Biomarkers for Underreported Alcohol Use

A significant clinical challenge in the field of Addiction Medicine is the underreporting or denial of alcohol use. This can be a particularly dangerous situation when an unexpected withdrawal occurs in the course of routine primary care treatment for other conditions or when the person in denial becomes confined (i.e., hospital, jail, etc.).

A frequent psychological feature in the addicted population is denial, where the level and degree of addiction behavior is minimized or lied about by the patient. This puts the treatment personnel in the difficult position of trying to second-guess the drug/alcohol status of their patient (sober/binging/using) while offering caring treatment.\(^1\)

We now have a number of biological markers that are useful for detecting recent heavy alcohol use and alcohol relapse before the patient is ready to admit to it. Combinations of two or more markers are more sensitive and accurate; also, the addition of one of the self-reports such as the CAGE or AUDIT increases the accuracy further.

The commonly used biochemical markers are the following blood tests:

1. BAL (blood alcohol level): The liver eliminates alcohol from the body at a fixed rate of approximately a half drink every four hours. If the patient abstains from drinking alcohol for 24 hours prior to the blood test, it will likely produce a false negative.

2. MCV (mean corpuscular volume) measures the average volume of the red blood cells (RBC) in a blood sample. The RBC’s become abnormally larger with excessive alcohol consumption. The RBC morphologic changes become evident after six weeks of alcohol misuse and last up to three months after drinking has stopped. Elevated MCV may be caused by other conditions than alcoholism; therefore it is not a reliable indicator of relapse, even though elevated MCV should raise your clinical awareness of the possibility of alcoholism.

3. LFT\(^2\): Liver function test measures enzymes and proteins in the blood produced in the liver. Since the liver is responsible for metabolizing alcohol, one of the key places in the body to show damage from excessive alcohol misuse is the liver. The most important proteins are ALT (Alanine aminotransferase), AST (aspartate aminotransferase) and GGT (gamma-glutamyl transferase). When the ratio of AST:ALT is greater then 2:1, the index

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of suspicion for alcoholism is raised. If the ratio is 3:1, the likelihood of alcoholic liver
disease is greater than 96%. GGT levels greater than 30 U/L tend to occur when the
patient consumes more than 4 drinks per day. GGT tends to remain elevated 4-6 weeks
after a binge and has a half-life of 14-16 days. GGT is a useful indicator for monitoring
abstinence. Like the MCV, other medical conditions may elevate the GGT. However,
elevated GGT occurs with alcoholism 50-72% of the time. CDT (carbohydrate deficient
transferrin) is the newest biomarker but also very expensive; therefore it is not
universally available in all clinical settings. In alcoholics who consume more than 4-5
drinks per day, the CDT rises to more than 1.3% of the total transferrin.

Blood test normal range:
  GGT: males: 0-53 U/L; females: 0-45 U/L
  AST: 10-34 U/L
  ALT: 8-37 U/L
  CDT: <60 mg/L
  MCV: 80-100 fl

Time to elevation:
  GGT: 24 hours to 2 weeks
  AST: 3-7 days
  ALT: 3-7 days
  CDT: 2-3 weeks
  MCV: 3 months

Time to return to normal levels:
  GGT: 2-6 weeks
  AST: half-life of 12-24 hours
  ALT: half-life of 37-57 hours
  CDT: 2 to 4 weeks
  MCV: 3 months

It is important to keep in mind that each biomarker has strengths and weaknesses in the
clinical setting. When these tests are used in combination along with the AUDIT questionnaire,
the predictive value increases markedly.

What you want in testing⁴ is a high degree of confidence in the predictive value for true
positives (namely alcohol misuse or that alcoholism is the cause) or true negatives (namely, the
cause is clearly other than alcoholism); also high sensitivity so that the test rules out alcohol liver
disease; and high specificity, so that to a high level of confidence, the diagnosis points to
alcoholism rather than some other medical condition.

Combination of the AUDIT with more than two abnormal biochemical markers brought
sensitivity to 94% and specificity to 98%. Some research studies have found 95% sensitivity
with the combined abnormal results for GGT plus MCV or GGT plus CDT; and 100% sensitivity
with the combination of GGT plus AST: ALT greater than 2:1.

Individually, each test has serious limitations: the AST:ALT ratio greater than 2:1 has a
sensitivity of only 70% but a specificity of alcoholic-induced liver disease of 92-100%. While
the negative predictive value (NPV) of the GGT (the patient does not have alcoholic liver

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disease) is 69-92%, the positive predictive value (PPV) is only 41%. The NPV for the MCV is 67% while the PPV is only 36%.

Relapse sensitivity of the AST:ALT ratio greater than 2:1 has 92-100% specificity for alcoholic liver damage while GGT is at 50% and MCV is only at 20%.

Summary:

Combinations of a questionnaire such as the AUDIT plus at least two laboratory markers give us the highest level of confidence for the diagnosis of alcohol-induced liver disease or relapse to further drinking, especially when the patient is in denial about heavy drinking. However, a comprehensive treatment plan and close follow-up are still most important ingredients for successful treatment of the addicted population.

References: