REVIEW

Ulcerative colitis and probiotics: An overview

Irfan Ahmad Rather[1], Rajib Majumder[1], Fanar Hamad Alshammari[1], Jae Gyu Park[2] and Vivek Kumar Bajpai[1]*

[1]Department of Applied Microbiology and Biotechnology, School of Biotechnology, Yeungnam University, Gyeongsan, Gyeongbuk, Korea

[2]Pohang Technopark, Pohang Center for Evaluation of Biomaterials, Jigok-ro, Nam-gu, Pohang, Gyeongbuk, Korea

Abstract: Ulcerative colitis is an inflammatory disease of the large intestine whose effects are bloody diarrhea, cramping and bloating. The disease is usually relapsing and remitting. However, the cause of ulcerative colitis is not yet known. Due to this reason, finding an effective treatment has been a great challenge. The suggested medical treatment is usually composed of two portions; keeping the flare up from happening and treating the flare up when it has happened. Active flare ups are treated with corticosteroids. There are several hypothesis which suggest that ulcerative colitis could be due to the micro flora present in gut. For this reason, several researchers tried to modify the gut microflora with probiotics. However, there is no probiotics found that can induce emission faster than the placebo. The ulcerative colitis patients taking probiotics showed fewer and less severe symptoms during the flare up. This means that even though the probiotics did not end up the flare up faster, it slowed up the severity of the symptoms of the patients.

Keywords: Ulcerative colitis, inflammation, probiotics.

INTRODUCTION

Ulcerative colitis (UC) is a chronic disease which is characterized by diffuse inflammation of rectal and colonic mucosa (Tannis 2008). The disease mainly affects the rectum, but extends to some parts of the large intestines. The most conspicuous classical clinical sign of this disease is bloody diarrhea from the patients, and the clinical course sign is a period of remission and exacerbation. The incidence of this disease has rapidly increased in the developing nations (Tannis 2008). Many reports confirm that there is an interaction between genetic and environmental factors in the etiology of the disease (Potter 2004). In order to reduce mortality and deaths, patients with this disease should be identified and treated early. (Potter 2004). There are many types of medication available to treat mild to severe forms of UC. The goal of each medication is to maintain remission and improve the quality of life. However, one of the serious concerns of all these medications is their adverse side effects. Therefore, finding new alternative treatments for UC have been always a new challenge. It believed that UC could be due to complex interactions of gut microbiome. Therefore, in past years many researchers try to modify the gut microflora with probiotics. The human gastrointestinal tract is usually covered with bacteria. Most of the bacteria are harmless; however, some are harmful and causes infection that leads to persistent intestinal dysbiosis (Janeway *et al*., 2001; Parfenov and Ruchkina 2011). The bacteria in the intestines are important in digestion and also prevent other types of bacteria from occupying their spaces. This is the basic concept of the probiotics referred to as the good bacteria. These probiotics work in different ways. First they act as barriers lining the intestinal tract where through competition inhibition, they are able to prevent other laminal bacteria from reaching the lamina propria and stimulate mucosal immune system (Tannis 2008). The second mechanism is by enhancing mucus production so that patients have a thicker mucus layer which is important in preventing invasion by bacteria. Probiotics are responsible in altering the consistency of mucus hence changing the bacteria adherence pattern (Kabelitz 2005). The probiotics also aid in production of protective immunoglobulins and protective defensins and bacteriosins into the body lumen (Baumgart 2012). In addition, probiotics help in altering the function of mucosal immune system making it less inflammatory (Lichtenstein 2014). However, it is still early to conclude if probiotics would be an alternative treatment for UC.

Epidemiology of ulcerative colitis

Ulcerative colitis is the most common type of inflammatory disease of the bowel. In the United Kingdom, its incidence is approximately 10 per 100,000 people per year (Wallace 2008), and prevalence is approximated to be about 240 per 100,000 (Singleton 2009). UC can develop to anybody at any age; but, its incidence peaks at the age of between 15 and 25 years, and also between 55 and 65 years. The effects of UC are seen in both men and women equally (Wallace 2008). In the United State, more than 200 per every 100,000 people

**Corresponding author:* e-mail: vbiotech04@gmail.com

are usually affected by this disease and is higher in whites and the Ashkenazi. Worldwide, this disease is mostly concentrated in Europe, North America and Australia. The effects of this disease have increased in the developed countries (Singleton 2009). However, there is a difference in the incidence and prevalence of the disease in these regions. The incidence rate ranges from 0.5 to 31.5 per 100, 000 people while the prevalence rate ranges from 5.3 to 63.6 per 100,000 people annually (Lichtenstein 2014). This range is however higher in North America where it ranges from 37.5 to 238 per 100, 00 people (Singleton 2009); however, in South America the prevalence is less. A study conducted in Puerto Rico show that the prevalence of the UC is 12.3per 100, 000 people while it is 14.81 per 100,000 people in Brazil (Wallace 2008).

Mortality rate of people with UC was high in the first half of the twentieth century; but, currently it has greatly reduced due to the usage of corticosteroids and sulfasalazine (Sutherland *et al.,* 2014). Surgical techniques have also been of great help in reducing mortality rate. However, mortality rate due to UC is higher than the rate in the general population (Sutherland *et al*., 2014).

The disease is more common in smokers than the nonsmokers. It mostly affects people in the urban areas compared to those in rural regions. This means that urbanization is a contributing factor to this infection (Potter 2004). This is as a result of westernization of lifestyle like change of diet, smoking, industrial chemicals, pollution and difference in exposure to sunlight (Martin *et al*., 2014). UC is more prevalent to people with white collar jobs (Wallace 2008). Many reports showed that the use of oral contraceptives, perinatal and child infections, a typical mycobacteria infections among others were the other factors that affected the rate of spread of the UC (Martin *et al*., 2014).

