Combination treatment for Gastric Helicobacter Pylori infection along with Periodontal Treatment -A Systematic Review

Dr. Ahmed Bin Khalid Khan[1] , Dr. Farzeen Tanwir[2], Dr. Seeme Nigar[3], Dr. Saima Mazhar[4], Dr. Shayan Ahmed[5], Dr Hira Khanzada[6].

[1]Assistant Professor, Department of Periodontology, Bahria University Health Sciences Campus. (BUHSC), Karachi, Pakistan

[2]Professor,Department of Periodontology, Bahria University Health Sciences Campus. (BUHSC) ,Karachi, Pakistan

[3]Demonstrator, Department of Oral pathology, Altamash Institute of Dental Medicine, Karachi, Pakistan

[4]Senior Registrar, Department of Periodontology, Bahria University Health Sciences Campus. (BUHSC), Karachi, Pakistan

[5] Senior Dental Surgeon at Executive Clinics , Altamash Institute of Dental Medicine, Karachi, Pakistan

[6]Demonstrator , Department of Oral Pathology, Altamash Institute of Dental Medicine, Karachi, Pakistan

Abstract

Objective: In this systemic review, we aimed to evaluate the combination of Anti- H. pylori treatment along with periodontal treatment to assess the rate of reinfection along with bacterial resistance against the drugs.

Materials and Methods: By using MeSH keywords such as "Helicobacter pylori and periodontal therapy", "Helicobacter pylori and periodontitis", "Helicobacter pylori and gingivitis", "Helicobacter pylori and dental plaque", and "Helicobacter pylori and oral cavity". Databases such as PubMed, Google Scholar, and Web of Science were used to search for relevant studies which fell within the eligibility criteria of this study. The selected articles were then screened to ensure being in the English language. The relevancy of the selected articles was assessed as per the

research question. The data of sample size, place of study, outcomes, and quality of assessment of the articles were extracted.

Results: In the initial search, a total of 801 articles were found, out of which 200 were initially eliminated. After further scrutinization, a total of 6 clinical trials were included. As per the results, reserves of Helicobacter pylori are present in the mouth. The combination of periodontal treatment with anti-H. pylori treatment resulted in a significant reduction in chances of reinfection with H. pylori along with the reduction in bacterial resistance to the drugs.

Conclusion: For doctors to diminish the chances of reinfection, complete eradication of H. pylori in gastric infection is of prime importance. To reduce the risk of reinfection, oral H. pylori can be eliminated by the use of mechanical instrumentation combined with treatment against helicobacter pylori for such patients.

Keywords: H. Pylori, Periodontal treatment, Gastric Treatment

Introduction

Helicobacter pylori also abbreviated as H. pylori, is a bacteria with high motility, possessing a spiral shape, that is an important gastrointestinal pathogen that has a causal link with pathologies like gastroenteric ulcers, gastritis, and gastric cancers [1]. H. pylori is one of the most common bacteria that cause gastric infections which has affected almost half of the population of the world [2]. In 1982, the human stomach was the first organ where this bacteria was first reported to exist, although, previously it was assumed that no bacteria were found in the stomach owing to its highly acidic pH [3]. Different approaches have been used in order to diagnose and treat the patients who have been infected with this pathogen. For the treatment of gastrointestinal infectious diseases, elimination of the pathogen is considered curative. The treatment regimen that is followed to eradicate H. pylori includes a 10-14 days triple regimen that includes a proton pump inhibitor (PPI) along with combination of antibiotics such as clarithromycin along with metronidazole or amoxicillin [4]. This treatment regimen is currently considered the first line of treatment.

Although first and standard option for treatment is the triple-drug regimen for the elimination of Helicobacter pylori pathology, drugs resistance has made the eradication of this bacterium a challenge [5]. Furthermore, even after the employment of triple therapy, the rate of recurrence is high amongst the patients [6][7][8]. One of the strategies that have been employed to overcome

such resistance includes the introduction of bismuth salicylate-based quadruple treatment. However, such a treatment's efficacy is often hampered by patient compliance along with resistance to bacteria. To overcome such barriers to eradication of H. pylori, alternative treatment strategies such as supplemental periodontal therapy with gastric H. pylori therapy offered an important insight.

