# To compare efficacy of 10-day sequential triple therapy versus 14-days sequential therapy for the eradication of *H. pylori.*

## Shiv Charan*, Rakesh Aggarwal**, Gurminder Singh***, Sudanshu Garg***, Robin Garg***, N. S.Neki****

*Associate Professor, **Assistant Professor, ***Junior Resident ****Professor, Department of Medicine, Govt. Medical College and Guru Nanak Dev Hospital, Amritsar, 143001, India
Corresponding Author: **Dr. Shiv Charan,** Associate Professor Medicine, Govt. Medical College, Amritsar, 143001, India.
E-mail: *drshiv2000@yahoo.com*

## Abstract

Background: *Helicobacter pylori* (*H.pylori*) colonization is the main main risk factor for peptic ulceration as well as for gastric adenocarcinoma and gastric MALT (mucosa-associated lymphoid tissue) lymphoma. Till date optimal therapeutic regimen has not been defined for *H.pylori* eradication, so present study is being conducted to compare efficacy of 10-day sequential triple therapy versus 14-days sequential therapy for the eradication of *H. pylori.*
Methods. Four hundred *H. pylori* positive patients (diagnosed by rapid urease test and histology), were randomized to receive 10-day sequential therapy as follows 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 and 14 Days Sequential Therapy with Omeprazole (20mg bid), Amoxicillin (1gm bid) for seven days, followed by Omeprazole (20mg) with Clarithromycin (500mg) and Tinidazole (500mg twice/day) for seven consecutive days respectively. Eradication rates were determined four weeks after treatment by rapid urease test.
Results. Though the eradication rate was 80 % and 86 in 10 days sequential therapy group and 14 days sequential therapy group respectively, there was no statistically significant difference in eradication rates in these two groups ('p'value>0.05).
Conclusions. 14 days Sequential therapy group had better eradication rates as compared to 10 days Sequential therapy group but results were not statistically significant when both the groups were compared together.

**Keywords:** *H.pylori* (*Helicobacter pylori*); MALT (mucosa associated lymphoid tissue); sequential therapy; PPI (Proton pump inhibitor)

## Background

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.[3]

Although *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. Failure of monotherapy has prompted the development of multidrug regimens, the most successful of which are triple and quadruple combinations. Initially these regimens produced Helicobacter pylori eradication rates of more than 90% in many trials; in recent years, however, resistance to key antibiotics has become more common, a trend leading to Helicobacter pylori eradication rates of only 75–80% for the most commonly used regimens. Current regimens consist of a PPI or $H_2$ blocker, bismuth citrate and two or three antimicrobial agents given for 7–14 days. Research on optimizing drug combinations to increase efficacy continues, and it is likely that guidelines will change as the field develops and as countries increasingly individualize treatment to suit local antibiotic resistance patterns and economic needs.[4] Resistance to clarithromycin and, to a lesser extent, to metronidazole are of growing concern. Clarithromycin resistance is less prevalent but, if present, usually results in treatment failure.[5] A specific mutation leading to clarithromycin resistance appears to be associated with the likelihood of eradication.[6] Of three point mutations associated with clarithromycin resistance (A2143G, A2142G, and A2142C), the A2143G mutation appears to be associated with the lowest eradication rates with clarithromycin containing regimens. Testing for these specific mutations is currently not widely available.

Therefore, an increasing number of patients require second therapeutic attempt to eradicate the infection after treatment with triple drug.

One promising approach is sequential therapy consisting of 10 days and 14 days. This regimen consists of 5 days and 10 days of amoxicillin and a PPI, followed by an additional 5 and 7 days of PPI plus tinidazole and clarithromycin respectively. Basis for this regimen is that by reducing bacterial load in first 5 and 7 days efficacy of tinidazole and clarithromycin increases. Initial studies have demonstrated eradication rates of more than 90% with good patient tolerance.[7]

Individuals may also have a primary resistance to antibiotics that are commonly used in a number of eradication regimens.[8]

