Culture and Susceptibility of Levofloxacin Resistant H.pylori

Thesis

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Ahmed Medhat Youssef Ibrahim Youssef

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List of Abbreviations

Abb.	Full term
*	Significant ($p<0.05$)
**	Highly significant ($p<0.001$)
ALP	Alkaline phosphatase
BMI	Body Mass Index
C/S	Culture and Sensitivity
Cag A	Cytotoxin associated gene A
Cag L	Cytotoxin associated gene L
CLO	Campaylobacter Like Organism
COPD	Chronic Obstructive Pulmonary Disease
CRP	C-Reactive Protein
CSR	Central Serous Retinopathy
CSU	Chronic Spontaneous Urticaria
CVD	Cardio Vascular Disease
DLBCL	Diffuse Large B Cell Lymphoma
DM	Diabetes Mellitus
EIA	Enzyme Immuno Assay
ERK	Extra-cellular signal-regulated kinases
E-Test	Epsilometer Test
FBS	Fasting Blood Sugar
FISH	Fluornascence in-situ Hybridisation
Fla A	Flagellins A
Fla B	Flagellins B
GERD	Gastro-esophagus Reflux Disease
GGT	Gamma-Glutamyl Transpeptidase
Hb	Hemoglobin
HR	Heart Rate
HTN	Hypertension
ICA	Immuno Chromatography
IDA	Iron Difficiency Anemia

List of Abbreviations Cont...

Abb.	Full term
Ig G	Immuno-globulins G
IL	Interleukin
INR	International Normalized Ratio
ITP	Idiopathic Thrompocytopenic Purpura
LDL	Low Density Lipoprotein
LPS	Lipopolysaccarides
MAPK	Mitogen-activated Protein kinase
MS	Multiple Sclerosis
NAP	Neutrophil-Activating protein
NMO	Neuromyelitis Optica
NSAID	Non-steroidal Anti-inflammatory Drugs
OAL	Ocular Adenxal Lymphoma
Oip A	Outer inflammatory protein A
PCR	Polymerase Chain Reaction
PE	Pre-Eclampcia
PMP	Pseudomyxoma Pertonitis
PNA	Peptide Nucleic Acid
PPI	Proton Pump Inhibitor
RPTP	Receptor-Like Protein Tyrosin Phosphatase
Sab A	Sialic acid binding adhesion
Th	T helper cells
TLC	Total Leukocytic count
TLR	Toll Like Receptors
TNF	Tumor Necrosing Factor
Vac A	Vacuolating Toxin A

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ABSTRACT

Background: Antibiotic resistance in Helicobacter pylori is the major cause of eradication failure. Prevalence of H.pylori antibiotic resistance is increasing worldwide, and it is the main factor affecting efficacy of current therapeutic regimens. Our aim is to investigate H.pylori resistant patients toward Levofloxacin and detect the most effective antibiotic in eradication of H.pylori.

Objective: To investigate H.pylori resistant patients toward Levofloxacin including regimens and to detect the most effective antibiotic in H.pylori eradication.

Patients and Methods: The present study aimed to investigate the Susceptibility of Levofloxacin Resistant H.pylori in patients who had been diagnosed and received any regimen including Levofloxacin and still signs and symptoms of H.pylori infection not releaved and after proper time of stoppage of PPI and antibiotics H.pylori Ag in stool still positive at the period from January 2019 to February 2020.

Results: In the present study we found a wide spectrum of resistance to rates of H. pylori, from nearly negligible rates of Rifampicin (0%), Imipenem (0%), Cefotaxime (2%), Tetracycline (6%), Doxycycline(10%), and Amoxicillin(38%). To high rates resistance to Metronidazole (100%), Erythromycin (72%), Clarithromycin (68%), Azithromycin (60%), Ciprofloxacin (52%), and Levofloxacin (48%).

Conclusion: Helicobacter pylori is the most common chronic bacterial infection in humans. Antibiotic resistance is a major issue nowadays. Prior use of macrolide antibiotics or metronidazole appears to increase the risk of H. pylori resistance. Clarithromycin resistance appears to be an "absolute" condition that can not be overcome by increasing the macrolide dose. Levofloxacin resistance seems to be increasing. Culture and susceptibility should be done before starting second line treatment.

Keywords: Cytotoxin associated gene A, cytotoxin associated gene L, campaylobacter like organism

INTRODUCTION

H.pylori is one of the most common bacterial infections in humans that affect most populations throughout the world ***(Hu, Zhu, and Lu 2017).***

The story of H. pylori and the recognition of its major role in gastric pathology originated from simple histological observations of the spiral organisms in the gastric mucosa of men and animals. W. Jaworski, Professor of Medicine at the Jagiellonian University of Cracow, Poland was first to de scribe the spiral organisms in the sediment of gastric washings obtained from humans. He noticed among the other rods, a bacterium with a characteristic spiral appearance and named it, Vibrio rugula, suggesting for the first time its possible pathogenic role in gastric diseases ***(Konturek 2003).***

