Prevalence Rate of Adverse Drug Reactions Caused by Eradicating Helicobacter Pylori in the Patients Treated by a Sequential Regimen

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ABSTRACT: H. pylori infection in adults is usually chronic and it does not improve without specific treatment. H. pylori eradication prevents recurrence of most of its related diseases and it is considered as the best method to treat peptic ulcer disease. Being aware of the side effects and its prevalence may be considered as a major factor in selecting more appropriate prescription drugs. Therefore, the present study aims at studying the prevalence rate of adverse drug reactions caused by eradicating H. pylori in the patients treated by sequential regimens. Materials and Methods: 89 patients with positive H. pylori test were included in the intervention study. They were treated in a double blind manner without notifying the patients, researcher and statistical team. The patients were treated by the standard three-medicine treatment of H. pylori eradication. After proving eradication, the patients were evaluated for three months as far as prevalence of side effects are concerned. Results: The study group consisted of 89 patients: 39 women, and 50 men. The mean age of the patients was 57.88 years. Ten (11.4%) of the patients, 5 men (5.5% of men patients) and 5 women (6.9% of women patients), developed adverse drug reactions. Conclusion: it is suggested that we help to gain more knowledge about these side effects, and that we help to reduce morbidity and fatality resulting from them, by increasing the monitoring of drug side effects in all treatment wards, especially in patients who are being treated for Helicobacter pylori eradication.
Key words: Adverse Drug Reactions, Helicobacter Pylori, Eradicating

INTRODUCTION

Helicobacter pylori (H. pylori) are gram-negative, 2.5-3 micron size microaerophilic bacilli. They are adapted to the ecological condition of gastric mucosa and may survive in the acidic conditions of stomach. The prevalence rate of H. pylori infection is different across the world and it depends on the lifestyle of each region. The diagnostic methods of H. pylori are invasive and non-invasive and selecting an appropriate method for each patient depends on its cost, availability, patient condition, infection prevalence and consumption of previous medicines [1 , 2]. H. pylori infection is common all over the world and it affects more than 50 percent of the population [3]. Its frequency is considerably different among countries and communities of each country. The frequency among the middle-aged adults exceeds 80 percent and it is higher than 20 percent among the European developed countries [4]. H. pylori infection is acquired through oral ingestion of the organism mainly during early childhood. So far, there has been no evidence proving transmission from animals and it seems that there are person-to-person, mouth-to-mouth and fecal-oral transmissions. Probably, spontaneous elimination of the bacteria in childhood is relatively more common; however, H. pylori infection in adults is usually chronic and it does not improve without specific treatment [5]. Moreover, one of the clinical manifestations of Helicobacter infection is in dyspepsia digestive system that has affected 15 percent of the individuals between 15-40 and causes spending high treatment costs and many working hours [6]. In 1994, WHO classified class I of H. pylori as a carcinogen. Gastric ulcer or duodenal ulcer, mucosal atrophy, gastric carcinoma and gastric lymphoma are considered as the potential complications of infection with Helicobacter pylori [7]. However, long-term improvement of symptoms was reported unexpectedly in randomized trials after eradication of infection. H. pylori eradication prevents recurrence of most of its related diseases and it is considered as the best method to treat peptic ulcer disease [8]. Infected with H. pylori usually accompanies chronic gastric [9]. Generation of basal and stimulated gastrin hormone increases in the infected individuals and simultaneously bicarbonate production in mucosa reduces. Infection with H. pylori is responsible for all the peptic diseases and ulcers of digestive system. It is also effective in formation of mucosal lymphomas of digestive system and gastric adenocarcinoma [10, 11]. Clinical experiences in Iran and most of the developing countries showed that the rate of eradication of H. pylori using similar treatment regimes is much lower than the one reported in western countries. Relapse or reinfection rates in a short time and/or a long time are much more than the ones reported in the western countries. The basic principle to treat these patients includes choice of medicines, prescription method and its duration. An ideal medicinal regime should be highly effective with low side effects, cheap, and prescribed easily. It should prevent relapse of the disease [12]. Although many attempts have been made to present such a regime, a long way should

be taken to access it. A wide variety of H. pylori strains and considerable resistance against antibiotics in different regions of the world have made us fail to access to such a regime. Among the medicines used in our center, consumption of Amoxicillin, Clarithromycin, and Pantoprazole was effective; however, being aware of the medicinal effects and its prevalence may be considered as a major factor in selecting more appropriate prescription drugs [13-15]. Therefore, the present study aims at studying the prevalence rate of adverse drug reactions caused by eradicating H. pylori in the patients treated by sequential regimens.

