Chapter 12

Helicobacterpylori Infection for Hemodialysis Patients

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1. Introduction

Helicobacter pylori (*HP*) infection is reported to be closely associated with upper gastrointestinal disorders, such as gastroduodenal ulcers, chronic gastritis, and gastric cancer. Furthermore, patients with chronic renal failure receiving hemodialysis often complain of digestive symptoms. There are many possible factors causing these symptoms, including reduced gastrointestinal motility attributable to diabetes mellitus, uremia, intestinal ischemia associated with circulatory failure, and adverse reactions to many oral medications including non-steroidal anti-inflammatory drugs. Although *HP* infection is amongthe factors that may cause upper gastrointestinal disorders in patients with chronic renal failure, the association with*HP* infection has not as yet been elucidated. According to recent reports, the prevalence of *HP* infection is significantly lower in patients with chronic renal failure than in controls with normal renal function, and the prevalence is even reported to decrease with longer duration of hemodialysis. However, there are also previous reports presenting contrary findings. This chapter describes *HP* infection and eradication therapy in hemodialysis patients.

2. Is the prevalence of *HP* infection low in hemodialysis patients?

It is often reported that the prevalence of *HP* infection tends to be lower in patients with chronic renal failure receiving hemodialysis than in control groups with normal renal function [1-19]. In a study conducted in 539 hemodialysis patients, the prevalence of *HP* infection was 48.6%, whereas health check-up examinees with normal renal function showed a significantly higher prevalence of 69.4% ($P < 0.001$) [15]. Another report also showed that, compared to a 27.5% prevalence of *HP* infection in hemodialysis patients, the prevalence in patients with chronic renal failure not receiving hemodialysis was significantly higher at 56.0% [4]. Although there is a report showing the prevalence of *HP* infection to also be low in patients undergoing renal transplantation, it seems that most had received hemodialysis

before transplantation [3]. Based on the above observations, the prevalence of *HP* infection would appear to be low in hemodialysis patients, suggesting that the hemodialysis procedure itself may be involved in the low prevalence of *HP* infection.

3. Are duration of hemodialysis and prevalence of *HP* infection inversely correlated?

How are duration of hemodialysis and prevalence of *HP* infection associated? There are reports that the prevalence of *HP* infection tends to be lower with longer duration of hemodialysis [9, 15, 20, 21]. Nakajima et al. report that the prevalence of *HP* infection gradually decreases with a 2-year or longer duration of hemodialysis, and Sugimoto et al reported that the prevalence gradually decreases within 4 years of hemodialysis [15]. Moriyama et al. report that such a tendency is revealed in patients receiving hemodialysis for 8 years or longer [20]. There is also a report that the prevalence of *HP* infection in health check-up examinees with normal renal function was similar to that in patients with chronic renal failure who had received hemodialysis for less than 1 year [15]. Meanwhile, other studies have shown that there is no such association [22, 23]. However, Sugimoto et al. conducted a 4-year follow-up study in hemodialysis patients with *HP* infection and found that the prevalence gradually decreased from 51.6% at the start to 38.3% at the end [15]. Given that the spontaneous elimination rate of *HP* infection is generally reported to be 0.6% annually [24], it must be assumed from these results that the hemodialysis procedure itself contributes to the observed decrease in the prevalence of *HP* infection.

4. Is there variation in *HP* infection rates among different countries?

The gastricmucosa of approximately 50% of the world's populationis infected with *HP*, and the infectionlevels exceed 70% in some developing areas [25, 26].

There is variation in *HP* infection ratesamong different countries. It may, therefore, be important to evaluate the infection rate in various countries. In East Asian countries, the prevalence of *HP*infection in patients receiving chronic hemodialysis is44.5% (95% confidence interval (CI): 41.5–47.6%], 474/1065), which is significantly lower than in all patients with nor malrenal function [54.0% [95% CI: 50.9–57.1%], 560/1038,*P* <0.001] [27]. On the other hand, because the prevalenceof *HP*in other areas, such as Europe, Middle East, and South Asia has a wide variation, it isdifficult to evaluate the prevalence of *HP*infectionin those areas.

5. Why does the hemodialysis procedure reduce the prevalence of *HP* infection?

One reason is eradication of *HP*by antibiotics that are administeredas therapy for other infections experienced by hemodialysis patients. Antibiotics are the most typically prescribed

drugs in general. In hemodialysis patients, antibiotics may be used for the treatment of bacterial infections as often as or even more frequently than in the general population. It is assumed that patients with renal failure are often prescribed reduced doses of antibiotics. However, compared to the general population with normal renal function, blood levels of antibiotics are likely to be higher after administration in patients with renal failure, and the elimination time is expected to be longer. Thus, in hemodialysis patients with a long duration of renal failure, the spontaneous elimination rate of *HP* infection might be increased by repeated administration of antibiotics. Because blood urea levels are increased in hemodialysis patients, urea levels in gastric juice are also high. The increased urea levels are considered to suppress the growth of *HP* in the stomach [28]. Another possible explanation is that up-regulation of pro-inflammatory cytokines in hemodialysis patients triggers the infiltration of inflammatory cells activated by the gastric mucosa, resulting in progression of gastric mucosal atrophy, an increase in pH, and ultimately *HP* elimination [29, 30]. While there are as yet no data clearly supporting this explanation, the prevalence of *HP* infection may be decreased by a combination of various factors.

