A New Century Approach for Alcohol Screen in the Insurance Industry

Pamela Bean, PhD, MBA; Elwood Kleaver, MCS; Bill Roberts, PhD; James Harasymiw, PsyD

Several recent studies point to the value of using combinations of biochemical markers for the identification of alcohol abuse. The Early Detection of Alcohol Consumption (EDAC) test uses a statistical method that combines the results of several routine laboratory tests to form a metabolic fingerprint for each subject. In this study, we evaluated the use of the EDAC test as a screening tool to assess heavy drinking in insurance applicants. The EDAC was calculated by linear discriminate function analysis using the results of 14 routine tests including liver enzymes, lipids, proteins, and blood sugars. We collected and analyzed 1680 random samples at Heritage Laboratories (Olathe, Kan). Alcohol Detection Services (Brookfield, Wis) and Millennium Strategies (Madison, Wis) collaborated in the data analysis and interpretation of laboratory tests results. Ninety-three percent of applicants showed a negative EDAC test. The 7% (n = 134) who screened positive for the EDAC test were then reflexed to carbohydrate deficient transferin (CDT) and whole blood associated acetaldehyde (WBAA). Sixteen percent (22/134) showed a positive confirmatory test. Among these 16% of subjects, 41% (9/22) showed no elevations in liver enzymes or HDL-C results. Four of these subjects were among the top one third with the highest elevations for the CDT test in the entire group and one of them was positive for both the CDT and WBAA tests. These results suggest that the EDAC screen may provide an efficient alternative screening tool for the identification of heavy alcohol consumption not HBA as it identifies applicants with both normal or abnormal liver enzymes and HDL-C.

Heavy alcohol consumption is a risk factor for increased morbidity and mortality. The life insurance industry, in an attempt to reduce losses related to heavy alcohol consumption, has for some years been testing applicants for heavy drinking. Insurance providers design their own algorithms of laboratory tests and health parameters for identification of alcohol abuse in the applicant populations. The traditional algorithm of laboratory tests consists of finding elevations of the liver enzymes AST, ALT and GGT or abnormal HDL-cholesterol, and positive urine codeine test. Applicants with abnormalities in any of these laboratory tests may undergo confirmatory reflex testing using carbohydrate deficient transferin (CDT), whole blood associated acetaldehyde (WBAA) or both.
Performance, assay and labor costs have limited the use of the CDT and WBAA tests as screening tools; however, they have been used widely since the early 1980s as reflex or confirmatory tests in the US.\(^2\)

CDT and WBAA are highly specific tests.\(^3\)

CDT is produced in the liver in subjects who drink the equivalent of 5 beers per day for 7–10 consecutive days.\(^4\)

However, volunteers who are exposed to a single episode of heavy drinking (80 grams of alcohol daily) for 2–3 weeks do not present CDT elevations, suggesting that CDT is a marker of chronic rather than acute drinking.\(^5\)

In contrast, blood acetaldehyde is a marker of both.\(^6\)

Indeed, WBAA is a marker of acute drinking because it is produced shortly after alcohol consumption and becomes elevated in conjunction with blood alcohol concentrations. WBAA is also a marker of chronic drinking because it accumulates in the circulation over time similar to the accumulation of glycated hemoglobin in diabetes. Since most of the acetaldehyde present in the blood is bound to hemoglobin, the WBAA test is also known as the hemoglobin associated acetaldehyde (HAA) test.\(^2\)

Several recent studies point to the value of using combinations of biochemical markers for the identification of alcohol abuse. A re-emerging approach is the “Early Detection of Alcohol Consumption” (EDAC) test, which uses a statistical method that combines the results of several routine laboratory tests to form a metabolic fingerprint for each subject.\(^7,8\)

This fingerprint is then compared to “model” fingerprints obtained from a database of subjects with a variety of known drinking patterns. The EDAC score computes the results of up to 36 routine laboratory tests. Smaller panels of 12, 14, or 25 constituents are effective as well.\(^9,10\)

The EDAC test was developed by Alcohol Detection Services, LLC (ADS, Brookfield, Wis) and patented by Jim Harasymiw in 1992. Today, the ADS database contains demographic information and drinking behavior for almost 1800 individuals recruited from multiple sites in different geographic areas in the US.

### STUDY OBJECTIVES

The main purpose of this study was to evaluate the use of the EDAC test as a screening tool to assess heavy drinking in insurance applicants.

