Helicobacter pylori in the critically ill patient
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Chapter 11

SUMMARY
In chapter 1 the literature is reviewed concerning stress ulcer pathogenesis and the potential role of *Helicobacter pylori* in stress ulcer formation in critically ill patients. Stress ulceration is a complex and multifactorial disease. Mucosal blood flow, endotoxins and cellular dysfunction all play an important role. *H. pylori* may theoretically contribute to the formation of stress ulceration.

In chapter 2 the incidence of gastrointestinal interventions is described in a mixed population of critically ill patients. Patients after uncomplicated cardiac surgery are excluded. Five to six percent of the included patients need gastrointestinal endoscopy. The most frequent indication for endoscopy is upper gastrointestinal bleeding. Upper gastrointestinal bleeding is the indication for admittance to the intensive care in 1.2% of all included patients. Esophageal varices are found in half of them. Bleedings that occur more than 24 hours after admission to the intensive care unit are usually defined as stress ulcerations. In this study, overt bleeding occurs more than 24 hours after admission in 1.9% of the patients. However, stress lesions in the upper gastrointestinal tract are identified in approximately half of these patients. Therefore, the incidence of bleeding as a result of stress ulceration appeared to be 1.0%. It is concluded that gastrointestinal endoscopy is indicated in 5.6% of critically ill patients. The incidence of overt upper gastrointestinal bleeding more than 24 hours after admission is 1.9% but stress ulceration is identified in only half of these patients.

The specific group of patients undergoing cardiac surgery is studied in chapter 3. Reviewing the literature, risk factors for upper gastrointestinal bleeding in this patient group are defined. Patients after cardiac surgery appear to have a very low incidence of upper gastrointestinal tract bleeding. In the reviewed literature 505 episodes of bleeding are found in 113323 patients. The incidence of these bleeding episodes under stress ulcer prophylaxis appears to be 0.35% (169 bleedings in 47868 patients) and in patients without pharmacological prophylaxis 0.51% (130 bleedings in 25609 patients). This difference is not statistically significant. Randomised controlled trials concerning stress ulcer prophylaxis in patients after cardiac surgery have not been performed. The conclusion from this literature review is that pharmacological stress ulcer prophylaxis in cardiac surgery patients is not indicated on a routine base.

Tests to detect *H. pylori* in critically ill patients should be validated to study the role of this micro-organism in gastric disease in these patients. Chapter 4 describes the Laser Assisted Ratio Analyser (LARA)-13C-urea breath test.
and serological assessment of antibodies in mechanically ventilated patients. The LARA-\(^{13}\)C-urea breath test is a non-invasive and relatively easy way to detect active \(H. \text{ pylori}\) infection in ambulant patients. It can also easily be used in mechanically ventilated patients. In addition, the test can be stored several weeks before analysis. Patients undergoing cardiac surgery are tested in both the pre-operative ambulant condition and post-operatively during mechanical ventilation. This study shows that with minor adaptations for breath collection this test is accurate in detecting \(H. \text{ pylori}\) in mechanically ventilated patients. However, serological antibody detection appears to be less reliable. Antibodies remain detectable in serum for months or years after eradication of \(H. \text{ pylori}\). False positive results may therefore occur. On the other hand, haemodilution and blood loss will result in false negative tests. The LARA-\(^{13}\)C-urea breath test is independent of these factors.

In chapter 5 it is described that detection of \(H. \text{ pylori}\) antigens in stools (HpSA) from critically ill patients has major disadvantages compared to the LARA-\(^{13}\)C-urea breath test. Most patients do not produce stools in the first three days of admission. Of the patients with \(H. \text{ pylori}\) antigens detected in a stool sample all have active \(H. \text{ pylori}\) infection as determined by LARA-\(^{13}\)C-urea breath test. Both the positive predictive value and the specificity of the HpSA are 100% compared to the LARA-\(^{13}\)C-urea breath test. However, false negative faecal tests result in a sensitivity of only 75% and a negative predictive value of 87.5%. The unavailability of stool samples in recently admitted critically ill patients and the false negative test results make the antigen detection in faeces not suitable for screening critically ill patients for the presence of active \(H. \text{ pylori}\) infection.