Marshall developed Warren's idea that H. pylori infection is associated with gastritis and duodenal ulcers and this was then confirmed independently by Rollason et al. and Steer, who reported that patients with these diseases were more often infected with spiral bacteria than healthy controls ***(Hagymási and Tulassay, 2014).***

The discovery of h.pylori and of its role in peptic ulcer disease constituted a breakthrough in the field of gastroenterology. Eradication treatment have been developed during the last 20 years leading to decrease in h.pylori-related

peptic ulcer disease and in the prevelence of the infection in the Western world. However, the success of these treatment s is now compromised by the increase in antimicrobal resistance of h.pylori ***(Tveit et al., 2011).***

Antibiotics are important ingredients in all of h.pylori eradication regimens. However, antibiotics resistance is common. Primary resistance to clarithromycin and metronidazole is common in our locality and signifcantly affect the effectiveness of standard eradication therapy ***(Abadi et al., 2012).***

Levofloxacin based therapies are recently found to be effective alternative therapy for h.pylori eradication, and is better than traditional therapy. However, recent studies showed that levofloxacin based therapies showed resistant cases ***(Hu et al., 2017).***

In our study we are trying to find the most effective antibiotic regimen in readdication of levofloxacin resistant H.pylori.

AIM OF THE WORK

The aim of study is to investigate H.pylori resistant patients toward Levofloxacin including regimens and to detect the most effective antibiotic in H.pylori eradication.

Chapter 1

H.PYLORI SIGNS, SYMPTOMS AND MICROBIOLOGY

Helicobacter pylori, previously known as Campylobacter pylori, is a Gram-negative, microaerophilic bacterium usually found in the stomach. It was identified in 1982 by Australian doctors Barry Marshall and Robin Warren, who found that it was present in a person with chronic gastritis and gastric ulcers, conditions not previously believed to have a microbial cause. It is also linked to the development of duodenal ulcers and stomach cancer. However, over 80% of individuals infected with the bacterium are asymptomatic, and it may play an important role in the natural stomach ecology ***(Reshetnyak and Reshetnyak, 2017).***

More than 50% of the world's population has H. pylori in their upper gastrointestinal tracts. Infection is more common in developing countries. H. pylori's helical shape (from which the genus name derives) is thought to have evolved to penetrate the mucoid lining of the stomach ***(Thung et al., 2016).***

Signs and symptoms

1. ***Asymtomatic infection:*** Up to 90% of people infected with H. pylori never experience symptoms or complications ***(Keshavarz Azizi Raftar et al., 2015).***

2. ***Symtomatic infection:*** Acute infection may appear as an acute gastritis with abdominal pain (stomach ache) or nausea. Where this develops into chronic gastritis, the symptoms, if present, are often those of nonulcer dyspepsia: stomach pains, nausea, bloating, belching, and sometimes vomiting or black stool ***(Aishwarya et al., 2016).***

Individuals infected with H. pylori have a 10 to 20% lifetime risk of developing peptic ulcers and a 1 to 2% risk of acquiring stomach cancer. Inflammation of the pyloric antrum is more likely to lead to duodenal ulcers, while inflammation of the corpus (body of the stomach) is more likely to lead to gastric ulcers and gastric carcinoma. However, H. pylori possibly plays a role only in the first stage that leads to common chronic inflammation, but not in further stages leading to carcinogenesis. A meta-analysis conducted in 2009 concluded the eradication of H. pylori reduces gastric cancer risk in previously infected individuals, suggesting the continued presence of H. pylori constitutes a relative risk factor of 65% for gastric cancers; in terms of absolute risk, the increase was from 1.1% to 1.7% ***(Hafez et al., 2011).***

Helicobacter pylori has been associated with colorectal polyps and colorectal cancer. It may also be associated with eye disease. Pain typically occurs when the stomach is empty, between meals, and in the early morning hours, but it can also occur at other times. Less common ulcer symptoms include nausea, vomiting, and loss of appetite. Bleeding can also occur;

prolonged bleeding may cause anemia leading to weakness and fatigue. If bleeding is heavy, hematemesis, hematochezia, or melena may occur ***(Keshavarz Azizi Raftar et al., 2015).***

Microbiology

- ***Morphology:*** Helicobacter pylori is a helix-shaped (classified as a curved rod, not spirochaete) Gram-negative bacterium about 3 μm long with a diameter of about 0.5μm. H. pylori can be demonstrated in tissue by Gram stain, Giemsa stain, haematoxylin–eosin stain, Warthin–Starry silver stain, acridine orange stain, and phase-contrast microscopy. It is capable of forming biofilms and can convert from spiral to a possibly viable but nonculturable coccoid form ***(Tveit et al., 2011).***

Helicobacter pylori has four to six flagella at the same location; all gastric and enterohepatic Helicobacter species are highly motile owing to flagella. The characteristic sheathed flagellar filaments of Helicobacter are composed of two copolymerized flagellins, FlaA and FlaB ***(Tveit et al., 2011).***