Rapid UTI Tests to Permit Point-of-Care Decisions

Personalized selection of agents may help fight antibiotic resistance.

BY CHRISTINE KILGORE

EXPERT ANALYSIS FROM THE ANNUAL MEETING OF THE AMERICAN UROLGICAL ASSOCIATION

WASHINGTON – Rapid molecular diagnosis of urinary tract infection will soon enable individualized, evidence-based selection of antibiotics "right at the point of care," according to Dr. Joseph C. Liao.

"Currently we rely on urine culture, which takes 2-3 days at a central microbiology laboratory," he said. "What if in the future [you] could obtain molecular diagnosis in less than 1 hour right there in your office? And what if we could tailor the choice of antibiotics for the patient sitting in your office [rather than start broad-spectrum antibiotics empirically]?"

Personalized, evidence-based selection of antibiotics has become an increasingly important goal – for both individual and public health – as the problem of antibiotic resistance has intensified, said Dr. Liao and other speakers at the meeting .

Over the past several years, Dr. Liao and his colleagues in the urology department at Stanford (Calif.) University have used biosensor technology to develop an assay for rapid pathogen identification, as well as a biosensor-based antimicrobial susceptibility test for urinary tract infection (UTI).

"We've been able to achieve pathogen identification within an hour, and antimicrobial susceptibility testing within 3 hours," Dr. Liao reported.

The biosensor (a molecular sensing device that generates a measurable signal in the presence of a target analyte) is already part of everyday clinical practice, he noted. The glucose sensor and the i-STAT portable clinical analyzer, for example, are commonly used biosensor-based devices.

The biosensor being utilized in the "next generation" of UTI diagnostic tools is composed of a chip about the size of a microscope slide with 16 individual sensors. "Like computer technology, it can be mass produced at a relatively low cost," said Dr. Liao, who is also chief urologist at the Veterans Affairs Palo Alto (Calif.) Health Care System.

This could further improve the now-challenging task of differentiating colonization, simple UTI, and early complicated UTI, 'and [could] help us better differentiate ... the severity of infection.'

The overall strategy for pathogen identification involves lysis of the bacteria present in a urine sample, followed by a hybridization process that enables the sensor to detect bacterial 16S rRNA, a kind of "bacterial molecular fingerprint." This results in a signal output.

"Essentially, we're converting a molecular hybridization event into an electrical signal," Dr. Liao explained. "And the higher the bacterial concentration, the higher the signal."

Bacterial 16S rRNA is also a marker of bacterial growth, a property that Dr. Liao's research group has exploited to develop a biosensor-based antimicrobial susceptibility test (AST).

By incubating a urine sample in the presence or absence of commonly used antibiotics, and quantifying the 16S rRNA level, "we can follow the differential growth and derive the AST," he said.

Dr. Liao and his colleagues recently completed a clinical validation study in which they compared results from their biosensor platform with results from standard microbiological analysis in more than 200 urine samples collected from patients at the Spinal Cord Injury Service at the Veterans Affairs Palo Alto system.

Pathogen detection sensitivity and specificity were 92% and 97%, respectively, and "in corresponding AST, we found an overall agreement of 94%," said Dr. Liao, whose study was published early this year (J. Urol. 2011;185:148-53).

In the future, Dr. Liao hopes to use biosensor technology to also detect biomarkers that are shown to be indicative of infection in the presence of pathogens, he said.

Such an integrated assay would detect both biomarkers and pathogens, and thus address the host immunity response as well as identify the pathogen.

This could further improve the now-challenging task of differentiating colonization, simple UTI, and early complicated UTI, "and [could] help us better differentiate and stratify the severity of infection," he said.

Dr. Liao reported that he had no disclosures. ■

WOCA, Botulinum Toxin Considered for Neurogenic Bladder

BY CHRISTINE KILGORE

EXPERT ANALYSIS FROM THE ANNUAL MEETING OF THE AMERICAN UROLOGICAL ASSOCIATION

WASHINGTON – How should one manage a 35-year-old woman with multiple sclerosis on self-clean intermittent catheterization who complains of pelvic pain and cloudy urine?

Such a patient with "neurogenic bladder" and possible urinary tract infection needs careful diagnosis, catheterization review, and possibly other management considerations, said Dr. Stephen R. Kraus during a panel discussion of recurrent UTIs at the meeting.

One study showed that UTI was five times less likely when CIC was performed six times per day rather than three times per day.

Patients with neurogenic bladder commonly have chronic bacteriuria and recurrent UTIs, and thus generally require a combination of bacteriuria and leukocyturia – as well as clinical symptoms or an increase in autonomic dysreflexia – for the initiation of empirical UTI therapy. Such criteria will help avoid unnecessary use of antibiotics.

"Original criteria were based on bacterial colonization counts but were criticized for being highly insensitive," said Dr. Kraus, professor and vice chairman of the department of urology at the University of Texas, San Antonio.

Assuming the patient has already had a video urodynamic test, Dr. Kraus said, he would obtain a catheterized specimen for urinalysis, culture, and a sensitivity test; treat as needed; and then consider increasing her catheterization frequency. A trial of a hydrophilic catheter could also be considered in the context of recurrent UTIs, he said.

Various catheter modifications – from silver alloy catheters to antibiotic-impregnated catheters – have been used with some success in reducing the risk of UTIs, but "they carry their own problems such as cost, development of resistance, and even, as one study suggested, the possibility of silver toxicity," Dr. Kraus said.

Two randomized, controlled trials have shown that hydrophilic catheters will reduce the risk of UTIs, compared with regular polyvinyl chloride catheters, he noted. Although the choice of single-use vs. reusable catheters is "always a point of contention," several studies have "clearly" shown that clean intermittent catheterization (CIC) poses no greater risk of recurrent UTIs than do single-use catheters, he added.

Frequent changing of intermittent catheters can prevent biofilm development, and one study showed that UTI was five times less likely when CIC was performed six times per day rather than three times per day, he noted.

Routine chronic antibiotic prophylaxis should be avoided in patients with neurogenic bladder, he said, but a short course of antibiotics could be useful during the initial CIC period, and is certainly prudent before any invasive genitourinary procedures are performed.

Dr. Kraus said he is intrigued by the concept of a weekly oral cyclic antibiotic (WOCA) program that uses weekly alternating antibiotics as a prophylactic measure. In one 2-year trial of WOCA, investigators "saw dramatic reductions in UTIs (from 9.4 to 1.8 per patient year) ... and most importantly, they did not see any change in the number of multidrug-resistant infections."

As a final management option for the above-described patient, Dr. Kraus said he would consider injections of botulinum toxin (Botox). This approach "has exploded in the market for neurogenic bladder management, and it has been associated with a significant reduction in UTI at 6 months ... presumably because the neurogenic bladder management is that much better."

The term "neurogenic bladder," Dr. Kraus noted, is one that's "not very precise." For the purposes of his discussion, he defined it as a condition in which the bladder is affected by a neurologic process and has an impaired ability to store and empty urine.

Dr. Kraus disclosed that he is an investigator for the National Institute of Diabetes and Digestive and Kidney Diseases, a course director for Laborie (which manufactures catheters and other products for urinary and pelvic disorders), and a consultant/adviser for Pfizer. ■