Recommended Treatment Regimens for *Helicobacter pylori.*[9]

| Regimen (Duration) | Drug 1 | Drug 2 | Drug 3 | Drug 4 |
|---|---|---|---|---|
| Regimen 1: OCM (7–14 days) | Omeprazole (20 mg bid) | Clarithromycin (500 mg bid) | Metronidazole (500 mg bid) | — |
| Regimen 2: OCA (7–14 days) | Omeprazole (20 mg bid) | Clarithromycin (500 mg bid) | Amoxicillin (1 g bid) | — |
| Regimen 3: OBTM (14 days) | Omeprazole (20 mg bid) | Bismuth subsalicylate (2 tabs qid) | Tetracycline HCl (500 mg qid) | Metronidazole (500 mg tid) |

| Regimen 4: sequential (5 days + 5 days) | Omeprazole (20 mg bid) | Amoxicillin 1 g bid | | |
| | Omeprazole (20 mg bid) | Clarithromycin (500 mg bid) | Tinidazole (500 mg bid) | |
| Regimen 5: OAL (10 days) | Omeprazole (20 mg bid) | Amoxicillin (1 g bid) | Levofloxacin (500 mg bid) | |
| Regimen 6: (7days + 7days) | Omeprazole (20 mg bid) | Amoxicillin 1 g bid | | |
| | Omeprazole (20 mg bid) | Clarithromycin (500 mg bid) | Tinidazole (500 mg bid) | |

The urea breath test, the stool antigen test, and biopsy-based tests can all be used to assess the success of treatment. However, because these tests are dependent on *Helicobacter pylori* load, their use less than 4 weeks after treatment may yield false-negative results. Furthermore, these tests are unreliable if performed within 4 weeks of intercurrent treatment with antibiotics or bismuth compounds or within 2 weeks of the discontinuation of proton pump inhibitor (PPI) treatment. In the assessment of treatment success, non-invasive tests are normally preferred; however, after gastric ulceration, endoscopy should be repeated to ensure healing and to exclude gastric carcinoma by further histologic sampling.[10,11]

## Tests Commonly Used to Detect *Helicobacter pylori* :[12]

| Test | Advantages | Disadvantages |
|---|---|---|
| Invasive (Based on Endoscopic Biopsy) | | |
| Biopsy urease test | Quick, simple | Some commercial tests not fully sensitive before 24 h |
| Histology | May give additional histologic information | Sensitivity dependent on experience and use of special stains |
| Culture | Permits determination of antibiotic susceptibility | Sensitivity dependent on experience |
| Non-invasive | | |
| Serology | Inexpensive and convenient; not affected by recent antibiotics or proton pump inhibitors to the same extent as breath and stool tests | Cannot be used for early follow-up after treatment; some commercial kits inaccurate, and all less accurate than breath test |
| [13]C urea breath test | Inexpensive and simpler than endoscopy; useful for follow-up after treatment | Requires fasting; not as convenient as blood or stool tests |
| Stool antigen test | Inexpensive and convenient; useful for follow-up after treatment; may be useful in children | May be disliked by people from some cultures; may be slightly less accurate than urea breath test, particularly when used to assess treatment success |

In view of increasing failure of treatment and rising resistance to antibiotics multiple randomised control trials are being conducted to look for best regimens that eradicates Helicobacter Pylori. Different regimens that are tried include Standard Triple regimen, Sequential Therapy, Quadruple therapy, Fluroquinolone based triple therapy.

In a meta-analysis and systematic review eradication 46 randomised controlled trials were reviewed and analysed. 5666 patients were randomised to sequential therapy and 7866 to other (established and new) treatments. Sequential therapy was superior to seven day triple therapy (relative risk 1.21, 95% confidence interval 1.17 to 1.25; I2=29.3%; number needed to treat 6, 95% confidence interval l5% to 7%), marginally superior to 10 day triple therapy (1.11,1.04 to1.19;I2=67.2%;NNT 10,7to15), but not superior to 14 day triple therapy (1.00,0.94 to1.06; I2=54.3%). This study also concluded that duration of therapy is important for eradication of Helicobacter pylori.[13]

