Review Article: A Mini Review on Lactic Acidosis Effect, Cause, Symptoms, Complications, Metabolism, and Pathodology with Its Diagnosis, Treatment, and Preventions

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ABSTRACT

Lactic acidosis is a condition characterized by an abnormal accumulation of lactic acid in the body, leading to a disturbance in the acid-base balance. It can occur due to various factors, including impaired oxygen supply, medication use, and liver dysfunction. The pathophysiology of lactic acidosis involves an imbalance between lactic acid production and elimination or utilization. Diagnosing lactic acidosis involves clinical evaluation, blood tests, and identification of underlying causes. Elevated lactate levels, arterial blood gas analysis, and electrolyte imbalances are commonly assessed. Imaging studies and electrocardiograms may be used to evaluate organ function and identify contributing factors. Treatment of lactic acidosis focuses on addressing the underlying cause and supporting organ function. Prompt resuscitation and oxygen therapy are crucial in cases of impaired oxygen delivery. Medications or toxins that contribute to lactic acidosis may need to be discontinued or managed differently. Fluid and electrolyte management is essential for correcting imbalances and optimizing organ function. In severe cases, interventions such as renal replacement therapy or hemodialysis may be required. Prevention of lactic acidosis involves managing underlying medical conditions and avoiding factors that can contribute to its development. Regular monitoring of medications that can cause lactic acidosis is necessary, with adjustments made if needed. Proper control of chronic conditions such as diabetes or liver disease can minimize the risk of lactic acidosis. Individuals engaging in intense physical activities should receive appropriate training, hydration, and pacing to prevent excessive lactic acid build-up. Lactic acidosis can have significant health effects and complications. Cardiovascular effects can occur, including arrhythmias, decreased cardiac output, and cardiac arrest. Organ dysfunction, such as acute kidney injury, liver failure, and pancreatitis, may result from lactic acidosis. Metabolic acidosis, electrolyte imbalances, and hypoxia are also common consequences. In severe cases, lactic acidosis can lead to confusion, altered mental status, and coma.

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Content

1. Introduction

Lactic acid is a small organic compound that plays a crucial role in various biological processes. It is produced in the body as a by-product of anaerobic metabolism, which occurs when there is an insufficient supply of oxygen to meet the energy demands of cells. Lactic acid is commonly associated with muscle fatigue and soreness, but it serves several important functions in the body, including as an energy source, a signalling molecule, and a regulator of pH balance. In addition, the detection of lactic acid levels in the body is of great importance for diagnosing and monitoring various medical conditions. One of the primary functions of lactic acid is to provide an alternative energy source for muscles and other tissues during times of increased energy demand (**Figure 1**). When the oxygen supply is limited such as during intense exercise or in hypoxic conditions, cells switch from aerobic metabolism to anaerobic metabolism [1-3]. This metabolic shift allows the body to produce energy quickly, albeit less efficiently. Lactic acid is produced as a result of this anaerobic metabolism and is utilized by muscle cells as an energy source. This process helps to sustain muscle contraction and maintain overall cellular function. In addition to its role as an energy source, lactic acid acts as a signalling molecule in the body. It has been shown to regulate gene expression and protein synthesis in various cell types. The accumulation of lactic acid in the muscles during exercise has been found to initiate the release of growth factors and other signalling molecules that promote muscle repair and adaptation. This mechanism helps to enhance muscle strength and endurance over time, making lactic acid an important player in exercise-induced muscle adaptation. Furthermore, lactic acid acts as a regulator of pH balance in the body. It is a weak acid, meaning that it can donate a proton and lower the pH of a solution [4-7]. During intense exercise, the accumulation of lactic acid in the muscles can lead to a decrease in pH, causing the surrounding tissues to become more acidic. This decrease in pH can impede the normal functioning of enzymes and other proteins, leading to muscle fatigue and discomfort. However, the body has mechanisms to buffer and remove excess lactic acid; helping to restore pH balance and minimize the negative effects of acidosis. The detection of lactic acid levels in the body is of high importance for diagnosing and monitoring various medical conditions. Elevated levels of lactic acid, known as lactic acidosis, can indicate underlying health issues such as infections, liver disease, kidney dysfunction, or impaired circulation. Lactic acidosis can also occur in individuals with certain metabolic disorders, such as mitochondrial diseases or pyruvate dehydrogenase deficiency [8, 9]. Detecting and monitoring lactic acid levels can provide valuable information about the severity and progression of these conditions. There are several methods for detecting lactic acid levels in the body. One commonly used technique is blood lactate testing which involves drawing a blood sample and measuring the concentration of lactic acid in the plasma. Blood lactate testing is often performed during exercise or in situations where there is a suspected imbalance

