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Detection and analysis of lactate metabolism in 192 healthy people

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ABSTRACT

This study aims to investigate lactate metabolism-related indicators in healthy individuals and explore their associations with the onset and development of diabetes. A total of 192 healthy individuals were subjected to lactate (LA), lactate dehydrogenase (LDH), and pyruvate dehydrogenase (PDH) measurements. The results showed a significant positive correlation between LDH and LA, and age-stratified analysis revealed significant differences in LA and LDH levels among different age groups. The correlation between LDH and LA may be related to lactate metabolism disruption in diabetic patients. Age trend analysis indicated higher LA and LDH levels during childhood, gradually declining with age, possibly due to growth and cellular metabolic changes. This study provides new perspectives and evidence for the early diagnosis and treatment of diabetes.

KEYWORDS

Diabetes; Lactate metabolism; Lactate dehydrogenase; Age trend

In recent years, the ongoing rise in the global diabetic population has placed diabetes and its complications at the forefront of global public health concerns. Diabetes, a metabolic disorder characterized by abnormal glucose metabolism, has far-reaching implications that extend beyond the individual patient. Lactate, a critical intermediate in the anaerobic glycolysis pathway, is typically processed in the liver into pyruvate, which is then channeled into the tricarboxylic acid (TCA) cycle for complete aerobic metabolism. Elevated lactate levels are often indicative of tissue hypoxia or metabolic disorders, suggesting a potential imbalance in the body's metabolic processes. Under normal physiological conditions, lactate is metabolized into carbon dioxide and water through aerobic pathways, ensuring that the body maintains a state of homeostasis. However, when the oxygen supply is insufficient, the rate of lactate production can surpass its clearance rate, leading to the accumulation of lactate and the subsequent risk of lactic acidosis.

In the context of diabetes, the intricate metabolic pathways are often disrupted due to a combination of factors including insulin resistance, insufficient insulin secretion, and other metabolic irregularities. These disruptions can significantly impair lactate metabolism, increasing the risk of lactic acidosis in diabetic patients. Lactate dehydrogenase (LDH), an enzyme that is present in nearly all cells, can have its levels elevated due to various factors such as cellular damage, necrosis, or inflammation. Persistently high levels of LDH may serve as a biomarker for a range of diseases or pathological states, including myocardial infarction, hepatitis, and pneumonia, highlighting the importance of monitoring LDH levels in clinical settings.

Pyruvate dehydrogenase (PDH), a key enzyme in the glycolytic process, plays a crucial role in the conversion of pyruvate into acetyl-CoA, which is essential for the TCA cycle. A decrease in PDH levels can be indicative of various factors, including poor diet, malnutrition, or other conditions that may impair metabolic function. A sustained decrease in PDH levels could be a sign of certain diseases or pathological states, such as anemia or hypothyroidism, emphasizing the need for a comprehensive understanding of metabolic enzymes in health and disease.

Given the complex interplay between lactate metabolism and diabetes, it is crucial to conduct thorough epidemiological surveys on lactate metabolism-related indicators within healthy populations. Such research can provide invaluable insights into the pathogenesis of diabetes and inform the development of more effective disease management strategies. By understanding the nuances of lactate metabolism, we can better identify early warning signs of metabolic disorders, enabling earlier interventions and potentially altering the disease trajectory for many individuals. Furthermore, these studies can contribute to the development of targeted therapies and preventive measures, ultimately aiming to improve patient outcomes and reduce the global burden of diabetes. In addition, the exploration of lactate metabolism in healthy individuals can help in establishing baseline values and identifying potential risk factors, which are essential for the early detection and management of metabolic disorders.

This study is a significant endeavor that seeks to delve into the intricate realm of lactate metabolism, particularly focusing on its relationship with diabetes. The ultimate goal is to uncover the intricate dynamics of lactate metabolism in healthy individuals and to identify any potential links that could be pivotal in the onset and progression of diabetes.

