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The Effect Of Helicobacter Pylori Eradication Treatment On Increasing Platelet Count In Patients With Thrombocytopenic Purpura

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Abstract

The effect of Helicobacter pylori eradication on platelet count in patients with immunosuppressive thrombocytopenic purpura is contradictory. In this clinical trial, the effect of Helicobacter pylori eradication on platelet count in adult patients with ITP was investigated.

materials and methods: Forty Iranian patients with ITP were studied in two groups. One group was treated with amoxicillin, clarithromycin and omeprazole. The other group received similar placebo values. Platelet count was assessed before treatment and in the first, second and third months after treatment.

Findings : The mean platelet counts before the intervention in the intervention and control groups were 67.85 and 69.4 thousand per cubic millimeter, respectively ($p = 0.82$). This rate was 107.15 in the intervention group and 71.15 thousand per cubic millimeter in the control group in the third month after treatment ($p <0.001$). Repeated measures analysis confirmed the effect of positive treatment for Helicobacter pylori eradication on platelet count ($p = 0.007$).

Conclusion : In this study, it was found that treatment of Helicobacter pylori eradication in patients with immune thrombocytopenic purpura causes a significant increase in platelet count.

Keywords: Immune thrombocytopenic purpura, Helicobacter pylori, Platelet count, Eradication

Introduction

Helicobacter pylori (Helicobacter pylori) is a gram-negative microaerophilic bacterium that colonizes the stomach of more than half of the human population(Suerbaum,2002و Michel,2004) .However, the prevalence of Helicobacter pylori worldwide is not homogeneous (Sherman, 2004 and Kato, 2005). In Western countries, the prevalence of infection has decreased over the past few decades (Kindermann, 2002 - Perez-Perez), but the rate of Helicobacter pylori infection in developing countries such as Iran has been reported to be about 90-80%.(Mansour-Ghanaei, 2009-, Massarrat, 1995). Helicobacter pylori is a major cause of chronic active gastritis and gastric and duodenal ulcers. Helicobacter pylori is a contributing factor in the development of gastric cancer and mucosa-associated lymphoid tissue

lymphoma (Suerbaum, 2002; Michel, 2004). Many diseases associated with platelet aggregation have been associated with Helicobacter pylori infection. For example, people with H pylori are more likely to have a heart attack, coronary heart disease, and stroke (Pietroiusti, 2002- Danesh, 2002). It has also been suggested that H pylori may initiate thrombotic thrombocytopenic purpura (TTP), inducing platelet aggregation through interaction with Willebrand von factor (Franchini, 2005). It is suggested that the chronic consequences of H pylori infection may be associated with idiopathic thrombocytopenic purpura (ITP), which has been shown to eradicate the bacterium from the gastric mucosa in some patients with ITP (Jackson, 2005). Campuzano-Maya, 2007). Clinically, Detection of Helicobacter pylori infection requires a diagnostic test that is cheaply and accurately available. Diagnosis methods can be divided into aggressive (direct) and non-invasive (indirect). Invasive methods include endoscopy, culture of biopsy specimens, staining of specimens, and identification of urease activity. Non-invasive methods include urea respiration test and serological techniques. Some of these studies have shown that treatment for Helicobacter pylori eradication has resulted in the treatment of patients with purpura thrombocytopenic immunity in 40 to 50% of cases. In contrast, some other studies have reported a lower incidence of Helicobacter pylori in patients with chronic thrombocytopenic purpura. Or eradication treatment was not effective in the addition of these germs. On the other hand, only three studies in this field have been performed in children.In addition, recent research findings on the role of this microbe in the incidence have been inconsistent with the persistence of the thrombocytopenic immunodeficiency purpura.Patients with a platelet count of less than 20,000 should be treated because of the possibility of spontaneous bleeding or mild trauma. The goal of treatment is to reduce antibody production, reduce platelet degradation, and increase platelet count.

