

Tigecycline Might Protect Against *C. difficile*

BY BRUCE JANCIN

FROM THE ANNUAL EUROPEAN CONGRESS OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

VIENNA — Treatment with the antibiotic tigecycline was associated with a sharply decreased risk of hospital-onset *Clostridium difficile* pseudomembranous colitis in a large case-control study.

This apparent protective effect has not been previously described, Dr. Matthew F. Emons said at the annual European Congress of Clinical Microbiology and Infectious Diseases.

The unexpected finding requires confirmation, given that exposure to other classes of antibiotics has consistently been shown to be a strong risk factor for *C. difficile* infection (CDI).

But the protective effect is biologically plausible. Tigecycline (Tygacil) has broad-spectrum in vitro activity against gram-positive and gram-negative agents as well as anaerobic organisms, and it reportedly has activity against toxigenic strains of *C. difficile*.

The retrospective study involved 1,454 adults who

developed laboratory-confirmed CDI at least 72 hours after admission to 74 hospitals of various sizes included in the Cerner Corp.'s proprietary Health Facts database. The control group consisted of 32,807 inpatients who did not develop CDI during hospital stays of 72 hours or longer.

The risk of hospital-onset CDI in tigecycline-treated patients was one-fifth that of patients not on the antibiotic. Exposure to tigecycline prior to onset of CDI was the only protective factor identified in the study, according to Dr. Emons of Cerner LifeSciences, Beverly Hills, Calif.

In contrast, exposure to carbapenems was associated with a 2.1-fold increased risk of CDI in a multivariate regression analysis, and third- or fourth-generation cephalosporins conferred a 1.6-fold increased risk. Patients who received two systemic antibiotics had a 1.5-fold greater risk than did those who hadn't received any systemic antibiotics, while those who got three or more antibiotics were at 1.8-fold increased risk.

Session chair Dr. Edward J. Kuijper deemed the tigecycline findings "very interesting."

"Based on this and other data, I think tigecycline is now a reasonable option with *C. difficile* infection resistant to first-line therapy," said Dr. Kuijper of University Medical Center Utrecht (the Netherlands).

The single most potent risk factor for hospital-onset CDI in the case-control study was impaired immune function, which was prevalent in 19.5% of cases and 4.3% of controls and was associated with a 4.8-fold increased risk.

Other notable risk factors included hospital admis-

sion from a skilled nursing facility, with a 3.5-fold increased risk, and acute renal failure, cardiac arrhythmia, heart failure, or cerebrovascular disease within 12 months prior to admission, each of which was associated with a 1.7- to 2.7-fold increased risk of CDI. Advanced age and a high burden of comorbidity were also risk factors, as previously reported by others.

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DR. EMONS

Liverpool. In this study, which included 296 patients with CDI and 296 controls, prior PPI therapy was associated with a threefold increased risk of CDI, but only in cases involving *C. difficile* ribotype 106, which accounted for 27% of all infections. Histamine₂-blocker therapy was associated with a significantly decreased risk of CDI in the British study.

Dr. Emons presented a second study that highlighted the impact of CDI on hospital resource utilization. It involved 1,312 patients with hospital-onset CDI and an equal number of hospitalized control subjects matched for comorbidity burden and demographic characteristics. The CDI group's in-hospital mortality rate of 8.7% was not significantly different from that of the matched controls. However, the mean hospital length of stay among CDI survivors was 20.8 days, compared with 9.9 days for controls. Moreover, 33% of patients discharged after CDI were readmitted within the next 90 days, a rate 56% higher than controls.



VITALS

Major Finding: The risk of hospital-onset *Clostridium difficile* pseudomembranous colitis in tigecycline-treated patients was one-fifth that of patients not on the antibiotic.

Data Source: Case-control retrospective study that included 1,454 adults with laboratory-confirmed CDI at least 72 hours after admission to 74 hospitals in the Cerner Corp.'s proprietary Health Facts database.

Disclosures: The studies were sponsored by Cerner LifeSciences, where Dr. Emons is employed.

