

Helicobacter Pylori Eradication in Renal Recipient: Triple or Quadruple Therapy?

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Abstract- Although triple (Omeprazole, Amoxicillin, and Metronidazole) and quadruple (Omeprazole, Tetracycline, Metronidazole, and Bismuth Subcitrate) therapeutic regimens for *H. pylori* eradication has been studied much in the general population, there is a lack of data in renal transplanted patients. So, this study aimed at comparing regimens in these patients who were considered being immunocompromised. The present clinical trial was carried out in Mashhad, Iran in 2010. Fifty-five patients who had received a kidney transplant in six months or earlier and referred for chronic dyspepsia were selected. They were resistant to H2-receptor antagonists or proton pump inhibitors therapy and had positive Rapid Urea Test. They randomly divided into two groups: triple and quadruple therapy. The treatment duration in both groups was similar (antibiotics for two weeks plus omeprazole for 4 weeks). Urea Breath Test (UBT) was performed two weeks after treatment for assessment of its result. Total numbers of 39 patients (71%) were positive for *H. Pylori* which were divided into triple therapy group (21 patients) and quadruple therapy (18 patients). Overall, the treatment was successful in 80% (71% in triple therapy and 89% in quadruple one) which was not different significantly between the groups ($p=0.247$). The result of this study revealed that the prevalence of *H. pylori* infection in renal transplant patients is similar to the normal population. In these cases, triple and quadruple therapies were similar in eradication of *H. pylori*. So, triple therapy can be recommended in renal transplant recipients.

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Introduction

Most kidney transplant recipients will have some gastrointestinal complications which are mostly secondary to opportunistic infections but can also be caused by iatrogenic injuries during the operation and/or metabolic toxicity caused by immunosuppressive drug regimens. These include oral lesions, esophagitis, peptic ulcer, diarrhea, colon disorders and malignancy. A kidney transplant recipient may be affected by MALTOMA (Mucosa Associated Lymphoid Tissue) which is a gastric lymphoma. This lymphoma may respond to Helicobacter pylori (*H. pylori*) eradication therapy (1). Peptic ulcer is the most common GI morbidity in the

kidney transplant recipients (2). Treatment of peptic ulcer has improved significantly since the introduction of the H2-receptor antagonists. Thus, it makes sense to use these medications as a preventive measure against peptic ulcer for all the kidney transplant recipients. However, the effects of H2-receptor antagonists on the function of allograft kidney and its pharmacological interaction with immunosuppressive agents are still controversial (3). As peptic ulcer is a chronic disease with recurrent relapses, most kidney recipients need the repeated treatment. Today, it is clear that *H. pylori* is the major cause of peptic ulcer, and its eradication affects the natural course of peptic ulcer that could significantly decrease the relapse rate (4,5). Some kidney transplant recipients may complain about

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nausea and vomiting and abdominal discomfort which are more common in those who use Cellcept® (Mycophenolate mofetil). Abdominal pain and discomfort are the Mycophenolate mofetil's side effects, which is probably secondary to direct irritation of gastric mucosa. In addition, cyclosporine, especially in high doses, can cause sickness and loss of appetite in some patients (6).

As kidney transplant recipients have to take immunosuppressive drugs for a lifetime and because these drugs have many side effects that may not be differentiated from *H. pylori* infection and also in order to reduce the use of medications – and subsequently to reduce the drug interactions- we aim to study the effect of triple and quadruple therapies in eradication of *H. pylori* infection in these patients. Obviously, if the difference between the two groups is not statistically significant, the triple therapy will be a better choice in patients who are immunocompromised.

Materials and Methods

This clinical trial was carried out in Mashhad, Iran in 2010. Fifty-five patients who had received a kidney transplant more than six months earlier and referred to the nephrology and gastroenterology clinics of Imam Reza Hospital for chronic dyspepsia were selected. Resistance patients to H₂-receptor antagonists (known as H₂-blockers) or proton pump inhibitors (PPI's) therapy underwent upper GI endoscopy with biopsy for Rapid Urea Test (RUT). Patients with positive RUT (39 patients, 71%) were considered eligible for intervention and randomly divided into two groups. The triple therapy (omeprazole 20 mg twice a day for six weeks, amoxicillin 1000 mg plus metronidazole 500 mg twice a day for two weeks) was used in group one (21 patients). In the second group, (18 patients) we used quadruple therapy (omeprazole 20 mg twice a day for 6 weeks, tetracycline 500 mg plus metronidazole 500 mg plus two tablets bismuth subcitrate every six hours for two weeks). In summary, both regimens had two weeks of antibiotic therapy and six weeks of PPI therapy. Urea Breath Test (UBT) was performed for all patients two weeks after the cessation of omeprazole treatment. The study had ethical approval from Mashhad University of Medical Sciences, and an informed consent was obtained from each patient.