A study of 10-day sequential or standard 10-day therapy (40 mg of pantoprazole, 500 mg of clarithromycin, and 1 g of amoxicillin, each administered twice daily) was conducted in two Italian hospitals. It was double blind randomised control trial. The eradication rate achieved with the sequential regimen was significantly greater than that obtained with the standard treatment in the intention-to-treat analysis (89% vs. 77%; P 0.0134; difference, 12% [95% CI, 3% to 20%]), the modified intention- to-treat analysis (91% vs. 78%; P 0.0022; difference, 13% [CI, 5% to 21%]), and the per-protocol analysis (93% vs. 79%; P 0.0013; difference, 14% [CI, 6% to 21%]).[14]

In an open-label, randomized, controlled trial of sequential therapy for 10 days, sequential therapy for 14 days, or standard triple therapy for 14 days in H pylori-positive individuals recruited from 6 gastroenterology clinics in Taiwan. Eradication rates were superior in the 14-day sequential therapy arm, compared with the 14-day triple therapy arm (90.7% vs 82.3%; P =.003), with a number needed to treat to prevent 1 patient failing

therapy of 12. There were no differences in eradication rates between 14- and 10-day sequential therapy (90.7% vs 87.0%), or 10-day sequential therapy and 14-day triple therapy (87.0% vs 82.3%). In this analysis, 14- or 10-day sequential therapy was superior to 14-day triple therapy in all regions, except those with high metronidazole and low clarithromycin resistance.[15]

The Lancet published a randomized controlled trial in January 2013 that compared sequential therapy with PPI- based triple therapy. It is found that the sequential treatment arm yielded superior eradication rates compared to Standard therapy, 87.0% and 82.3% respectively. This trial also tested 14- days sequential therapy, which proved even more efficacious with a 90.7% success rates.[16]

A prospective randomised study comparing 10- or 14-day sequential therapy with 10- or 14-day concomitant therapy. This Study showed that All four regimens achieved eradication rates > 90% in PP analyses in a country with high clarithromycin resistance. There was no difference in tolerability among the four regimens.[17]

A multi-center, single site, pilot study in which H. pylori-infected patients received a 14-day sequential therapy. The eradication rate was 93.9% (95% confidence interval [CI], 89.5–98.3%) by PP and 91.9% (95% CI, 87.1–96.7%) by intention-to-treat analysis. Study showed that extending sequential therapy to 14 days did not result in improving the treatment outcome to 95% or greater.[18]

## Aim and Objectives

Comparative study of 10 days sequential therapy versus 14 days sequential therapy for eradication of Helicobacter pylori infection.

## Materials and Methods

The study included 400 patients attending OPD / admitted in various wards of Guru Nanak Dev Hospital and allied group of hospitals attached to Government Medical College, Amritsar

diagnosed to be helicobacter pylori positive by rapid urease test, after obtaining informed consent. Sample size of 400 was taken as under:

Based on the efficacy rates of 86% and 80% in two groups respectively, taking alpha error probability 0.05, power required 90% effect size was calculated as 0.173, it was seen that sample size required was 352. However by taking sample size 400 i.e. 200 each in both groups power achieved was 93.32%

² **tests -** Goodness-of-fit tests: Contingency tables

**Analysis:** A priori: Compute required sample size

| **Input:** | Effect size w | = |
|---|---|---|
| | 0.1729171 | |
| | err prob | = 0.05 |
| | Power (1- err prob) | = 0.90 |
| | Df | = 1 |

| **Output:** | Noncentrality parameter | = |
|---|---|---|
| | 10.5249139 | |
| | Critical ² | = |
| | 3.8414588 | |
| | Total sample size | = 352 |
| | Actual power | = |
| | 0.9004726 | |

² **tests -** Goodness-of-fit tests: Contingency tables

**Analysis:** Post hoc: Compute achieved power

| **Input:** | Effect size w | = 0.173 |
|---|---|---|
| | err prob | = 0.05 |
| | Total sample size | = 400 |
| | Df | = 1 |
| **Output:** | Noncentrality parameter | = |
| | 11.9716000 | |
| | Critical ² | = |
| | 3.8414588 | |
| | Power (1- err prob) | = |
| | 0.9331975 | |

