from chronic pouch inflammation and use several courses of antibiotics each year. In addition, in 46% of UC patients with a pouch, pouchitis will occur at least once in the first five years after the pouch has been constructed. This can be accompanied by symptoms including diarrhoea, cramps, urge, loss of blood and weight loss, and it therefore strongly affects the patient’s quality of life.

Extensive research notwithstanding, the exact causes of IBD are not known. It is a multifactorial condition involving the gut microbiota, the immune system, the patient’s genetic background, nutrition and environmental factors. In addition, it seems that a disturbed intestinal barrier, and the resulting increased permeability of the gut wall, plays an important role in the inflammation and its persistence.

**Ulcerative colitis, pouchitis and microbiota management**

The microbiota composition of patients with IBD is off balance (dysbiosis) and differs from that of healthy people. What is particularly notable is that, in addition, the microbiota of ulcerative colitis patients is clearly different from that of patients with Crohn’s disease.
Dysbiosis has a range of consequences. It has been demonstrated that, in people with inflammatory bowel disease, the production of short-chain fatty acids in particular decreases. This effect is enhanced by an increased concentration of sulfate-reducing bacteria. These bacteria produce toxic hydrogen sulfide which damages epithelial cells by blocking short-chain fatty acid absorption. This results in increased permeability of the gut wall. In addition, gut wall permeability is regulated by tight junctions. These are protein structures which interconnect the epithelial cells. Under normal conditions, these tight junctions form a closed barrier and harmful substances cannot pass between the epithelial cells (which is referred to as paracellular transport). If the intestinal barrier function is disturbed, these tight junctions will be open, so that the gut wall becomes more permeable and not only nutrients but toxic substances and pathogens as well will enter the bloodstream, resulting in overactivation of the immune system (Figure 1). Moreover, due to reduced production of defensins and mucus, the gut wall will also be exposed more to the intestinal content, causing damage to the gut wall.
Figure 2: As a result of several factors, the intestinal barrier function can be disturbed, resulting in large spaces between the cells of the gut wall. Through these openings – the tight junctions – bacteria, fungi, parasites and the toxins they produce (such as LPS), undigested food particles and waste products can reach the bloodstream. This will place a heavy burden on the immune system, which can cause inflammation, among other things.

Microbiota management to restore the balance therefore seems an important therapeutic option for these disorders. One approach that has received a great deal of attention in this context is faecal microbiota transplantation (FMT). This involves replacement of a patient’s microbiota with the microbiota of a healthy person, so that the microbiota of the patient changes dramatically. In people with IBD this has had varying results. Apart from the treatment itself being thought of as controversial (for reasons including the lack of a method to verify the composition of donor microbiota and the need to screen donors for various infectious diseases), there are still many questions to be answered with regard to the results obtained. These are mainly related to cause and effect, the genetic and immunological background, and the natural microbiota of the patient. Against that background, it is unlikely that FMT will be used as a treatment method for IBD in the short term.

**Ulcerative colitis, pouchitis and probiotics**

The use of probiotics for the treatment of inflammatory bowel disease has been studied extensively over the past few years. As indicated previously, both UC and pouchitis are characterized by alternating periods without inflammation (remission) and periods of exacerbation (flare-ups). An important observation with regard to the use of probiotics is that it prolongs this remission period in particular.

Researchers studying the use of probiotics have addressed both single-strain and multiple-strain formulas. The effects of multispecies probiotics generally seem more convincing. A notable fact here is that probiotics seem to be especially effective in patients with UC and pouchitis, but much less so in patients with Crohn’s disease. Its deeper impact and the fact that it can occur in the entire gastrointestinal tract are probably part of the reason why the use of probiotics has far less of an effect.
on Crohn’s disease.

The effects of probiotics on ulcerative colitis and pouchitis are linked to an effect on the microbiota itself, effects on the immune system and an effect on the intestinal barrier. Based on the above, Winclove developed its Ecologic® 825 formula. The strains in this product were selected mainly for their ability to strengthen the intestinal barrier and also for their ability to stimulate the production of anti-inflammatory cytokines.

Winclove developed the indication-specific probiotic formulation Ecologic® 825 with the following strains:

- *Bifidobacterium bifidum* W23,
- *Bifidobacterium lactis* W51,
- *Bifidobacterium lactis* W52,
- *Lactobacillus acidophilus* W22,
- *Lactobacillus casei* W56,
- *Lactobacillus paracasei* W20,
- *Lactobacillus plantarum* W62,
- *Lactobacillus salivarius* W24
- *Lactococcus lactis* W19.

The effectiveness of this formula has been demonstrated in a study conducted at the University of Linköping in Sweden (Figure 3). In this study, 16 patients were given the Ecologic® 825 formula for 8 weeks after being treated with antibiotics for pouchitis. During this 8-week period, no recurrence was seen in any of these patients. In addition, it was demonstrated that the barrier function had strongly increased.

![Figure 3: Study design of Persborn et al, 2013](image)

In a different study, in which the Ecologic® 825 formula was given to 40 UC patients, 77% of them indicated that the use of the probiotics during a period of two months had clearly caused improvement. 68% of patients had already reported improvement after one month. A factor that does not receive a lot of attention in research into IBD is the fact that many IBD patients experience considerable gastrointestinal problems during periods of remission as well. The main improvements reported in this study were reduced diarrhoea, bloating and stomach cramps. Of the patients using the formula, 56% indicated after two months that they were generally feeling better than before their use of the product.
Because several studies have since shown that the use of multispecies probiotics can prolong remission periods (and in the case of pouchitis even in prevention of inflammation), it is now recommended in the guidelines of the European Crohn's and Colitis Organisation. In addition, in the Netherlands probiotics are recommended by the Dutch Digestive Foundation (Maag Lever Darm Stichting) for patients who have just been given a pouch in order to reduce their chance of developing pouchitis.


The research formulation Ecologic® 825 is not sold as a consumer product. However our worldwide business partners offer the formulation Ecologic® AAD as their own branded product. Thus the specific bacterial composition can be found in different products around the world.

**References**


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