The therapeutic effects of corticosteroid drugs, intravenous immunoglobulin have been proven. Immunosuppressant such as virginChristine, cyclic andCyclophosphamide, cyclosporine, azathioprine, Mycophenolate may not be used in severe cases .According to studies, the frequency of Helicobacter pylori infection among patients with LTP has been reported to be between 29 and 100%, depending on the sampling method and the study site. Helicobacter pylori infection in adults is usually chronic. A causal relationship between H pylori infection and ITP has been suggested in studies showing improved platelet counts after eradication in infected patients. The prevalence of H pylori infection in patients with ITP has been systematically studied and no differences have been found with the healthy general population matched by age and geographical area. In contrast, a study from Colombia reported a very high prevalence of H pylori infection in patients with ITP (90.6%), which differed significantly from controls (43.8%).Numerous studies in adults have shown the positive effect

of H. pylori eradication with triple standard treatment on platelet count in patients (Kohda, 2002; Hino, 2003; Veneri, 2002; Sato, 2004: Liebman, 2007) in cohort studies. Higher response rates have been reported in Japan and Italy than in other countries.The association between H pylori infection and ITP was first described in 1998, when an Italian group reported a significant increase in platelet count in 8 of 11 ITP patients in whom the bacterium had been eradicated (Gasbarrini , 1998). However, the results are contradictory in subsequent reports. Studies often include patients with mild thrombocytopenia who are not usually treated.Therefore, the role of Helicobacter pylori eradication in the management of patients with ITP needs further investigation, but there is growing evidence of an association between Helicobacter pylori eradication and platelet recovery in patients with ITP. And ITP is not available and

there are many inconsistencies in the few studies. Past studies have suggested further research in this areaScreening and eradicating H. pylori infection may be an easier and safer treatment option than suppressing the immune system or removing the spleen in patients with ITP (Inaba, 2005; Kuwana, 2006).The results of many studies in this regard have shown that the eradication of Hicobacter pylori infection has led to a significant and continuous increase in platelet count in patients with LTP.Helicobacter pylori eradication is now considered as one of the treatments for LTP, even as the first line of treatment. However, the response to this treatment is not yet complete and its mechanism is not fully understood .In addition, there is a great deal of disagreement about the association between Hicobacter pylori infection and LTP, pathogenesis, and treatment of this group of patients.Pylori may have a positive effect on treatment with mediators independent of the eradication of this bacterium and due to the modification of the host's immune responses or the elimination of the size of the companion bacteria in the host body. However, the latter theory has been rejected according to the conclusions of meta-analysis studies. The common treatment for LTP today is the use of immunosuppressive drugs such as corticosteroids to modulate the immune responses that have been implicated in the development of this complication. And as we know, the use of alternative drugs that have less side effects can be beneficialRecently, contradictory results from a study suggest that the eradication of Helicobacter pylori in patients with LTP may have a positive effect on this group of patients who are also infected with the bacterium.The British Hematology Association now recommends screening and eradicating H. pylori as an ITP (Evidence Level III) treatment (British Committee, 2003). To date, no reports of these patients have been published in Iran.

Research methodology

This study is an interventional study. Intervention studies: the effect on independent variables and the effects of these changes on dependent variables such as evaluation of Helicobacter pylori eradication treatment on platelet count in patients with immunosuppressive thrombocytopenic purpura referred to Shahid Beheshti Hospital inMilad

Research community

All patients referred to Shahid Beheshti Hospital in millad with a diagnosis of immune thrombocytopenic purpura

Research unit

Any patient with immune thrombocytopenic purpura

Research environment

Blood and Oncology Department of Shahid Beheshti Hospital, Milad

Sampling

Permuted-block randomization

How to calculate the sample size

Using the formula of comparing 2 means and considering the mean and standard deviation from similar studies and 95% confidence and 80% power in finding the differences between groups, the maximum number required in each group was calculated 20 cases.

Method of data collection

Patients with definitive diagnosis of immune thrombocytopenic purpura (ITP) according to the criteria of the American Society of Hematology (history, physical examination, CBC, peripheral blood smear and bone marrow examination) and examination of an experienced hematologist, who were referred to Shahid Beheshti Hospital in Milad

Examination of inclusion and exclusion criteria were included in the study. After providing information on how to conduct the study, all patients were informed about the informed written consent to participate in the study. Demographic information of patients (including age, sex and duration of disease onset) was recorded in a questionnaire. Stool samples were taken from all patients to evaluate for the presence of Helicobacter pylori antigen. Patients who tested negative for fecal antigen were excluded from the study. The patients were divided into case and control groups using Permuted-block randomization with 4 and 6 blocks. The study was a double-blind study and the patients were in charge of group therapy. In the case group, Helicobacter pylori eradication regimen containing the following drugs was prescribed:

Clarythromycin	500 mg	BD	N= 28
Amoxicylin	1 gr	BD	N= 28
Omeprazol	20 mg	BD	N= 90

The control group received the same placebo in terms of number and shape as the case group. At the end of the treatment period, the patients underwent fecal examination again to ensure the eradication of Helicobacter pylori.During the treatment period, platelet count was monitored three times (intervals of one, two and three months) and in case of an increase in platelet count before the end of the treatment period, the person was excluded from the study and was considered spontaneously improved. The effectiveness of treatment was evaluated according to platelet count.