Probiotic Reduced Diarrhea Due to Antibiotics, *C. difficile*

BY DAMIAN McNAMARA

FROM THE INTERNATIONAL PROBIOTICS ASSOCIATION WORLD CONGRESS

MIAMI — A proprietary probiotic combination of two live *Lactobacillus* organisms significantly reduced the incidence and severity of antibiotic-associated diarrhea, as well as the incidence of *Clostridium difficile*-associated diarrhea, compared with placebo in a prospective, double-blind study.

Researchers at Shanghai Jiao Tong University in China randomized 255 hospitalized patients, aged 50-70 years, within 36 hours of antibiotic initiation to one of three groups: 86 patients took two probiotic capsules daily, 85 took one probiotic capsule plus one placebo capsule daily, and 84 took two placebo capsules daily. Each capsule contained 50 billion colony forming units (c.f.u.) of *L. acidophilus* CL1285 and *L. casei* LBC80R (made by Bio-K Plus International, which funded the trial). The regimen continued for 5 days after the usual course of antibiotics, then patients were monitored for another 21 days.

The incidence of antibiotic-associated diarrhea—the primary study outcome—was 29% overall, affecting 74 patients. Specifically, diarrhea occurred in 16% of the patients who took two active capsules, 28% of those who took one active and one placebo capsule, and 44% of those who took two placebo capsules. Con-

trolled comparisons were statistically significant between the groups, suggesting a dose-response relationship, Kerry Diaz said in an interview at a poster presentation.

The second outcome, severity of diarrhea, was likewise lower with the 100 billion c.f.u. daily dose. The researchers tracked the mean number of days that patients reported three or more episodes of liquid to soft stool. Patients in the high-dose probiotic group had a mean 2.8 days of severe diarrhea, compared with 4.1 days for those in the low-dose group and 6.4 days in the placebo group. Again, the differences were statistically different.

The researchers also found a significant difference in the incidence of *C. difficile*-associated diarrhea: 1% in the high-dose probiotic group, 9% in the low-dose group, and 24% in the placebo cohort—a "huge difference," Ms. Diaz said. The full study findings were published earlier this year (Am. J. Gastroenterol. 2010 Feb. 9 [doi:10.1038/ajg.2010.11]).

The product is sold as a supplement in the United States, Ms. Diaz said, and has been available for more than a decade in Quebec, where Bio-K Plus is based. The product has not been reviewed by the U.S. Food and Drug Administration for antibiotic-associated and *C. difficile*-associated diarrhea, she added.

Disclosures: Ms. Diaz is a clinical research manager at Bio-K Plus International.

Hospitals Take Aim at *C. difficile* Infections

Health care facilities around the country have added new infection prevention measures aimed at stopping the spread of *Clostridium difficile* infections, but few have been able to add staff to help cope with the problem, according to an online survey conducted by the Association for Professionals in Infection Control and Epidemiology.

Overall, 53% of the health care facilities surveyed by APIC had adopted new interventions to address *C. difficile* in the last 18 months; of those that had not, 21% were planning to do so in the next year. But only 23% of the facilities reported that they had added more infection prevention staff or increased the hours dedicated to infection prevention. And about 34% of the respondents said that their facility could be doing more to control the spread of *C. difficile*.

APIC conducted the survey in February and March of this year to gauge progress following a November 2008 APIC report showing that the prevalence of *C. difficile* was 6-20 times greater than previously estimated. The survey yielded responses from nearly 1,800

APIC members, most of whom are nursing directors or patient safety officers working in acute care facilities.

The survey findings suggest that some hospitals are heeding the data on increased prevalence as a call to action. For example, over the past 18 months, about 60% of the facilities surveyed have implemented additional or more aggressive hand hygiene interventions, 77% have started staff education programs about *C. difficile*, and 50% have added patient education programs about the infection.

But the survey also showed that hospitals could be doing a better job when it comes to tracking colectomies, which can indicate the presence of a more severe strain of *C. difficile*. Fewer than 30% of facilities reported that they monitor the number of colectomies performed, and 46% said they didn't know if the colectomy rate had increased during the past 18 months.

—Mary Ellen Schneider

The full survey report is available at www.apic.org.