Patients were randomly divided into two groups each of 200, group A was given 10 days 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. Group B received 14 Days Sequential Therapy with Omeprazole(20mg bid) , Amoxicillin(1gm bid) for seven days, followed by Omeprazole (20mg) with Clarithromycin(500mg) and Tinidazole (500mg twice/day) for seven consecutive days. Patients were followed up at 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. The statistical software SPSS(Statistical package for Social Sciences) Ver. 21 was used for statistical analysis. The qualitative variables were compared using the chi-square test and $p < 0.05$ was taken as statistically significant.

This study shows eradication rate of 80 % and 86% in 10 days sequential therapy group and 14 days sequential therapy group respectively. However, there was no statistically significant difference in eradication rates in these two groups ('p'value >0.05).

## Inclusion criteria

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

## 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
- Known allergy to the prescribed antibiotics
- Pregnant or breastfeeding women
- Any other clinically significant medical condition that could increase risk of side effects.

- Patients with severe psychiatric or neurological disorder
- Eradication rates in two groups will then be analyzed statistically.

## Results

The study included 400 patients diagnosed to be helicobacter pylori positive by rapid urease test, the patients were randomly divided into two groups each of 200, group A and group B.
Group A: 10 days sequential therapy group
Group B: 14 days sequential therapy group

### Table 1 Main clinical characteristic of all patients

| Parameters | Group A | Group B | P value |
|---|---|---|---|
| **Total number** | 200 | 200 | |
| Sex (M/F) | 136/64 | 148/52 | $0.186^{NS}$ |
| Age ( years; range) | 19 – 73 | 18 – 75 | |
| GERD | 56 | 44 | $0.166^{NS}$ |
| Erosive gastritis | 140 | 148 | $0.373^{NS}$ |
| Gastric ulcer | 80 | 88 | $0.418^{NS}$ |
| Duodenal ulcer | 4 | 16 | 0.006* |

Table 2 shows mean age of population in two groups. There was no significant difference in age distribution in both the groups ('p' value >0.05).

### Table 2 Age distribution of population in study group

| Age group (years) | Group A | | Group B | |
|---|---|---|---|---|
| | No. | % | No. | % |
| ≤20 | 8 | 4.0 | 6 | 3.0 |
| 21-30 | 16 | 8.0 | 16 | 8.0 |
| 31-40 | 66 | 33.0 | 64 | 32.0 |
| 41-50 | 70 | 35.0 | 72 | 36.0 |
| 51-60 | 27 | 13.5 | 26 | 13.0 |
| 61-70 | 10 | 5.0 | 12 | 6.0 |
| >70 | 3 | 1.5 | 4 | 2.0 |
| Total | 200 | 100.0 | 200 | 100.0 |
| $X^2$ | 0.688 | | | |
| Df | 6 | | | |
| p-value | $0.995^{NS}$ | | | |

NS; p > 0.05; Not significant

Table 3 shows side effect profile in both groups at follow up. Diarrhoea was the most common side effect and constipation was least common side effect reported. There was no significant difference in side effect profile in both the groups 'p' Value >0.05 for all the reported side effects.

Table 3  Comparing side effects

| Side effects | Group A | | Group B | | P value |
|---|---|---|---|---|---|
| | N | % | N | % | |
| Taste | 4 | 2.0 | 8 | 4.0 | $0.241^{NS}$ |
| Abdominal Pain | 12 | 6.0 | - | - | <0.001* |
| Bloating | 12 | 6.0 | 8 | 4.0 | $0.359^{NS}$ |
| Nausea/vomiting | 8 | 4.0 | 16 | 8.0 | $0.092^{NS}$ |
| Constipation | 4 | 2.0 | 4 | 2.0 | $1.000^{NS}$ |
| Diarrhoea | 32 | 16.0 | 12 | 6.0 | 0.001* |

Table 4 shows that eradication rate was 80 % and 86 in 10 days sequential therapy group and 14 days sequential therapy group respectively.

