

Title: PREVENTION OF STRESS BLEEDING AND THE RISK OF NOSOCOMIAL PNEUMONIA IN VENTILATED ICU-PATIENTS

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The current concept of stress bleeding prophylaxis aims to increase the intragastric pH to a level of at least 4. Both antacids and H<sub>2</sub>-antagonists proved to be effective in reducing the gastric acidity in ICU-patients. In several prospective studies particularly antacids could reduce the frequency of stress bleeding (1), while even in large placebo-controlled studies H<sub>2</sub>-antagonists proved to be ineffective (2). The fact that, to date, no reduction in mortality rates as a result of medicinal prophylaxis for stress bleeding could be proved seems even more significant. This lack of improvement in outcome could be due to the side-effects of the stress bleeding prophylaxis.

The overgrowth of gramnegative bacteria in the stomach with an intragastric pH of over 3.5 has been confirmed by several investigations (3). The same gramnegative bacteria were also found in the tracheas of the patients 24 to 48 hours later (4). As a consequence in ventilated patients treated with antacids and/or H<sub>2</sub>-antagonists nosocomial pneumonia occurred significantly more often than in patients without medicinal prophylaxis (5).

Until now the risk of nosocomial pneumonia in relation to stress bleeding prophylaxis has not been investigated in prospective controlled trials. In initial studies (6) sucralfate proved to be an efficient substance for stress bleeding prophylaxis. The effectiveness of this drug could not be explained by an increase of the pH level to above 3.5. We therefore conducted a prospective controlled study to investigate the incidence of pulmonary infections and stress bleedings in ventilated patients treated with antacids or sucralfate.

**METHODS:** The study was carried out with the approval of the local ethical committee. 100 ventilated patients received, in a random order, either an antacid (70 mval neutralizing capacity) 2-hourly or 1 g sucralfate 4-hourly through a stomach tube. Exclusion criteria were initial gastrointestinal hemorrhage and gastric or duodenal ulcer. The acidity of the gastric juice was measured 8-hourly. Macroscopically visible bleeding was used as the criterion for stress bleeding. The diagnosis of pneumonia was made by a doctor who was unaware of the object of the study. Criteria for pneumonia were pulmonary changes on X-ray and at least three of the following findings: temp > 38.5° C, leucocytosis, bacteria in the smear and suspicious changes in the arterial blood gases. Patients showing signs of pneumonia on admission to the ICU or those with a thoracic trauma were excluded from the analysis of pneumonia rates. Student's t-test, chi-square and Fisher's exact test were used for the analysis of the results with a level of significance of p < 0.05.

**RESULTS:** Both groups were comparable on basic clinical parameters and risk factors (Table). In each group one patient showed signs of an acute gastrointestinal hemorrhage. Both of the patients were in the high risk group. 1370 determinations of the gastric pH were taken from the 100 patients. Only 3.9 % of the samples in the antacid group were < 4, in contrast, only 53.5 % of the pH samples in the sucralfate group were > 4 (p < 0.01). 61 patients fulfilled the criteria for the analysis of pulmonary infections. Three of 29 sucralfate treated patients (10.3 %) developed nosocomial pneumonia. This was significantly lower (p < 0.05) than the 34.4 % incidence (11 of 32 patients) in the antacid group.

TABLE

	antacids	sucralfate
N	50	50
male/female	28/22	31/19
age (x± SD)	43.7 ± 20.1	44.9 ± 20.6
days on therapy	5.6 ± 4.0	6.2 ± 4.6
days on ventilator	4.8 ± 3.5	5.8 ± 4.8
risk factors	3.7 ± 0.9	3.9 ± 1.0
mortality (%)	34	30
gastric pH > 4 (%)	89.6	53.5 <sup>§</sup>
pneumonia (%)	34.4	10.3 <sup>*</sup>

\*: p < 0.05    §: p < 0.01

**DISCUSSION:** Nosocomial pneumonia is the most common lethal complication in ventilated ICU-patients. In the present study it could be shown for the first time that the risk of pneumonia in these patients can be significantly reduced when a stress bleeding prophylaxis is used which does not rely on raising the intragastric pH. Sucralfate also provides adequate protection against stress bleeding. These findings must be seen as of critical importance where the choice of medication for stress bleeding prophylaxis is concerned.

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