MATERIAL AND METHODS

Eighty-nine patients were included in an intervention study after obtaining permission from the Ethics Committee of Ahvaz Jondishapour University of Medical Sciences (AJUMS). The patients were selected among those referred to the internal medicine ward of the training hospitals of AJUMS. Exclusion criteria included record of gastrointestinal bleeding, record of H pylori eradication, pregnancy, cirrhosis, any type of malignancy, endoscopically proved peptic disease record, severe and/or chronic renal failure, decompensated heart failure, and the patients with severe physical conditions. After examining such features, the patients were examined as far as H. pylori infection was concerned. A stool antigen test was used for screening infected with H. pylori. Then 89 patients with positive H. pylori test were included in the study. They were treated in a double blind manner without notifying the patients, researcher and statistical team. The patients were treated by the standard three-medicine treatment of H. pylori eradication using Amoxicillin regime with D 2-gram dose and Clarithromycin with 500 mg dose BID and Pantoprazole with D 40 mg dose for ten days. The patients will be controlled by three calls in a day in terms of medicines consumption and prevalence of complications. A test to prove eradication will be performed through examining stool antigen four weeks after treating the target group. After proving eradication, the patients were evaluated for three months as far as prevalence of side effects are concerned. Finally, the descriptive statistic methods and central indices were used for analyzing data and describing the variables under study. It was then analyzed using the statistical analyses of T-test, Chi square test and ANOVA. Significance level of the above tests was considered lower than 0.05 and the data were analyzed using SPSS Version 20.

RESULTS

The study group consisted of 89 patients: 39 women, and 50 men. The mean age of the patients was 57.88 years. Ten (11.4%) of the patients, 5 men (5.5% of men patients) and 5 women (6.9% of women patients), developed adverse drug reactions (ADRs) Figure (1).
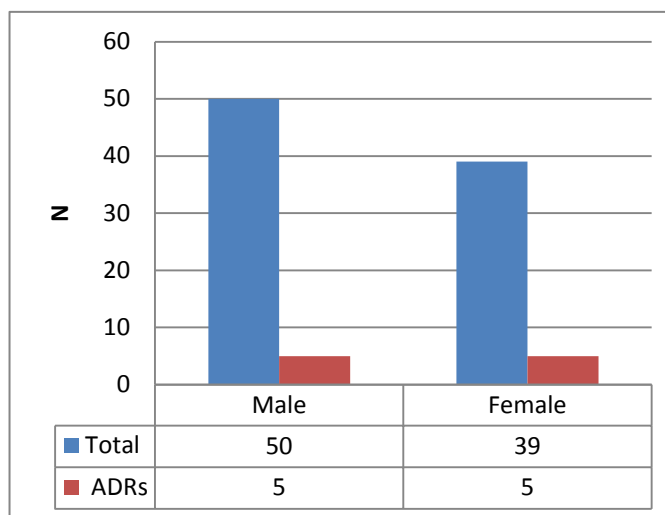
Figure 1. Adverse drug reactions

	Male	Female
■ Total	50	39
■ ADRs	5	5

DISCUSSION AND CONCLUSIONS

Although results of this study indicated low prevalence of ADRs among the studied patients, even this low prevalence is very important and considerable. ADRs greatly influence patients' health and their degree of satisfaction with the treatment process because they influence patients' lives and have financial consequences for them. It is necessary to mention that three lines of treatment are usually used to eradicate Heliobacter pylori. If the observed is to clarithromycine (in 15-20% of resistance cases), it is better to use the standard regimen of first-line therapy [16, 17]. If resistance to metronidazole in the area is less than 40%, metronidazole can replace amoxicillin. The success of the 14-day first-line treatment is greater than the 7-day treatment period [17, 18]. Although this regimen is considered first-line treatment, its capacity to eradicate Helicobacter pylori is low, and it does not have much therapeutic effect, the most important reason for which is the resistance Helicobacter has shown to antibiotics (and especially to clarithromycine) in the past decade [19-21]. About 5 to 35 % of people

