Original Research Article

Efficacy of sequential therapy versus standard triple therapy versus quinolone-based triple therapy for eradication of Helicobacter pylori infection

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ABSTRACT

Background: Helicobacter pylori colonization is a risk factor for Adenocarcinomas of the distal (noncardia) stomach. The presence of Helicobacter pylori is strongly associated with primary gastric lymphoma. The urea breath test, the stool antigen test, and biopsy-based tests can all be used to assess the success of treatment. Helicobacter pylori is susceptible to a wide range of antibiotics in vitro, monotherapy is not usually successful, probably because of inadequate antibiotic delivery to the colonization niche. Current regimens consist of a PPI or H2 blocker, bismuth citrate and two or three antimicrobial agents given for 7-14 days. Research on optimizing drug combinations to increase efficacy continues. Efficacy of Sequential Therapy versus Standard Triple Therapy versus Quinolone-based Triple Therapy for eradication of Helicobacter pylori infection is done in this study.

Methods: This study had been conducted on 150 patients divided into three groups randomly 50 Patients each and were treated with Sequential, Standard and Quinolone based triple therapy respectively. Patients were followed up no sooner than four weeks of completing therapy by rapid urease test to confirm eradication.

Results: There was no significant difference with regards to presence of GERD, Gastric Ulcers, Duodenal Ulcers (p value>0.05) except for presence of erosive gastritis which was significantly higher in patients in quinolone group (p value<0.05). The eradication rate was 90%, 86%, 82% in Sequential therapy group, Triple therapy group and Fluroquinolone group respectively. However, there was no statistically significant difference in eradication rates in these groups (p value>0.05).

Conclusions: Sequential therapy group had better eradication rates (90%) as compared to standard triple therapy group (86%) and fluroquinolone therapy group (82%) but results were not statistically significant when all three groups were compared together.

Keywords: Fluroquinolones, Helicobacter pylori, Mucosa associated lymphoid tissue, Triple therapy

INTRODUCTION

Helicobacter pylori resides in the stomachs of half of the world's human population throughout their lifetimes.¹ Infection with this organism is the main risk factor for peptic ulceration as well as for gastric adenocarcinoma and gastric MALT (mucosa-associated lymphoid tissue) lymphoma.² Treatment for Helicobacter pylori infection
has revolutionized the management of peptic ulcer disease, providing a permanent cure in most cases. Such treatment also represents first-line therapy for patients with low-grade gastric MALT lymphoma. In view of rising resistance present study was undertaken to identify the most appropriate regimen for Helicobacter pylori eradication in Punjab.

METHODS

The study included 150 patients diagnosed to be Helicobacter pylori positive by rapid urease test, after obtaining informed consent, admitted between December-2013 to July-2016. The patients were then randomly divided into three groups each of 50, one received Sequential Therapy with Omeprazole (20 mg) plus Amoxicillin (1 g) twice/day for five days, followed by Omeprazole (20 mg) with Tinidazole (500 mg) twice/day and Clarithromycin (500 mg) twice/day for five consecutive days. Standard triple therapy group received Omeprazole (20 mg), Amoxicillin (1g) and Clarithromycin (500mg) twice/day for 14 days and third group received Quinolone-Based Triple Therapy Omeprazole (20mg bid), Amoxicillin (1gm bid), Levofloxacin (500mg bid) for 10 days. Patients were followed up no sooner than four weeks of completing therapy by rapid urease test to confirm eradication. In cases of duodenal or gastric ulcers compelling continued use of proton-pump inhibitors after completion of antibiotic therapy, patients were followed up four weeks after stopping proton-pump inhibitors.

Inclusion criteria

- Individuals of age more than 18 years age.
- Randomized after positive rapid urease test.

Exclusion criteria

- Chronic use of PPIs or H2-receptor antagonists.
- Use of antibiotics in the previous two weeks
- Concomitant anticoagulant or nonsteroidal anti-inflammatory drug use.
- Zollinger-Ellison syndrome.
- Known allergy to the prescribed antibiotics.
- Pregnant or breastfeeding women.
- Severe or unstable cardiovascular.

- Clinically significant renal or hepatic disease or dysfunction.
- Any other clinically significant medical condition that could increase risk of side effects.
- Patients with Barrett’s esophagus and high-grade dysplasia.
- Patients with severe psychiatric or neurological disorder.

Eradication rates in three groups were then analyzed statistically using standard statistical methods mentioned with each parameter.

RESULTS

Endoscopic diagnosis in three groups was not significant with regards to presence of GERD, Gastric Ulcers, Duodenal Ulcers (p value>0.05) except for presence of erosive gastritis which was significantly higher in patients in quinolone group (p value<0.05) (Table 1).

Eradication rate was 90%, 86%, 82% in sequential therapy group, triple therapy group and fluroquinolone group respectively. However, there was no statistically significant difference in eradication rates in these groups (p value>0.05) (Table 2).

