UPPER GASTROINTESTINAL DISEASES CORRELATED TO HELICOBACTER PYLORI INFECTION: COMPARISON BETWEEN UREMIC AND NON-UREMIC PATIENTS. REVIEW OF THE LITERATURE

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[Patologie del tratto gastrointestinale superiore correlate ad infezione da Helicobacter Pylori: confronto fra pazienti uremici e non uremici. Revisione della letteratura]

ABSTRACT

Helicobacter Pylori is the first cause of infection of the upper gastrointestinal tract in hemodialysis patients. The hemodialytic treatment can lead to spontaneous eradication of this bacteria, but the frequency of pathologies involving the upper gastrointestinal tract is still higher in these patients compared to hemodialysis patients negative for the infection and normal patients. In consideration of virulence and pathogenicity of Helicobacter Pylori infection, there is the strong recommendation for eradication therapy in uremic patients, that it has been demonstrated to reduce the incidence of benign and malignant of the upper gastrointestinal tract.

Key words: Helicobacter Pylori, end renal stage disease, hemodialysis, uremia.

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Introduction

Helicobacter Pylori (HP) is, for sure, the bacterium which could be isolated in the most of benign and malignant diseases of the Upper Gastrointestinal Tract, and assumes a fundamental pathogenic role in the development of the mucosal associated lymphoid tissue (MALT) lymphoma, gastric adenocarcinoma, chronic gastritis, gastric ulcer, gastrointestinal bleeding, ileus, gastrointestinal perforation and hyperplastic and adenomatous tumors[(1)].

The role of chronic renal failure and uremia on the onset of the HP-related lesions on the upper gastrointestinal tract is still under debate, even if HP infection can be evidenced in 21-64% patients affected with end stage renal disease (ESRD)[(2;3)]. The bacteria possess factors of virulence due to its own structure, the expression of adhesins, and the production of enzymes such as Urease, CagA, and VacA. A permissive role is given from host inflammatory response to infection with production of pro-inflammatory cytokines. The final results of this interaction are the signs and symptoms at the expense of the upper gastrointestinal tract.

In uremic patients infected by HP, gastrin renal clearance reduction, associated with gastric G Cells hypertrophy, can be responsible of the onset of the symptomatology on the upper gastrointestinal tract[(4)].

HP-positive patients affected by ESRD manifest symptoms like nausea, dyspepsia, lack of appetite, epigastric and thoracic pain[(5;6)].

Discussion

HP is a Gram-negative, microaerophilic bacterium, identified for the first time in 1983 by Marshall and Warren[(7)] in gastric biopsies of patients affected with chronic gastritis.

About 50% of the population shows the bacterium on the gastric mucosa and, in certain areas the percentage can increase to the 70%[1].

The upper gastrointestinal tract mucosa is characterized by a rapid epithelial turnover and the homeostasis is mainly controlled by apoptotic mechanism. In different studies it has been shown how the apoptotic cells are increased in HP positive patients and how the number of these cells decrease as HP is eradicated[8;9]. It is considered that the harmful mechanism responsible of the apoptosis is determined by ammonium production from urea degradation by bacterial urease[6]. Because of the increased urea concentration in the stomach of ESRD patients, the level of ammonium produced by HP is consequently increased. Furthermore, it is thought that the damage on the upper gastrointestinal tract can be also connected with a reduction of gastrointestinal motility[11] and with amyloid protein laying[1].

HP is responsible of the onset of the signs and symptoms of the upper gastrointestinal tract in ESRD patients that underwent dialysis. Among HP-related pathologies in uremic patients, it has been mentioned gastric metaplasia, even though the erosive gastritis is the most common pathology among these patients. According to a study headed by Huang C. et al.[12] it has been shown how a longer hemodialysis timing can be followed by an increased incidence of gastric metaplasia ($p < 0.05$). Moreover it has been demonstrated that a percentage ranging between 24%[10] and 36.4%[12] of ESRD patients who undergone hemodialysis were HP positive. On a 4 years follow up, the longer the dialysis period lasts, the higher is the reduction of HP infection[1]. The prevalence of HP infection in patients undergoing hemodialysis is significantly lower than not-dialyzed ones (27.5% vs 56%)[13]. This finding suggests that the hemodialysis treatments explicate a protective role against the bacterial infection.

According to Cocchiara et al.[14], analyzing two patients groups, both with ESRD, the incidence of gastrointestinal ulcer was proved higher in the HP positive group not treated with eradication therapy compared to the HP positive group undergone eradication therapy (5 vs 1, $p = 0.05$). Furthermore the comparison between the HP positive untreated patients and the HP negative patients showed a sharp incidence of gastro-duodenal ulcer on the first compared to the second one (5 vs 0, $p = 0.05$).

Many authors wonder about the need of treating HP positive patient affected with ESRD with eradication therapy. About 1/3 of patients undergone hemodialysis for a duration of 4 years headed for spontaneous eradication[1]. Anyway is clear how in this patients the frequency of peptic ulcer is increased compared to HP negative ones and to normal renal function subjects[5].

HP eradication in ESRD patients associates with a reduction of the clinical symptomatology, insomuch as the eradication therapy is recommended both for prevention and the treatment of peptic pathology of the uremic patient undergoing hemodialysis[12]. In any case, it is unclear if the mere presence of HP could be directly connected to renal dysfunction progression and to the ESRD patients prognosis[1].

A therapeutic protocol for the ESRD patients is the 7-days omeprazole-based triple therapy in low doses, which consists of omeprazole (40mg/die), amoxicillin (500mg/die) and clarithromycin (500mg/die). After four week of therapy, it was possible to show the efficacy and the safety of this protocol using histological examination of the gastric mucosa and rapid urease test. In this study[15], eradication was effective in the 84% of uremic patients who underwent hemodialysis.

As this drugs are excreted in the urines an evaluation of the creatinine clearance and a dosage adjustment of the mentioned drugs is needed, keeping the posology as lower as possible[12], even though Authors do not report any severe side effects following amoxicillin therapy[1] due to the reduction of serum concentration of these drugs after hemodialytic treatment[16-17].

It has been widely demonstrated a relationship between HP positivity and MALT lymphoma onset in patients who underwent renal transplantation: this lymphoma can be treated by HP eradication[3,18].

Conclusions

In ESRD patients undergone dialysis, HP represents the main cause of infection of the upper gastrointestinal tract. HP infection is frequently found in patients with chronic renal failure. These patients, if treated with hemodialysis for a period of at least four years, can head to spontaneous eradication in 1/3 of the cases. Despite this, the frequency of pathologies involving the upper gastrointestinal tract is higher in hemodialysis HP positive patients compared to HP negative and normal patients. For this reason authors agree on recommending eradication therapy for HP positive patients.

Eradication therapy demonstrated to reduce the incidence of benign and malignant of the upper gastrointestinal tract[14].

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