infected with Helicobacter pylori respond to the standard regimen of using the three drugs of the first-line treatment [19, 22]. If the four-drug regimen that includes bismuth (the second-line treatment), is available, it can be used instead of the first-line treatment [17]. If resistance is observed, regimens based on bismuth, levofloxacin, and rifabutin or furazolidone (the third-line treatment regimen) can be employed. In some countries, the above-mentioned regimen is employed as first-line treatment, but studies have shown the effectiveness of these regimens also differs for various populations [16, 19]. It seems low pH, excessive secretion of gastric acid, drug intolerance in patients, and substantial accumulation of bacteria in the stomach and duodenum are other reasons besides bacterial resistance for the failure in eradicating Helicobacter pylori [23]. In case resistance is reported, it is better to culture the microbe after the failure of the first-line of treatment and prepare an antibiogram [24]. In general, the first-line treatment must be simple, tolerable, and cost effective, but the second-line treatment is effective too. Among regimens that can be employed in the second-line treatment after the failure of the first- line treatment, or in case patients are sensitive to penicillin compounds, the 4-drug regimen including bismuth together with tetracycline, metronidazole, and acid- suppressing drugs is the best option [16]. However, some researchers believe the above-mentioned regimen is not a good one because of its long treatment period and adverse side effects, the large number of pills that have to be taken every day, and the fact that bismuth may not be available everywhere [25]. If bismuth is not available, the 4-drug regimen can be converted to the 3-drug regimen and be used as the second-line treatment [26]. If the tetracycline in this 3-drug regimen is not available either, amoxicillin can replace it [17]. If an antibiogram is not prepared after the failure of the first-line treatment, the second-line treatment cannot act effectively, together with metronidazole/clarithromycin, as a suppressor of protein pumps [22]. Unlike clarithromycin, metronidazole exhibits the therapeutic advantage of having a desirable eradicative effect even if the bacteria are resistant to it [26], while in cases where there is resistance to clarithromycin, treatment failure rate with repeating clarithromycin administration is very high. If the preliminary second-line treatment administered by a general practitioner fails, the patients must be referred to specialists who, by taking gastric mucus samples and culturing them, and by preparing antibiograms, determine the suitable antibiotic. Moreover, specialists must investigate and control failures that follow [27]. Finally, the third-line treatment can be based on furazolidone and rifabutin. If there is strong bacterial resistance and eradication is disrupted, antibiotic sensitivity tests must be conducted [19]; however, if we want to use the life-saving 3-drug third-line treatment of rifabutin + levofloxacin + furazolidone, preparing antibiograms is not recommended [28]. Other third-line treatment regimens, 3-drug regimens based on rifabutin/ furazolidone/levofloxacin/tetracycline together with amoxicillin and a proton pump suppressor/or amoxicillin at high dosages are recommended [21, 29, and 30]. In any case, all these strategies are prone to result in ADRs in patients for whom they are prescribed. Hospitalization due to ADRs constitutes about 5% of all hospital admissions [31], and undesirable drug side effects are one of the important causes of impairment and death in the world. In England, drug side effects are responsible for about 6.5% of hospital admissions and at least 5000 deaths per year [32]. In the United States, drug side effects are the fourth cause of death and result in a greater number of fatalities than pneumonia and accidents, AIDS, pulmonary diseases, diabetes, and driving accidents [33]. In general, undesirable drug side effects are a general important problem that in most cases can be prevented [34]. Based on the definition by the World Health Organization (WHO), undesirable drug side effects are unwanted harmful effects that happen when drugs are used at dosages to prevent, diagnose, or treat diseases, or to correct physiological functions in human beings [35]. Therefore, in conclusion, it is suggested that we help to gain more knowledge about these side effects, and that we help to reduce morbidity and mortality resulting from them, by increasing the monitoring of drug side effects in all treatment wards, especially in patients who are being treated for Helicobacter pylori eradication.

Acknowledgement

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