to achieve this, a large-scale, population-based approach will be adopted, which will involve the collection of extensive data from a diverse and representative sample of the population. This method will ensure that the findings are robust and applicable to a wide range of individuals. By amassing this wealth of data, researchers aim to establish a comprehensive understanding of the normal range and variability of lactate metabolic indicators. the study will also explore the multifaceted factors that could be associated with an increased risk of diabetes. This will involve a meticulous examination of various biochemical, physiological, and environmental factors that may influence lactate metabolism. Identifying these factors could provide crucial insights into the mechanisms that contribute to the development of diabetes. one of the innovative aspects of this study is the planned stratified analysis, which will segment the population by age and gender. This approach will allow researchers to examine the sex differences and age-related trends in lactate metabolism. Such an analysis is vital because it is known that both age and gender can significantly influence metabolic processes, including lactate metabolism. by conducting this stratified analysis, the study will be able to provide a more nuanced understanding of lactate metabolism across different demographics. This could reveal important patterns and variations that may not be evident through a more generalized approach. For instance, it may uncover whether lactate metabolism differs significantly between males and females or if it changes in predictable ways as individuals age.the findings from this study are expected to have profound implications for the field of diabetes research and treatment. A deeper understanding of lactate metabolism could lead to the identification of new biomarkers for diabetes risk, which could be used in early detection and prevention strategies. Moreover, this knowledge could inform the development of more personalized treatment plans for diabetic patients, taking into account their unique lactate metabolic profiles. furthermore, the insights gained from this study could also contribute to the broader understanding of metabolic disorders and their interplay with lactate metabolism. This could potentially open up new avenues for research and treatment across a range of metabolic conditions.in conclusion, this study represents a significant step forward in the quest to understand the complex relationship between lactate metabolism and diabetes. By conducting a comprehensive investigation of lactate metabolic indicators and exploring their association with diabetes risk factors, this research aims to provide a new perspective and a solid foundation for the prevention and treatment of diabetes. It is anticipated that the results will not only enhance our understanding of lactate metabolism but also pave the way for innovative strategies and approaches in the management of diabetic patients, ultimately leading to improved health outcomes for those affected by this condition.

1 Object and methodsubject investigated

From March 2019 to September 2021, 192 subjects were randomly selected from our hospital, and during the subject selection process, we excluded individuals with chronic diseases or who were using drugs affecting lactate metabolism to ensure that the study subjects were relatively healthy. These included 93 women and 99 men, ensuring a gender balance. The sampling was stratified by age, and the population was divided into different age groups to ensure full representation of each age group.

Childhood group: age <= 4 years, 38 people.

Child group: 4 <age <=10 years, with 38 people.

Juvenile group: 10 <age <= 18 years, a total of 38 people.

Adult group: 18 <age <= 59 years, with 38 people.

Age group: age> = 60 years, with 40 people.

Through the stratified analysis of people in different age groups, we will have a more comprehensive understanding of the differences in the indicators related to lactate metabolism between age groups and sexes.

1.1 Sample collection

In our study, meticulous attention was given to the selection of the optimal timing and technique for collecting venous blood samples from our subjects. This careful approach was crucial to ensure the integrity and quality of the samples, which would later be used for detailed analysis. The blood was drawn at a time chosen based on scientific considerations, such as the circadian rhythms of the subjects or the specific biomarkers we intended to measure.

Upon collection, the blood samples were immediately processed to prevent any degradation of the biomarkers. This involved placing the samples on ice to maintain a low temperature, which helps preserve the biochemical properties of the blood. Following this, cold centrifugation was employed, a method that spins the blood at a low temperature to separate the serum from the blood cells. This step is essential as it allows for the isolation of the serum, which is the liquid component of the blood that remains after the clotting process and contains the majority of the proteins and other soluble factors we are interested in.

Once the serum was isolated, it was carefully transferred to cryovials or other suitable containers designed for long-term storage at ultra-low temperatures. These containers were then stored in a -80°C refrigerator, which is a specialized piece of equipment capable of maintaining a stable and extremely cold environment. The purpose of this storage condition is to preserve the serum samples for an extended period without compromising their biochemical properties.

The decision to store the samples at such a low temperature was strategic, as it allows for the possibility of centralized testing at a later date. This centralized testing approach is beneficial for several reasons. It enables the pooling of resources and expertise, ensuring that the analysis is conducted under the most stringent and controlled conditions. Additionally, it allows for batch processing, which can lead to more efficient use of laboratory equipment and personnel, and ultimately, more reliable and consistent results.

In summary, the careful selection of collection time, the immediate processing of the samples, and the storage of the isolated serum at -80°C are all critical steps in our study's methodology. These steps are designed to maintain the quality and integrity of the samples, ensuring that the subsequent centralized testing yields accurate and meaningful data that can contribute to our understanding of the subject matter at hand.

