Multicenter Study Evaluating the Role of Enterococci in Secondary Bacterial Peritonitis

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A 1-year prospective multicenter study was performed to explore the significance of the presence of enterococci in cultures of peritoneal fluid from patients with secondary bacterial peritonitis in seven Spanish hospitals. The clinical records of patients with positive peritoneal fluid cultures were reviewed and distributed into cases (patients with cultures yielding enterococci) and controls (patients with cultures not yielding enterococci). Of a total of 158 records, 38 (24.1%) were cases and 120 (75.9%) were controls. The percentages or the scores (cases versus controls) for the variables included in the multivariate analysis were as follows: age of >50 years, 89.5% versus 68.3%; malignancy, 39.5% versus 18.3%; chronic obstructive pulmonary disease (COPD), 15.8% versus 4.2%; postoperative peritonitis, 55.3% versus 30.1%; nosocomial onset, 57.9% versus 34.2%; a higher Charlson comorbidity index, 3.29 ± 3.38 versus 1.84 ± 2.31; APACHE II score, 10.71 ± 4.37 versus 8.76 ± 5.49; ultimately or rapidly fatal disease, 63.2% versus 34.8%; need for surgical reintervention, 36.1% versus 15.1%; and admission to an intensive care unit, 45.9% versus 30.8%. In the multivariate analysis, enterococci were associated only with postoperative peritonitis (P = 0.009; odds ratio [OR] = 5.0; 95% confidence interval [CI] = 1.49 to 16.80), a higher Charlson comorbidity index (P = 0.002; OR = 1.30; 95% CI = 1.11 to 1.54), and COPD (P = 0.046; OR = 6.50; 95% CI = 1.04 to 40.73). The results of this study showed that enterococci were associated with comorbidity. An association with mortality could not be demonstrated.

Aggregation substances and the extracellular protein Esp have been identified as virulence factors in enterococci, and both play a role in colonization of the host (5, 10). In addition, resistance to multiple antimicrobial agents allows enterococci to proliferate in patients receiving antimicrobial chemotherapy (14). The factors enabling enterococci to cause human infections have yet to be clarified, although the development of traits that make it possible for the microorganism to occupy new niches, evade host defenses, or exploit a weakened host immune system go some way to providing an explanation (10).

It has been suggested that enterococci act synergistically with other bacteria and thus increase the rates of morbidity and mortality (15). Nevertheless, most reports of high rates of mortality in association with enterococcal bacteremia involve series that include severely debilitated patients; therefore, bacteremia could be a marker of this state and not the cause of it (15).

Although the role of enterococci in intra-abdominal infections has not been fully defined, it is clear that they can cause peritonitis (in patients with nephrotic syndrome or cirrhosis and in patients undergoing peritoneal dialysis) (17) and that perioperative treatments with active agents during abdominal surgery decrease the probability of development of subsequent enterococcal wound infections (24). More recent studies excluding postoperative cases have reported on the minor role of enterococci in secondary peritonitis in relatively healthy patients (20), although others report that the presence of this entity in cultures of peritoneal fluid significantly increases the rate of morbidity but not the rate of mortality (6).

Few recent series have reported on the rate of isolation of enterococci in secondary peritonitis, and their role in this disease remains undefined (15, 16). Therefore, we carried out a prospective multicenter study in Spain to evaluate the role of enterococci in secondary bacterial peritonitis.

MATERIALS AND METHODS

We studied all peritoneal fluid samples from patients with secondary peritonitis received in the microbiology departments of seven Spanish hospitals in 2004. Sample collection was done by the hospital-specific routines. Peritoneal
Wilcoxon test. Statistical significance was established at a p value of \( p < 0.05 \). A table shows data for the cases and the controls were not yielding the growth of enterococci. Data for the cases and the controls were not yielding the growth of enterococci and were defined as “controls.” Table 1 lists the microorganisms isolated from the cases and the controls. No significant differences in isolation rates were obtained for the controls versus the cases for all bacterial types isolated. Table 2 shows the comorbid conditions of the controls and the cases. The cases tended to be older, with a significantly higher percentage of the case patients being over 50 years of age (89.5% versus 68.3% for the controls; \( P = 0.011 \)). As for comorbid conditions, a significantly higher percentage of cases presented with malignancy (39.5% versus 18.3% for the controls; \( P = 0.014 \)) and chronic obstructive pulmonary disease (COPD; 15.8% versus 4.2% for the controls; \( P = 0.014 \)).

