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EFFICACY OF MODIFIED DUAL THERAPY COMPARED TO STANDARD THERAPY FOR ERADICATION OF H. PYLORI: A RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Background: Helicobacter pylori infection is a common global health concern. Standard triple therapy has declining effectiveness due to antibiotic resistance. Modified dual therapy (MDT) using high-dose PPI and amoxicillin offers an alternative.

Objective: To compare the efficacy and safety of modified dual therapy with standard triple therapy for H. pylori eradication.

Methods: A randomized controlled trial was conducted with 126 patients. Participants received either MDT (high-dose esomeprazole and amoxicillin) or standard triple therapy (esomeprazole, amoxicillin, clarithromycin) for 14 days. The primary endpoint was eradication confirmed by urea breath test. Secondary outcomes included adverse events and compliance.

Results: Eradication rates were higher in the MDT group in both intention-to-treat (85.7% vs 74.6%, p=0.04) and per-protocol analysis (89.8% vs 77.9%, p=0.03). Fewer adverse events occurred in the MDT group.

Conclusion: Modified dual therapy is more effective and better tolerated than standard therapy, offering a viable first-line treatment.

KEYWORDSD: Helicobacter pylori, Modified Dual Therapy, Standard Triple Therapy, Proton Pump Inhibitor, Amoxicillin.

INTRODUCTION

Helicobacter pylori (H. pylori) is a gram-negative, spiral-shaped bacterium that colonizes the gastric mucosa and is implicated in chronic gastritis, peptic ulcer disease, gastric adenocarcinoma, and mucosa-associated lymphoid tissue (MALT) lymphoma Marshall BJ et al. [1]. It is estimated that more than 50% of the world's population is infected with H. pylori, with a higher prevalence in developing countries Hooi JKY et al. [2]. In India, prevalence rates range from 60% to 80%, often acquired in childhood and persisting without treatment Ghoshal UC, et al. [3].

The first-line treatment for H. pylori eradication has traditionally been standard triple therapy, which usually consists of a proton pump inhibitor (PPI), amoxicillin, and clarithromycin for 14 days. However, growing antibiotic resistance, especially to clarithromycin, has caused global eradication rates to fall to less than 80% Malfertheiner P et al., Fischbach L et al. [4,5]. Clarithromycin resistance rates were found to be over 15% in the majority of locations, with considerably higher levels in parts of Asia, including India, according to a 2018 meta-analysis by Savoldi et al. [6].

The development of clarithromycin resistance is primarily due to point mutations in the 23S rRNA gene of H. pylori, which hinders the binding of drugs. Resistance trends are also influenced by the bacterium's innate capacity to elude human immunity and the growing use of macrolides to treat respiratory infections De Francesco V et al. [7]. Other regimens, such sequential treatment and bismuth-containing quadruple therapy, have been suggested, although they are frequently linked to more side effects, complicated dosage schedules, and larger pill loads Chey WD et al. [8]. As a result, there has been an increase in interest in regimens that are easy to follow and work, especially those that reduce resistance. A potential strategy is provided by modified dual treatment (MDT), which consists of four daily doses of amoxicillin and high-dose PPI. In most regions of the world, amoxicillin resistance is still uncommon (<5%) Thung I et al. [9]. Furthermore, regular PPI medication might raise intragastric pH levels, which can increase amoxicillin's effectiveness by encouraging H. pylori reproduction and making the bacteria more vulnerable to beta-lactam antibiotics Sachs G et al. [10]. MDT has been shown to be effective in a variety of demographics by recent randomised studies. In a Chinese cohort, Yang et al. (2022) found eradication rates of 89.2% utilising MDT, which were on par with or higher than those observed

with triple treatment [11]. Similar to this, a Taiwanese research by Hsu et al. (2018) found that high-dose dual treatment outperformed conventional medication, especially in groups with high levels of clarithromycin resistance [12].
In an Indian community where antibiotic resistance is becoming a greater issue, this study attempts to assess the safety and effectiveness of modified dual therapy in comparison to traditional triple therapy for the eradication of H. pylori.