SPSS 16 was used for data analysis. Frequency (%) and mean (standard deviation) were used for the description of variables and a chi-squared test, and independent-sample t tests were used for analytical

purposes.

Result

The mean (SD) of age and time duration after kidney transplantation of all patients were 45±12 years and 43±19 months, respectively. There were no significant statistical differences between the two groups in terms of age and time duration after kidney transplantation ($P=0.069$ and $P=0.882$, respectively).

At the end of the treatment period, the UBT was negative (responded to treatment) in 31 patients (80%) and positive (treatment failure) in the remaining. Again, the two groups did not differ significantly in terms of age and time duration after kidney transplantation ($P>0.05$). The UBT test was negative in 15 (71%) of triple therapy group and in 16 (89%) of quadruple group. However, there was no significant difference between the two groups in terms of treatment success ($P=0.247$)

Patients who did not respond to the triple therapy (six patients) were treated again with quadruple therapy regimen in which five patients (83%) responded to the treatment.

No side effects were found among patients except some mild epigastric discomfort at the beginning of treatment in some patients which resolved with continuation of treatment.

Discussion

This study shows a high prevalence of *H. pylori* infection in kidney transplant recipients (71%) which is consistent with the high prevalence of *H. pylori* infection in the report of Asl and Nasri that shows its prevalence in stable hemodialysis patients to be about 70% (7), whereas it has been reported to be 23% by Teenan *et al.*, 29% by Davenport *et al.*, 31% by Sarkio *et al.*, 38.5% by Yildiz *et al.*, 70% by Ozgür *et al.*, and finally 60.5% by Abu Farsakh *et al.* (8-13). Most reports are from developed countries, in which the prevalence of *H. pylori* among the adult population is almost 30%.

We agree with Farsakh *et al.*, that the prevalence of gastrointestinal symptoms and endoscopic and histological findings in stable renal transplant recipients are similar to those in the controls, and there was no increase in opportunistic infections of the gastrointestinal tract or of gastric *H. pylori* in these patients (13).

The mean age of the patients was 45 years old, and the mean time duration after transplantation was 43

months. Our results showed that the time duration after transplantation and patient age had no effect on the results of the triple or quadruple therapy regimens, and this result shows that immunosuppression has no negative effect on the treatment regimens of the *H. pylori* eradication. Primary resistance to antibiotics commonly used to treat *H. pylori* varies widely throughout the world (14,15). In the United States, resistance to metronidazole can be detected in up to 40% of stains, whereas resistance to tetracycline and amoxicillin is unusual, generally less than 1% (14,16,17).

Also, the present study shows that the overall eradication rate of *H. pylori* infection was 80% (89% for quadruple therapy and 71% for triple therapy) which does not show statistically significant difference. Of course, the treatment rate in kidney transplant recipients in our study was higher than the patients in the general population (71% and 50%, respectively) which could be due to the younger age of our sample. In a study done by Moradimoghadam and Khosravi in 2009, it was shown that the rate of *H. pylori* eradication by triple therapy will decrease when the age increases (18). In several studies, it has been shown that the rate of *H. pylori* eradication with this regimen is less than 80% (19-21).

In our study, six patients who initially did not respond to the triple therapy were treated with quadruple therapeutic regimen in which five patients responded to this regimen and became negative UBT. So, we could offer quadruple therapeutic regimen as a second line of treatment in those who failed to respond to 3-drug regimen. The limitation of our study includes the small number of patients in each group. In this study, we did not have any serious side effect that resulted in the reduction of dosage or cessation of the treatment; of course some of the patients complained about mild epigastric upset after the onset of treatment that were removed immediately. However, we need more studies to take into account the side effects of drugs and the type of the gastric lesions.

The result of this study revealed that the prevalence of *H. pylori* infection in renal transplant patients is similar to the normal population and triple and quadruple therapies have similar results in eradication of *H. pylori*. So, triple therapy can be recommended in renal transplant recipients.

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