The presence of Helicobacter pylori, other than the human stomach, is reported to exist in the oral cavity in areas such as dental plaque, gingiva, mucosal lesions, and saliva [9]. Such findings suggest that reserves of helicobacter pylori exist at these sites. Therefore, from the mouth, such bacteria should be eliminated which can lead to completed eradication along with decreasing the chances of encountering resistance and reinfection [10]. The effective of the Systemic antibiotics has been thoroughly studied for elimination of helicobacter pylori from the gastric region, however, the impact of these systemic antibiotics is minimal to none on the oral plaque [11]. For the removal of these bacteria from the dental plaque, mechanical removal is required. Such supplemental elimination of these bacteria from the mouth can reduce chances of administrating repeated antibiotics in cases of reinfection. Furthermore, it has been reported that after employment of the triple therapy, the rate of recurrence of H. pylori infection was higher amongst the patients with oral health categorized as poor as compared to those whose oral health was categorized as good [12]. This further signifies the importance of the reservoirs of H. pylori in the oral cavity and the need for its eradication to eliminate its reoccurrence.

For the evaluation of the effectiveness of supplemental periodontal treatment with gastric helicobacter pylori treatment, this systemic review intended for determination of supplemental periodontal treatment to anti-H. pylori treatment to assess rate of reoccurrence and bacterial resistance.

Materials and Methods

2.1 Question of Focus

As per the Preferred Reported Items for Systemic Review and Meta-Analysis (PRISMA) guidelines, this systemic review was conducted. Our question for this systemic review was "Effect of Periodontal Therapy as an adjunct to Gastric Helicobacter Pylori infection for prevention of

reinfection and bacterial resistance". The question was formulated according to Participants Intervention Comparison Outcome Study (PICOS) strategy.

Participant: Patients who were suffering from gastric helicobacter pylori infection

Intervention: Patients receiving H. pylori treatment and patients receiving H. pylori treatment along with supplemental periodontal treatment for evaluation of adjunct effectiveness of administration of periodontal treatment on such patients.

Comparison: Comparison of H. pylori treatment alone and supplemental periodontal treatment along with H. pylori treatment

Outcome: Analyse and assess the effect of the addition of periodontal treatment to patients for the prevention of reoccurrence and to decrease the risk of bacterial resistance.

Study design: In this systemic review, we included only interventional studies such as clinical trials that have been published in the English language only.

2.2 Eligibility criteria:

About the inclusion criteria, following was the criteria:

a) Study types: Clinical trials
b) Clinical trials which provided the association between H. pylori and periodontal therapy
c) Studies that have been published to date of September 2022
d) Articles that have been published in the English language
e) Articles with full texts available

About the exclusion criteria, following was the criteria:

a) Researches which fail to conclude any association between Helicobacter pylori and Periodontal therapy
b) Researches which demonstrated results of associations of H. pylori with other oral diseases
c) Researches such as cross-sectional studies, review articles, letters to editors, commentaries, non-clinical trials
d) Articles that were published in languages other than English

2.3 Search Methodology:

Databases such as PubMed, Google Scholar, and Web of Sciences were used to identify relevant articles by using search terms (MESH terms) such as: "Helicobacter pylori and periodontal therapy", "Helicobacter pylori and periodontitis", "Helicobacter pylori and gingivitis", "Helicobacter pylori and dental plaque", and "Helicobacter pylori and oral cavity". The articles which were published till the date of September 2022 were extracted. All extracted studies were thoroughly checked and any relevant article was excluded from the study. The articles were cross-checked with the eligibility criteria of the study. For extraction of relevant information from the selected articles, full texts were read.

2.4 Extraction of Data and Quality Assessment of the studies

Independently there were two authors who went through the abstracts and titles of the studies. To further improve the search, the bibliography of the articles was also assessed. To avoid discrepancy and biasness, a third author was involved to solve the conflict.