Comparison of follow-up rapid urease test in sequential vs standard triple therapy group. Eradication rate in sequential group was 90 percent whereas in standard triple therapy group was 86 percent. However, this difference was not statistically significant (p value >0.05) (Table 3).

Side effect profile in sequential vs standard triple therapy group. There was no significant difference in two groups in terms of side effects (Table 4).

Follow-up rapid urease test in sequential vs quinolone therapy group. With eradication rate in sequential group was 90 percent whereas in quinolone therapy group was 82 percent. However, this difference was not statistically significant (p value >0.05) (Table 5).

Side effect profile in sequential vs Quinolone therapy group. There was no significant difference in two groups in terms of side effects (p value >0.05) (Table-6).

<table>
<thead>
<tr>
<th>Endoscopic diagnosis</th>
<th>GERD no. (%age)</th>
<th>Erosive gastritis no. (%age)</th>
<th>Gastric ulcers no. (%age)</th>
<th>Duodenal ulcers no. (%age)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sequential</td>
<td>20 (40% )</td>
<td>30 (60%)</td>
<td>16 (32%)</td>
<td>2 (4%)</td>
</tr>
<tr>
<td>Standard Triple</td>
<td>17 (34%)</td>
<td>27 (54%)</td>
<td>20 (40%)</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Quinolone</td>
<td>18 (36%)</td>
<td>42 (84%)</td>
<td>13 (26%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Total</td>
<td>55 (36.7%)</td>
<td>99 (66%)</td>
<td>49 (32.7%)</td>
<td>7 (4.7%)</td>
</tr>
<tr>
<td>p value</td>
<td>0.818NS</td>
<td>0.004*</td>
<td>0.326NS</td>
<td>0.350NS</td>
</tr>
</tbody>
</table>

NS; p >0.05; Not Significant; *p < 0.05; Significant
Table 2: Comparison of follow-up rapid urease test of three groups.

<table>
<thead>
<tr>
<th>Follow-up rapid urease test</th>
<th>Group</th>
<th>Sequential Therapy no. (%age)</th>
<th>Triple Therapy no. (%age)</th>
<th>Quinolone Therapy no. (%age)</th>
<th>Total no. (% age)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>45 (90%)</td>
<td>43 (86%)</td>
<td>41 (82%)</td>
<td>129 (86%)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>5 (10%)</td>
<td>7 (14%)</td>
<td>9 (18%)</td>
<td>21 (14%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>50 (100%)</td>
<td>50 (100%)</td>
<td>50 (100%)</td>
<td>50 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

\[ x^2 = 1.329; \text{df} = 2; p = 0.515 (> 0.05); \text{Not Significant} \]

Table 3: Comparison of follow-up rapid urease test in sequential vs standard triple.

<table>
<thead>
<tr>
<th>Follow-up rapid urease test</th>
<th>Group</th>
<th>Sequential therapy no. (%)</th>
<th>Standard triple therapy no. (%)</th>
<th>Total no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>45 (90%)</td>
<td>43 (86%)</td>
<td>88 (88%)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>5 (10.0%)</td>
<td>7 (14.0%)</td>
<td>12 (12%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>50 (100.0%)</td>
<td>50 (100.0%)</td>
<td>100 (100.0%)</td>
<td></td>
</tr>
</tbody>
</table>

\[ x^2 = 0.379; \text{df} = 1; p = 0.538 (> 0.05); \text{Not Significant} \]

Table 4: Side effects of patients in sequential vs standard triple therapy groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Taste no. (%)</th>
<th>Abdominal pain no. (%)</th>
<th>Bloating no. (%)</th>
<th>Nausea/Vomit no. (%)</th>
<th>Diarrhoea no. (%)</th>
<th>Constipation no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sequential</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
<td>3 (6%)</td>
<td>4 (8%)</td>
<td>7 (14%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Standard Triple</td>
<td>1 (2%)</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
<td>6 (12%)</td>
<td>6 (12%)</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>3 (3%)</td>
<td>3 (3%)</td>
<td>4 (4%)</td>
<td>10 (10%)</td>
<td>13 (13%)</td>
<td>1 (%)</td>
</tr>
<tr>
<td>p value</td>
<td>0.558\text{NS}</td>
<td>0.558\text{NS}</td>
<td>0.307\text{NS}</td>
<td>0.505\text{NS}</td>
<td>0.766\text{NS}</td>
<td>0.315\text{NS}</td>
</tr>
</tbody>
</table>

NS: p > 0.05; Not Significant

Table 5: Follow up rapid urease test comparison of sequential vs quinolone therapy.