### STUDY DESIGN

We analyzed 1680 samples randomly selected from the pool of specimens obtained daily at Heritage Laboratories (Olathe, Kan). From the original 1680 samples, 20 samples were removed because they did not contain the gender information for the applicants, and an additional 16 were removed because the age of the applicants was not disclosed.

Heritage's staff collected all the specimens and performed the laboratory testing according to their established insurance industry protocols with two exceptions. First, Heritage sent the results of the routine laboratory panel to ADS for calculation of the EDAC test. Second, Heritage Laboratories performed CDT and WBAA test in those applicants with a positive EDAC test and provided the results.
Table 1. Laboratory results for EDAC+ confirmed with CDT/HAA

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<th>Subject #</th>
<th>Sex</th>
<th>Age</th>
<th>ALT &gt;5 U/L</th>
<th>AST &gt;40 U/L</th>
<th>GGT &gt;65 U/L</th>
<th>HDL &gt;75 U/L</th>
<th>CDT &lt;6%</th>
<th>WBAA &lt;15.0 μM</th>
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to ADS. ADS in conjunction with Millennium Strategies (Madison, WI) collaborated in the data analysis and interpretation of laboratory tests results.

**STUDY METHODS**

The population analyzed consisted of 1644 subjects including 944 men and 700 women. Average age was 42.1 ± 11.5 years for the males and 40.4 ± 12.0 years for the females.

The EDAC test utilized Heritage's standard routine insurance profile of 15 markers: albumin, globulin, albumin/globulin ratio, alkaline phosphatase, ALT, AST, GGT, blood urea nitrogen, cholesterol, HDL-cholesterol, triglycerides, total bilirubin, total protein, creatinine, and glucose.

For liver enzymes and HDL-C we used the thresholds described in Table 1. Since women (particularly premenopausal women) have considerably higher HDL-C levels than men, we analyzed the correlation between HDL-C and alcohol markers using different HDL-C cutoffs for males (>70 mg/dL) and females (>75 mg/dL).

CDT was performed in serum using the %CDT TIA, a commercial kit HDL-C (from Biorad Laboratories, Hercules, CA). The %CDT TIA procedure had two steps: normal transferrin is separated from CDT on a charged matrix (anion exchange chromatography). Next, CDT was detected and quantified using a turbidimetric immunoassay called nephelometry. The reference range used for CDT was <6%.

The HAA assay was performed on a specimen of EDTA preserved whole blood and used a high performance liquid chromatography (HPLC) method previously published and licensed exclusively by Primus Corporation (Kansas City, MO). The procedure had three steps: release of hemoglobin bound acetaldehyde by heat, formation of a fluorescent compound with the released and free acetaldehyde present in the blood sample, and separation and quantification of all the pertinent
acetaldehyde peaks by HPLC. The reference range used for HAA was <15.0 μmol/L.

RESULTS

The testing algorithm used in this study is shown in the figure. The first step was to test all applicants by the EDAC test; the results show 92.8% (1510/1644) with a negative EDAC test and 8.2% (134/1644) with a positive EDAC test. No further testing was done in those 1510 applicants with a negative EDAC test.

The 134 applicants who screened positive for the EDAC test were submitted to reflex testing by CDT and HAA. Average age for the group was 46.9 ± 14.9 years. Overall, the results showed 16.4% (22/134) of subjects with a positive confirmatory test. Of these, 17 tested positive for CDT only, 2 subjects (#21 and 22) tested positive for HAA only and 3 subjects (#5, 6, and 14) tested positive for both tests (Table 1). The CDT+ applicants showed values ranging from 6.3 to 16.4% and the HAA+ applicants showed values ranging from 17.9 to 45 μmol/L. The only female in this group showed a mildly elevated CDT test (6.4%) and a negative HAA test (8.3 μmol/L).

Next, we analyzed the test results of liver enzymes and HDL-C for those who tested positive for both EDAC and either or both confirmatory tests. Six of these 22 individuals (#3, 8, 10, 12, 14, and 20) had abnormal elevations in a single test result and 7 subjects (#4, 6, 9, 11, 17, 18, and 21) showed abnormal elevations in at least two laboratory tests. Interestingly, the data show that 9 subjects (#1, 2, 5, 7, 13, 15, 16, 19, and 22) with positive confirmatory tests after positive EDACs had no elevations in liver enzymes or HDL-C results. Even more, 4 of these subjects (#1, 2, 5, and 7) were among the top one third with the highest elevations for the CDT test in the entire group and one of them (subject #5) was positive for both the CDT and HAA tests.

