Henry Ford Hospital Medical Journal

Volume 3 | Number 4 Article 7

12-1955

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PRELIMINARY EXPERIENCE WITH THE GLUTAMIC OXALOACETIC TRANSAMINASE DETERMINATION IN ACUTE MYOCARDIAL INFARCTION IN HUMANS

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Transaminase is an enzyme which catalyzes the tranfer of the amino group of a dicarboxylic amino acid to a keto acid to form a second amino acid and a second keto acid, thereby accomplishing the process of transamination. This reaction was first described by Braunstein and Kritzman in 1938. Since that time investigators have simplified the original and rather complex methods of assaying transaminase activity, and have established the presence of this activity in various tissues of the human body[1,2,3,4,5]. Glutamic-oxaloacetic transaminase, one of several different such enzymes, has been established as one of the most widely distributed, being found in decreasing concentration in the myocardium, liver, skeletal muscle and kidney. The advent of a reasonably practical method for assay of transaminase activity in human serum allows a more widespread utilization of this test as a clinical tool.

Use of this determination has recently been instituted here on a limited scale. This is a review of those reports appearing in current literature and leading to or supporting our decision to investigate the procedure, and a report of our preliminary findings. Assays were made on the serum of patients admitted for definite or suspected myocardial infarction either transmural or non-transmural. Two serial assays, 24 hours apart, were made. No attempt was made to follow the evolution of the reaction until increased activity returned to a normal level, except in two cases. Patients suspected of having co-existing destructive disease of the liver, skeletal muscle and/or kidney, conditions which may give rise to positive assays, were eliminated.

LaDue, Wroblewski and Karmen[5,6] have reported the only work done in humans in which a series of patients with myocardial infarction are included. After measuring transaminase activity in 50 normal individuals these investigators reported a normal range of 10 to 40 units. Activity in sera of 30 patients having incurred transmural infarctions yielded values of 100 to 6000 units on at least one occasion during the first five days following onset of the infarct. The sera of only 2 patients, of a total of 22 patients studied, with arteriosclerotic heart disease uncomplicated by myocardial infarction exhibited elevated levels of activity. This elevation was minimal. Increased activity could be obtained from sera of patients with destructive inflammatory lesions of the liver and kidney or lesions allowing tissue destruction due to sudden circulatory derangement in these organs. However, these yields were substantially below levels obtained in sera of patients with myocardial infarction.

To substantiate these findings this same group working alone and in conjunction with a second group[7,8] produced experimental infarcts in a total of 21 dogs. In 12

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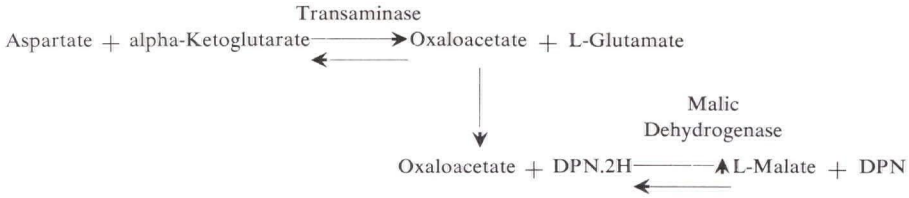
animals plastic microspheres were introduced into the coronary circulation resulting in coronary embolization and myocardial infarction. In the remaining 9, ligatures were placed about the coronary arteries and subsequently these arteries were closed after sufficient time had elapsed for the dogs to recover from effects of the anesthesia and thoracotomy. Since liver damage due to anesthesia or tissue destruction due to surgical procedure caused increased transaminase activity no ligations were done in the latter group until this activity had returned to normal and so remained for several days. In each instance of infarction a prompt and sustained elevation of transaminase activity was found. Following death portions of infarcted and healthy myocardium were removed. After homoginization of these sections transaminase activity was determined in each homoginate. Much less activity was consistently found in homoginates of infarcted myocardium than in homoginates of healthy myocardium.

The spectrophotometric method of Karmen, Wroblewski, and LaDue[6] was used for the assay of transaminase activity. The method has previously proven reliable by comparison of paired sera assay using the quantitative paper chromatographic technique. Assay of activity is predicated upon the measurement of the rate of oxydation of DPN.2H to DPN+ by oxyaloacetate, obtained during the transamination of aspartate and alpha-ketoglutarate (see Figure 1). The rate may be followed at wave length 340 mu in the model DU Beckman spectrophotometer. One unit of glutamic-oxaloacetic transaminase activity represents a decrease in optical density of 0.001/cc of serum/minute when measured at this wave length under specified conditions.

FIGURE 1

Reactions Utilized in the Assay of Glutamic Oxaloacetic Transaminase by the Spectrophotometric Method.



One unit of Glutamic Oxaloacetic Transaminase Activity represents a decrease in optical density of 0.001/cc of serum/minute when measured at wave length 340 mu at room temperature.

TABLE 1

Maximal Glutamic-Oxaloacetic Transaminase Activity in Nine Patients With Proven Myocardial Infarction.

Patient Number	Units of Activity
1	55 F
2	55 F
3	136 R
4	73 F
5	94 F
6	720 R
7	62
8	50 R
9	54 R

Capital letters following units of activity indicate whether this reaction fell below or above the preceding reaction.

Assays on three normal sera here have yielded values of 8 units, 14 units and 38 units. Twelve patients admitted to the cardiology service with proven or suspected infarcts have had serum transaminase assays on a minimum of two specimens. Nine patients had at least one serum yielding elevated activity, more than 40 units, (Table 1) each patient having EKG evidence of acute infarction. Three patients exhibited normal assays. Two of these did not have infarctions and the third incurred the infarction 10 days previous to admission.

One patient with a transmural posterior infarct had serial determination daily for 3 days. The first assay yielded 290 units, the second 580 units and the third 720 units. Death occurred during the night of the 3rd day.

One patient with a non-transmural anteroseptal infarction had serial determinations, done daily on each of 5 days. Units of activity in order were 12, 50, 32, 20 and 28.

It would seem that we may conclude from review of existing reports and our preliminary experience that: (1) the spectrophotometric assay of glutamic-oxaloacetic transaminase is a reasonably practical and reliable laboratory procedure. (2) increased activity may be found in sera of patients having incurred either transmural or non-transmural myocardial infarction. (3) increase in activity may be found within a short time after the occurrence of the infarct and may be sustained for a period of a few days or may return promptly to normal. (4) that cellular destruction in the liver or kidney gives rise to increased transaminase activity. (5) further utilization of the test is warranted.

It would seem reasonable to suspect that the degree of increase of transaminase activity is related to the amount of tissue damaged, but it probably is premature to declare that degree of damage may be estimated from the amount of elevation found.

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