FACTORS AFFECTING FAILURE OF FIRST LINE CLARITHROMYCIN BASED THERAPY FOR HELICOBACTER PYLORI INFECTION

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BACKGROUND

- Helicobacter pylori (H. pylori) is a motile, curved and Gram-negative bacillus that is associated with a wide array of digestive and extra-gastric disorders.
- Successful eradication of H. pylori will therefore benefit in improvement of histologic gastritis and prevention of gastric cancer development.
- A major challenge is failure of therapy which can be associated with advanced age, smoking, gastric acidity, high intragastric bacterial load before treatment, bacterial genotype, and host genetic polymorphisms of the cytochrome-P450 isoenzymes that are specifically involved in the metabolism of proton pump inhibitors.
- The most common reason for treatment failure among these is due to antibiotic resistance, especially to the macrolide Clarithromycin used in the triple therapy.

OBJECTIVES

- To determine the eradication rate of gastric H. pylori infection with first-line therapy.
- To determine the contributing factors for failure of first-line therapy.

METHODS

- Design – Retrospective, single-center, cohort study.
- Location – Outpatient clinic located in New Brunswick, NJ.
- Duration – From 10/2014 to 01/2021.
- A total of 299 patients with H. pylori infection were obtained from electronic health record using the ICD-10 code. All of the included patients had a second diagnostic method to determine treatment success and failure.
- Among those treated with clarithromycin based triple therapy (C3), subjects were categorized into C3 success and C3 failure groups for comparative analysis.
- Univariate logistic regression was used for comparison of continuous data (reported as mean ± standard deviation) and χ² test for comparison of categorical data (reported as counts and percentages) between the cohorts. Multivariate logistic regression model was used to determine independent predictors of C3 failure. A p value < 0.05 was considered significant. All data were analyzed with the software Stata/SE version 17.

RESULTS

- Clarithromycin based triple therapy (C3) is the most commonly used first line therapy in 279 (93.3%) of 299 patients with H. pylori gastritis.
- C3 treatment failure was observed in 69 (24.7%) patients, leading to an eradication rate of 75.25%.
- Patients in C3 failure were older (odds ratio [OR] 1.02, 95% CI 1.00–1.04, p = 0.04) when compared to C3 success. This was no longer significant in the multivariate model.
- There was no statistically significant difference in the BMI, Helicobacter pylori. history of recent NSAID use, PPI use, modality of first diagnostic method and endoscopic histopathology between the C3 success and failure groups.
- After multivariate logistic regression analysis, we found a strong association of female sex (OR 2.86, 95% CI 1.23–6.62, p = 0.01) and medication non-compliance (OR 4.98, 95% CI 1.80–13.8, p = 0.002) in C3 failure group.

DISCUSSION

- Bismuth based quadruple therapy (B4) was the most commonly used second line therapy in 37/69 (53.6%) patients, followed by levofloxacin based triple therapy (L3) in 16/69 (23.2%) patients.
- Among those who had a third diagnostic testing performed, 15/28 (53.6%) patients in B4 group and 6/11 (54.5%) in L3 group had successful eradication of H pylori.

CLINICAL IMPORTANCE

- Appropriate selection of first line therapy is crucial in preventing primary treatment failure.
- Patients with risk factors for clarithromycin resistance based on the medical history and geographic resistance pattern can be considered to be treated with either B4 or L3 as first line.

Table 1. Comparison between patients with C3 success and C3 failure

<table>
<thead>
<tr>
<th>Variable</th>
<th>C3 success (n = 210)</th>
<th>C3 failure (n = 69)</th>
<th>Odds ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>48.7 ± 13</td>
<td>52.4 ± 13</td>
<td>1.02 (1.00–1.04)</td>
<td>0.04</td>
</tr>
<tr>
<td>Female sex</td>
<td>143 (68.1%)</td>
<td>58 (84%)</td>
<td>2.47 (1.21–5.00)</td>
<td>0.01</td>
</tr>
<tr>
<td>BMI</td>
<td>20.6 ± 4.7</td>
<td>30.5 ± 6.1</td>
<td>1.03 (0.98–1.09)</td>
<td>0.18</td>
</tr>
<tr>
<td>Ethnicity</td>
<td>182 (96.6%)</td>
<td>57 (82.6%)</td>
<td>0.73 (0.34–1.52)</td>
<td>0.4</td>
</tr>
<tr>
<td>Current smoking</td>
<td>11 (5.2%)</td>
<td>0</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Alcohol use</td>
<td>41 (19.9%)</td>
<td>15 (21.7%)</td>
<td>1.11 (0.57–2.17)</td>
<td>0.74</td>
</tr>
<tr>
<td>Recent NSAID use</td>
<td>21 (11.7%)</td>
<td>11 (17.4%)</td>
<td>1.68 (0.74–3.65)</td>
<td>0.22</td>
</tr>
<tr>
<td>Recent antibiotic use</td>
<td>5 (2.6%)</td>
<td>6 (8.8%)</td>
<td>2.55 (0.66–9.81)</td>
<td>0.16</td>
</tr>
<tr>
<td>Recent PPI use</td>
<td>48 (25%)</td>
<td>15 (24.4%)</td>
<td>0.95 (0.49–1.86)</td>
<td>0.9</td>
</tr>
<tr>
<td>Treatment completion</td>
<td>200 (95.2%)</td>
<td>54 (83%)</td>
<td>0.24 (0.09–0.60)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Medication non-compliance</td>
<td>10 (4.8%)</td>
<td>12 (19%)</td>
<td>4.68 (1.91–11.4)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Table 2. Multivariate logistic regression model