

# C. difficile Outbreak Is Tied to Fluoroquinolones

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SAN FRANCISCO — The use of fluoroquinolones, but not of proton pump inhibitors alone, was strongly associated with an outbreak of *Clostridium difficile* diarrhea in a hospital in the Netherlands, according to data presented at the annual Interscience Conference on Antimicrobial Agents and Chemotherapy.

A second study that was conducted at the same hospital indicated that the outbreak was associated with *C. difficile* ribotype 027, a strain that appears to cause a more severe course of illness and to result in more deaths than do other strains of *C. difficile*.

The findings shed more light on suspicions that proton pump inhibitors and antibiotics, especially fluoroquinolones, are associated with nosocomial outbreaks of *C. difficile* diarrhea.

The data, which suggest that the risk of *C. difficile* diarrhea is not directly associated with proton pump inhibitors, also strongly implicate the use of fluoroquinolones.

**The odds ratio that someone taking a fluoroquinolone would develop *C. difficile* diarrhea was 15 times that of someone not on a fluoroquinolone.**

Cephalosporins were used by more of the patients who developed *C. difficile* diarrhea during the outbreak than by those who did not develop such illness, said Dr. Norbert Vaessen of the Leiden University Medical

Center, the Netherlands.

But in the statistical analysis of the case-control study of the outbreak, which occurred at St. Jansdal Hospital, Harderwijk, the fluoroquinolone association was found to be significantly stronger, Dr. Vaessen reported.

The odds ratio that someone taking a fluoroquinolone would develop *C. difficile* diarrhea was 15 times that of someone not on a fluoroquinolone. The odds ratio for cephalosporin use was 5.7.

The odds ratios of fluoroquinolone or cephalosporin use in controls who had diarrhea that was not caused by *C. difficile* were 2.2 and 0.9, respectively.

Intriguingly, in two instances, the cases no longer occurred when fluoroquinolone use was halted at the hospital, Dr. Vaessen said at the meeting, sponsored by the American Society for Microbiology.

The initial outbreak began in March 2005. Overall, the case rate at the hospital rose from 4-5 cases/10,000 admissions to 58 cases/10,000 admissions between April and September 2005.

The hospital had a total of 51 *C. difficile* cases between April and November. Three patients died from direct complications.

In June, the hospital instituted infection control measures and the number of cases began to fall. In July, the hospital stopped using fluoroquinolones, and almost no cases occurred in that month.

Case numbers rebounded in September when fluoroquinolone use was reinstated, and that number fell dramatically again when fluoroquinolones were halted once more in October.

"Fluoroquinolones seemed very important, at least in this outbreak," Dr. Vaessen said.

Proton pump inhibitors were used by a total of 47% of the case patients; however, these patients were not found to be associated with an increased odds ratio of

risk in the analysis of this outbreak, Dr. Vaessen said.

The cases in Harderwijk were caused by the *C. difficile* ribotype 027 strain. Since about 2003, this strain has appeared with greater frequency in Canada, the United States, and Europe, according to Dr. Vaessen.

In the related presentation, Dr. Ed J. Kuijper, also of the Leiden University Medical Center, reported that confirmed cases of ribotype 027-associated diarrhea

have occurred in 35 hospitals in the Netherlands. The strain also appears to have spread to Belgium and France, he said.

In Great Britain, the ribotype 027 strain has been observed in 24% of the isolates that have been tested, and it appears to have become the second-most-common strain found there.

The ribotype 027 strain has not yet been detected in cases in Spain, Turkey, or Greece, Dr. Kuijper added. ■

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