Original Articles

Platelet Count Response to Helicobacter pylori Eradication in Iranian Patients with Idiopathic Thrombocytopenic Purpura

Mehrdad Payandeh 1, 2, Nasrollah Sohrabi 1, Mohammad Erfan Zare 2, 3, Atefeh Nasir Kanestani 2, 3, Amir Hossein Hashemian 4

1Department of Medical Laboratory Sciences, Paramedicine Faculty, Kermanshah University of Medical Sciences, Kermanshah, Iran.
2Medical Biology Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran.
3Student Research Committee, Kermanshah University of Medical Sciences, Kermanshah, Iran.
4Department of Biostatistics, Faculty of Public Health, Kermanshah University of Medical Sciences, Kermanshah, Iran.

Correspondence to: Mohammad Erfan Zare, BSC student of Medical Laboratory Sciences. Medical Biology Research Center, P.O.Box: 1568, Sorkheh Lizheh, Kermanshah University of Medical Sciences, Kermanshah, Iran. Tel: +98 831 4276473, Fax: +98 831 4276471. E-mail: mezarelab@yahoo.com

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Abstract. Idiopathic thrombocytopenic purpura (ITP) is an autoimmune hematological disorder characterized by auto antibody-mediated platelet destruction. Although the main cause of ITP remains unclear, but its relationship with some infection was demonstrated. In recent years, many studies have demonstrated improvement of platelet counts in ITP patients after treating Helicobacter pylori infection. The aim of this study was to investigate the effects of H. pylori eradication on platelet count response in Iranian ITP patients.
A total of 26 patients diagnosed with both ITP and H. pylori infection. ITP were diagnosed whose platelet counts were less than 100×10^3/μL. These patients were tested for H. pylori infection by Urea Breath Test and serum H. pylori antibody. All patients received triple therapy for 7 or 14 days to eradicate H. pylori infection. These patients followed for six months.
Prevalence of H. pylori was 67.3%. H. pylori eradication achieved in 89.5% (26/29). Of the 26 patients, 15 (57.7%) exhibited a complete response (CR) and 11 (42.3%) were unresponsive. We did not find partial responders. There was a significant difference in the baseline platelet count of responders and non-responders patients (p<0.001). All responders had platelet count ≥50×10^3/μL and all non-responders had platelet count <50×10^3/μL.
Results of this study revealed that eradication therapy of H. pylori infection can improve platelet counts in ITP patients especially with mild thrombocytopenia and support routine detection and treatment of H. pylori infection in ITP patients in populations with a high prevalence of this infection.
**Introduction.** Helicobacter pylori (H. pylori) is the most common chronic pathogen that colonizes the human gastric mucosa. It has been recognized as the causative agent of chronic gastritis, gastro duodenal ulcers, adenocarcinoma and mucosa-associated lymphoid tissue lymphoma (MALT).1,2 The prevalence of H. pylori infection in geographic regions of the world is different.2 This rate in the most of the Asian countries such as Japan, South Korea and Iran is too high, but in Western countries is much lower.3,6 In recent years, several studies have proposed that H. pylori infection may be associated with some extra gastric disease especially hematological disorders such as iron deficiency anemia, pernicious anemia and idiopathic thrombocytopenic purpura (ITP).7,9

ITP is an autoimmune hematological disorder characterized by auto antibody-mediated platelet destruction. Although the main cause of ITP remains unclear, but its relationship with some infection was demonstrated.10-12 In 1998, Gasbarrini, for first time, observed increased platelet counts after H. pylori eradication in ITP patients.9 In recent years, many studies have demonstrated improvement of platelet counts in ITP patients after treating H. pylori infection.13-18 But in some studies, were observed no favorable effect on patients with ITP.19,20 The discrepancy might be due to different strains of H. pylori in these geographic regions. In this study we investigated the effects of H. pylori eradication on platelet counts in ITP patients in a teaching hospital in Kermanshah, west of Iran.

