ORIGINAL RESEARCH

LACTATE DEHYDROGENASE AS AN INDICATOR OF LIVER DISEASES

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ABSTRACT:

To determine lactate dehydrogenase (LDH) level as an indicator of liver, muscular or cancer diseases in patients of more than 40 years of age. Hundred and ten patients had been tested for LDH and liver function tests (LFTs). Creatine kinase (CK) levels were measurement only in patients who had high levels of LDH. As an indicator for liver diseases, high levels of LDH, had been observed in many patients. For muscular damage, measurement of CK in patients with elevated levels of LDH. Whereas high LDH levels, as an indicator for cancer diseases, were found in three males and one female who had normal values of LFTs and CK. LDH can be regarded as a good biomarker for diagnosis of liver, muscular and cancer diseases. There is little variable between males and females in the elevated value of LDH. Patients who had high values of LDH and CK are proposed to have unidentified cancer disease.

Keywords: LDH, Liver Diseases, Muscular Diseases, CK

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NTRODUCTION

Lactate dehydrogenase (LDH) found in different types of human tissues is an oxidoreductase enzyme. Although LDH is tetrameric enzyme, only two subunits have been determined: H for heart and M for muscle.¹ The main function of LDH is

converting pyruvic acid, the final product of glycolysis, to lactic acid and vice versa in muscle through production of cellular energy.²However, it is normally located in small amounts in most of active organs. Thus, high level of this enzyme may indicate unusual conditions that can result from liver, muscular disorder (e.g. acute myocardial infarction) and even from cancer disease. Moreover, total LDH level may elevate in blood of patients suffering from various diseases such as allergy, but not in patients with chronic obstructive pulmonary disease.³

Serum lactate dehydrogenase, a ubiquitous cellular enzyme is increased following tissue breakdown.

Consequently elevated serum LDH1 is present in numerous clinical conditions, such as hemolysis, cancer, severe infections and sepsis brain infarcts, meningitis, encephalitis, pulmonary infections and infarcts, liver diseases, pancreatitis, muscle injury and myositis, hematologic malignancies, human immunodeficiency virus infections, and many others. As a diagnostic and prognostic marker, serum LDH has previously been reported mainly as a marker of ominous outcome in cancer patients, including a variety of solid tumors and hematologic malignancies.⁴ In addition, the prognostic value of serum LDH was shown in patients with sepsis. However, despite the ubiquitous presence of elevated serum LDH in numerous disease states, it is not known whether high LDH would be a useful diagnostic and/or prognostic marker in patients admitted to the internal medicine ward.⁵

High level of LDH also described in other types of cancer, such as in 13.5% of non-small cell lung

cancer patients and in children with Hodgkin lymphoma. The measurement of LDH as indicator for liver or muscular disorder or as biomarker for cancer disease in suspected patients was the main aim of this study.

MATERIALS & METHOD

Hundred Ten out and in patients (65 females and 45 males) in Gujarat Adani Institute of Medical Science at Bhuj (India) were involved in our study from January to August 2010. All patients age up to 40 years old. The clinical examination by physician confirmed that all patients showed signs of abnormal liver functions. Thus, liver function tests (LFTs) were suggested for those patients.

Serum of all patients was collected with all due precautions and LDH levels were measured by using liquid UV method that modified based on the recommendations of the Scandinavian Committee on Enzymes. Briefly, 20 µL of each patient serum was mixed first with 1000 µL of buffer (pH 7.35) supplied by the manufacturing company and incubated for 1-5 min at 25 °C. A volume of 250 µL of substrate that composed of nicotinamide-adenine dinucleotide (0.75 mmol/L) and sodium azide in-hospital outcome of admitted medical patients is (0.095%) was added to the mixture. After mixing, the absorbance at 340 nm was read by UV-visible spectrophotometer (CECiL, CE 1021, England) after 1 min. CK levels were assayedaccording to Humazym M-test as described by the instructions of the produced company.

