Makati Medical Center

Makati City

The effect of Adding *Saccharomyces boulardii* in Triple Therapy of *Helicobacter Pylori* Eradication

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CHAPTER 1

INTRODUCTION

Background of the Study

Infection of *Helicobacter pylori* is the leading cause for gastric ulcers and duodenum ulcers. It also affects an estimated 50% of the population around the world (Zojaji et al, 2013). The prevalence of being infected with *Helicobacter pylori* (*H.pylori*) depends on the country, socio-economic status and age (Suerbaum & Michetti, 2002). In most cases, especially in industrialized countries, transmission is by vomiting, saliva or feces. However, transmission in developing countries is often through water routes. Because of this it has been found out that infection of *Helicobacter pylori* contributes to the incidence of gastric cancer, and impacts 75% of adults worldwide (Peleteiro, Bastos, Ferro and Lunet, 2014). Prevalence of infection of *Helicobacter pylori* appear higher in developing countries such as those found in Asia and South America, and this also showed greater incidences of gastric cancer among these countries. Prevalence of infection of *Helicobacter pylori* is estimated to be 80% in developing countries, compared to a 20% incidence in industrialized countries (Suerbaum & Michetti, 2002).

In the Philippines, there are very few data on the prevalence of *Helicobacter pylori* infection. A few unpublished reports showed a 60% prevalence among adults and 42% among patients in the Philippine General Hospital (Destura et al, 2004). Many methodological difficulties in the country has made it unpopular to detect the organism *Helicobacter pylori*.

The first line therapies for the eradication of *Helicobacter pylori* often utilizes treatment with a proton pump inhibitor (PPI) such as omeprazole and antibiotics amoxicillin and clarithromycin. (Zojaji et al, 2013). Other first-line therapies available are ranitidine bismuth citrate in dual therapy with clarithromycin and amoxicillin or substituted with a combination of clarithromycin and nitroimidazole (Suerbaum & Michetti, 2002). These citrate-based therapies are found to be also as effective as proton pump inhibitor based therapies, and are found to be less influenced by antibiotic resistance. Another equally effective option are bismuth-based therapies, in which a triple therapy of furazolidone, amoxicillin and bismuth are also found to be successful. However, citrate-based therapies are not yet approved, while bismuth-based therapies have negative side effects. As such, proton pump inhibitor based therapies are most popular in eradicating *Helicobacter pylori* infection. The problem however, is the risk for antibiotic resistance.

There has been treatment failures in eradicating *Helicobacter pylori* infection due to anti-biotic resistance. Physicians have begun considering alternative options, such as addition of probiotics to therapy.

Probiotics are live microorganisms that can be used for beneficial effects to prevent and treat certain pathological organisms. A specific yeast probiotic that been proven to be effective is *Saccharomyces boulardii* (Czerucka, Piche & Rampal, 2007). Many countries have used *Saccharomyces boulardii* as a treatment and preventive agent against diarrhea and other gastrointestinal disorders. This is because *Saccharomyces boulardii* belongs to the category of

eukaryotic cells, thereby differentiating it from other bacterial probiotic prokaryotes. As such, it can survive the environment inside the gastrointestinal tract and inhibits the growth of other microbes and bacterial infections.

Many animal and human studies have been conducted to document the efficacy of using probiotics in the treatment of *Helicobacter pylori* infection (Lesbros-Pantoflickova, Corthesy-Theulaz & Blum, 2007). Animal studies revealed that treatment with probiotics have reduced *Helicobacter pylori* gastric inflammation and human studies showed that administering probiotics have improved symptoms of gastritis and reduced *Helicobacter pylori* in the gut. These probiotics inhibits growth of *Helicobacter pylori* by reducing pH of the gastric environment, reducing adhesion to gastric cells, which stabilizes the function of the intestines and gastric barriers and reduces the negative side effects of antitiobiotic therapy (Zojaji et al, 2013). However, there have been conflicting information in these previous studies, and there is a dearth of research of the efficacy of *Saccharomyces boulardii* in triple-therapy combination for the eradication of *Helicobacter pylori.* The present study aims to address this research gap, and hopes to bridge the medical knowledge in the use of *Saccharomyces boulardii* or probiotics in the treatment of *Helicobacter pylori* infection, especially in the Philippines.