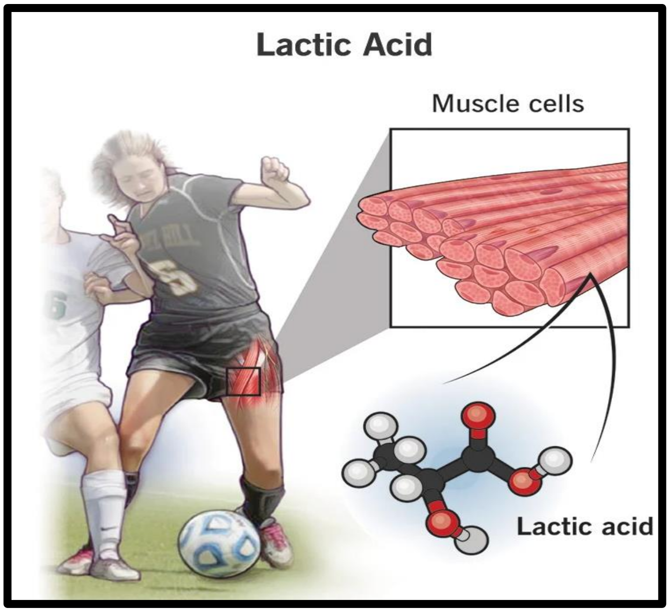

Figure 1. The presence of lactic acid in muscle cells [13]

in oxygen supply and demand, such as in cases of sepsis or cardiac arrest. Elevated blood lactate levels can indicate tissue hypoxia and the presence of underlying medical conditions. Another method for detecting lactic acid levels is through the use of lactate meters. These portable devices allow for quick and easy measurement of lactic acid levels in the blood. Lactate meters are commonly used in sports medicine and exercise physiology to monitor lactate production during exercise and determine an individual's lactate threshold. This information can be used to optimize training programs and improve athletic performance [10-13].

Lactic acid detection is not limited to blood testing; it can also be measured in other body fluids such as cerebrospinal fluid, urine, or sweat. Elevated levels of lactic acid in these fluids can provide valuable diagnostic information in cases of metabolic disorders or certain types of cancer. For example, high levels of lactic acid in cerebrospinal fluid can indicate bacterial or viral meningitis, while increased lactic acid in urine may be a sign of kidney dysfunction. The detection of lactic acid levels in the body is of great importance for understanding the metabolic status and overall health of an individual. It can help diagnose and monitor various medical conditions, guide treatment decisions, and optimize athletic performance. By understanding the functions and significance of lactic acid, healthcare professionals can better assess and manage the health of their patients [2, 5, 9].

Prior research on lactic acid has focused on various aspects, including its production, applications, and health effects. Here is a brief overview of some key findings:

(a) Production: Lactic acid is primarily produced through the carbohydrates fermentation by lactic acid bacteria. Research has explored optimizing the production process by investigating various factors such as substrate selection, fermentation conditions (temperature, pH, and oxygen supply), and strain selection. This research has led to the development of more efficient and cost-effective methods for lactic acid production.

(b) Applications: Lactic acid has a wide range of applications. It is commonly used in the food and beverage industry as a food additive, preservative, and flavouring agent. It is further used in the production of biodegradable plastics, cosmetics, pharmaceuticals, and as a precursor for other chemicals. Research has focused on exploring and expanding these applications, as well as developing new applications for lactic acid.

(c) Health effects: Lactic acid has been studied for its health effects, particularly in the context of exercise physiology. During intense exercise, lactic acid accumulates in muscles, leading to fatigue and muscle soreness. However, recent research suggests that lactic acid may not be the primary cause of muscle soreness, and that it may have some beneficial effects on muscle recovery and adaptation. Furthermore, lactic acid has been investigated for its potential as an antimicrobial and anti-inflammatory agent [14]. Prior research on lactic acid has explored its production, applications, and health effects, leading to advancements in various fields. Further research is ongoing to uncover new uses and potential benefits of lactic acid [13-19].

Here are some additional details about prior research on lactic acid. It has been extensively studied in the biomedical field. It has been explored as a biomaterial for tissue engineering and drug delivery systems. Lactic acid-based polymers, such as polylactic acid (PLA) and poly(lactic-co-glycolic acid) (PLGA), have been widely investigated due to their biocompatibility and biodegradability. These polymers have been used for scaffolds in tissue engineering, as well as for the controlled release of drugs in various medical applications [20]. Recent research has focused on improving the efficiency of lactic acid fermentation processes which includes studying and optimizing fermentation parameters such as pH, temperature, substrate concentration, and fermentation mode (batch, fed-batch, and continuous). By identifying optimal conditions, researchers aim to enhance the yield and productivity of lactic acid production [21-23].