Chapter 6 describes the measurement of gastric permeability in critically ill patients. The relation between gastric permeability and both \(H. \text{ pylori}\) infection and severity of disease is described. Gastric permeability is determined by measuring the sucrose excretion in the urine after the ingestion of 100 g sucrose in 250 ml of water. Previously it was shown that an abnormal sucrose loading test is related to gastric mucosal ulceration and NSAID induced mucosal injury. In this study the sucrose excretion is not related to the severity of disease measured by APACHE II score or other scores. In contrast, patients with \(H. \text{ pylori}\) infection have a significantly higher sucrose excretion compared to non-infected patients. Thus, \(H. \text{ pylori}\) infection leads to an increase in gastric permeability which underlines the possible role of \(H. \text{ pylori}\) in the pathogenesis of stress ulceration.
The prevalence of *H. pylori* in critically ill patients is described in chapter 7. Active *H. pylori* infection as determined by the LARA-\(^{13}\)C-urea breath test is present in 37% of the 300 included patients. Three days after intensive care admission the infection rate falls to 7.7% and in none of the patients *H. pylori* can be detected after 7 days. Antibiotic treatment for selective decontamination of the digestive tract is the proposed mechanism for this decline. It is also shown that *H. pylori* prevalence as detected by serology is 57%. The three patients with stress ulcer related bleeding (1.0%) are not infected with *H. pylori*. The suppression of *H. pylori* infection may have eliminated *H. pylori* associated stress ulcer formation which may be the reason for the observed low incidence of stress ulcer related bleeding.

The observed suppression of *H. pylori* infection during intensive care treatment using SDD is further studied in chapter 8. *In vitro* and *in vivo* studies show that *H. pylori* is susceptible for two of the four antibiotics used for selective decontamination of the digestive tract. Both cefotaxime intravenously and tobramycin topically applied are antimicrobial agents with anti-*H. pylori* properties. Prolonged topical treatment with tobramycin effectively suppresses *H. pylori* infection.

Chapter 9 describes the role of *H. pylori* in the pathogenesis of stress ulceration. Gastric mucosal injury is detected in mechanically ventilated patients by upper gastrointestinal endoscopy within 6 hours after admission to the intensive care. The endoscopical mucosal injury score (EMIS) is determined. Major mucosal injury is significantly related to the presence of *H. pylori* infection as detected by the LARA-\(^{13}\)C-urea breath test and to the use of NSAID's. However, in a multiple regression analysis *H. pylori* infection appears to be the only risk factor (p=0.019).

Whether the presence of *H. pylori* in critically ill patients is an occupational hazard for intensive care nurses is described in chapter 10. A group of nurses from a unit were *H. pylori* is suppressed in the patients by gut decontamination (group I) is compared with a group of nurses from a unit where gut decontamination is not used (group II). It is shown that *H. pylori* prevalence is 11% and 25% in these groups of nurses respectively (p=0.027). The duration of nursing time is significantly higher in group II but the distribution of *H. pylori* infection in time supports acquisition on the intensive care unit in these nurses.

In this thesis it is shown that upper gastrointestinal bleeding occurs infrequently in a population of patients with selective gut decontamination.
Moreover, in only half of these patients stress related lesions are found. *H. pylori* infection is effectively suppressed in these patients. Suppression of *H. pylori* infection in critically ill patients reduces the occupational hazard of *H. pylori* acquisition by intensive care nurses. *H. pylori* infection is a risk factor for gastric mucosal injury in mechanically ventilated critically ill patients and the suppression of this micro-organism may well be the reason for the low incidence of stress ulcer related bleeding in an intensive care unit where SDD is used.

However, the definite prospective study comparing the incidence of stress ulcer related bleeding in an ICU where SDD is used and an ICU where SDD is not used, was not performed for this thesis. A major drawback for such a study is that the two ICU's that would be compared should have identical treatment protocols. The only difference should be the lack of SDD in one ICU. At this moment I do not have access to ICU’s with these qualifications. However, this thesis provide enough circumstantial evidence to consider this hypothesis seriously.

In this thesis it is shown that *H. pylori* is strongly related to gastric mucosal injury in critically ill patients. Apparently, during critical illness severe gastric mucosal injury occurs when *H. pylori* is present. Therefore I conclude that the formation of these lesions known as stress ulcerations is enhanced by *H. pylori* infection.