**RESULTS**

A total of 158 evaluable samples were processed, and the corresponding clinical records were reviewed. Of these, 38 (24.1%) yielded the growth of enterococci and were defined as “cases,” while the remaining 120 (75.9%) did not yield the growth of enterococci and were defined as “controls.” Table 1 lists the microorganisms isolated from the cases and the controls. No significant differences in isolation rates were obtained for the controls versus the cases for all bacterial types isolated. Table 2 shows the comorbid conditions of the controls and the cases. The cases tended to be older, with a significantly higher percentage of the case patients being over 50 years of age (89.5% versus 68.3% for the controls; \( P = 0.011 \)). As for comorbid conditions, a significantly higher percentage of cases presented with malignancy (39.5% versus 18.3% for the controls; \( P = 0.014 \)) and chronic obstructive pulmonary disease (COPD; 15.8% versus 4.2% for the controls; \( P = 0.014 \)).

Table 2 also shows the characteristics of secondary peritonitis. While no differences in the origin of peritonitis were found between the study groups, for the cases significantly higher percentages of postoperative peritonitis (55.3% versus 30.1% for the controls: \( P = 0.005 \)) and nosocomial onset (57.9% versus 34.2% for the controls; \( P = 0.009 \)) were found. Table 3 shows the prognoses and the outcomes for both the controls and the cases. The incidence of comorbidities was significantly higher in the cases than in the controls according to both the Charlson comorbidity index \((3.29 \pm 3.38\) and \(1.84 \pm 2.31\), respectively; \( P = 0.011 \)) and the prognoses of the underlying diseases (McCabe and Jackson score) \((P = 0.003\)). The prognosis of mortality assessed by use of the APACHE II score also showed differences between the groups, with a higher score being achieved for the cases than for the controls \((10.71 \pm 4.37\) and \(8.76 \pm 5.49\), respectively; \( P = 0.011 \)). There were no differences between the cases and the controls for preoperative physical health in the global analysis \((P = 0.036\), lower percentage of controls presented ASA I (18.2% and 40.2%, respectively; \( P = 0.006 \)), as was fungal superinfection (21.6% and 5.8%, respectively; \( P = 0.011 \)). In the multivariate analysis, the logistic regression was sta-
from bloodstream infections in the United States (7, 10). It is important to determine whether this pathogen should be covered in the empirical treatment of secondary peritonitis, since several studies have found a significant relationship between inappropriate therapy and lower clinical success rates (11, 23) and have concluded that the selection of inappropriate antibiotics for treatment increases the rate of clinical failure 3.4-fold and the mortality rate by about 30% (4, 12).

The bivariate analysis showed that enterococci were isolated from patients with significantly higher ages, comorbid conditions (according to the Charlson and the McCabe and Jackson scores), a worse prognosis (according to the APACHE II score), and the need for surgical reintervention. However, in the multivariate analysis, only comorbid conditions (as determined by the Charlson score), postoperative peritonitis, and the presence of COPD were significantly associated with the presence of enterococci, although the coefficient of determination was low (Cox $R^2 = 0.191$). Therefore, it seems that enterococci are associated with comorbidity, but we could not demonstrate an association with mortality. In a previous study, the presence of enterococci in peritoneal fluid cultures significantly increased the rate of morbidity but not that of mortality (6), while other authors established an association between polymicrobial infections involving enterococci and increased mortality (3, 20, 21).

In the view of the presence of enterococci in more severely ill patients with secondary peritonitis (mainly postoperative peritonitis), our results suggest, but do not demonstrate, the need for coverage in this group. In this sense, the guidelines of the Infectious Diseases Society of America for the selection of anti-infective agents for complicated intra-abdominal infections do not recommend routine coverage of enterococci in patients with community-acquired intra-abdominal infections, although they do recommend coverage (with a moderate quality of evidence for the recommendation, based on clinical experience and expert committee opinions) when enterococci are recovered from health care-associated intra-abdominal infections (22). Although clinical success depends on many factors, the choice of effective empirical therapy is important, as indicated in a pharmacodynamic analysis of empirical therapy for secondary peritonitis carried out by using a Monte Carlo simulation, in which the probability of target attainment and the cumulative fraction of the response decreased for β-lactams when enterococci were included in the model (4).

As in previous studies in which the presence of enterococci in peritoneal fluid cultures significantly increased the rate of morbidity but not the rate of mortality (6), our analysis shows that the presence of enterococci might be a biomarker of a poor prognosis. Further studies are needed to fully and definitively clarify the exact role of enterococci in secondary peritonitis.

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