Its production traditionally relies on carbohydrate-rich substrates, such as glucose or corn starch. However, recent research has explored the use of alternative feedstock, such as lignocellulosic biomass and agro-industrial waste, to produce lactic acid. These studies aim to enhance the sustainability and cost-effectiveness of lactic acid production using renewable and abundant resources [23-25]. Lactic acid bacteria (LAB) are the primary producers of lactic acid. Research has focused on exploring the microbial diversity within LAB to identify strains with improved fermentation capabilities. This includes studying the genetic and metabolic characteristics of LAB strains, as well as developing genetic engineering techniques to enhance lactic acid production [26, 27]. Furthermore, lactic acid has also been investigated for its potential health benefits, particularly in the context of gut health. Research suggests that lactic acid produced by certain strains of LAB can help maintain a healthy gut microbiota, enhance digestion, and improve the absorption of nutrients. Moreover, lactic acid bacteria-based probiotics have been studied for their potential to improve immune function and prevent gastrointestinal disorders [28-30].

Overall, the prior research on lactic acid encompasses a wide range of areas, including production optimization, applications in various industries, biomedical uses, alternative feedstock, microbial diversity, and health benefits. Ongoing research continues to expand our understanding of lactic acid and its potential applications.

2. Metabolism and Pathodology of Lactic Acid in Living Bodies

The metabolism of lactic acid in living bodies involves a process called lactic acid fermentation, which occurs primarily in muscle cells during periods of intense exercise or when there is a lack of oxygen supply to the tissues. During exercise, muscle cells require a high amount of energy to perform their functions. Initially, glucose is broken down through a process called glycolysis to produce energy in the ATP form. However, when the oxygen supply becomes limited such as during intense exercise then the glycolysis continues without the involvement of oxygen leading to the production of lactic acid. Lactic acid fermentation involves the conversion of pyruvate, a product of glycolysis, into lactic acid by the enzyme lactate dehydrogenase. This conversion helps to regenerate the supply of NAD^+ in the absence of oxygen, which is required for glycolysis to continue. In the liver, lactic acid can be converted back into glucose through a process called gluconeogenesis. This glucose can then be released into the bloodstream and used by other tissues for energy. This is an important pathway as it helps

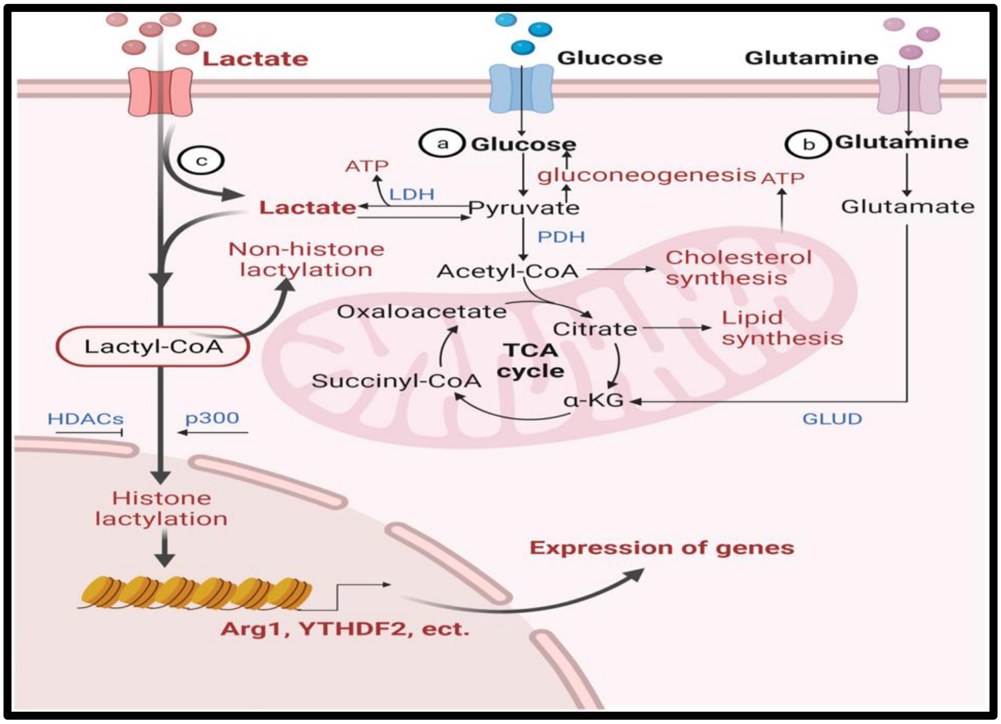

Figure 2. A Schematic for metabolism and pathodology of lactic acid in living bodies [30]

to maintain blood glucose levels and supports energy production in various organs (**Figure 2**). The metabolism of lactic acid also plays a crucial role in buffering the effects of acidosis, which is the accumulation of excess hydrogen ions in the body. Lactic acid acts as a proton donor and helps to maintain pH balance by neutralizing the acidity caused by the breakdown of glucose. Overall, the metabolism of lactic acid provides an alternative pathway for energy production when oxygen supply is limited and helps to maintain energy homeostasis and pH balance in living bodies [19, 21, 25, 28-34].

3. Causes of Lactic Acidosis

Lactic acidosis occurs when there is an imbalance between lactic acid production and its elimination or utilization. There are several factors that can contribute to the development of lactic acidosis, including:

3.1. Impaired oxygen supply

In conditions such as shock, heart failure, respiratory failure, or severe anemia, the delivery of oxygen to tissues is compromised which leads to anaerobic metabolism, where glucose breakdown produces lactic acid instead of energy [35, 36].

3.2. Medications and toxins

Certain medications, such as metformin (used for diabetes management) and nucleoside reverse transcriptase inhibitors (used in the treatment of HIV), can interfere with mitochondrial function and promote lactic acidosis. In addition, toxins like ethanol or methanol can disrupt cellular metabolism and cause lactic acid accumulation [37-39].

3.3. Liver dysfunction

The liver plays a crucial role in metabolizing lactic acid by converting it back into glucose through gluconeogenesis. Liver diseases, such as liver failure or cirrhosis, can impair this metabolic pathway, leading to lactic acidosis [40-42].

4. Symptoms and Complications

The severity of lactic acidosis symptoms can range from mild to life-threatening. Common symptoms include [43-46] rapid breathing known as tachypnea (to compensate for the excessive lactic acid, the body increases its respiratory rate to eliminate carbon dioxide, which is produced during lactic acid breakdown), nausea and vomiting (lactic acidosis can cause gastrointestinal disturbances, including nausea, vomiting, and abdominal pain), fatigue and weakness (body's energy production is compromised in lactic acidosis, leading to fatigue, muscle weakness, and a general feeling of malaise), confusion and altered mental status (severe lactic acidosis can affect brain function, causing confusion, disorientation, and even coma).

If left untreated, lactic acidosis can lead to various complications such as cardiovascular effects where high levels of lactic acid can disrupt normal cardiac function, leading to arrhythmias (abnormal heart rhythms), decreased cardiac output, and even cardiac arrest. This can be particularly dangerous in individuals with pre-existing heart conditions. Organ dysfunction in which lactic acidosis can impair the function of various organs, including the kidneys, liver, and pancreas. In severe cases, it can lead to acute kidney injury, liver failure, and pancreatitis. Metabolic acidosis is characterized by an imbalance in acid-base regulation, resulting in a decrease in blood pH. This metabolic acidosis can further disrupt normal cellular processes and lead to electrolyte imbalances.

Hypoxia conditions where lactic acidosis is caused by inadequate oxygen supply, such as in shock or respiratory failure, the underlying hypoxia (low oxygen levels) can have detrimental effects on multiple organ systems.

5. Diagnosis and Treatment

The diagnosis of lactic acidosis involves a combination of clinical evaluation, blood tests, and assessment of underlying causes. Blood tests can measure lactate levels, arterial blood gases, and electrolyte imbalances. The other diagnostic tools, such as imaging studies or electrocardiograms, may be used to evaluate organ function and identify any underlying conditions. Treatment of lactic acidosis involves addressing the underlying cause and supporting vital organ function. In cases where lactic acidosis is caused by impaired oxygen delivery, such as in shock or respiratory failure, prompt resuscitation, and oxygen therapy are essential. Medications or toxins contributing to lactic acidosis may need to be discontinued or managed differently. Supportive measures, such as fluid and electrolyte management, may be necessary to correct imbalances and optimize organ function. In severe cases, interventions such as renal replacement therapy or hemodialysis may be required to remove lactic acid from the bloodstream and support kidney function [47-52].