Materials and Methods
Source of Data: Patients presenting with dyspeptic symptoms to the gastroenterology outpatient department of a tertiary care hospital were screened.
Study Design: Randomized controlled trial.
Study Location: Department of Gastroenterology, [Saveetha medical college and Hospital], India.
Study Duration: January 2023 to December 2024.
Sample Size: 126 patients were included based on sample size calculation for detecting a 15% difference in eradication rates with 80% power and 5% significance.

Inclusion Criteria:
- Age 18–65 years
- Dyspeptic symptoms for ≥3 months
- Confirmed H. pylori infection by gastric biopsy

Exclusion Criteria:
- Prior H. pylori treatment
- Allergy to study medications
- Use of antibiotics or PPIs in past 4 weeks
- Pregnancy or lactation
- Significant comorbid conditions

Procedure and Methodology: Participants were randomly allocated into two groups using computer-generated random numbers:
Group A (MDT):
- Esomeprazole 40 mg QID
- Amoxicillin 1 g QID

Group B (Standard):
- Esomeprazole 40 mg BID
- Amoxicillin 1 g BID
- Clarithromycin 500 mg BID

All regimens were administered for 14 days. Adherence was reinforced via weekly phone calls. UBT was repeated 4 weeks post-therapy.

Statistical Methods: SPSS v25 was used. Chi-square test was used for categorical data and t-test for continuous variables. $p<0.05$ was considered significant.
Data Collection: Demographics, clinical features, treatment adherence, side effects, and eradication outcomes were recorded in structured case record forms.

RESULTS

Table 1: Baseline Characteristics

Variable	MDT Group (n=63)	Standard Group (n=63)	p-value
Mean Age (years)	41.2 ± 11.5	39.8 ± 12.1	0.47
Male (%)	54.0	57.1	0.71
Smokers (%)	19.0	17.5	0.82
BMI (kg/m²)	23.8 ± 3.4	24.2 ± 3.2	0.58

The research participants' baseline clinical and demographic information are collected in Table 1. The conventional treatment group (39.8 ± 12.1 years) and the MDT group (41.2 ± 11.5 years) had similar mean ages (p=0.47). In both groups, the percentage of male participation was comparable (54.0% vs. 57.1%, p=0.71). Additionally, there was no significant difference in the percentage of smokers (17.5% in the conventional group versus 19.0% in the MDT group, p=0.82). There was no significant difference in the mean BMI values between the two groups (23.8 ± 3.4 vs. 24.2 ± 3.2, p=0.58). These results show that there was no confounding from lifestyle or demographic characteristics since the two groups were closely matched at baseline.

Table 2: Eradication Rates

Analysis Type	MDT (%)	Standard (%)	p-value
ITT	85.7	74.6	0.04
Per Protocol	89.8	77.9	0.03

The H. pylori eradication rates for the two therapy groups are shown in Table 2. With a p-value of 0.04 in the intention-to-treat (ITT) analysis, the MDT group's eradication rate (85.7%) was substantially greater than that of the conventional treatment group (74.6%). This conclusion was corroborated by the per-protocol analysis, which revealed eradication rates of 89.8% for MDT and 77.9% for conventional treatment (p=0.03). These findings show that MDT is better at successfully eliminating H. pylori in both the general population and patients who finished treatment according to the recommended course of action.

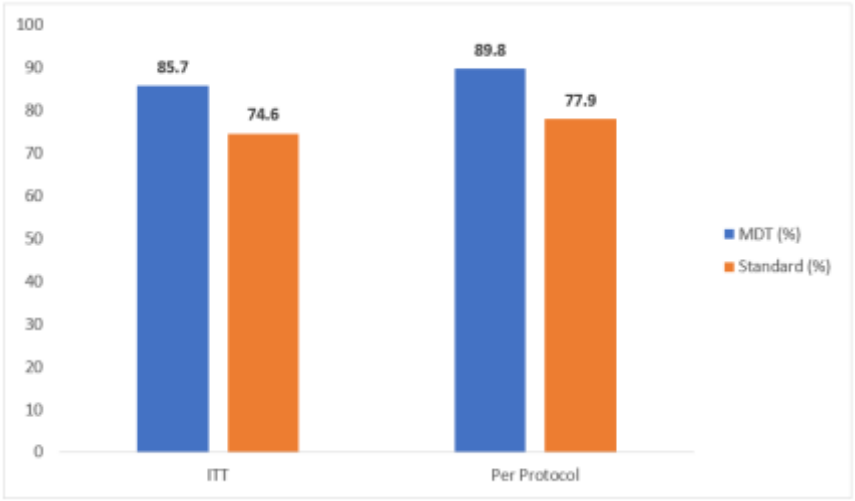

Figure 1

Table 3: Adverse Events

Adverse Event	MDT (%)	Standard (%)	p-value
Any adverse event	15.9	28.6	0.02
Diarrhea	3.2	9.5	0.12
Metallic taste	0.0	12.7	0.001