1.2 Test method

In this study, a meticulous examination was conducted to evaluate the levels of lactate (LA), as well as the enzymatic activities of lactate dehydrogenase (LDH) and pyruvate dehydrogenase (PDH), employing a series of standardized biochemical assays. These assays are pivotal in understanding the metabolic processes and the role of these enzymes in various physiological and pathological conditions.

The process of lactate content detection commenced with the selection of an appropriate volume of serum samples. Subsequently, a buffer solution and a microstandard solution provided within the kit were added to the samples. This mixture was then thoroughly mixed to ensure homogeneity. Following this, the mixture was subjected to spectrophotometry at a specific wavelength, which is optimal for the detection of lactate. By comparing the absorbance readings to a pre-established standard curve, the concentration of lactate in the samples was accurately calculated.

The detection of LDH activity involved a slightly different procedure. Initially, 50 microliters of serum samples were combined with the enzyme's reaction substrate. Throughout the reaction, LDH facilitated the conversion of the substrate into a product. This biochemical transformation was accompanied by a reduction of nicotinamide adenine dinucleotide (NAD+) to its reduced form, NADH. The activity of LDH was then deduced by monitoring the change in absorbance of NADH, which is directly proportional to the rate of the enzymatic reaction.

Similarly, the detection of PDH activity also required the mixing of 50 microliters of serum samples with the respective enzyme reaction substrate. During the reaction, PDH catalyzed the conversion of the substrate into the product, which was coupled with the oxidation of NADH back to NAD+. The PDH activity was quantified by examining the absorbance change of NAD+, which mirrors the enzymatic activity.

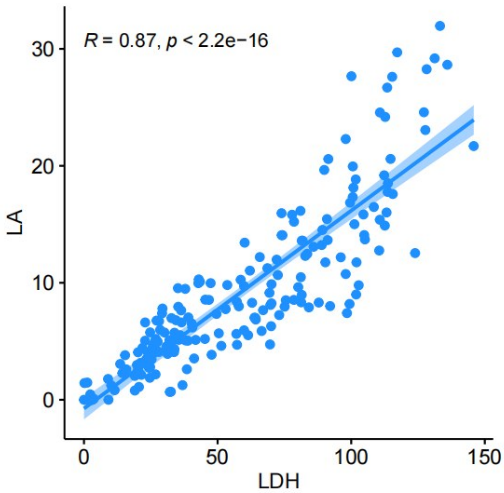
Each of these steps was meticulously designed to provide a precise and reliable measure of the LA content and the activities of LDH and PDH. These assays are not only crucial for clinical diagnostics but also for research purposes, as they offer insights into the metabolic pathways and the enzymatic mechanisms that underpin various diseases and conditions. The findings from such studies can significantly contribute to the development of therapeutic strategies and the advancement of medical knowledge.

1.3 statistical method

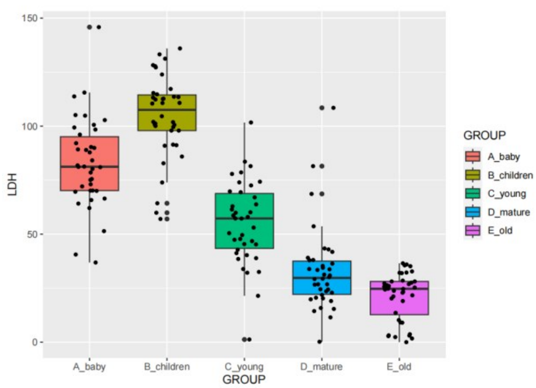
ANOVA analysis: one-yuan analysis of variance (One-Way ANOVA) was used to compare whether the test results of LA, LDH and PDH in different age groups. In the ANOVA test, the significance level was set ($\alpha = 0.05$), and if the calculated p value is <0, the $p < 0.05$.

Correlation analysis: Association between LA, LDH and PDH was assessed using Pearson's correlation coefficient. After calculating the correlation coefficient, the significance level is also set. If the calculated correlation coefficient is> 0.75 (or <-0.75), and the p-value is less than the set significance level ($\alpha = 0.05$).bear fruit

A significant positive correlation between LDH and LA ($R = 0.87$, $P < 2.2e-16$), indicating that increased LDH levels were closely associated with increased LA levels and the correlation was extremely significant. There was a degree of correlation between LDH and PDH, with statistical significance, although weak (R = 0.38, P = 4.3e-16). However, the correlation between LA and PDH was not significant (R = 0.17, P = 0.016), indicating that the changes in the levels of LA and PDH were statistically independent.



