Clinical Evaluation of two Immunoassay Methods for the Rapid Detection of Chlamydia trachomatis

Antigen in Endocervical Specimens from High Risk Female Patients

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Leknablaðið 1995; 81: 541–4

Two rapid immunoassay methods, QuickVue-Chlamydia (Quidel Corp., San Diego California) and Kodak Surecell (Kodak Corp. Rochester, N.Y.) were evaluated for the detection of Chlamydia trachomatis antigen in endocervical swabs from high risk females attending a sexually transmitted disease clinic. The results were compared to McCoy cell culture and a polymerase chain reaction assay (Amplisor®-PCR, Roche Molecular Systems). Of the 240 females enrolled in the study 45 were considered infected (18.8%). Sensitivity, specificity, predictive value of a positive (PVP) and predictive value of a negative (PNV) of the QuickVue-Chlamydia assay were 96%, 99%, 96% and 99% respectively. Sensitivity, specificity, PVP and PNV of the Surecell assay were 96%, 100%, 100% and 99% respectively. The performance of the two immunoassay methods was similar, the sensitivity was the same and the specificity of the Kodak Surecell was slightly better than that of the QuickVue. On the other hand, the QuickVue-Chlamydia assay was considerably simpler to perform (fewer steps) than the Kodak Surecell assay and took significantly less of technologists time.

Introduction

Genital infections caused by Chlamydia trachomatis have been a significant health care problem in the Western world in recent years (1,2). Cell culture has traditionally been the gold standard for diagnosing these infections but it is expensive and time consuming. Rapid diagnosis of Chlamydia infections is obviously of major importance for treatment of individual patients and for effective contact tracing. Since a significant number of patients is asymptomatic, screening of asymptomatic populations may be of major importance (3). In recent years a number of rapid methods have been introduced for direct detection of Chlamydial antigens in patient specimens (4-8). These rapid tests have come into widespread use although they lack sensitivity compared to culture. Initially, most of these new rapid tests were intended for use in laboratories, but more recently, tests have been introduced for use in physicians offices or at the bedside (9,10). Taking the test to the patient instead of having to send a specimen to a laboratory can obviously save significant time and save patients some anxiety. The performance of two of these rapid tests was compared to the results of culture in high risk females. The tests were the Kodak SureCell which has been on the
Materials and methods

Patient population and specimen collection: The patients were high risk females attending the State Clinic for Sexually Transmitted Diseases (STD) in Reykjavík, Iceland. Patients were enrolled in the study if they had symptoms or were contacts of patients, known to be infected with *Chlamydia trachomatis*. Patients were excluded if they had received antibiotics during the two weeks prior to specimen collection. Four cervical specimens were collected for the detection of *Chlamydia*. First, three specimens were collected for culture, QuickVue and the Kodak SureCell in an alternating sequence. Then a fourth specimen was collected for Amplicor® PCR. The sample intended for culture was collected on a cotton swab (Medical wire Co) and put in 1.0 ml of 0.2 M sucrose phosphate buffer, antibiotics and 10% foetal calf serum and cooled with ice. The samples for QuickVue and SureCell were collected on solid shaft dacron swabs. The specimen for PCR was collected with collection kits supplied by the manufacturer. Specimens were delivered to the laboratory within three hours. Specimens for QuickVue and SureCell were processed upon arrival to the laboratory. Specimens for culture and PCR were either processed upon arrival to the laboratory or frozen at -70°C until processing.

Test procedures: Specimens for culture of *C. trachomatis* were agitated with glass beads and 0.6 ml of the buffer was added to two tubes with a monolayer of McCoy cells. The cells were centrifuged for one hour at 5000 g at 35°C. The supernatant was aspirated and replaced with maintenance media containing cycloheximide. The tubes were incubated at 35°C for 48–72 hours and the slide from one of the tubes was examined stained with Fluorescent Antibody (Syva MicroTrak FA). If the slide was conclusively positive or negative the slide from the second tube was stained with iodine. If the examination of the first tube was inconclusive the second was subcultured and the procedure repeated. The number of inclusions was recorded. The QuickVue and the SureCell tests were performed according to the manufacturer's recommendations in the package inserts.

The Amplicor® assay was performed on a Perkin Elmer thermocycler. The test was performed according to manufacturer's instructions. Discrepant results were resolved at the Indiana School of Medicine, Infectious Disease Laboratory, by doing Amplicor® PCR and DFA (Syva MicroTrak) on the leftover culture transport medium. A patient was considered infected if culture was positive or if the rapid tests and a confirmatory test were positive.

Results

Results from 240 high risk female patients were evaluated in the study. The patients were 13 to 54 years of age with the median age of 20 (figure). The infected patients were 15 to 31
years of age with the median age of 19. Ninety-eight patients had symptoms and 142 were asymptomatic. Of those 240 patients, 45 were considered to be infected, giving a prevalence of 18.8% in this population. The performance of the two different tests is shown in table I. The sensitivity, specificity, predictive value of a positive (PVP) and the predictive value of a negative (PVN) for the different assays is shown in table II. The calculation was not performed for PCR because of the bias caused by the specimen collection sequence. In the two instances where culture was false negative the three other tests and the confirmatory tests were in agreement. The majority of the culture positive patients had high inclusion counts. Only four had five or fewer inclusions per cover slip. The two false negative QuickVue tests were among those four as was one of the false negative SureCell tests. The other false negative SureCell test had a high inclusion count but the specimen was collected last in the collection sequence.

**Discussion**

Many new diagnostic tests have come available for the diagnosis of *Chlamydia trachomatis* infections in recent years. None of them are perfect nor are any of them ideal for use in all situations. The traditional gold standard, cell culture, is time consuming and expensive and although it is highly specific it lacks in sensitivity (11). Also, the specimens used for cell culture need to be transported rapidly to the laboratory and under controlled conditions (12). The antigen detection tests, which are in most widespread use at present, give more rapid results and are the least expensive methods for diagnosing these infections. Many of the antigen detection tests are intended for use in clinical laboratories but some, such as the two evaluated here, are intended for use in physicians offices. The antigen detection methods have traditionally been less sensitive than cell culture for the detection of these infections (8). The sensitivity is though, heavily dependent on the types of patients studied, the lack of sensitivity being most pronounced in asymptomatic males (4,8). All diagnostic tests perform best, in terms of sensitivity and predictive value of a positive, in populations as the one studied in this evaluation, young high risk females. The two tests, QuickVue and the SureCell performed extremely well compared to culture in this study and the latter better than previously reported (10). The reason is without doubt the quality of the specimen and the rapid delivery to the laboratory. The amount of antigen in an infected cervical canal is related to age, decreasing with increased age of the patient. Our patients were mostly young high risk females with high inclusion counts on culture.

The new DNA amplification methods like PCR and LCR have been shown to be more sensitive than culture (11–16) and the inferior performance of PCR in this study is undoubtedly caused by bias in the specimen collection sequence, the specimen for this test always being collected last.

In conclusion it can be said that both of the
antigen detection tests studied are likely to perform quite adequately when used on the appropriate patients, and when full advantage can be taken of the rapidity with which the results can be achieved, such as in physicians offices. The QuickVue test has the added advantage over the SureCell test of being simpler to perform.

REFERENCES