Comparison of Murex Single-Use Diagnostic System with Traditional Enzyme Immunoassay for Detection of Exposure to Human Immunodeficiency Virus

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Because a retrospective study detected 13 negative Western blots out of 38 single-use diagnostic system (SUDS)-positive cases over a 1-year period, we performed a prospective study to compare the performance of the SUDS test with that of enzyme immunoassay (EIA). Of 888 SUDS-tested sera, 875 (98.4%) were both SUDS and EIA negative and 5 (0.6%) were SUDS positive, and Western blot positive. The rate of SUDS-positive samples decreased from 3.16/month in the retrospective study to 1.33/month in the prospective study. The immunoassays had sensitivities and specificities of 100 and 99.7 (SUDS) and 100 and 99.4% (traditional EIA), respectively. In laboratories with experienced personnel, the SUDS test performs as well as the EIA as a screen for infection with the human immunodeficiency virus.

Occasionally, the human immunodeficiency virus (HIV) status of an individual is needed urgently. For example, a rapid HIV status result may be needed for initiating prophylactic therapy after possible HIV exposure (1), prior to listing patients for organ transplantation (4, 6, and in a public health setting (3). The Food and Drug Administration-approved Murex Single-Use Diagnostic System (SUDS; Abbott Laboratories), a rapid qualitative immunoassay, is in wide use in our region (lower Michigan). The purpose of this two-armed study was to compare the standard enzyme immunoassay (EIA) screen with the SUDS test.

The retrospective study evaluated the Western blot assay results of 38 consecutive SUDS-positive sera received at our reference laboratory (Ann Arbor, Mich.) from January 1998 through February 1999. These samples were received from several Michigan hospital laboratories and represented patients involved in health care worker exposures as well as patients being screened for HIV infection. The last six SUDS-positive cases received were tested further by the third-generation Abbott HIV1/2 EIA.

The prospective study collected 896 SUDS-tested sera referred from seven hospital laboratories from July 1999 through December 1999. Eight of these sera were excluded due to incomplete information; therefore, 888 specimens were entered into the study. Sera from all of these SUDS cases were also tested by traditional third-generation EIA at our reference laboratory. Any SUDS- or EIA-positive cases were confirmed by Western blotting. All laboratories submitting SUDS test results provided the SUDS grade of reactivity in triplicate (from negative to 4+) and information as to why the test was ordered.

In the SUDS test, HIV antigen is a suspension of p24 Gag lysate and a synthetic envelope protein. The test consists of a subjective determination by examining the blue color produced in three circles on the bottom of the test cartridge. A positive test can result in several shades of blue, which are graded from 1+ to 4+. After the initial positive result, the test is repeated in duplicate; if two of the three tests are positive, the final conclusion is that the test is positive. Patient serum is then sent for confirmatory Western blot assay. The SUDS portion of the study was performed in the field. We do not know if the sera were recentrifuged prior to testing. The Abbott third-generation EIA and the Organon Teknika Western blot assay were performed in our laboratory according to the instructions in the product inserts. Positive samples were defined according to Centers for Disease Control and Prevention criteria; at least two of the following bands were present: gp160/120, gp41, and p24. The presence of any pattern lacking two of these three HIV-associated bands was read as indeterminate (any nonspecific band qualifies as indeterminate). When no bands were present, the sample was read as negative.

The retrospective study showed that 17 (44.7%) of 38 SUDS HIV-positive cases were confirmed by Western blotting, 8 (21.1%) were indeterminate, and 13 (34.2%) were Western blot negative. The last six SUDS-positive cases submitted were tested by EIA. Three were both Western blot and EIA positive. However, three were Western blot negative (false positives) and nonreactive by EIA.

The prospective study compared the results for 888 specimens assayed by SUDS tests done in the field with the results of the traditional EIA. Of these, 394 (44.4%) were ordered due to employee exposure to patient fluids, 479 (53.9%) were ordered to screen patients for HIV infection, 4 (0.5%) were part of prenatal work-ups, 3 (0.3%) were ordered as part of an employee physical, and 8 (0.9%) had no reason listed. Of the 888 specimens, 875 (98.5%) were both SUDS and EIA negative. There were five (0.6%) SUDS-, EIA-, and Western blot-positive cases (true HIV-positive cases) and three (0.3%) SUDS-false-positive cases that were both EIA and Western blot negative (Table 1). Two of these three SUDS-false-posi-
tive cases were initially graded 1+, 1+, 1+, and 2+, 1+, 1+, while the third case was graded 3+, 3+, 3+. There were also three (0.3%) EIA-negative samples that were SUDS negative and Western blot negative. In two of the EIA false-positive cases, the test signal was just above the cutoff, while the third case produced signals between 1.447 and 1.872 with a cutoff of 0.113. The last case also tested negative by a separate anti-HIV type 2 EIA. An additional two (0.2%) EIA-positive cases were SUDS negative and Western blot indeterminate (Table 1). Finally, 5 of 8 (62.5%) SUDS-positive cases and 5 of 10 (50.0%) EIA-positive cases were confirmed by Western blotting.