Statement of the Problem

The study seeks to investigate the efficacy of adding *Saccharomyces boulardii* in proton pump inhibitor based triple therapy of *Helicobacter Pylori* Eradication. The study will describe the clinical profile of patients from Makati Medical Center who tested positive for *Helicobacter Pylori* infection. It shall look into the difference in treatment efficacy with or without probiotics. Lastly, it shall investigate on whether adding *Saccharomyces boulardii* in triple therapy will have significant effects on the number of side effects experienced by the patients.

Objectives of the study

1. To determine the clinical profile of patients from Makati Medical Center who tested positive for *Helicobacter Pylori* infection
2. To determine the prevalence of *Helicobacter Pylori* infection among patients of Makati Medical Center
3. To determine the effectiveness of adding *Saccharomyces boulardii* for *Helicobacter Pylori* triple therapy in decreasing the side effects

Significance of the Study

It is essential to investigate the efficacy of probiotic treatment in decreasing the side effects associated with *Helicobacter Pylori* infection treatment, to be able to recommend alternative therapies to combat anti-biotic resistance treatments, and provide more affordable treatment alternatives for *Helicobacter Pylori* infection.

Specifically, the study will be beneficial to the following:

Hospitals and health centers. The study will increase the awareness of hospitals and health centers on the prevalence of *Helicobacter Pylori* infection and the clinical profile of patients who are positive for *Helicobacter Pylori* infection. Raising awareness can facilitate in improving the existing health management programs of these facilities.

Doctors, nurses and health practitioners. The study will aid the doctors, nurses and health practitioners to identify the clinical profile of patients with *Helicobacter Pylori* infection. In this way, doctors, nurses and health practitioners will be able to devise measures and mechanisms to identify such patients. In addition, they can recommend probiotics as another alternative therapy for eradication of *Helicobacter Pylori* infection.

Patients and family members. The study will increase the awareness of patients and family members as to prevalence and clinical profile of patients with *Helicobacter Pylori* infection. In addition, patients and family members can act as active agents in probiotics as a treatment alternative, and in communicating to their own communities about the relevant information pertaining to *Helicobacter Pylori* infection, to ensure that treatment will be successful.

Medical research institutions and future medical researchers. This study will add to the body of knowledge on the prevalence and clinical profile of patients with *Helicobacter Pylori* infection. It shall also aid in coming up with

recommendations on how to improve treatment regimens and therapies for the eradication of *Helicobacter Pylori* infection, using probiotics.

Scope and Delimitations of the Study

The scope of the study is limited in one hospital, which is the Makati Medical Center, located in the National Capital Region. Most of the participants are out-patients who come from Metro Manila or nearby provinces and have tested positive for *Helicobacter Pylori* infection.

The study is also limited by the quasi-experimental nature of the research design. It is also limited by the extraneous variables to treatment of *Helicobacter Pylori* infection, such as patient compliance to treatment.

CHAPTER 2

METHODOLOGY

Study design

The research design is a prospective randomized experimental-control group study, which shall employ experimental method in its data gathering process, by collecting quantitative data. It shall utilize carefully controlled procedures to ensure successful control of relevant variables in its its data gathering procedure and data analysis. The duration of the study will be for six months, from August 2017 until January 2018.

Population and Sampling Technique

Inclusion Criteria

The participants in the present study are all Makatie Medical Center out-patients, who tested positive for *Helicobacter Pylori* infection after undergoing the endoscopic procedure. Patient cases will be selected using the sampling design of purposive sampling method, based on the inclusion criteria. The inclusion criteria are the following: 1) patients were detected positive for *Helicobacter Pylori* infection thru endoscopic procedure, and 2) patients were out-patients of Makati Medical Center.