However, there was no statistically significant difference in eradication rates in these two groups ('p'value>0.05).

Table 4 Comparison of follow-up rapid urease test of three groups

| Followup | Present | | Absent | |
|---|---|---|---|---|
| | No. | % | No. | % |
| Group A | 40 | 20.0 | 160 | 80.0 |
| Group B | 28 | 14.0 | 172 | 86.0 |
| Total | 68 | 17.0 | 332 | 83.0 |
| $X^2$ | 2.551 | | | |
| Df | 1 | | | |
| p-value | $0.110^{NS}$ | | | |

NS: p > 0.05; Not significant

## Discussion

Present study included 400 patients attending OPD / admitted in various wards of Guru Nanak Dev Hospital and allied group of hospitals attached to Government Medical College, Amritsar diagnosed to be helicobacter pylori positive by rapid urease test, after obtaining informed consent. The patients were then randomly divided into two groups each of 200, group A will receive 10 Days 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.  Group B will receive 14 Days Sequential Therapy with Omeprazole(20mg bid) , Amoxicillin(1gm bid) for seven days,  followed by Omeprazole (20mg) with Clarithromycin (500mg) and Tinidazole (500mg twice/day) for seven consecutive days.  Patients were followed up atleast four weeks after completion of treatment.

There was no significant difference in age distribution in both the groups ('p' value>0.05). There was no significant difference in sex distribution in both the groups ('p' value >0.05).

In our study eradication rate for 10 days sequential therapy group was 80 percent and 14 days sequential therapy group was 86 percent. Though eradication rate was slightly higher in 14 days sequential therapy group (86 percent) compared to 10 days sequential therapy group (80 percent) results were statistically insignificant (p value>0.05) when both the groups were compared together suggesting both the regimens were equivalent in terms of achieving *Helicobacter pylori* eradication. No significant difference was found in terms of side effect profile in both the groups.

These findings were consistent with an open-label, randomized, controlled trial where sequential therapy for 10 days was compared with sequential therapy for 14 days, or standard triple therapy for 14 days conducted by Liou JM.[15] No difference was noted in eradication rates or adverse effects in two groups.

Our results were consistent with a randomised controlled trial published by lancet that shows 87 percent eradication rate with 10 days sequential therapy and extending to 14 days sequential therapy yielded 90 percent eradication rate.[16]

Also, a prospective randomised study comparing 10- or 14-day sequential therapy with 10- or 14-day concomitant therapy concluded that All four regimens achieved eradication rates > 90% in PP analyses.[17]

Similarly a multi-center, single site, pilot study conducted by Ping I etal where 123 subjects were given 14 days sequential therapy and the results were consistent with findings of our study. It was shown that extending sequential therapy to 14 days did not result in improving the treatment outcome to 95% or greater.[18]

## Conclusion

Helicobacter pylorus infection is a global problem specially in developing countries. Colonization 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. Despite the number of studies, the optimal therapeutic regimen has not yet been defined.

Following conclusions were drawn from study:

- 14 days Sequential therapy group had better eradication rates as compared to10 days. Sequential therapy group but results were not statistically significant when both the groups were compared together.
- Side effects profile in both the groups were similar when compared together and there was insignificant difference in side effects of both groups.

- Resistance is an evolving process and hence antibiotic susceptibility and local treatment success rates must be monitored to update treatment selections.
- Though statistically insignificant, 14 days sequential therapy group had slight better eradication rates than 10 days sequential therapy group further studies with large sample size are needed to recommend it as replacement for 10 days sequential therapy.
- In case of treatment failure antibiotic resistance should be evaluated before selecting next regimen for best outcomes.
- Limitations of our Study:
- Small sample size.
- Study was not multicenter.
- Antibiotic sensitivity testing in patients who did not achieve eradication was not done in our study.
- Thus large multicenter studies, meta-analysis are required to recommend best eradication regimen for Indian Population.

