Journal of Microbiology, Immunology and Infection (2014) **47**, 429—437

Available online at www.sciencedirect.com

SciVerse ScienceDirect

journal homepage: www.e-jmii.com

BRIEF COMMUNICATION

Clinical application of probiotics in the treatment of *Helicobacter pylori* infection—A brief review

Ami Patel*, **Nihir Shah**, **J.B. Prajapati**

Dairy Microbiology Department, Sheth Mansukhlal Chhaganlal (SMC) College of Dairy Science, Anand Agricultural University, Anand, Gujarat, India

Received 5 December 2012; received in revised form 6 March 2013; accepted 28 March 2013
Available online 10 June 2013

KEYWORDS
Eradication treatment;
Gastritis;
Helicobacter pylori;
Interleukin-6;
Lactobacillus;
Stomach cancer

The role of probiotics in the treatment of gastrointestinal infections is increasingly being documented as an alternative or complement to antibiotics, with the potential to decrease the use of antibiotics or reduce their side effects. Although antibiotics-based *Helicobacter pylori* eradication treatment is 90% effective, it is expensive and causes antibiotic resistance associated with other adverse effects. Probiotics have an *in vitro* inhibitory effect on *H. pylori*. Animal studies demonstrated that probiotic treatment is effective in reducing *H. pylori*-associated gastric inflammation. About 12 human studies investigated the efficacy of combinations of antibiotics and probiotics, whereas 16 studies used probiotic alone as an alternative to antibiotics for the treatment of *H. pylori* infection. Most of the studies showed an improvement of *H. pylori* gastritis and decrease in *H. pylori* colonization after administration of probiotics. However, no study could demonstrate complete eradication of *H. pylori* infection by probiotic treatment. Probiotic combinations can reduce adverse effects induced by *H. pylori* eradication treatment and, thus, have beneficial effects in *H. pylori*-infected individuals. Long-term intakes of products containing probiotic strains may have a favorable effect on *H. pylori* infection in humans, particularly by reducing the risk of developing disorders associated with high degrees of gastric inflammation.

* Corresponding author. Dairy Microbiology Department, Sheth Mansukhlal Chhaganlal (SMC) College of Dairy Science, Anand Agricultural University, Anand 388110, Gujarat, India.
E-mail address: amiamipatel@yahoo.co.in (A. Patel).

1684-1182/$36
http://dx.doi.org/10.1016/j.jmii.2013.03.010

Introduction

For a long time, ulcers were considered to be a result of stress and improper diet. The important discovery that ulcers are caused by a bacterial infection (*Helicobacter pylori*), which was rewarded with the 2005 Nobel Prize in Medicine, has changed gastroenterological practice worldwide. After its discovery, many gastroduodenal diseases became curable infectious diseases. *H. pylori* is a highly prevalent pathogen associated with chronic gastritis and peptic ulcer, and is a risk factor for gastric malignancies. The prevalence rate of *H. pylori* infection in the adult population of industrialized countries is estimated to be at 20—50% and in developing countries, the rate is as high as 80%.[1] *H. pylori* colonizes the stomach and induces chronic gastritis, a long-lasting inflammation of the stomach. The bacterium persists in the stomach for decades in many cases. However, most infected people may never experience clinical symptoms despite having chronic gastritis; 10—20% of those colonized by *H. pylori* may ultimately develop peptic ulcers.[2] *H. pylori* infection is also associated with 1—2% lifetime risk of stomach cancer and a less than 1% risk of gastric mucosa-associated lymphoid tissue (MALT) lymphoma. This pathogen was designated as a class-I carcinogen for stomach cancer in 1994, after epidemiological investigation by the International Agency for Research on Cancer (IARC), a subordinate organization of the World Health Organization.[3] The infection is generally acquired during childhood and can persist indefinitely, if not treated systematically.[4] It has been suggested that *H. pylori* infection rates vary with age, ethnicity, socioeconomic status, sanitary environments, and lifestyle.[5]