The EDAC test was able to identify 41% (9/22) of applicants who would have been missed by the traditional insurance screen.

In order to determine what was causing the elevations in the EDAC test and the confirmatory tests of these 9 subjects with normal liver enzymes and HDL-C, we analyzed the test results in the rest of the components of the EDAC panel (Table 2). The analysis shows that these subjects are identified by the EDAC test because the EDAC test weights the contribution of several routine chemistry analyses avoiding the selection bias that occurs when screening is based solely on a single abnormal test.

DISCUSSION

In this study, we describe the results of an alternative approach to screen for heavy drinking using the EDAC test. EDAC alike tests have been used successfully for many years.8,13,14 Indeed, most of the EDAC-alike tests developed during the early 1980s using quadratic discriminant analysis concluded that routine laboratory tests provided important prognostic information and should be an integral part of the assessment of individuals with hazardous alcohol consumption.14 However, cumbersome hole-punching computer systems limited further developments in this area until user-friendly statistical packages became available in the 1990s. Today, the EDAC test is used to assess heavy alcohol consumption and monitor compliance in individuals attending selected primary care settings in the midwest.9 It is also an integral part of a study on relapse prevention being conducted at Rogers Memorial Hospital (Oconomowoc, WI) and funded by the National Institute on Alcohol Abuse and Alcoholism in the U.S. (Grant # 1R43AA12366).

The results of this study show that the traditional algorithms used by the insurance industry to screen applicants for heavy drinking may be missing many subjects with positive CDT and/or HAA results. The EDAC identified the two applicants with the highest CDT results in this group and another one with abnormal CDT and abnormal HAA results but normal liver enzyme tests.

In the absence of alcohol consumption
data, the question still remains. Is the EDAC specific? In other words, how do we know if the EDAC+/CDT+/HAA+ applicants with normal liver enzyme tests represent "true" heavy drinkers or whether the test results represent merely false-positives? To answer this question, the reader is referred to examine many recent scientific reports describing all three biochemical markers as highly specific tests. Indeed, the insurance industry in the US has relied on the use of these tests since the early 1990s with successful results.

The diagnostic performance of the EDAC was evaluated in studies with well-characterized alcohol abusers and light drinker controls to show sensitivity values ranging from 80 to 87% at >90% specificity rate. Best performance for the EDAC was obtained when heavy drinking was identified in the over 40 year olds (84% sensitivity at 97% specificity). Performance in females showed 73% sensitivity at 94% specificity, rates higher than the ones obtained with any single biochemical marker previously examined. ROC plot analysis showed areas under the curve of 0.94 for females and 0.95 for males (P < .0001).

The EDAC has also been studied for identification of at-risk drinking in young adults. The alcohol consumption data of EDAC positive males showed they were drinking an average of 3.6 drinks per day and drank an average of 6.6 drinks on a typical drinking day for the 42 days before blood sampling. EDAC positive females showed average daily alcohol consumption of 1.5 drinks per day and drank an average of 3.7 drinks per typical drinking day in the same time period. Thus, in this separate validation sample attending a primary medical care setting at the University of Missouri, the EDAC test showed better sensitivity and same specificity than most biochemical markers in young adults. Results were especially encouraging in females.

A third study used the EDAC combined with CDT in heavy drinking males. The EDAC alone showed 88% (122/138) sensitivity rate when identifying heavy drinking males and 98% (48/49) specificity rate when
assessing light drinkers. The CDT test alone showed a sensitivity rate of 58% (80/138) and a corresponding specificity rate of 96% (47/49). When analyzed simultaneously, 92% (127/138) of heavy drinkers showed abnormal EDAC and/or CDT tests and 94% (46/49) of light drinkers were negative for both tests. When analyzed sequentially, the CDT test confirmed 61% (75/122) of the heavy drinkers identified by the EDAC test. The specificity rate for this testing strategy was 100% because the only false positive for EDAC tested negative for CDT. This preliminary study shows that EDAC and CDT may react independently to alcohol intake and they can be combined for maximum diagnostic accuracy.

In summary, these results suggest that the EDAC screen may provide an improved screening tool for the identification of heavy alcohol consumption in the insurance population as it identifies applicants who are missed by the liver enzyme tests.

REFERENCES