6. Prevention

Preventing lactic acidosis involves managing underlying medical conditions and avoiding factors that can contribute to its development. This may include regular monitoring of medications that can cause lactic acidosis and adjusting dosages if necessary. It is also important to maintain good control of chronic conditions such as diabetes or liver disease to minimize the risk of lactic acidosis. In individuals who engage in intense physical activities, proper training, hydration, and pacing can help prevent excessive lactic acid build-up during exercise (**Figure 3**). Ensuring adequate oxygen supply and avoiding prolonged periods of intense anaerobic exercise can help reduce the risk of lactic acidosis [53-56]. Here are some preventive measures:

6.1. Regular medical check-ups

Routine check-ups and monitoring of medications can help identify any potential risk factors for lactic acidosis. It is important to inform healthcare professionals about any medications or supplements being taken to ensure they are not contraindicated.

6.2. Managing chronic conditions

If you have chronic conditions like diabetes, liver disease, or heart failure, it is crucial to follow the recommended treatment plans, including medication management, lifestyle modifications, and regular monitoring of the relevant parameters.

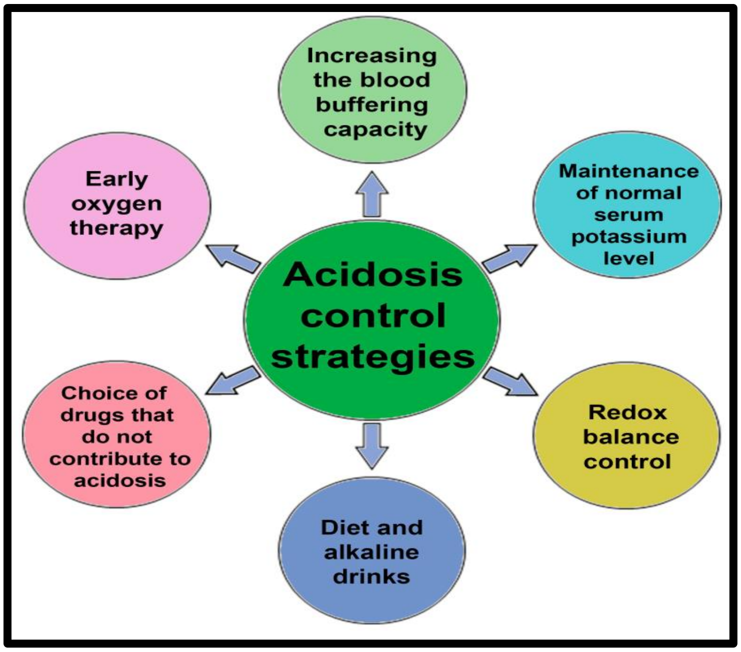

Figure 3. Diagram of strategies used for acidosis control [57]

6.3. Balanced exercise routine

When engaging in physical activity, it is important to maintain a balanced routine that includes both aerobic and anaerobic exercises. Gradually increasing intensity and allowing for adequate rest periods can help prevent excessive lactic acid build-up.

6.4. Hydration and nutrition

Proper hydration and a balanced diet can support optimal metabolic function and energy production. Ensuring adequate fluid intake and consuming various nutrient-rich foods can help maintain overall health and prevent metabolic imbalances.

7. Conclusion

Lactic acidosis is a condition characterized by an imbalance in lactic acid production and elimination, resulting in elevated levels of lactic acid in the body. It can occur due to various causes, including impaired oxygen supply, medication or toxin-induced mitochondrial dysfunction, and liver dysfunction. Lactic acidosis can lead to a range of symptoms, from mild fatigue and weakness to severe complications involving vital organs and metabolic disturbances. Early diagnosis and treatment are essential to prevent further complications. Prevention of lactic acidosis involves managing underlying medical conditions, taking medications as prescribed, and maintaining a balanced exercise routine. Furthermore, regular medical check-ups, hydration, and proper nutrition play a crucial role in preventing this condition.

If you suspect lactic acidosis or experience symptoms, it is important to seek medical attention promptly for proper diagnosis and treatment. In conclusion, lactic acidosis is a condition characterized by the abnormal accumulation of lactic acid in the body. Prompt diagnosis, treatment, and prevention are essential for managing this condition. Timely intervention, addressing underlying causes, and supportive measures to optimize organ function are crucial in the management of lactic acidosis. By understanding the pathophysiology and implementing appropriate strategies, healthcare professionals can effectively mitigate the health effects of lactic acidosis and improve patient outcomes.

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Declaration of competing interest
All the authors declare that they have no known competing financial interests to declare.

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