Long-term antibiotics and PPI's induce bacterial translocation in patients with cirrhosis: Antibiotics are not always ANTI-biotics

O'Leary JG, Reddy KR, Wong F, et al. Long-term use of antibiotics and proton-pump inhibitors predict development of infections in patients with cirrhosis. Clin Gastroenterol Hepatol 2014; pii: S1542-3565(14)01146-X. doi: 10.1016/j.cgh.2014.07.060. [Epub ahead of print].

O'Leary et al. (1) prospectively analyzed 188 patients with cirrhosis who were hospitalized for infection from 12 centers (North American Consortium for the Study of End-Stage Liver Disease). They investigated and characterized risk factors for repeat infections in these patients. Patients were followed for 6 months after hospital discharge and data were analyzed on type of infections and factors associated with subsequent infections. Just after 6 months after hospital discharge, only 59% of them were alive and 14% had liver transplant.

Following discharge, 45% had subsequent infections, but only 26% of the subsequent infections occurred at the same site. Compared to patients not re-infected, patients with repeat infections were older and a higher proportion used proton-pump inhibitors, rifaximin, or prophylactic therapy for spontaneous bacterial peritonitis. Statistical analyses revealed four independent risk factors for re-infection: 1) SBP prophylaxis (OR: 3.44), PPI use (OR: 2.94), SBP at hospital admission (OR: 0.37) and age (OR: 1.06).

According to these solid findings above, there is about to be major turning point in liberal prescription of PPI's and prophylactic (long-term) antibiotics in cirrhotics. Last year, a meta-analyses indicated the cautionary hazard of PPI use, which was associated with increased occurrence of SBP (2). The hypothesis behind this association was sound, that PPI usage led to small intestinal bacterial overgrowth and subsequent infection in the ascitic fluid. However, what about prophylactic antibiotics and increased secondary infections?

Literally, antibiotics leading to increased bacterial infection rate is a paradox. But, the explanation come from a recent study published this month (3). Antibiotic treatment induced-dysbiosis predisposes exogenous infection and causes systemic dissemination of both antibiotic resistant and commensal bacteria through transcytotic route across epithelial layers of the gut (3).

In summary, O'Leary et al. (1) published an extra-ordinary paper which has the potential to alter our daily practice. They stated that "Patients hospitalized with cirrhosis and infections are at high risk for subsequent infections, mostly at different sites, within 6 months of index infection resolution. Those at highest risk include previously infected older patients receiving PPIs and/or SBP prophylaxis, although these associations do not prove that these factors cause the infections. New strategies are needed to prevent infections in patients with cirrhosis". The "New Strategies" mentioned above might be microbiota modulation without antibiotics in the future.

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