Turk J Gastroenterol *2016; 27: 294-5*

Empirical antibiotic treatment of nosocomial spontaneous bacterial peritonitis: Should we start direct broader-spectrum antibiotics or not?

Piano S, Fasolato S, Salinas F, et al. The empirical antibiotic treatment of nosocomial spontaneous bacterial peritonitis: results of a randomized, controlled clinical trial. Hepatology 2016; 63: 1299-1309.

Spontaneous bacterial peritonitis (SBP) is one of the major life threatening infectious complication of decompensated cirrhosis. In recent years, a new nomenclature was carried out in SBP by the presentation type of the patients, defined as community acquiered, health related and nasocomial SBP (1). Third-generation cephalosporins are the first choise of the antibotic treatment, however up to 75% resistance has been defined in the nasocomial SBP patients to the third-generation cephalosporins (2). These high resistance rates may increase the mortality and complications in both health related and nasocomial SBP patients (3). For that reason, recently, treatment of nasocomial SBP was modified by the experts to use of broader spectrum antibiotics (4). However concerns about the usage of broader-spectrum antibotics should be discussed. This aproach may increase the resistance to these last salvage weapons againts the nasocomial infections and may reduce our success rate to this complicated infections in the future.

In the last issue of Hepatology (Hepatology, Vol. 63, No. 4, 2016), Piano et al. (5) presented an elegant prospective randomized study which compared the effectivenes of third-generation cephalosporin, ceftazidime versus meropenem plus daptomycin (MER/DAPTO), (dosages were adjusted according to the GFR) for at least 7 days treatment in 31 patients with nasocomial SBP. In patients without response by the results of PMN count in the ascitic fluid, to the treatment with ceftazidime after 48 hours, ceftazidime was discontinued and replaced by a rescue therapy with MER/DAPTO as provided for the experimental arm. Primary endpoint was effectivenes of treatment defined as reduction of PMN count at least 25% of baseline after 48 hours of starting the antibiotics and PMNC count below 250 mm^3 at the 7^{th} day of the treatment. Secondary endpoints included: (1) 90-day transplant free survival (TFS); (2) length of hospital stay; (3) cost of hospitalization (4) cost of antibiotic treatment (5) safety of the treatment (6) the efficacy of daptomycin in the treatment of intra-abdominal infections. Results of this study showed that MER/DAPTO group has more effectively cleared the SBP infection when compared to Ceftazidime group (86.7% versus 25%, $p<0.001$). However, there was no difference in 30-day or 90-day transplant free survival between the groups (86.7% versus 81.3% 30-day and 79.4% versus 68.8% 90-day for MER/DAPTO and Ceftazidime groups, respectively). Patients who have no response to the treatment had more usage of Norfloxacin prohpylaxis when compared to the responsive patients. In multivariate analysis, they also found that ineffective first-line treatment (hazard ratio: 20.6), development of acute kidney injury during hospitalization (hazard ratio: 23.2), and baseline mean arterial pressure (hazard ratio: 0.92) were independent predictors of 90-day transplant-free survival. In discussion part, authors discussed the possible concerns of starting highest borad-spectrum antibiotics as a first line treatment might posibly increase the more resistant bacteria in the hospitalized patients. Finally, in conclusion they recomended that based on the early results of cultures, antibiotics may be changed to the specific ones and this aproach may partially overcome to this problem. The other important finding of this study is that patients who have responded both of the treatment regimes have longer transplant free survival than the non-responder patients. However, there is no statistical significant difference in both treatment arms. Authors suggested that this non-significance between the treatment arms may be due to the lack of adequate sample size. Finally, Authors concluded that MER/DAPTO combination should be started as a first choise antibiotic treatment in patients with nasocomial SBP. In editorial of the same issue of Hepatology, Ison critizied the authors' conclusion and suggested that "although this study provides evidence to the usage of broad-spectrum antibiotics to nasocomial SBPs, development of resistance to these salvage antibiotics is a major concern" (6). In Editorial, Ison con-

cluded that empirical antibiotic treatment should be tailored in each hospital by the bacterial resistance data of its own, in community acquired, health care related and nasocomial SBP patients.

I agree with Ison's conclusion, that starting with the third generation cephalosporins and changing the antibotics based on the results of 48th hour responses in patients with nasocomial or health care related SBP may be an acceptable option which decreases unneccesary usage of broader spectrum antibiotics. By this aproach at least 25% of patients who will have respond to the third generation cephalosporins are not going to be treated with those broader spectrum antibiotics. However, one concern of this aproach might be that 48 hour of ineffective treatment may cause any increase in the mortality. Piano's data clearly showed that there is no increased mortality in patients whom have no response to ceftazidime and switched to MER/DAPTO at the 48th hour (5).

At the end of the day, selection of a cephalosporin with Pseudomonas coverage will be appropriate for centers with high rates of pseudomonal nosocomial SBP. Additionally, every center should consider its own bacterial resistance situation and decide to the first line antibiotic treatment not in only SBP but also for the other nasocomial infections.

Osman Cavit Özdoğan
Department of Gastroenterology, Marmara University School of Medicine, İstanbul, Turkey
Received: April 6, 2016 Accepted: April 6, 2016
DOI: 10.5152/tjg.2016.160001

REFERENCES

1. Bunchorntavakul C, Chamroonkul N, Chavalitdhamrong D. Bacterial infections in cirrhosis: A critical review and practical guidance. World J Hepatol 2016; 8: 307-21. **[CrossRef]**
2. Fernandez J, Acevedo J, Castro M, et al. Prevalence and risk factors of infections by multiresistant bacteria in cirrhosis: a prospective study. Hepatology 2012; 55: 1551-61. **[CrossRef]**
3. Ariza X, Castellote J, Lora-Tamayo J, et al. Risk factors for resistance to ceftriaxone and its impact on mortality in community, healthcare and nosocomial spontaneous bacterial peritonitis. J Hepatol 2012; 56: 825-32. **[CrossRef]**
4. Jalan R, Fernandez J, Wiest R, et al. Bacterial infections in cirrhosis: a position statement based on the EASL Special Conference 2013. J Hepatol 2014; 60: 1310-24. **[CrossRef]**
5. Piano S, Fasolato S, Salinas F, et al. The empirical antibiotic treatment of nosocomial spontaneous bacterial peritonitis: results of a randomized, controlled clinical trial. Hepatology 2016; 63: 1299-309. **[CrossRef]**
6. Ison MG. Empiric Treatment of Nosocomial Spontaneous Bacterial Peritonitis: One Size Does Not Fit All. Hepatology 2016; 63: 1083-5. **[CrossRef]**