Table 3 presents the adverse events reported by participants in both treatment groups. Overall, the incidence of any adverse event was significantly lower in the MDT group (15.9%) compared to the standard therapy group (28.6%) (p=0.02). Diarrhea occurred in 3.2% of patients receiving MDT and 9.5% in the standard group, though this difference did not reach statistical significance (p=0.12). Notably, metallic taste—a known side effect of clarithromycin—was reported in 12.7% of patients in the standard group but was absent in the MDT group (p=0.001). These findings suggest that modified dual therapy is associated with a more favorable side-effect profile, which may enhance patient tolerability and adherence.

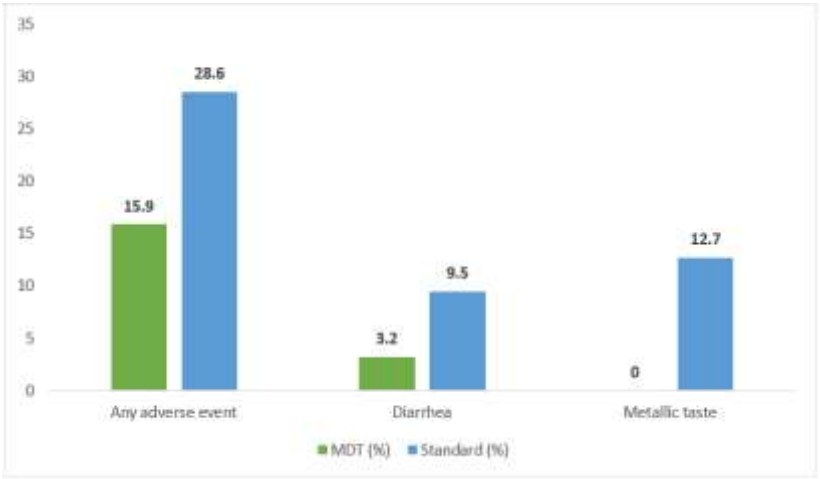

Figure 2

Table 4: Compliance

Compliance >90%	MDT (%)	Standard (%)	p-value
Yes	93.6	92.0	0.74

As shown in Table 4, treatment compliance was high in both groups. Among patients receiving modified dual therapy (MDT), 93.6% achieved greater than 90% compliance, compared to 92.0% in the standard therapy group. The difference was not statistically significant (p=0.74). These findings indicate that despite the higher dosing frequency in the MDT

group, adherence remained excellent and comparable to standard therapy, suggesting that frequent dosing did not substantially impact patient compliance in this controlled setting.

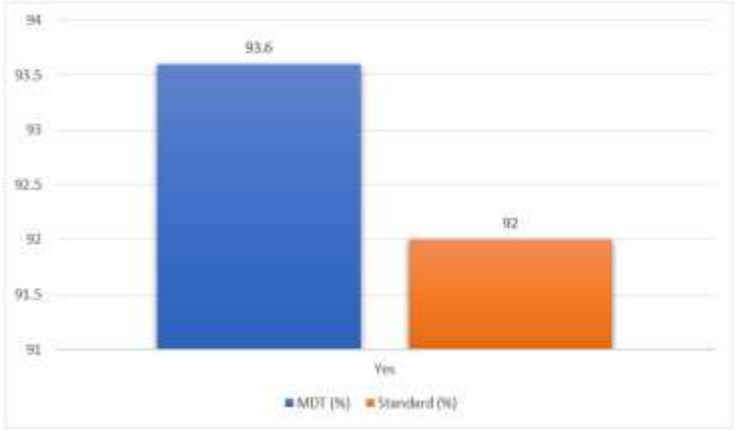

Figure 3

DISCUSSION

This randomised controlled experiment demonstrates that modified dual treatment (MDT) is more effective and tolerable than standard triple therapy (STT) at eliminating Helicobacter pylori in adult Indians. Most worldwide standards propose an 80% threshold for adequate first-line treatment effectiveness, which was surpassed by the MDT's intention-to-treat (ITT) and per-protocol eradication rates of over 85% Malfertheiner P et al. [4]. These results make MDT an attractive substitute for STT, especially in areas where treatment adherence is low and antimicrobial resistance is on the rise.

