18

Biological Markers of Alcoholism

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18.1. Utility of a Biological Marker of Alcoholism

18.1.1. Practical Application of a Marker of Alcoholism

A biological marker of ethanol consumption would be a valuable tool in the diagnosis and treatment of alcoholism. There are several areas of potential clinical application. First, a biological marker would be useful for the early detection of alcoholism, as many patients do not seek medical attention at an early stage (Clark, 1981). Previous studies have demonstrated the medical and social advantages of early intervention in the treatment of alcoholism (Reiff, 1985; Paredes, 1985). In addition, a biological marker would improve the monitoring of sobriety in alcoholics undergoing treatment. Furthermore, many patients who are suffering from a disease in which alcoholism is the suspected etiological agent (e.g., chronic pancreatitis, cirrhosis) fail to give an accurate history of their alcohol consumption. These patients are then subjected to an exhaustive diagnostic workup to rule out other etiological factors. A reliable biological marker of alcoholism would expedite the diagnostic workup and perhaps avoid invasive procedures (e.g., endoscopic retrograde pancreatography, liver biopsy). Finally, selected patients with alcohol-induced liver disease may become candidates for liver transplantation if there is a proven record of abstinence (Maddrey and Van Thiel, 1988); a reliable biological marker would provide objective verification of abstinence and thus improve the selection process.

A biological marker of alcoholism would also be valuable in clinical research. Currently, clinical trials evaluating the efficacy of various treatment modalities of alcoholism usually rely on the patient's self-report of alcohol consumption as the therapeutic endpoint. Because the patient's self-report may not always be reliable (Sobell et al., 1979; Orrego et al., 1979; Watson et al., 1984; Peachey and Kapur, 1986; Fuller et al., 1988), a biological marker of alcohol consumption may provide a more objective assessment of abstinence. In addition, a reliable biological marker would be a valuable tool for epidemiologic studies investigating the incidences of alcoholism in different communities.

A marker of alcohol consumption would have useful forensic applications. Individuals arrested for driving while intoxicated could be screened for chronic alcohol consumption and then referred to an appropriate treatment program (Luchi et al., 1978; Gjerde and Morland, 1987). In addition, workers involved in areas of public safety could be effectively monitored for alcohol abuse.

18.1.2. Limitations of Patient History and Screening Instruments

Although chronic ethanol consumption produces diverse biochemical and physiological changes, a reliable and simple marker is still not available. Presently, the diagnosis of alcoholism by physicians is primarily based on a patient's history. However, because denial may play an important role in alcoholism, patients may be reluctant to seek medical care (Moore and Murphy, 1961; Clark, 1981; Spickard, 1986). In a prospective
study of patients admitted to the medical and orthopedic services of a community hospital, only 29% of patients with a history of alcohol dependence or alcohol abuse considered themselves to be alcoholic (Bush et al., 1987). Even when the alcoholic patient comes to medical attention, the diagnosis of alcoholism is frequently overlooked in a variety of clinical settings (Barrison et al., 1980). Thus, physicians were only able to identify correctly 25% of alcoholics attending a general medical clinic (Persson and Magnusson, 1988).

Even when the alcoholic patient is identified and referred for treatment, the long-term monitoring of sobriety is suboptimal. Physicians mainly rely on a patient's self-report of alcohol consumption for identifying relapse. However, various studies have demonstrated the lack of reliability of a patient's self-report of alcohol consumption. In clinical studies in which alcohol consumption was monitored by both patients' self-report and daily urine specimens for ethanol (Orrego et al., 1979; Peachey and Kapur, 1986), more than half of the alcoholic patients who drank while undergoing therapy denied any alcohol use. In the Veterans Administration Cooperative Study, which evaluated the efficacy of disulfiram (Fuller et al., 1988), drinking behavior was assessed using patients' self-report, collateral history, and serial urine or blood tests for ethanol. Approximately 35% of patients who claimed to be abstinent were indeed drinking during the study period, as confirmed by collateral history or laboratory tests. Furthermore, the number of drinking days was underestimated by at least 28% when compared to collateral history. Thus, a patient's self-report is insensitive in the detection of relapse and will underestimate the patient's alcohol consumption.

Since the previous studies used blood or urine ethanol determination as a gold standard, the drinking behavior may be further underestimated. Because the rate of ethanol metabolism is about 10 g/hr (Rowland and Tozer, 1989), blood or urine ethanol testing will only identify recent intake. Furthermore, blood ethanol determination cannot discriminate between sporadic drinking and excessive alcohol consumption.

A number of questionnaires have been developed in order to improve the detection of alcoholism. Most of the questions inquire about the social consequences related to drinking behavior rather than directly asking the patient to quantify his alcohol consumption. One of the most investigated questionnaires is the 25-item Michigan Alcoholism Screening Test (MAST), dealing with social, legal, and medical effects of alcoholism (Selzer, 1971). The MAST has been demonstrated to have clinical value (Moore, 1971, 1972), but its format and length have limited its application. Various modifications of the original MAST have included the ten-item brief MAST (Pokorny et al., 1972), the 35-item Self-Administered Alcohol Screening Test (SAAST) (Swenson and Morse, 1975), and the nine-item SAAST (Davis et al., 1987). These modifications have generally improved the simplicity of administration without sacrificing diagnostic accuracy (Kristenson et al., 1983; Davis et al., 1987). Two other screening items, the four-item CAGE (Mayfield et al., 1974) and the five-item Skinner Trauma Questionnaire (Skinner et al., 1984), are easy to administer and have greater sensitivity and specificity than standard laboratory markers of alcoholism (Kristenson and Trell, 1982; Bernadt et al., 1982; Skinner et al., 1984), but, nevertheless, they have several limitations. First, these tests are dependent on patient cooperation and veracity. In addition, their accuracy may be affected by socioeconomic and cultural factors (Walters et al., 1983; Monteiro et al., 1986; Bilal et al., 1987). Finally, the utility of these questionnaires in monitoring alcoholic patients undergoing treatment has not been validated.

18.1.3. Clinical Utility of Laboratory Tests

When clinical evaluation results in a diagnostic uncertainty, physicians may turn to laboratory tests for further assistance. The principles for evaluating diagnostic tests have been discussed in several review articles (McNeil et al., 1975; Gottfried and Wagar, 1983; Sox, 1986). These principles are summarized below to serve as a basis for evaluating the utility of laboratory markers of alcohol consumption.

The usefulness of a diagnostic test lies in its ability to discriminate accurately between patients with a disease and patients without a disease. The diagnostic characteristics used to assess the discriminating ability of a laboratory test include sensitivity and specificity. Sensitivity is the proportion of patients with a disease who have a positive (i.e., abnormal) test. Specificity is the proportion of patients without the disease who have a negative (i.e., normal) test. Both the sensitivity and specificity will vary with the cutoff point used to define a positive test (McNeil et al., 1975). In addition, sensitivity is dependent on the population being studied. Several laboratory markers of alcoholism are only abnormal in patients at advanced stages of their disease. Because many of these markers may be less sensitive in detecting alcoholics at an early stage, the sensitivity of these markers determined in hospitalized alcoholics