Exclusion Criteria

The exclusion criteria are the following: 1) cases in which patients' did not undergo endoscopic procedure; 2) cases of attrition, in which patients dropped out during the research conduct; 3) cases when patients refused

participation; 4) cases of mortality, in which patients died during the research conduct.

Data collection procedure

A letter of permit was forwarded to the medical directors of Makati Medical Center, requesting the conduct of research among out-patients who sought services from its Endoscopic Unit. Once approved, medical professionals shall aided in the data collection procedure, thru performing endoscopic services and confirming the presence of *Helicobacter Pylori* infection among out-patients who tested positive. In addition, patients' clinical charts and patient information shall be gathered, to gain additional data regarding their clinical profile. Demographic characteristics of the participants were obtained through a uniform data collection sheet and follow-up throughout the duration of the study.

Identified patients will be randomized between two groups. The first group shall receive the standard triple therapy of antibiotics and proton pump inhibitor. The second group shall receive the same standard triple therapy, but will be adding *Saccharomyces boulardii* in the treatment regimen. Patients will be asked for a weekly checkup to monitor side effects of treatment and symptoms. After _____ days, patients will be requested for a follow-up check for final assessment and evaluation.

Data processing and analysis

The data collection sheet were be quantitatively analyzed. Data completeness will be checked for each variable and demographic characteristic. Data were entered and analyzed in the MS Excel Program. A statistician will be consulted for the validity of data analysis. Descriptive statistics such as frequency counts and percentage, and inferential statistics such as t-test for independent samples will be utilized to obtain a quantitative analysis of data gathered from the study.

Ethical Considerations

The study protocol will be presented to the Institutional Review Board responsible for medical researches conducted at the Makati Medical Center. Once approved, all patients will be provided with an informed consent form, to ensure voluntary participation and an understanding of their ethical rights as a participant in the study.

The template for the informed consent will be patterned after the World Health Organization informed consent template for clinical studies and designed by the WHO Research Ethics Review Committee. The template can be readily accessed from the WHO online website by medical and clinical researchers in the health industry (http://www.who.int/rpc/research_ethics/informed_consent/en/). The principal investigator, with the assistance of medical aides, shall provide the informed consent to potential participants, during the recruitment phase. The informed consent process will be conducted during recruitment. The selected

participants will be informed of the following: 1) that the data gathered from them will be held with the utmost prudence and confidentiality, and that identifying information shall be private during the data gathering and analysis procedure; 2) that the data collection and consultation shall be conducted in a close, private room, and the principal investigator shall personally talk and interview the participants; 3) that participants from minority groups, low socio-economic status, or from any vulnerable and at-risk groups shall be treated and dealt with the utmost dignity and respect, to reduce unfair treatment; 4) that participants who agreed to participate might be exposed to risks of discomfort stemming from the drugs' side effects; 5) that there shall be no monetary compensation provided while participating the study; 6) that the benefits which participants can have is the potential to takeaway some insights and new knowledge and awareness of *Helicobacter pylori* infection and its treatment, 7) that participation in the study will have tremendous impact on increasing medical knowledge and treatment of *Helicobacter pylori* infection in the medical profession.

Results of the study will be communicated in the medical community, and national medical conventions. The principal investigator shall choose a reputable medical journal, and shall plan to submit the study for peer-review and publication. Research publication of the results of the study in an accredited and peer-reviewed journal shall ensure that it can be replicated by other medical researchers who might be interested in investigating the efficacy of probiotic treatment of *Helicobacter pylori* infection, particularly in the Philippines. Only the principal investigator will publish the research.

Study timeline

Activity	Target Date
Presentation and approval of study protocol by the research committee	December 2017
Screening and patients' voluntary participation	January 2018
Data collection	February – May 2018
Data encoding, organizing and analysis	June 2018
Writing the research manuscript	July 2018
Research presentation and publication	August 2018

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