**Material and Methods.** In this retrospective study, between June 2009 and November 2010, 52 patients with ITP who attended the Taleghani hospital in Kermanshah, west of Iran, were evaluated. ITP was diagnosed according to the standard criteria and defined by thrombocytopenia (platelet counts ≤100×10^9/L).21 Other causes of thrombocytopenia such as thrombocytopenia caused by drugs, pseudothrombocytopenia, hepatitis C virus infection, hepatitis B virus infection, human immunodeficiency virus infection and autoimmune disorders were excluded. The patients also were excluded if they had been received eradication therapy for H. pylori infection within 2 years or an antibiotic or proton pump inhibitor within the previous 4 weeks.

We used Urea Breath Test (UBT) and serum H. pylori antibody for diagnosis of H. pylori infection.22 All patients with H. pylori infection was treated with standard eradication therapy included amoxicillin 1000 mg twice daily, clarithromycin 500 mg twice daily, and a proton pump inhibitor 40 mg twice daily for 2 weeks.23 Eradication of H. pylori was evaluated two weeks after treating by the same tests which we used for diagnosis of H. pylori infection. Platelet counts were monitored every 2 weeks for the first 2 months, every month for the next 4 months after the end of treatment. Complete response (CR) was defined as a platelet count ≥100×10^9/µL at month 6. Partial response (PR) was defined by a platelet increase of ≥30×10^9/µL and at least a doubling of the base line count at month 6. No response (NR) was defined a platelet count <30×10^9/µL or a count increase less than 2-times the baseline count after month 6.21 According to declaration of Helsinki; we took consent from all patients before H. pylori eradication for remedy of their ITP disorders.

Differences of platelet count are expressed as the mean (SD) as appropriate. An ANOVA test was used for analysis of platelet differences in 3 groups (CR, PR and NR); the t-test was used to compare positive and negative response. A P-value of less than 0.05 was considered statistically significant. All statistical analysis were performed by using SPSS software version 16.0.

**Results.** Of 52 patients with ITP, H. pylori infection was found in 67.3% (35/52) of patients. Three patients with autoimmune disorders, two patients with HBV infection and one patient with HCV infection were excluded. Thus 29 patients were considered whom 26 (13 males, 13 females, mean age 38.2 years) achieved H. pylori eradication (89.6%). After H. pylori eradication, CR was obtained in 57.7% (15/26) of patients (CR= platelet count ≥100×10^9/µL ; 11 patients (42.3) were unresponsive . No PR was found. (Table 1). There is a significant difference between the platelet counts of responders and non-responders (p<0.001) (Table 2). All responders had platelet count ≥50×10^9/µL and all non-responders had platelet count <50×10^9/µL (Table 1 and Figure 1).

**Discussion.** ITP is an autoimmune blood disorder in which platelet destruction is mediated by anti-platelet antibodies.7,9 The mechanisms of anti-platelet antibodies development are still a little known. The association between ITP and some infections has been reported previously.10-12 For first time, Gasbarrini in 1998 proposed that H. pylori infection may be associated with ITP.9 In recent years, many studies have demonstrated improvement of platelet counts in ITP patients after treatment of H. pylori infection.13-18 In our study, the prevalence of H. pylori infection in ITP patients was 69.3%. This rate similar to prevalence of H. pylori infection in the general population in Iran.5 These results also were comparable to those of previous studies which were done in Asian countries.6
Table 1. Clinical and platelet response characteristics by Patient

| Patient | Baseline platelet count×10^3/µL | Mount 6 platelet count×10^3/µL | Response status |
|---------|---------------------------------|---------------------------------|-----------------|
| 1       |                                 |                                 | CR              |
| 2       |                                 |                                 | CR              |
| 3       |                                 |                                 | CR              |
| 4       |                                 |                                 | CR              |
| 5       |                                 |                                 | CR              |
| 6       |                                 |                                 | CR              |
| 7       |                                 |                                 | CR              |
| 8       |                                 |                                 | CR              |
| 9       |                                 |                                 | CR              |
| 10      |                                 |                                 | CR              |
| 11      |                                 |                                 | CR              |
| 12      |                                 |                                 | CR              |
| 13      |                                 |                                 | CR              |
| 14      |                                 |                                 | CR              |
| 15      |                                 |                                 | CR              |
| 16      |                                 |                                 | CR              |
| 17      |                                 |                                 | CR              |
| 18      |                                 |                                 | CR              |
| 19      |                                 |                                 | CR              |
| 20      |                                 |                                 | CR              |
| 21      |                                 |                                 | CR              |
| 22      |                                 |                                 | CR              |
| 23      |                                 |                                 | CR              |
| 24      |                                 |                                 | CR              |
| 25      |                                 |                                 | CR              |
| 26      |                                 |                                 | CR              |