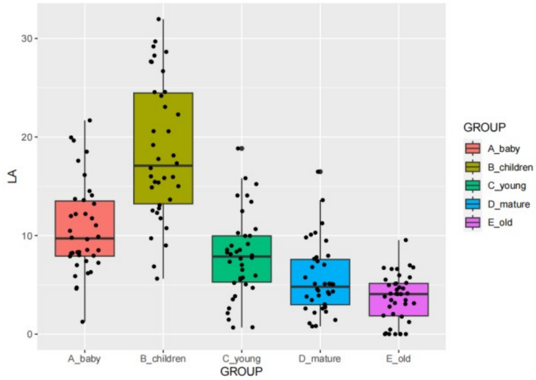
There were significant differences between LA and LDH levels in each age groups. Specifically, both LA and LDH levels showed an upward growth trend from early childhood to childhood. However, both indicators decreased significantly with increasing age. This finding suggests that LA and LDH may play different roles in cellular metabolic and physiological processes at different ages.



In conclusion, this study found a significant positive correlation between LDH and LA, suggesting that LDH and LA may co-change in some physiological or pathological state. In addition, for the results of the age group analysis, we observed that LA and LDH levels increased from early childhood to childhood, and then showed a significant decline with age. This may be related to factors such as growth and development and cell metabolism changes, but the specific mechanism still need to be further studied and explored.

2 Discuss

Diabetes mellitus and its complications have become one of the most important public health



problems worldwide. This study investigated a comprehensive survey of lactate metabolism in healthy people and explored its potential association with the onset and development of diabetes. Through the detection of 192 healthy people from different age and gender of lactate (LA) content, lactate dehydrogenase (LDH) activity and pyruvate dehydrogenase (PDH) activity of the test, we found a significant positive correlation between LDH and LA, according to the age stratified analysis found significant difference in LA and LDH levels at different age.

LDH is an important intracellular enzyme class, involved in lactate production and metabolism. Under normal conditions, lactate is oxidized to carbon dioxide and water by aerobic metabolism, but during hypoxia or insufficient oxygen supply, the rate of lactate production may exceed its scavenging rate, leading to lactate accumulation. Due to insulin resistance, insufficient insulin secretion and other metabolic abnormalities, lactate metabolism is often affected, easily leading to lactic acidosis 4,5,6. This study found a significant positive correlation between LDH and LA, which may mean that the activity of LDH and LA content are somehow affected simultaneously, which may be related to the disorder of lactate metabolism in diabetic patients. The production of antilactate is an important metabolic feature of adipocytes, and lactate is the end product of lactate dehydrogenase (LDH) conversion from pyruvate to anaerobic or aerobic glycolysis. It has been shown that adipocyte-specific Ldha deficiency prevents mice from diet-induced insulin resistance. Therefore, further studies could explore the physiological regulation mechanisms between LDH and LA and whether this correlation is more significant in diabetic patients.

By stratifying people of different age groups, we found that LA and LDH levels increased from early childhood to childhood, followed by a significant decline with age. This may be related to factors such as growth and development and changes in cell metabolism. In childhood, rapid growth and frequent cell division and metabolic activity, result in elevated LA and LDH levels. However, the cellular metabolism gradually stabilizes with increasing age, which may cause a decrease in LA and LDH levels 7,8,9.

In conclusion, In this comprehensive study, we delved deeper into understanding the intricate relationship between lactate metabolism and its biomarkers, particularly in the context of healthy individuals. We meticulously analyzed various indicators that are pivotal in the metabolic pathway of lactate, aiming to uncover any discernible patterns or trends that may correlate with age. Our findings have shed light on the potential predictive capabilities of these lactate-related biomarkers in assessing the risk of developing diabetes. The implications of this research are profound, as it offers a novel lens through which we can view the early signs of diabetes, which could be instrumental in its early diagnosis and intervention. By identifying these trends, we aim to pave the way for more personalized diabetes management strategies. The data collected and analyzed in this study could be a cornerstone in the development of targeted treatment approaches, which are tailored to the specific needs of individuals at risk of diabetes. Ultimately, we aspire for our research to contribute to the broader medical community's efforts in combating diabetes mellitus, ensuring that patients receive the most effective and personalized care possible. This research is not just a step forward in scientific discovery but also a commitment to enhancing the quality of life for those living with diabetes.

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