American Journal of Biomedical Science & Research

www.biomedgrid.com

ISSN: 2642-1747

Mini Review

Lactate Dehydrogenase: Physiological Roles and Clinical Implications

Ahed J Alkhatib[1]* and Nawaf Abduallah Mohammad Alrakaf[2]

[1]*Department of Legal Medicine, Jordan University of Science and Technology, Jordan*

[2]*MOH, Saudi Arabia*

***Corresponding author:** Ahed J Alkhatib, Department of Legal Medicine, Toxicology and Forensic Medicine, School of Medicine, Jordan University of Science and Technology, Jordan.

To Cite This Article: *Ahed J Alkhatib. Lactate Dehydrogenase: Physiological Roles and Clinical Implications. Am J Biomed Sci & Res. 2019 - 3(5). AJBSR.MS.ID.000705. DOI: 10.34297/AJBSR.2019.03.000705*

Received: June 10, 2019 | **Published**: July 03, 2019

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 1[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.

References

1. Priya Shirish Joshi, Madhuri Chougule, Mahesh Dudanakar, Someshwar Golgire (2012) Comparison between salivary and serum lactate dehydrogenase levels in patients with oral leukoplakia, and oral squamous cell carcinoma - A pilot study. International Journal of Oral and Maxillofacial Pathology 3(4): 7-12.
2. Swetha Acharya, Jyoti Kale, Kaveri Hallikeri, Anil Desai (2018) Prognostic Significance of Preoperative Salivary and Serum Lactate Dehydrogenase in Oral Squamous Cell Carcinoma Patients. Acta Scientific Cancer Biology 2(8): 2-10.
3. Sivaramakrishnan M, Sivapathasundharam B, Jananni M (2015) Evaluation of lactate dehydrogenase enzyme activity in saliva and serum of oral submucous fibrosis patients. J Oral Pathol Med 44(6): 449-452.
4. Pincus MR, Abraham NZ, Carty RP (2011) Clinical enzymology. In: McPherson RA, Pincus MR, (Eds.). Henry's Clinical Diagnosis and Management. (22nd edn), Elsevier Saunders, Philadelphia, PA, USA, pp. 273-295.
5. Panteginini M, Bais R. Serum enzymes. In: Burtis C & Bruns D (Eds.), Teitz (2014) Fundamentals of Clinical Chemistry and Molecular Diagnostics. (7th edn), St Louis, Elsevier Saunders, MO, USA, pp. 318-336.
6. Jialal I, Sokoll LJ (2015) Clinical Utility of Lactate Dehydrogenase: A Historical Perspective. Am J Clin Pathol 143(2): 158-159.
7. Lokesh K, Kannabiran J, Rao MD (2016) Salivary lactate dehydrogenase (LDH) – A novel technique in oral cancer detection and diagnosis. J Clin Diagn Res 10(2): 34-37.
8. Joshi PS, Golgire S (2014) A study of salivary lactate dehydrogenase isoenzyme levels in patients with oral leukoplakia and squamous cell carcinoma by gel electrophoresis method. J Oral Maxillofac Pathol 18(Suppl 1): S39-S44.
9. Nagler RM, Lischinsky S, Diamond E, Klein I, Reznick AZ (2001) New insights into salivary lactate dehydrogenase of human subjects. J Lab Clin Med 137(5): 363-369.
10. Glenn Hernandez, Rinaldo Bellomo, Jan Bakker (2019) The ten pitfalls of lactate clearance in sepsis. Intensive Care Med, 45(1): 82–85.
11. Tapia P, Soto D, Bruhn A, Alegría L, Jarufe N, et al. (2015) Impairment of exogenous lactate clearance in experimental hyperdynamic septic shock is not related to total liver hypoperfusion. Crit Care 19: 188.
12. Garcia Alvarez M, Marik P, Bellomo R (2014) Sepsis-associated hyperlactatemia. Crit Care 18(5): 503.
13. Stacpoole PW, Wright EC, Baumgartner TG, Bersin RM, Buchalter S, et al. (1992) A controlled clinical trial of dichloroacetate for treatment of lactic acidosis in adults. The Dichloroacetate-Lactic Acidosis Study Group. N Engl J Med 327(22): 1564-1569.
14. Figge J, Bellomo R, Egi M (2018) Quantitative relationships among plasma lactate, inorganic phosphorus, albumin, unmeasured anions and the anion gap in lactic acidosis. J Crit Care 44: 101-110.
15. Mohr NM, Vakkalanka JP, Faine BA, Skow B, Harland KK, et al. (2018) Serum anion gap predicts lactate poorly, but may be used to identify sepsis patients at risk for death: a cohort study. J Crit Care 44: 223-228.
16. Brooks GA (2009) Cell-cell and intracellular lactate shuttles. J Physiol 587(Pt 23): 5591-600.
17. Gotmaker R, Peake SL, Forbes A, Bellomo R, ARISE Investigators (2017) Mortality is greater in septic patients with hyperlactatemia than with refractory hypotension. Shock 48(3): 294-300.
18. Milanovic N, Matkovic S, Ristic D, Jelic S, Petrovic M (2012) Significance of tumor burden, vascular endothelial growth factor, lactate dehydrogenase and beta-2 microglobulin serum levels in advanced diffuse large B cell lymphoma. J BUON 17(3): 497-501.
19. Smolewski P, Robak T, Krykowski E, Blasiñska-Morawiec M, Niewiadomska H, et al. (2000) Prognostic Factors in Hodgkin's Disease: Multivariate Analysis of 327 Patients from a Single Institution. Clin Cancer Res 6(3): 1150-1160.
20. García R, Hernández JM, Caballero MD, González M, Galende J, et al. (1993) Serum lactate dehydrogenase level as a prognostic factor in Hodgkin's disease. Br J Cancer 68(6): 1227-1231.
21. Lindh J, Lenner P, Osterman B, Roos G (1993) Prognostic significance of serum lactic dehydrogenase levels and fraction of S-phase cells in non-Hodgkin lymphomas. Eur J Haematol 50(5): 258-263.