Table 2. Differences of platelet according to outcome groups

| Outcome           | N (%) | Median | Minimum | Maximum | Mean SD        | P-Value |
|-------------------|-------|--------|---------|---------|----------------|---------|
| No response       | 11 (42.3) | 10000  | 4000    | 19000   | 11000 +/- 3974.9 | < 0.001 |
| Complete response | 15 (57.3) | 67000  | 34000   | 112000  | 79917 +/- 20042.9 |        |
| Total             | 26 (100) | 43000  | 4000    | 112000  | 69000 21851.8 |         |

In general, the prevalence of *H. pylori* infection varies according to geographic location and in Asian countries such as Japan and South Korea but this rate is in contrast studies were conducted in Western countries. In this study all patients with *H. pylori* infection were treated with triple therapy regimen and eradication rate was 86.5%. This finding is in agreement to other studies which have showed successful eradication greater than 70% using triple therapy.

In this study 65.6% of ITP patients had an increase of platelet counts after eradication of *H. pylori* infection. We found that there is a significantly association between overall response rate and eradication therapy infections (*p*<0.001). According our data in other studies, conducted by Emilia *et al*, Fujimara *et al* and Inaba *et al* respectively 68%, 63% and 44% of ITP patients showed significant increase in platelet count after *H. pylori* eradication. In contrast
the effects of eradication therapy had no favorable effect on platelet count in other series. Ahn et al reported increased platelet count only in 7% of treated patients, no platelet response were observed in ITP patients after eradication therapy of H. pylori infection in studies done by Micheal et al and Stasi et al. The discrepancy among these studies might be due to geographic variation in expression of some proteins such as Cag A (Cytotoxin-associated gene A) in different H. pylori genotypes. The prevalence of Cag A-positive H. pylori strains is different in geographical regions of the world. In Asian countries such as Japan, South Korea and Iran, most of H. pylori strains express Cag A; whereas the frequency of Cag A positive H. pylori strain in Western countries is lower. Franceschi et al and Takahashi et al. documented association between H. pylori eradication with disappearance of anti Cag A antibodies and significant increase in platelet counts in ITP patients; they attributed the effect of HP eradication on platelet increase to HP Cag A molecular mimicry to platelet antigens. Thus, difference in the H. pylori genotypes and prevalence of Cag A positive H. pylori strains may explain variability in improvement of platelet counts after treatment in studies that were done in different geographic areas, but more work is needed to evaluate it formally.

In this study, all responders had platelet count $\geq 50 \times 10^3$\/$\mu$L and we observed poor response to treatment in ITP patients with severe thrombocytopenia. Accordingly an other study, done by Stasi et al., 32% of patients with mild thrombocytopenia had a platelet response, but platelet response was observed only in one patient with severe thrombocytopenia. The reason of this situation has not been addressed in most reports, but these results show that the chance of obtaining a response by HP treatment is lower in patients with severe thrombocytopenia.

Conclusions. Results of this study revealed eradication therapy of H. pylori infection can improve platelet counts in ITP patients especially with mild thrombocytopenia. Also, our results show that H. pylori eradication cannot have a major role in the treatment of severe ITP patients. On the other hand; treating of H. pylori infection compared to conventional ITP treatment has some advantages such as the low cost, the non-invasiveness of diagnostic methods and favorable toxicity of drugs. Thus, this study supports routine detection and eradication of H. pylori infection in ITP patients in populations with a high prevalence of this infection such as Iran.

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