Risk factors of ulcerative colitis

- Genetic factors: Ulcerative disease can be hereditary. Therefore, patient's family or relatives could be at a high risk of being infected.
- Environmental factors: Environmental changes such as exposure of body with pollen, bacteria and chemicals could result in uncontrolled inflammation of gastrointestinal tract.
- Geography: UC is common in the northern America and northern Europe than in other parts of the world like Asia and Africa.
- Working place: UC is common in people working indoors than outdoors or manually.
- Age: Ulcerative disease is common in people who are aged 20 to 30 years and between 55 and 65 years.
- Medications: Long-term use of nonsteroidal anti-inflammatory disease has led to relapse of the UC. Women taking contraceptives are at a higher risk of developing this disease (Khalili, 2013).

Current treatment of ulcerative colitis

It has been seen that patients with mild to moderate distal or left sided colitis, therapy includes oral or topical mesalamine (5-ASA) agents or both (Baumgart 2012). The combination of two is more active than neither alone. This therapy maintains UC and remission and superior to corticosteroids for distal disease. Steroid enemas are used for the active diseases; but, cannot be used in maintaining remission (Kabelitz 2005). Some of the medications used for these kind of patients are; sulfasalazine, olsalazine, balsalazide, mesalamine (pentasa, asacol, asacol HD, liada, apriso) mesalamine suppository and mesalamine rectal suspension (Potter 2004). In addition, there are number of new drugs of UC in pipeline (Table 1) and many drugs have been stopped after clinical trials due to poor results.

Probiotics for ulcerative colitis

It is still assumed that UC is caused by integrative factors, such as genetic susceptibility which is an imbalance between gastrointestinal probiotics and pathogens, an impairment of intestinal epithelial cells and host immune dysfunctions (Rutgeerts 1999). The human intestinal tract plays host to approximately 100 trillion microorganisms, with at least 15,000-36,000 bacterial species. The intestinal microbiota is now considered to be a functional organ associated with normal physiological processes, such as metabolism, immunological response and intestinal epithelium morphogenesis. Thus, there are many areas of host health that can be compromised when the microbiota is drastically altered. Many probiotics are effective as traditional ulcerative medications like the gold-standard treatment mesalamine and have been reported both had the same effects on the patients (Jewell *et al*., 2006). Recently, it was reported that probiotics suppress colitis-associated carcinogenesis (Do *et al*, 2015). However, these probiotics can influence the activity of the immune cells and the cells that lines the intestines. The intestinal flora dysbacteriosis contributes to the pathogenesis of UC. Probiotics are nonpathogenic beneficial flora, which have important effects on maintaining the balance of intestinal flora (Onderdonk 2000). Probiotics can adjust the metabolic activity of the intestinal flora and their components by preventing bacterial overgrowth and by maintaining the integrity of the intestinal mucosal barrier, thereby adjusting and stabilizing the intestinal environment (Rutgeerts 2009). The effects of the probiotics are important in treating the pathogenic mechanisms of the inflammatory bowel diseases in the body. However, it is still early to conclude if probiotics could be an ultimate treatment for UC.

Future prospectus of the ulcerative colitis

The UC has been with us for the last few decades; however, gained attention of researchers a decade or two ago. There is no direct cure for this infection (Wallace 2008). The only available treatment for mild pan or left sided colitis is still mesalamine. These formulations

Table 1: New drugs for ulcerative colitis (Crohnology.com, 2015)

	Phase 1/2	Phase 3	Registered	Launched
	Generic name			
Anti-TNF		HMPL-004 (Herbal extract)	Infliximab biosimilar (CT-P13)	Adulimimad
				Infliximad
				Certolizumad pegol
Anti-adhesion molecules	Alicaforsen	None	Vedolizumad	None
	Etrolizumad			
	Vatelizumab			
	Abrilumab			
Downstream signaling blockade	Eldelumab	Tofacitinib	None	None
	Peficitinib			
	Ozanimod			
Immunomodulator	Abatacept	Cobitolimod	None	None
	Rituximab			
	Visilizumab*			
Cytokine	Low dose IL-2	None	None	None
	ActoGenix*			
IL-inhibitor	Bertilimumab	None	None	None
	Anrukinzumab*			
	Tralokinumab			

*Have been stopped due to poor results in clinical trials.

allowing for once daily dosing are not only equally effective, but even facilitate the implication of long-term therapy in daily life (Baumgart 2012). In case steroids are frequently required to control the disease, further immunosuppressive therapy should be introduced in order to minimize steroid exposure. Thiopurines shows the first choice immunosuppressive medication. In more severe cases, early escalation to combinatory therapies with anti TNF antibodies should be considered with the possibility of therapy de-escalation after induction of remission. Major difficulties arise with steroid refractory acute flares. Probiotics are not useful in inducing a faster remission during the flare up of the UC, but the preparation of healthy bacteria makes the symptoms less severe. Probiotics increase the time between flare ups (Tannis 2008) and still there is a need of huge number of clinical trials at large scale using different types of probiotics. Additionally, it also depends on a particular strain of probiotics, not every probiotics would have similar effects.

CONCLUSION

In conclusion, UC occurs in genetically predisposed people. Even though probiotics are helpful for the ulcerative patients, they offer a very small benefit, but do not cure. They therefore do not replace the convection medication for patients with UC disease. It is important to notice the effect of probiotics after taking it. Probiotics doesn't have any side-effects; however a proper consultation from doctor is mandatory.

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