Data of all biochemical tests were expressed as mean \pm SD. The value were analyzed statistically with paired t-test between test value of patient and normal individual. The minimum level of P value was < 0.01 considered as significant level.

RESULTS

The values of LDH in males and females were variable. From 110 patients, 25 females and 20 males showed normal levels of LDH. High LDH level are observed in large number in females (40 patients) than in males (30 patients). Increased LDH levels in blood could not be indicator for liver diseases only, but it may be resulted from damage in muscular tissues. 40 females and 30 males who possessed high level of LDH were investigated for CK, as monitor for muscular injury. Additionally, ten patients (male and female) showed increased levels of LDH and CK in their blood which means they may sever from muscular damage.

None of our patients revealed abnormal levels of LDH that associated with normal level of CK which eliminated the possibility of severing from liver cancer disease. However, three males and one female who had high level of LDH showed normal levels of CK which increase the possibility for those patients to sever from one types of cancers with excluded liver cancer disease.

DISCUSSION

LDH is an enzyme present in all human cells catalyzing the pH dependent interconversion of lactate into pyruvate. Characteristically, human LDH can be separated into five different isoenzymes (LDH1 through LDH5), based on their electrophoretic mobility (Kory and Susan 1993).⁶ Our preliminary observations suggested that a slight to moderate increase in serum LDH in admitted medical patients is very common, but not specific, probably reflecting the ubiquitous distribution of LDH in tissues. In contrast, a very high and isolated serum LDH might be a marker of specific diagnostic groups. Furthermore, whether isolated very high serum LDH would be an independent predictor of largely unknown and should be addressed further.⁷

LDH plays an important role in human body represented by anaerobically converting of pyruvic acid to lactic acid and vice versa. Under normal conditions, LDH produced in human body in little amounts with low monitory value. There are many factors responsible for increasing LDH levels in blood stream that distributed between temporary conditions such as prolonged exercise and some of physiological disorder i.e. severity of preeclampsia, ascites and allergy.⁸

For clinical values, LDH is useful for diagnosis or as an indicator for many diseases in liver and muscles and also for cancers.⁸ The main goal of our study is to determine if the increasing levels of LDH may result from either liver, muscular or cancer diseases in patients of more than 40 years of age. The present of LDH in muscle regarded to play a very important role for muscular tissues through its ability to convert muscular lactic acid into pyruvic acid, an essential step in producing cellular energy.⁹ Moreover, LDH is not restricted in specific type of muscle, it can be found in various types of muscle, especially skeletal and cardiac muscles. These muscles are also known to contain CK rather than LDH which may release in blood with greater levels as result from various muscular diseases such as

skeletal muscle necrosis, andDuchenne muscular dystrophy. Thus, If we need to confirm that high level of LDH is resulted from muscular disorder and not from other things, it's important to measure the CK level. CK is a better indicator of heart or muscular damage. Therefore, estimation of CK along with LDH may serve as suitable diagnostic marker for muscular damage i.e. Rhabdomyolysis, manifestations that associated cardiac with organophosphorus poisoning, acute myocardial infarction and patients with prosthetic heart valves. However, in the present of normal CK levels, it's unlikely that the elevated levels of LDH derive from myocardial necrosis.¹⁰

There are many explanations for increasing LDH level in blood of patients whom suffering from cancer diseases. First, the increase number of cells during cancer development will consume great amount of glucose to get energy by glycolysis which increasing LDH level when the condition is anaerobic.¹¹ Second, growing cancer cells will destroy other tissues and causing release of intracellular enzyme like LDH into the blood stream by the injury or dying cells. Third, increase LDH level by activating its production by tyrosin phosphorylation mechanism in cancer cells.⁴ In D 8. Pandey CK, Nath SS, Tripathi M: Hepatic and Biliary conclusion, LDH can use as a good biomarker for diagnosis of liver, muscular and even cancer diseases. There is little variable between males and females in the elevated values of LDH. Patients with normal values of CK and high level of LDH suggested to have unidentified cancer disease, except liver cancer, and for that other specific tests are required.

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