<table>
<thead>
<tr>
<th>Follow-up rapid urease test</th>
<th>Groups</th>
<th>Sequential therapy no. (%)</th>
<th>Quinolone therapy no. (%)</th>
<th>Total no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>45 (90.0%)</td>
<td>41 (82%)</td>
<td>86 (86.0%)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>5 (10.0%)</td>
<td>9 (18.0%)</td>
<td>14 (14.0%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>50 (100.0%)</td>
<td>50 (100.0%)</td>
<td>100 (100.0%)</td>
<td></td>
</tr>
</tbody>
</table>

\[ x^2 =1.39; \text{df} = 1; p = 0.249 (> 0.05); \text{Not Significant} \]

Table 6: Side effects of patients in sequential vs quinolone groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Taste no. (%)</th>
<th>Abdominal pain no. (%)</th>
<th>Bloating no. (%)</th>
<th>Nausea/vomit no. (%)</th>
<th>Diarrhoea no. (%)</th>
<th>Constipation no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sequential</td>
<td>2 (4%)</td>
<td>1 (2%)</td>
<td>3 (6%)</td>
<td>4 (8%)</td>
<td>7 (14%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Quinolone</td>
<td>-</td>
<td>2 (4%)</td>
<td>2 (4%)</td>
<td>4 (8%)</td>
<td>6 (12%)</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Total</td>
<td>2 (2%)</td>
<td>3 (3%)</td>
<td>5 (5%)</td>
<td>8 (8%)</td>
<td>13 (13%)</td>
<td>2 (2%)</td>
</tr>
<tr>
<td>p value</td>
<td>0.153\text{NS}</td>
<td>0.558\text{NS}</td>
<td>0.646\text{NS}</td>
<td>1\text{NS}</td>
<td>0.766\text{NS}</td>
<td>1\text{NS}</td>
</tr>
</tbody>
</table>

NS: p > 0.05; Not Significant

Table 7: Follow-up rapid urease test comparison of triple therapy vs quinolone groups.

<table>
<thead>
<tr>
<th>Follow-up rapid urease test</th>
<th>Groups</th>
<th>Triple therapy no (%)</th>
<th>Quinolone therapy no (%)</th>
<th>Total no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative</td>
<td>43 (86.0%)</td>
<td>41 (82%)</td>
<td>84.0% (n=84)</td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>7 (14.0%)</td>
<td>9 (18.0%)</td>
<td>16.0% (n=16)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>50 (100.0%)</td>
<td>50 (100.0%)</td>
<td>100.0 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

\[ x^2 =0.298; \text{df} = 1; p = 0.585 (> 0.05); \text{Not Significant} \]
Follow-up rapid urease test in standard triple therapy group vs quinolone therapy group. Eradication rate in standard therapy group was 86 percent whereas in quinolone therapy group was 82 percent. However, this difference was not statistically significant (p value >0.05) (Table 7). There was no significant difference in two groups in terms of side effects (Table 8).

**DISCUSSION**

Present study included 150 patients diagnosed to be *Helicobacter pylori* positive by rapid urease test, after obtaining informed consent. The patients were then randomly divided into three groups each of 50, one received Sequential Therapy, Standard Triple Therapy group and third group received Quinolone-Based Triple Therapy and patients were followed up atleast four weeks after completion of treatment.

Eradication rate for sequential therapy group was 90 percent. This finding was consistent with study conducted by Vaira et al, in Italy between 2003 and 2006 where eradication rate of 89 percent was obtained with sequential therapy. Similar results were obtained in a study conducted by Zullo et al. Eradication rate for 14 days standard triple therapy was 86 percent and this finding was consistent with results of study conducted by Yuan et al, where eradication rate of 84.4 percent was obtained with 14 days standard triple therapy. Eradication rate for 10 days fluoroquinolone based triple therapy was 82 percent. This finding was consistent with results of study conducted by Gisbert et al, where eradication rate of 83 percent was obtained with levofloxacin containing regimen.

Eradication rate was slightly higher in sequential therapy group (90 percent) compared to other two groups, however the results were statistically insignificant (p value>0.05) when all three groups were compared together suggesting all three regimens were equivalent in terms of achieving *Helicobacter pylori* eradication. No significant difference was found in terms of side effect profile in three groups

These findings were consistent with a multi-center randomised control trial where in 10 days sequential therapy was compared with 14 days Triple Therapy conducted by Liou JM. No difference was noted in eradication rates or adverse effects in two groups. Also, a meta-analysis and systematic review consisting of 46 randomised controlled trials concluded that eradication rates in 10 days sequential therapy and 14 days standard triple therapy were statistically insignificant. The study included 150 patients diagnosed to be *Helicobacter pylori* positive by rapid urease test, after obtaining informed consent. The patients were then randomly divided into three groups each of 50, one received Sequential Therapy, Standard Triple Therapy group and third group received Quinolone-Based Triple Therapy and patients were followed up atleast four weeks after completion of treatment.

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as first line regimen. In case of treatment failure antibiotic resistance should be evaluated before selecting next regimen for best outcomes. A large multicenter study, meta-analysis are required to recommend best eradication regimen for Indian population.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES