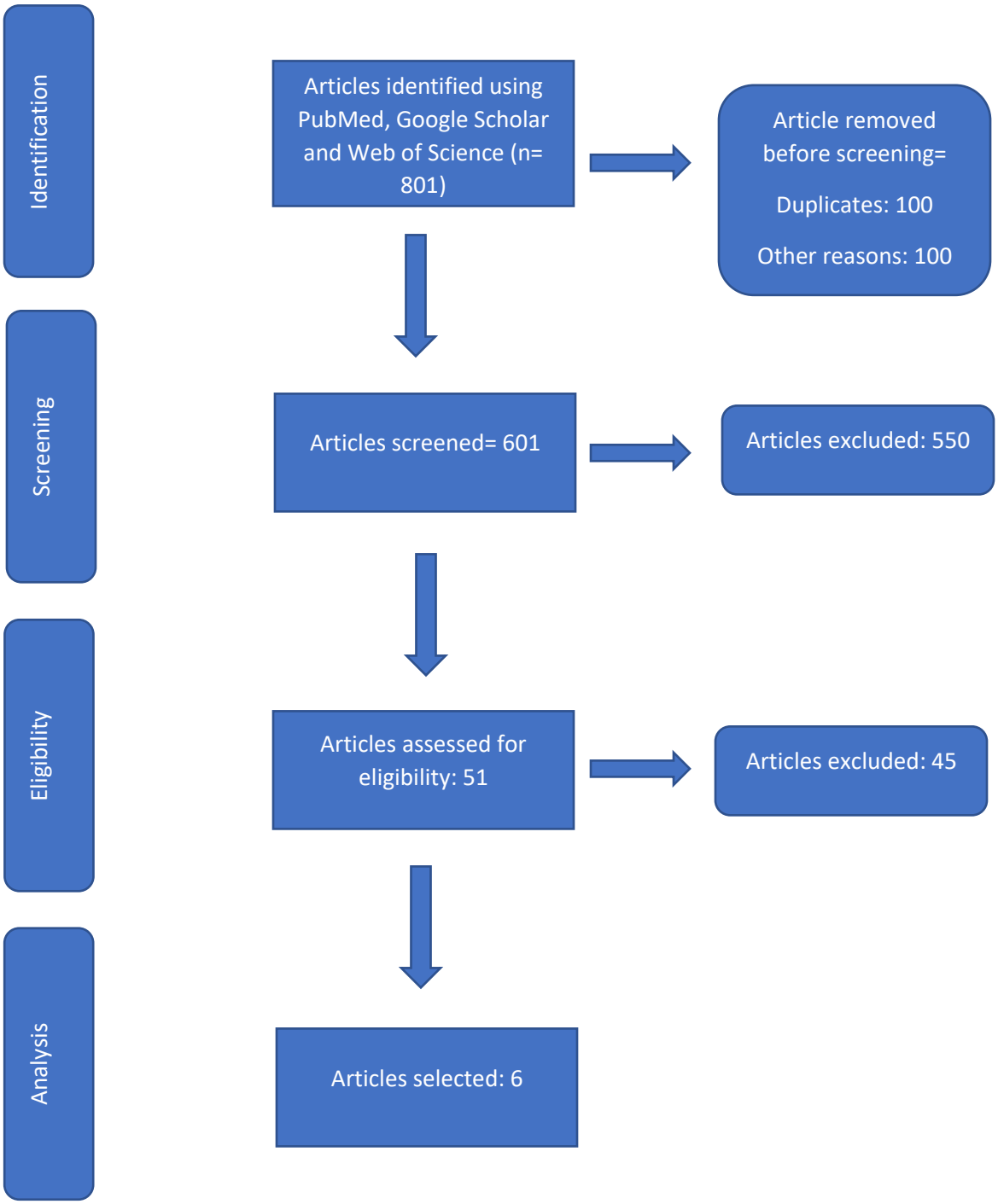
By using Newcastle-Ottawa scale (NOS), studies which were part of this review were checked for quality purposes. The NOS has three parameters: Firstly, the target sample, Secondly, comparability of the samples, and lastly, outcome of interest. For each study, a score will be assigned which ranges from zero to nine. Articles that have scores ≥ 7 were categorized as high quality, studies with scores between 4 to 6 were categorized as moderate quality, and 1 to 3 scores were categorized as low quality.

Results

Characteristics of the eligible studies

For this systemic review, a total of 801 articles were screened for eligibility that was published till the date of September 2022. Out of the 801 articles, 200 articles were excluded on the basis of duplication and ineligibility. After exclusion, for this systemic review a total of 6 articles were selected, as shown in **figure 1.**

Figure 1. PRISMA Flowchart of the literature analysis for this systemic review



All of the six articles that were included in this study were clinical trials. The sample size of these studies ranged from 96 up to 698, with a total of 1,549 patients in all of these six studies. Out of the 6 studies, 4 studies were from China, 1 study each was from Thailand and Turkey, respectively. The general features of the articles part of this systemic review are presented in **table 1.**

Table 1. Characteristics of the studies included in this systemic review

References	**Sample population**	**Design of Study**	**Country**	**Year of Publication**
Jia et al [13]	107	Clinical Trial	China	2009
Tongtawee et al [14]	698	Clinical Trial	Thailand	2019
Gao et al [15]	96	Clinical Trial	China	2011
Sert et al [16]	98	Clinical Trial	Turkey	2019
Song et al [17]	391	Clinical Trial	China	2013
Wang et al [18]	159	Clinical Trial	China	2014

Additionally, some studies which were excluded from this systemic review are presented in **table 2** along with their reason for exclusion.

Table 2. List of the studies excluded from this systemic review

Authors and References	**Reason for exclusion**
Jin et al [19]	Article in the Chinese language
Jin et al [20]	Article in the Chinese language
Lv et al [21]	Article in the Chinese language
Liu et al [22]	Article in the Chinese language

General outcomes of the studies

Different studies have evaluated the effects of the adjunctive introduction of periodontal treatment to anti-H. pylori treatment to decrease the chances of reoccurrence of infection and bacterial resistance. H. pylori in the oral cavity can be identified using the ^{13}C urease test. When dental plaque control measures have been provided to the patient, the prevalence of H. pylori has been significantly lower, as compared to not receiving dental plaque control methods [13]. Therefore, emphasizes the fact of regular and long-term dental plaque control can help decrease the chances of reoccurrence of H. pylori infection [13]. When gastric helicobacter pylori treatment alone is compared with gastric helicobacter pylori along with periodontal treatment, it has been noted that supplementary introduction of periodontal therapy results in enhancing the gastric helicobacter pylori treatment to diminish the reoccurrence of gastric Helicobacter pylori pathology [14]. Furthermore, bismuth triple therapy when given in combination with periodontal therapy has shown considerable decrease in detection rate of this bacteria that enhances the prolonged elimination of Helicobacter pylori in chronic periodontitis and gastric diseases patients [15]. Oral hygiene is also termed important eradication of this bacterium. Maintenance along with anti-H. pylori treatment and periodontal treatment result in greater eradication of the bacterium as compared to neglecting oral hygiene measures [16]. Moreover, the employment of mouth rinses alone or when combined with periodontal therapy possibly can provide improvement in eradication of the bacteria [17]. When systemic therapy is provided for removal of Helicobacter pylori, it has minimal effects on oral colonies of this bacteria. Therefore, removal of the oral colonies of Helicobacter pylori can lead to successful eradication as it has a vital and paramount relationship with gastric colonies of Helicobacter pylori [18].

Assessment of Quality of the studies

For quality assessment of the studies included, the Newcastle-Ottawa scale was used where each study was assigned a score ranging from 0 to 9, as presented in **table 3.**

Table 3. Newcastle-Ottawa Scale for quality assessment of the included studies

References	Selection	Comparability	Result	Score
Jia and colleagues [13]	****	*	***	8
Tongtawee and colleagues [14]	**	*	**	5
Gao et al [15]	**	*	**	5
Sert and colleagues [16]	**	**	**	6
Song and colleagues [17]	***	**	****	9
Wang and colleagues [18]	**	*	**	5

Note: A study can be awarded a maximum of one star (*) for each numbered item within the Selection and Exposure categories. A maximum of two stars can be given for Comparability.

Discussion

This systemic review's purpose was "Effect of Periodontal Therapy as an adjunct to Gastric Helicobacter Pylori infection for prevention of reinfection and bacterial resistance". We analyzed different clinical trials for evaluation of supplemental use of periodontal therapy along with anti-H. pylori treatment.

Helicobacter pylori is one of the most common bacteria that leads to gastric infections such as chronic gastritis and gastric ulcers. At times, untreated infections can contribute to gastrointestinal cancers. According to some studies, oral colonies of Helicobacter pylori contribute to development oral squamous cell carcinoma, halitosis, and the burning of the tongue [23].

In terms of reinfection and bacterial resistance against H. pylori, oral colonies of these bacteria is considered a possible routes for these occurrences due to the existence of these bacteria in the mouth [24]. Literature states a causal relationship between the presence of H. pylori in the oral

cavity and resultant gastric infection along with the severity of periodontal disease [9][25][26]. The existence of these bacteria in the oral cavity is found to be variable among different researchers. Davin et al conducted a study where existence of Helicobacter pylori in the oral cavity has been concluded at 41%, whilst some studies report the prevalence up to 97% from the samples that were obtained from dental plaque [27][28]. In contrast to these findings, one study by Shimoyama found that in healthy male patients that was reduction in probability of tooth loss when patients were infected with gastric helicobacter pylori. Such findings present the further need for evaluation of this bacteria in the oral cavity with infection in the gastrointestinal system.

Kadota et al in their research found that the participants who had positive Helicobacter pylori status, count of bacteria such as Porphyromonas gingivalis, Prevotella intermedia, and Treponema denticola was higher as compared to patients who were H. pylori negative [29]. Such results may indicate the co-existence of periodontopathic bacteria along with H. pylori, however, the associations between these two bacterial species are yet to be demonstrated. Furthermore, in a study by Umeda et al, significance of eradication of these bacteria from oral region was highlighted as danger exists for developing gastric infection due to colonization of such bacteria in periodontal pockets [30]. Such results put forward the question that Helicobacter pylori from mouth can lead occurrence of infection again in the gastric region which can render resistance to systemic antibiotics [31].

The effectiveness of systemic antibiotics in the removal of gastric infection against H. pylori has been well established. However, the studies regarding the effects of these antibiotics against oral H. pylori are limited. It is known that the bacteria that have colonized inside the dental plaque are about a thousand times resistant to systemic antibiotics [32]. To remove such bacteria, mechanical removal of the dental plaque is required. Many studies have evaluated the adjunctive use of periodontal therapy to anti-H. pylori treatment regimen [33][34][35]. The therapies which are used to eradicate gastrointestinal Helicobacter pylori disease are not effective against these bacteria in oral cavity, therefore, chances exist for the oral H. pylori to reach the stomach [36]. Such situations can potentially lead to reinfection. This necessitates equipping of periodontal therapy depending on the periodontal health of the patient.

A study by Tongtawee et al, concluded that the reoccurrence rate of treatment of periodontium in combination with gastric Helicobacter pylori infection treatment resulted in lower rates of

reoccurrence as compared to the use of anti-H. pylori therapy alone [14]. The reason for the lower reoccurrence rates with the potential addition of periodontal therapy is primarily due to the fact that the oral cavity acts as a reservoir of H. pylori such as in periodontal pockets and dental plaque [37]. Therefore, a successful reduction such bacteria from the oral cavity leads to a decrease in rates of reinfection. Furthermore, a study by Iwai et al concluded that the samples from the oral cavity did express H. pylori bacteria along with finding that the primary reserve center for Helicobacter pylori are dental pulp [38]. Moreover, in a study by Sruthi et al, they found that H. pylori bacteria is found within the dental caries of children [39].

Gao and colleagues in their study found that the first and standard treatment i.e. triple drug treatment along with periodontal therapy can lead to prolonged elimination of Helicobacter pylori in subjects who are suffering from chronic gastritis and periodontitis both [15]. All of the studies that were reviewed in this study did report and conclude that periodontal therapy as an adjunct to gastric Helicobacter pylori infection treatment can possibly pave way for successful decrease in chances of reinfection as well as bacterial resistance.

Although the association between oral helicobacter pylori and stomach reinfection has been studied, further clinical trials should be carried out to evaluate the effectiveness of multidisciplinary therapeutic regimen for eradication of oral helicobacter pylori and reduce the risk of reinfection.

Conclusion

Currently, periodontal therapy is not frequently used along with the first line of therapy against gastric infection with H. pylori. However, based on the findings of this systemic review, we conclude that:

1) The reserves of Helicobacter pylori in the oral cavity are present in localities like plaque and periodontal pockets
2) Oral H. pylori can potentially travel to the stomach as a result of deglutition.
3) Accumulation of Helicobacter pylori from oral cavity in the stomach can potentially lead to reinfection with H. pylori as well as leading to bacterial resistance against drugs

4) There is a significant decrease the risk of reinfection by the elimination of H. pylori from the oral cavity by the use of periodontal treatment

Conflict of Interest:

The author declare that they have no conflict of interest.

Authors Contribution:

- **Dr Ahmed Bin Khalid Khan :**Writing-original draft preparation, Methodology
- **Dr Farzeen Tanwir:** Formal analysis, Supervision, Visualization
- **Dr Seeme Nigar:** Review and editing, Methodology
- **Dr Saima Mazhar:** Article Processing & Publication, Literature Review
- **Dr Shayan Ahmed**: Methodology, Supervision
- **Dr Hira Khanzada :** Literature Review, Methodology.

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