None of the antimicrobials is effective enough to eliminate *H. pylori* when given as a monotherapy; only a combination of these can wipe out *H. pylori* effectively.[4] According to Malfertheiner et al,[6] the first-line recommended eradication treatment of *H. pylori* consists of a combination of two antimicrobials and an acid-suppressive drug. This triple therapy used for the treatment of *H. pylori* has several adverse effects, such as diarrhea, nausea, bloating, and taste disturbance, possibly leading to discontinuation of the treatment, and limited efficacy principally because of antimicrobial resistance of the pathogen.[7]

Alternative anti-*H. pylori* treatments are currently becoming more popular than the traditional eradication methods. Components that may be used either as a monotherapy or, synergistically, in combination with antimicrobials, resulting in a more effective anti-*H. pylori* therapy or an alternative way of controlling *H. pylori* infection, have been investigated in depth by several researchers.[2] It is believed that these novel therapies can potentially cut down the costs related to the treatment of *H. pylori*-associated diseases. One of the potential therapies involves an application of probiotic cultures; promising results have been observed in initial studies with numerous probiotic strains. Nevertheless, many questions remain unanswered. As defined by the Food and Agriculture Organization (FAO)/World Health Organization (WHO),[8] probiotics are live microorganisms that may confer a health benefit on the host. The most commonly used probiotic bacteria belong to the genera *Lactobacillus* and *Bifidobacterium*, and these also include several yeasts such as *Saccharomyces boulardii*.[9]

In the current article, the possible mechanisms of action of probiotics on *H. pylori* infection, as reported by *in vitro* cell line and animal studies, are narrated, followed by the outcomes of the available *in vivo* evidences for the effect of probiotics on *H. pylori* infection in humans. The effect of the addition of probiotics to the standard *H. pylori* eradication therapy is also discussed.

Mechanisms of probiotic action on *H. pylori*

A number of mechanisms have been anticipated or hypothesized from *in vitro* studies of host intestinal epithelial or immune cell responses to probiotic strains. In that context, probiotic bacteria can inhibit *H. pylori* by either immunological or nonimmunological mechanisms. According to Haller et al,[10] distinct probiotic strains may generate divergent immune responses depending on the host's immune status.

Animal studies suggested that the immunomodulatory effects of probiotic bacteria may be mediated through immune regulation, particularly through controlling the balance of proinflammatory and anti-inflammatory cytokines and chemokines, which in turn would reduce gastric activity and inflammation.[11] Probiotic bacteria can bind to recognition receptors, such as Toll like receptors (TLRs) expressed on the surface of epithelial cells, and thus trigger a cascade of immunological defense mechanisms.[9] In that TLR4 can recognize lipopolysaccharide of Gram-negative bacteria, whereas TLR2 can recognize a variety of microbial components, such as peptidoglycan and teichoic acids, present in Gram-positive bacteria.[12] The cytokine response is initially manifested by the release of interleukin (IL)-8, which leads to the migration of neutrophils and monocytes to the mucosa.[13] These activated monocytes and dendritic cells stimulate production of various cytokines together with IL-4, IL-5, IL-6, and interferon-γ. According to Gill,[14] probiotics can modify the immunologic response of the host by interacting with epithelial cells and modulating the secretion of anti-inflammatory cytokines, resulting in a reduction of gastric activity and inflammation. In one of the earlier studies, Kabir et al[15] demonstrated that *Lactobacillus salivarius* inhibits *H. pylori*-stimulated secretion of IL-8 by gastric epithelial cells. During several animal studies, a decrease in specific IgG antibodies to *H. pylori* infection, parallel to a fall in gastric inflammation, was observed following a probiotic intake.[16,17] Also, enhancement of secretory IgA production in the intestinal epithelium may have a role in pathogen defense through strengthening of the mucosal barrier.[13,18] It was also established that *H. pylori* infection induces production of Smad7, nuclear factor (NF)-κB, IL-8, and tumor necrosis factor-α *in vitro*. In a recent investigation, Yang et al[19] observed that pretreatment of *Lactobacillus acidophilus* at higher doses reduced *H. pylori*-induced inflammation through the inhibition of *H. pylori*-induced Smad7 transcription, by inactivating the Jak1 and Stat1 pathways, and subsequently reduced nuclear NF-κB production.

Nonimmunological mechanisms of probiotics include strengthening of mucosal barrier by producing