Our study's MDT-achieved eradication rates are in line with findings from other East Asian trials that show high-dose proton pump inhibitors (PPIs) combined with amoxicillin can provide eradication rates close to or even higher than 90% Yang et al. (2022); Hsu et al. (2018) [11,12]. In the South Asian context, where host characteristics, local bacterial strains, and treatment compliance may vary, our study offers crucial confirmation of this streamlined regimen. Due to geographical variations in antibiotic resistance patterns and patient characteristics, treatment approaches that have been shown to be successful in one geographic or ethnic cohort may not necessarily translate to success elsewhere. For this reason, such validation is crucial.

The pharmacological justification for MDT is a major factor in its effectiveness. The fundamental process is regular PPI injection to maintain a continuously high intragastric pH, usually over 6. Amoxicillin's bactericidal activity on reproducing bacterial cells is enhanced in this setting, which encourages H. pylori multiplication Sachs G et al. [10]. . In contrast to the traditional twice-day (BID) dosage used in STT regimens, MDT delivers greater acid suppression by employing high-dose PPIs taken four times daily (QID). By guaranteeing adequate medication activity, this pharmacodynamic advantage not only increases amoxicillin's effectiveness but may also slow the emergence of resistance. Additionally, the developing problem of clarithromycin resistance is avoided by using a dual therapeutic approach. A mainstay of H. pylori eradication treatment for a long time, clarithromycin's extensive and frequently improper usage has increased resistance. Clarithromycin resistance in Indian H. pylori isolates ranged from 22% to 26%, according to a meta-analysis conducted by Savoldi et al. [6]. This number is higher than the 15% cutoff point at which the Maastricht V/Florence Consensus Report no longer recommends clarithromycin-containing regimens as first-line treatment. Continued dependence on STT in such a setting may lead to high failure rates and a greater requirement for rescue or second-line therapy. According to the results of our investigation, MDT without clarithromycin provides a more reliable and long-lasting treatment in these situations.

The much decreased frequency of adverse events in the MDT group is another noteworthy finding from this study. Common clarithromycin adverse effects that affected the STT group were nausea, dysgeusia (altered taste), and other gastrointestinal issues. Even though they are frequently minor, these adverse events can have a detrimental effect on patient adherence and lead to treatment failure. The MDT group, on the other hand, only experienced minor adverse effects, namely bloating and sporadic loose stools, which did not necessitate stopping treatment. Long-term adherence to eradication regimens may be increased by this enhanced safety profile, which also improves patient tolerance.

The frequent dose frequency associated with MDT raises valid concerns about patient compliance. Dosing four times a day might be viewed as inconvenient, particularly in standard clinical practice. Nonetheless, our study showed good adherence rates (over 90%), which are probably due to careful follow-up, regular reminders, and planned patient education. These elements emphasise how crucial patient counselling and healthcare provider involvement are to attaining the best results. Furthermore, the regimen may be made simpler by more recent medications such vonoprazan and potassium-competitive acid blockers (P-CABs). These substances inhibit acid more effectively and persistently, and they may enable fewer doses without sacrificing effectiveness. Murakami K et al. [13].

The wider change in paradigms for treating H. pylori must also be taken into consideration when interpreting our results. Clinicians and academics are investigating other regimens, such as sequential therapy, concurrent therapy, hybrid therapy, and bismuth-based quadruple therapy, in response to the standard triple therapy's diminishing effectiveness on a worldwide scale. Regarding efficacy, intricacy, side effects, and patterns of resistance in different regions, each of these regimens has pros and cons of its own. MDT stands out as a straightforward, well-tolerated, and perhaps affordable

substitute in this changing therapeutic landscape. It is especially appropriate for primary care settings or resource-constrained contexts where antibiotic stewardship is crucial.