The retrospective study suggested to us that the SUDS test could produce a moderate number of false-positive results (34.2%). Furthermore, since most indeterminate Western blot assay results do not represent HIV infection, the SUDS false-positive rate might approach 55% (2). This retrospective study had several limitations: only SUDS-positive cases were studied, no information about SUDS reactivity was provided, not all sites were strictly adhering to the SUDS insert procedure, and EIA comparison was only performed on the last six SUDS-positive cases.

In our prospective comparison, the two immunoassays performed similarly. The vast majority (98.5%) of sera submitted for testing were both SUDS and traditional EIA negative. There was complete agreement between the two immunoassays in detection of the five (0.6%) true HIV-positive cases. Both SUDS and EIA produced three false-positive results (0.3%). In two cases (0.2%), the traditional EIA was positive while the SUDS test was negative and the Western blot assay was indeterminate. Lacking follow-up information, we cannot say with absolute certainty whether these two cases represented additional traditional EIA false-positive cases or SUDS false-negative cases. However, these two cases most likely represent traditional EIA false positives. Based on this assumption, the sensitivities and specificities of the tests are 100 and 99.7 (SUDS) and 100 and 99.4% (traditional EIA), respectively. Schwartz et al. reported sensitivity and specificity rates similar to ours (7). In another paper, Phillips et al. evaluated the performance of a number of rapid tests in detection of HIV infection (5). They reported a SUDS sensitivity of 100% and a specificity of 93.2% (5 false-positive cases out of 69 known seronegative specimens). The lack of SUDS false negatives in all three studies indicates that the test performs well as an HIV screen in various clinical settings, but specific confirmatory tests are necessary to establish HIV status.

Our retrospective study found SUDS false-positive results in 34.2 to 55.3% of cases (the latter, if Western blot-indeterminate cases were assumed to be HIV negative). In the prospective study, the corresponding SUDS test and traditional EIA false-positive rates were 37.5 and 37.5 to 50.0% (the latter, if Western blot-indeterminate cases were assumed to be HIV negative). Chi-squared analysis of the two study periods’ SUDS false-positive rates did not show statistical significance ($P = 0.36$; SAS program, SAS Institute, Cary, N.C.). The positive predictive value of the SUDS test calculated from the prospective data is 62.5%. Therefore, in our Midwestern American population that is screened by the SUDS method, a SUDS-positive result indicates infection with HIV only approximately 60% of the time. This positive predictive value reflects the relatively low prevalence of HIV in our region. Indeed, of the 394 SUDS tests ordered because of employee exposure, only 2 (0.5%) were HIV positive.

Between the two study periods, there was a decrease in the number of SUDS-positive cases from 3.16/month in the retrospective study to 1.33/month in the prospective study. We speculate that the decrease could be due to fewer false-positive SUDS test results because of several differences between the two studies. First, during the retrospective study, not all laboratories had been performing repeat SUDS assays on initial positive samples. Second, in the retrospective study, all laboratories were required to provide data on the grade of test reactivity. Third, as technologists gain experience in the performance and interpretation of the subjective SUDS test, false-positive results may decrease. All of the laboratories had been using the test between 6 months and 1 year during the retrospective study and between 18 months and 2 years during the prospective arm of the study. This “hands-on” time is especially important in the distinction of weak positive results (1+ and 2+) from negative results. Indeed, two of the three SUDS-false-positive cases in the prospective study involved such weak results. Other technical variables, such as particulate matter in the serum and overincubation, can also cause false-positive results.

The SUDS test offers on-site availability, apparent simplicity, and rapid turnaround time (30 to 60 min) compared to the EIA. However, the validity of the test results depends on the technical experience of the individual performing the test and subjective interpretation of the colorimetric end point. In conclusion, the SUDS test performs as well as the traditional EIA as a screen for HIV infection in laboratories with experienced personnel. A confirmatory test, such as the Western blot assay, must be done on all serologically HIV-positive cases before a final decision regarding disease status is made.

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