Inclusion and exclusion criteria

Inclusion criteria

Existence of ITP diagnosis based on the criteria of the American Hematology Association and experienced hematologist examinations

Platelet count between 30 and 150 thousand

Non-wet purpura

Absence of life-threatening bleeding

Helicobacter pylori positive stool test

Exclusion criteria

History of allergy to penicillin

Irregular drug use by the patient

Existence of diseases related to malabsorption

Method of describing and analyzing information

The data obtained from this study were statistically analyzed using SPSS software version 16. Chi-square, Independent T test and Repeated measures were used in data analysis. The significance level of P is considered less than 0.05.

3. Research findings

In this study, 40 patients with immune thrombocytopenic purpura in both intervention and control groups underwent eradication of Helicobacter pylori. The mean age of the patients was 34.82 9 9.06 years, which in the intervention group was 35.2 9 9.64 years and, in the control, group was 34.45 8 8.68 years (p = 0.8).

Gender	Group		Sum
	control	Intervention	
Male	14 70%	10 50%	24 60%
Female	6 %30	10 50%	16 40%
Sum	30 100%	20 100%	40 100%
P value			0/2

According to the table above, 50% of the patients in the intervention group and 70% of the patients in the control group were male. The two groups were in a similar situation in terms of gender (p = 0.2).

Group	Item	Average	Standard deviation	p-value
Intervention	20	18/45	12/46	0/26
Control	20	22/45	9/54	

The mean duration of immune thrombocytopenic purpura in all patients was 20.45 11 11.14 months (with a median of 23 months), which was 18.45 12 12.46 months in the intervention group and 54.45 months in the control group. It was 22.45 9 9.9 months that the difference between the two groups was not statistically significant (p = 0.26).

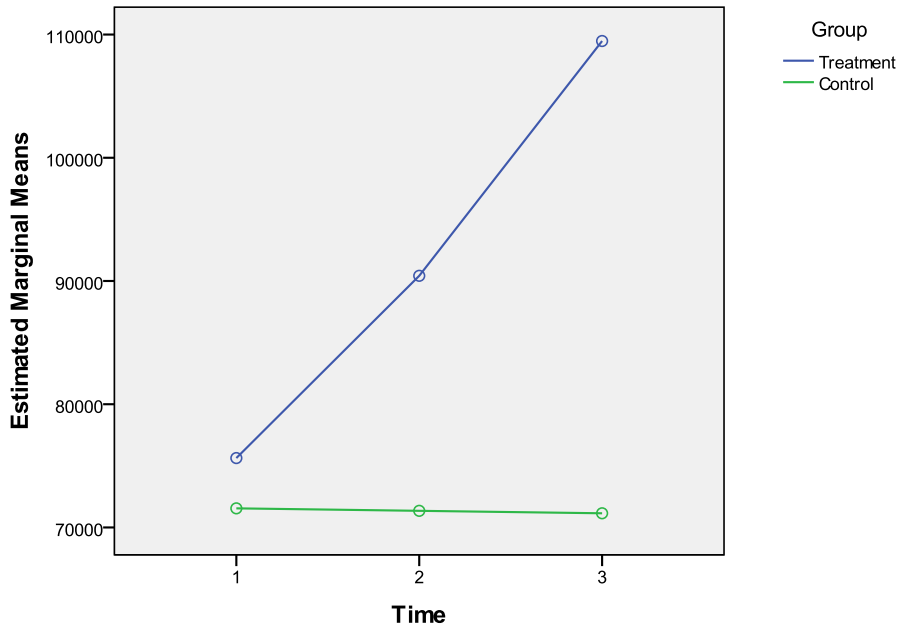
Group	Item	average	Standard deviation	p-value
Intervention	20	6785%	19770/46	0/82
Control	20	6940%	2368/22	

Comparison of the mean platelet count before the intervention in the study groups showed that the two groups had a similar status in terms of platelet count (p = 0.82).

Time	Group	Average	Standard deviation	p-value
first month	Intervention	7420%	20255/21	0.7
	Control	71550%	23520/37	
The second month	Intervention	88600%	27660/25	0.03
	Control	71350%	21947/96	
Third month	Intervention	10715%	31843/82	<0.001
	Control	71150%	20171/04	

According to the results of the above table, it was found that the mean platelet count in the first month after treatment was similar in the two groups.