6. What are the harmful effects of a decreased prevalence of *HP* infection on hemodialysis patients?

In general, *HP* infection is considered to be a cause of gastroduodenal ulcers, and a decrease in the prevalence of *HP* infection is favorable in this regard. It is widely known that *HP* eradication suppresses gastric acid secretion, which causes gastric erosion [31]. The frequency of endoscopically detected gastric erosion is reported to be high in hemodialysis patients [20, 32, 33], which may be associated with a decrease in *HP* infection. Because gastric erosion may cause gastrointestinal bleeding, caution is required especially in hemodialysis patients [20]. They are often receiving anticoagulant or antiplatelet drugs, and gastrointestinal bleeding can thus be fatal.

Prophylactic administration of anti-acid secretory drugs, such as proton pump inhibitors (PPI), is recommended. While long-term hemodialysis is reported to carry a high risk for reflux esophagitis [32-34], this may also be attributable to suppressedgastric acid secretion due to a decrease in *HP* infection. In patients receiving long-term hemodialysis, administration of anti-acid secretory drugs is recommended to prevent reflux esophagitis.

7. Is *HP* eradication necessary for hemodialysis patients?

While the previous section described the harmful effects of a reduced prevalence of *HP* infection on hemodialysis patients, the harmful effects of *HP* infection include the aforementioned association with gastroduodenal ulcers, chronic gastritis and gastric cancer, as well as gastric mucosa associated-lymphoid tissue lymphoma, etc. Especially in hemodialysis pa-

tients, the frequency of gastroduodenal ulcers and gastric cancer is reported to be higher than in healthy people [3, 35]. Because hemodialysis patients are often receiving anticoagulant or antiplatelet drugs, bleeding from gastroduodenal ulcers may be fatal. Thus, *HP* eradication is considered to be an important treatment for hemodialysis patients in order to prevent gastroduodenal ulcers and gastric cancer. Although spontaneous elimination of *HP* infection can be expected in hemodialysis patients, the earliest possible *HP* eradication is recommended especially in those with a history of gastroduodenal ulcer and confirmed current *HP* infection.

8. How is *HP* eradication best achieved in hemodialysis patients?

According to recent reports, the major regimen is a combination of a PPI selected from among omeprazole, lansoprazole, and esomeprazole and 2 antibiotics selected from among clarithromycin, amoxicillin, and metronidazole, which are administered for 1 or 2 weeks [1, 6, 36-40]. Although the eradication rate fluctuates slightly from 72.7 to 96.0%, it averages around 90%. There seems to be no substantial difference in comparison with the eradication rate of *HP* infection in the general population. The factors contributing to eradication failure include a history of previous eradication therapy, suggesting that the presence or absence of resistant strains to antibiotics iskey to the success of eradication therapy [6].

9. What are the precautions for *HP* eradication therapy in hemodialysis patients?

Caution should be considered in performing eradication therapy for hemodialysis patients to avoidexcessive doses of drugs. Administration of low doses results in high blood levels. However, hemodialysis removes both PPI and antibiotics, lowering their blood levels. In consideration of this fact, without adjustment of the therapy by administering the drugs after the hemodialysis session on the day of hemodialysis, the eradication rate of *HP* infection may be decreased. Safe and effective optimal dosages and administration procedures should be established. In patients with chronic renal failure before the initiation of hemodialysis, attention should be paid to the nephrotoxicity of amoxicillin, and the eradication therapy needs to be adjusted by substituting amoxicillin with metronidazole [39, 41, 42].

Moreover, hemodialysis patients often receive oral antibiotics, and the duration of circulation of these antibiotics in the body is prolonged due to delayed metabolism. Thus, it seems that *HP* often acquires resistance to antibiotics. According to a report on resistance to clarithromycin, resistant *HP* strains were detected in 36.4% of patients with renal failure and 15.2% of healthy volunteers, showing the prevalence of resistant *HP* strains to be significantly lower in the latter [43].

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10. Conclusion

This chapter has described *HP* infection in hemodialysis patients. Because the prevalence of *HP* infection is lower in these patients than in healthy people, attention should be paid to symptoms due to gastric hyperacidity. For those with *HP* infection, eradication therapy is recommended in order to prevent gastrointestinal ulcers and gastric cancer. Even after *HP* eradication, prophylaxis against gastric erosion and reflux esophagitis should be performed with anti-acid secretory drugs.

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