Lactate Dehydrogenase: Physiological Roles and Clinical Implications

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Abstract

The present study aimed to review the literature about lactate dehydrogenase regarding physiological roles and clinical implications. The enzyme lactate dehydrogenase (LDH) is widely spread in almost each cell in the body, and its prime function is to convert lactate to pyruvate through oxidation process. LDH exists in the cytoplasm of cell and when cell dies it becomes extracellular. The levels of LDH vary according to metabolic needs of each tissue such as development, biological conditions, and pathological aspects. Its levels are increased in a variety of clinical situations from inflammatory conditions to malignancies. The specificity of LDH cannot be taken as a single parameter but helps with other biochemical investigations.

Keywords: Lactate dehydrogenase; Inflammation; Malignancy; Metabolism; Specificity; Clinical implication

Introduction

Importance of lactate dehydrogenase (LDH)

The enzyme lactate dehydrogenase (LDH) is widely spread in almost each cell in the body [1,2]. The prime function of LDH is to convert lactate to pyruvate through oxidation process. LDH exists in the cytoplasm of cell and when cell dies it becomes extracellular [3]. The levels of LDH vary according to metabolic needs of each tissue such as development, biological conditions, and pathological aspects [1].

Biochemistry of LDH

The molecular weight of LDH is 134 kDa, and it is consisted of a tetramer including two subunits, H and M. there are 5 isoenzymes, LD1 to LD5. Although LDH is considered as a ubiquitous enzyme that exists in the cell cytoplasm of each cell, but its isoenzyme structure varies in different tissues. As an example, LD1 is mainly abundant in cardiac tissue, red blood cells, and renal cells; and on the other hand, LD5 exists mainly in hepatocytes and skeletal muscles [4-6].

Clinical implications of LDH

The indications for requesting a serum LDH have become less important with time. For example, the use of LDH for evaluation of liver function is of limited implications because of its involvement in different areas of the body from one side, and from another side the use of transaminases and alkaline phosphatase is more important than LDH [4]. Its implication in the assessment of muscle disease is limited because creatine kinase is more specific and important than LDH [4].

The levels of LDH are highly elevated due to alterations in carcinogenic status that can lower the conversion rate of lactate to pyruvate ending with increased nicotinamide adenine dinucleotide (NAD+) that has the ability to interact with metabolic pathways of carbohydrate. A high glycolytic activity is thought to increase the likely of cancer development [7]. Tissues damaged by tumours release LDH into bloodstream which participates to increased levels of this enzyme [8]. The levels of serum LDH are used to diagnose a variety of cancers including oral, laryngeal and breast cancer [9].

From a clinical point of view, the variation in the levels of lactate with time reflects directly its production changes. Elevated levels of lactate give a clue for circulatory alterations, while its lowered levels pointed to improved circulation [10]. The clearance of lactate is a very important aspect in assessing the clinical status of patients [10]. Although clearance decreases in some cases such as septic...
conditions in humans and animals, hyperlactemia may reflect lowered clearance instead of increased production [11].

Metabolic aspects of lactate implied that increased rates of glucose metabolism or lowered rates of pyruvate increase the levels of lactate [12]. It is worth mentioning that controlling the levels of lactate is not necessarily improving the survival because the real cause is not addressed [13]. The adjustment of pH when there are increased levels of lactate may not improve survival because the relationships between pH and anaerobic glycolysis as well as lactate levels are not fully clear [14,15].

It has been reported that lactate can act as a substrate and involved in different metabolic pathways. In case of sepsis, lactate undergoes various metabolic aspects and provides cellular energy.

**Metabolic aspects of LDH**

Lactate metabolism is mediated through liver and kidneys at the organ level, whereas it can be mediated on cellular level as a preferred source of energy than glucose [16].

The nervous system has a role in the metabolism of lactate through transporting lactate from astrocytes into neurons and then converted to pyruvate through the effect of lactate dehydrogenase type I[10].

It seems to be a big assumption that the levels of lactate represent a chemical marker of severity of illness under all conditions. As an example, in case of sepsis, lactate levels are considered as a strong predictor of mortality [17].

**LDH and lymphoma**

The results of the study of [18] showed that increased levels of serum LDH were significantly associated poor outcome of tumour. Furthermore, an association between serum LDH level and non-Hodgkin's lymphoma (NHL) was indicated.

A previous study indicated that serum LDH levels were not statistically significant as an independent prognostic factor. Neither treatment response nor the survival time was impacted by LDH levels [19]. Other studies showed that serum LDH in cases of NHL and paediatric HD is considered as an important prognostic factor [20,21]. According to [19], increased activities of LDH reflected poor treatment prognosis, and it is considered the single parameter that has an independent prognostic importance.

**Conclusion**

The results of this study showed that serum levels of HDL have varied clinical implications, but its specificity cannot be taken as a single parameter but helps with other biochemical investigations.

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