## References

1. Brown LM. Helicobacter pylori: epidemiology and routes of transmission. Epidemiol Rev.2000;22(2):283–97.
2. Eidt S, Stolte M, Fischer RJ. Helicobacter pylori gastritis and primary gastric non-Hodgkin's lymphomas. Clin Pathol. 1994; 47(5):436-9.
3. Wündisch T, Thiede C, Morgner A, Dempfle A, Günther A, Liu H, et al. Long-term follow-up of gastric MALT lymphoma after Helicobacter pylori eradication. J ClinOncol. 2005;23(31):8018-24.
4. Graham DY, Lew GM, Evans DG, Evans DJ, Klein PD.Effect of triple therapy (antibiotics plus bismuth) on duodenal ulcer healing. A randomized controlled trial. Ann Intern Med. 1991; 115(4):266-9.
5. Megraud F. Helicobacter pylori and antibiotic resistance. World J Gastroenterol. 2007; 56: 1502.

6. De Francesco V, Margiotta M, Zullo A. Clarithromycin-resistant genotypes and eradication of *Helicobacter pylori*. Ann Intern Med. 2006; 144:94.

7. Graham DY, Lew GM, Malaty HM, Evans DG, Evans DJ, Klein PD, et al. Factors influencing the eradication of Helicobacter pylori with triple therapy. Gastroenterology. 1992;102(2):493-6.

8. Malfertheiner P, Megraud F, O'Moran C. Current concepts in the management of *Helicobacter pylori* infection. The Maastricht III Consensus Report.World J Gastroenterol.2007;56:72–81.

9. Mana F, Van Laer W, Bossuyt A, UrbainD . The early effect of proton pump inhibitor therapy on the accuracy of the 13C-urea breath test. Dig Liver Dis. 2005;37(1):28-32.

10. Laine L, Estrada R, Trujillo M, Knigge K, Fennerty MB. Effect of proton-pump inhibitor therapy on diagnostic testing for Helicobacter pylori. Ann Intern Med. 1998;129:547–50.

11. Atherton JC, Blaser MJ. *Helicobacter pylori* Infections. In: Lango DL, Kasper DL, Jameson JL, Fauci AS, Hauser SL, Loscalzo J, editors. Harrison's Principles of Internal Medicine. 18th edition. McGraw Hill Education;2012.p.1261-5.

12. Valle JD. Peptic ulcer disease and related disorder. In: Lango DL, Kasper DL, Jameson JL, Fauci AS, Hauser SL, Loscalzo J, editors. Harrison's Principles of Internal Medicine. 18th edition. McGraw Hill Education;2012.p.2438-59.

13. Gatta L, Scarpignato C, Vakil N, Vaira D. Global eradication rates for *Helicobacter pylori* infection: systematic review and meta-analysis of sequential therapy. Brit Med J. 2013;347:f4587.

14. Vaira D, Zullo A, Vakil N, Gatta L, Ricci C, Perna F, et al. Sequential Therapy versus Standard Triple-Drug Therapy for *Helicobacter pylori* Eradication A Randomized Trial. Ann Intern Med. 2007;146(8):556-63.

15. Liou JM, Chen CC, Chen MJ, et al. Sequential versus triple therapy for the first-line treatment of *Helicobacter pylori*: a multicentre, open-label, randomised trial. Lancet. 2013;381:205-13.

16. Edwards P. Eradicating Helicobacter pylori: what is the latest recommended therapy? CurrTher. 1996;jan:49-54.

17. Park SM, Kim JS, Kim BW, Ji JS, Choi H. A randomised clinical trial comparing 10- or 14-day sequential therapy and 10- or 14-day concomitant therapy for the first line empirical treatment of *Helicobacter pylori* infection. Journal of gastroenterology and hepatology.2016 Aug 9 pg.

18. Ping I. Hsu, Deng-Chyang Wu, Jeng-Yih Wu, David Y. Graham. Is There a Benefit to Extending the Duration of *Helicobacter pylori* Sequential Therapy to 14 Days? Helicobacter. 2011;16(2):146-52.

| **Access this Article in Online** | |
|---|---|
| | Website: www.ijcrims.com |
| Quick Response Code | Subject: Medicine |