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New antibiotic drug combo to speed up treatment of tuberculosis

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A team of tuberculosis (TB) experts at Johns Hopkins and in Brazil have evidence that substituting the antibiotic moxifloxacin in the regimen of drugs used to treat the highly contagious form of lung disease could dramatically shorten the time needed to cure the illness from six months to four.

Adding moxifloxacin to a standard combination of other antibiotics increased by 17 percent the number of patients who cleared active infections from their lungs (raising cure rates from 68 percent to 85 percent), after just two months of therapy, and when compared to patients taking the standard combination with another, older antibiotic, ethambutol.

“This is the most compelling evidence in nearly 25 years that a novel antibiotic drug combination works better than the current gold standard at curing active TB infection,” says study senior author Richard E. Chaisson, M.D., a professor of medicine, epidemiology and international health at The Johns Hopkins University School of Medicine and founding director of its Center for Tuberculosis Research. Chaisson will present his team’s findings Sept. 18 in Chicago at the 47th Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC).

“Beyond the obvious value of healing patients more quickly, a shorter treatment time could also cut down on transmission of the disease to others and make it easier for health care workers worldwide, who are overwhelmed by large numbers of patients, to treat more people and to

treat them faster," says Chaisson, who started the study in 2003.

He notes that worldwide, each year, nearly 9 million new cases of TB are diagnosed, and more than one and a half million people die from the disease, caused by Mycobacterium tuberculosis.

TB also remains the leading cause of death worldwide among those with HIV and AIDS and is epidemic in developing countries with the highest HIV-infection rates.

The new study of more than 170 men and women in Rio de Janeiro, Brazil – all with active TB – showed that combination drug therapy with moxifloxacin was more potent than combination therapy with an older, more traditional anti-TB drug, ethambutol. Symptoms of active TB include fever, cough, night sweats and weight loss.

After two months of combination therapy, cultured sputum samples from patients taking moxifloxacin were significantly less likely to grow TB bacteria than samples from those on traditional ethambutol therapy. The time to clear the infectious organism from sputum was also significantly shorter in the moxifloxacin group.

Conventional TB therapy prescribes a mix of antibiotics, typically four, given in view of a caregiver and taken together for six months. Commonly known by its acronym DOTS, short for Directly Observed Therapy Short-Course, the treatment cures on average 95 percent of patients who finish taking their medications as originally prescribed.

But experts say the lengthy treatment period has proven a problem for patients, who sometimes miss taking their drugs on time, minimizing the therapy's effectiveness and increasing the risk that drug-resistant strains will develop.

History, says Chaisson, demonstrates that shorter regimens boost drug compliance and cure rates, often by as much as 50 percent. In the 1950s, TB treatment lasted from 18 to 24 months, and nearly a quarter of patients failed to complete therapy. It was not until new drugs appeared in the 1970s and 1980s, when treatment times were shortened to an average of six months, that cure rates shot up.

In the latest study, all participants were given a standard combination of three antibiotic pills – isoniazid, rifampin, and pyrazinaminde – and then randomly assigned to receive a fourth pill, either moxifloxacin or ethambutol. Moxifloxacin, approved for use in the United States since 1999 as a treatment for pneumonia, is not currently approved as a treatment for TB. However, ethambutol has been approved to treat TB since 1962.

The three combination drugs, which must be taken several times daily for six to eight months, have all been widely used to treat TB disease for decades: isoniazid (since 1952), rifampin (1968) and pyrazinamide (1954).

“It was remarkable to see just how potent moxifloxacin was,” says Chaisson. After just two weeks of therapy with moxifloxacin, 21 percent of the sputum samples were negative and cleared of visible disease, while in the ethambutol study group, it was just 3 percent. After four weeks, the gap widened to 51 percent and 29 percent, respectively.

Chaisson says substituting moxifloxacin for one of the key ingredients in DOTS could also make treatment far less costly overall, allowing TB programs to expand their coverage. The medication currently costs $10 per day for short-term use, but the researcher says the drug’s manufacturer, Bayer Healthcare AG, has promised to make the drug available at affordable prices in poor countries should it gain approval for use in TB.

Chaisson and his team next plan to investigate a potentially even more potent drug combination that includes traditional DOTS drugs with yet another substitution, rifapentine in place of rifampin. Rifapentine became available in the United States in 1998 and scientists say it is more effective against drug-resistant strains of TB.

Chaisson and colleagues conducted their research with funding from the U.S. Food and Drug Administration's Office of Orphan Product Development. The study was part of a series of studies on moxifloxacin that are being coordinated by the nonprofit Global Alliance for TB Drug Development (GATB) in collaboration with Bayer.

The GATB estimates that 1 billion people worldwide will be infected with tuberculosis by the year 2020, of whom 200 million will fall ill and 35 million will die.

As part of the research program, Bayer donated supplies of moxifloxacin.

Source: Johns Hopkins Medical Institutions