While in the second and third months after the start of treatment, this mean in the intervention group was significantly higher than the control group.



Repeated measures analysis of platelet count at different times of the study showed that the two groups were different in terms of platelet count changes ($p = 0.007$) that the intervention group was better than the control group in all stages of the study.

This study was performed to evaluate the effect of Helicobacter pylori eradication treatment on platelet count in patients with immune thrombocytopenic purpura. The results of this study showed that eradication of Helicobacter pylori significantly increases the number of platelets in patients.

Different studies in this field have had different results in different geographical areas. According to the results of our study in a study conducted by Kohda et al

It was found that 62.5% of patients with ITP were infected with Helicobacter pylori, which with platelet eradication treatment increased significantly in more than 63.2% of patients within 15 months after treatment. Hino et al. Reported Helicobacter pylori infection in 85.7% of ITP patients, and eradication treatment was successful in more than 55% of patients. The study of patients showed that with the eradication of the infection, the platelet count increased significantly in the following months. Similar results to the present study and the studies cited in other studies have been reported (Inaba, 2005, 2003, Ando K, Shimamoto 2004, Nomura).

Contrary to the above studies, a number of studies have pointed to the ineffectiveness of Helicobacter pylori eradication treatment in increasing platelet count. Jarque et al. Examined the effect of Helicobacter pylori eradication on platelet count in patients with chronic ITP and found that only 5% of these patients had increased platelet count following treatment for Helicobacter pylori. In a study conducted by Payendeh et al. On 92 patients with ITP in Iran, it was found that eradication of Helicobacter pylori infection using the three drugs amoxicillin, clarithromycin and omeprazole significantly improved platelet count in patients with mild ITP. While in patients with severe ITP, this treatment has little effect on platelet count. This discrepancy has been reported in other studies.

Although the number and quality of studies that have pointed to the positive role of Helicobacter pylori eradication in the course of ITP treatment is higher, but the observed discrepancy can be justified in some ways. Pathogenic differences between different strains of Helicobacter pylori are one of the most important possible causes of the inconsistency. Studies have shown that Helicobacter pylori genotypes have significant differences in the development of gastrointestinal symptoms. Although it is not clear to what extent bacterial genotypic differences are involved in the development of extraintestinal symptoms, the geographical dispersion of the positive results of studies suggests the effect of these differences. Most of the previously mentioned studies that have confirmed the positive effect of Helicobacter pylori eradication on platelet count have been performed in Asian regions, especially in the eastern part, and most of the studies with negative results have been related to European and American regions. Regional differences in Helicobacter pylori and response to eradication treatment in ITP patients have been addressed, but it is difficult to draw conclusions due to the lack of information on the infectious strains of ITP patients.

Another possible factor in the different responses of patients with ITP to the treatment of Helicobacter pylori infection is the duration of the disease. A limited number of studies in this field have reported the duration of ITP patients. Comparison of mean platelet count changes after eradication of Helicobacter pylori indicates the fact that platelet counts are higher in patients with a shorter duration of infection than in patients with chronic ITP.Further studies in this area and meta-analysis of the results will help to better understand this relationship.

summary and Conclusion

This study was performed to evaluate the effect of Helicobacter pylori eradication treatment on platelet count in patients with immune thrombocytopenic purpura. The results of this study showed that eradication of Helicobacter pylori significantly increases the number of platelets in patients.

The duration of infection and Helicobacter pylori infection in patients is another possible factor that can affect the response to eradication treatment. Various mechanisms have been suggested to justify the role of Helicobacter pylori in the development or exacerbation of ITP, such as the production of antibodies, interference with von Willebrand factor, activation of B lymphocytes, increased phagocytic activity of monocytes, etc. (35, 58-55). Eradication therapy before stabilizing these immunological processes appears to increase the success of platelet-lowering control. It is difficult to investigate this factor due to the available facilities.

Although the etiological role of Helicobacter pylori in the pathogenesis of ITP has been established, it should be borne in mind that other factors such as viral infections (HIV, CMV and VZV) and immune system disorders have been implicated in the pathogenesis of this disease. They can also be effective in responding to any treatment, including Helicobacter pylori eradication therapy.

suggestions

- Frequency of association between different strains of Helicobacter pylori in patients with ITP
- Investigating the relationship between ITP onset time and platelet status improvement with Helicobacter pylori eradication treatment

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