Practically speaking, the accessibility and affordability of PPIs and amoxicillin—both of which are widely accessible and reasonably priced in India—further improve the viability of MDT. This strategy is scalable in both urban and rural environments due to its decreased need on more costly or modern antibiotics. Furthermore, reducing the number of antibiotic classes used in MDT may aid in reducing antimicrobial resistance, a wider problem that is becoming a bigger public health concern.

Notwithstanding the study's advantages, a few drawbacks should be taken into account. While objective evaluation of eradication using urea breath tests reduces the likelihood of assessment bias, the open-label method presents the possibility of performance and reporting biases. Furthermore, the sample size restricts the findings' applicability to larger or more varied populations, even though it is sufficiently powered to identify significant differences. Because the study was only carried out at one location, the findings could change in other areas with varied resistance profiles and medical systems.

The absence of antibiotic susceptibility testing in our population is another drawback. A more accurate relationship between resistance patterns and treatment results would have been possible with direct culture and sensitivity testing, even though resistance statistics were deduced from earlier regional investigations. Such microbiological data should be taken into account in future research to further improve therapy recommendations.

To sum up, this study adds important data in favour of modified dual therapy being used as India's first line of treatment for H. pylori infection. The regimen's simplicity, good safety profile, and high eradication rates highlight its potential use in clinical practice. Regimens like MDT provide a practical and evidence-based choice that is consistent with the ideas of patient-centered care and rational medication usage as regional and international recommendations change to address antibiotic resistance and therapeutic effectiveness. In order to optimise H. pylori care options across a range of populations and shape future recommendations, further research—including multicenter trials and cost-effectiveness analyses—will be crucial.

CONCLUSION

For the eradication of Helicobacter pylori in an Indian population, this randomised controlled trial shows that modified dual therapy—which consists of high-dose esomeprazole and amoxicillin given four times a day—is both significantly more effective and better tolerated than the conventional triple therapy. In both ITT and PP studies, the eradication rates with MDT exceeded 85%, satisfying the current consensus recommendations' gold criterion for successful regimens. The conventional triple treatment group, on the other hand, demonstrated unsatisfactory eradication, which is in line with the general trend of diminishing effectiveness brought on by clarithromycin resistance. Crucially, a much decreased rate of adverse events was linked to MDT. The MDT regimen had a good safety profile with little complaints, whereas clarithromycin-based treatment had serious adverse effects such metallic taste and gastrointestinal problems. These results imply that MDT can improve patient satisfaction and adherence.

In light of the concerning increase in clarithromycin resistance, particularly in developing nations like India, MDT stands out as a workable, affordable, and efficient alternative. Amoxicillin is still widely accessible and reasonably priced, and high-dose PPI regimens are simple to administer. Additionally, MDT contributes to wider antimicrobial management by maintaining other antibiotic classes. In conclusion, especially in regions with significant macrolide resistance, modified dual therapy need to be seriously explored as a first-line treatment for H. pylori. Although more research is needed to assess resistance profiles and long-term effects, our results provide credence to the use of MDT in standard clinical practice.

LIMITATIONS OF THE STUDY

1. **Open-label Design:** Because this trial used an open-label design, participants and researchers were both aware of the therapy being given. Observer bias could have been created as a result, particularly when reporting and assessing subjective outcomes like side effects.
2. **Lack of Antibiotic Susceptibility Testing:** For patients that were enrolled, antibiotic susceptibility testing was not done. This may have an impact on how therapeutic failures are interpreted and reduced our capacity to link treatment results with resistance tendencies.
3. **Single-center Study:** One tertiary care facility served as the study's site. The data' generalisability may be limited as a consequence of findings that are not typical of various patient demographics, healthcare environments, or geographic areas.
4. **No Long-term Follow-up:** Four weeks following treatment, the trial evaluated the effectiveness of eradication; however, it did not analyse long-term outcomes like resistance development, reinfection, or recurrence. To really comprehend MDT's longevity, this is necessary.
5. **High Pill Burden in MDT Group:** QID (four times daily) dose was necessary for the modified dual treatment, which would not be practical for individuals with poor adherence or in environments with limited resources. This restricts how MDT may be used practically in some groups.

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