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L. Lactic Acid Homeostasis - A Comprehensive Perspective on its Role in Health and Disease

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Abstract: ***This article provides a comprehensive overview of L. Lactic acid homeostasis, its metabolic pathways, and its role in various physiological and pathological conditions, including cancer. The article further discusses the implications of lactic acid accumulation and its relevance in the context of increasing cancer cases and survivors.***

Keywords: L. Lactic Acid, Homeostasis, Metabolism, Cancer, Acidosis

1. Introduction

Lactic acid is the end product of anaerobic glycolysis. **The purpose of this article is to provide a comprehensive overview of L. Lactic acid homeostasis, its metabolic pathways, and its role in various physiological and pathological conditions, with a particular focus on cancer.**

This article is significant as it provides insights into the role of L. Lactic acid homeostasis in health and disease, potentially contributing to the understanding and treatment of various conditions, including cancer.

Formation of Lactic Acid

Lactic acid is formed from Pyruvic acid by the action of Lactic acid dehydrogenase. It is a reversible reaction. **Lactic acid dehydrogenase is an enzyme that plays a key role in the conversion of Pyruvic acid to Lactic acid. This enzyme is specific to certain tissues and has multiple forms, resulting in five different isoenzymes.** . There are also two different forms of the enzyme based on its stereospecificity-D and L form of the enzyme. In human metabolism L-LDH plays an important role and the product formed from D. Pyruvic acid is L. Lactic Acid.1

One of the outcomes of the reaction is to regenerate NAD from NADH formed during glycolysis. The intermediate glyceraldehyde-3-phosphate is phosphorylated by glyceraldehyde-3-phosphate dehydrogenase to form 1, 3-bisphosphoglycerate. This step requires NAD+ as a coenzyme. The NADH formed as a bye product of this reaction is oxidized through oxidative phosphorylation so the NAD is available for continuity of glycolysis. With the absence of mitochondrion in say RBS, NAD is generated through LDH action.2

Various sources of Lactic acid formed in the body

Lactate is produced continuously even under aerobic condition. Lactate is one of the main substrates of gluconeogenesis in liver. It is recently shown that lactate also contributes to TCA cycle acting as a primary source of carbon in majority of the tissues except the brain. But the major organ of lactate production and utilization is skeletal muscle.[3-4]

Daily about 1500 m. moles of L. lactate is generated by the tissues with a measurable blood level of 0.5-1.5m. mol/L.

Conditions in which blood lactate levels increase beyond 5. om. moles leads lactic acidosis. (pH <7.35). Apart from that small amounts of D. Lactic is produced by the intestinal micobiome (5-20 micromoles/L). Minimal amounts of D. Lactate is contributed by the minor methylglyoxal pathway.

Methyl glyoxal by the action D. LDH produces D. Lactate. Overgrowth of bacteria in the colon is shown to be cause of short bowel syndrome causing D. lactic acidosis due to defective removal of from the colon.[3-4]

Most common cause of lactic acid accumulation is tissue hypoxia due to inadequate perfusion of tissues or reduced oxygen level which is common feature of critical illness. blood lactate measurement therefore is a routine investigation in a critical care unit.[5]

Metabolic acidosis is a condition in which blood pH is <7.35 with a fall plasma bicarbonate levels. (<22meq/L). Normal blood pH is 7.35 to 7.45 and normal plasma bicarbonate level is 22-28meq/L. It can be classified as high anion gap and normal anion gap metabolic acidosis. Anion is usually calculated by Blood level of sodium say 140meq/L minus blood chloride level (100meq/L) and Blood bicarbonate level (25 meq/L).

Anion Gap = Na+ – (Cl-+ HCO3 -)-Normal AG reference value= 4 to 12meq/l.

If AG > 30 mmol/L then metabolic acidosis invariably present.

If AG 20-29mmol/L then 1/3 will not have a metabolic acidosis.

K can be added to Na+, but in practice offers little advantage

For every gram decrease albumin level AG will decrease by 0.25meq/L.) Anion gap is due to unmeasured anions like organic acids, plasma proteins particularly aalbumin.

High anion gap metabolic acidosis is associated with diabetic ketaoacidosis, lactic acidosis, renal failure, drugs or toxins. Normal AG is observed in gastrointestinal tranct loss

due to diarrhea or renal loss. Exogenous causes may due to ethylene glycol or methanol exposure or ingestion because of accumulation of oxalic acid or formic acid respectively.
Lactic acidosis is classified as:

Type A-hypoproteinemia, cyanosis, poor tissue perfusion or hypoxemia. This can be over production of lactic acid due to circulatory or pulmonary diseases or under utilization due to live disease, thiamine deficiency or uncoupling of oxidative phosphorylation.

Type B-
B1-systemic disease such as renal hepatic failure, diabetes
B2-Drugs-biguanides, alcohol, isoniazid, zidovudoine or salicylate oisoning.

B3-in born erros of metabolism like mitochondrial disorders, von-Gierke disease.6

Lactic acid accumulation in various forms of cancer is reported. The liver plays a vital role in lactic acid metabolism along with kidneys that utilize 30 percent of lactate production. Extensive metastasis may lead to liver failure. Hypocapnea and metabolic alkalosis present in these patients may be responsible in converting liver into lactic acid producer in spite of changes in carbon di oxide tension.[7-8]

Therefore an introspection and overview of status of lactic acid and its metabolism in general and cancer in particular will be relevant with increasing number of cancer cases and survivors.;

In conclusion, L. Lactic acid plays a crucial role in various physiological and pathological conditions. Understanding its homeostasis and metabolic pathways can provide valuable insights into the treatment of various conditions, including cancer. Further research is needed to explore the potential therapeutic applications of this knowledge.

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