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Diseases associated with abnormal tyrosine metabolism

(Literature research according to the standard EN 13612: 2002)

No.: DAATE/ZYB/2021

Introduction

Carry out a literature search in accessible scientific publications and find out, according to the categories (Parkinson's disease, Mild depression, Albinism, Pigment disorders (freckles, brown spots) and malignant melanoma tumors, Phenylketonuria, Tyrosinemia, Malignant tumors), summarize the abnormal tyrosine metabolism related diseases which probably affect the results of CarciReagent test.

Content:

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1, Name of in vitro diagnostic device for self-testing
CarciReagent

2, Description of in vitro diagnostic device for self-testing
Test kit for the detection of the approximate amount of monohydroxyphenol metabolites (tyrosine) in urine (Lay semi-quantitative test for self-testing) (Chemical chromogenic method)

3, Intended use of the in vitro diagnostic device for self-testing
"CarciReagent - an in vitro diagnostic device for self-testing, intended for the detection of monohydroxyphenol metabolites (tyrosine) and its approximate amount in the patient's urine (Lay semiquantitative test)"

4, Principle and function of in vitro diagnostic device for self-testing
The basic principle of the test is based on the improved method of Millon's reagent (Millon's reagent), which monitors the increased amount of tyrosine (monohydric phenolic amino acids and their metabolites) in the urine. By changing the color of the mixture in the ampoule after adding 3 ml of morning urine (middle urine stream), the reaction color cascade can be used to determine if urine samples contain increased amounts of these metabolites. The reagents in the ampoule and the tyrosine content in the urine show a characteristic chromogenic response that can be used for the clinical diagnosis of intracellular metabolic abnormalities (detection of possible changes or disorders in metabolism within the human cell). The determined approximate content of tyrosine in urine (according to the attached table from 0–2000 mg per liter of urine) reacts with the chemical reagent and, depending on its amount, turns colored. According to the enclosed color scale, the test result can be read from No. 1 to No. 8. The result from No. 1 to No. 3 is the amount of tyrosine in the normal concentration, so the result is considered negative, and no increased amount of tyrosine has been demonstrated. With results No. 4 and No. 5, it is already a positive finding of an increased amount of tyrosine in the urine. If the tyrosine concentration is higher than 500 mg per liter of urine, ie result No. 6, No. 7, No. 8, this is a positive result, a high content of tyrosine in the urine may indicate a more serious disease. In case of positive results, it is recommended to perform a more thorough examination by a general practitioner in order to exclude the risk of a possible serious illness.

5, Objective of literature research for functional evaluation of in vitro diagnostic device for self-testing
Carry out a literature search in accessible scientific publications and summarize the abnormal tyrosine metabolism related diseases which probably affect the results of CarciReagent test.

6, Plan of literature research for functional evaluation of in vitro diagnostic device for self-testing

6a, Responsible person of literature research for functional evaluation of in vitro diagnostic device for self-testing
Huang Ganhui (Professor at Nanchang University)

6b, Timetable for literature research for functional evaluation of in vitro diagnostic device for self-testing
1.2.-15.4.2021

6c, Design of literature research for functional evaluation of in vitro diagnostic device for self-testing

This literature research is about the abnormal tyrosine metabolism related diseases, include Parkinson's disease, Mild depression, Albinism, Pigment disorders (freckles, brown spots) and malignant melanoma tumors, Phenylketonuria, Tyrosinemia, Malignant tumors. To summarize the probably affect the results of CarciReagent test.

6d, Key words of literature research for functional evaluation of in vitro diagnostic device for self-testing

Key words: tyrosine, melanin, tyrosinemia, urine, amino acid metabolites, malignant, tumors

7, Structure of literature research for functional evaluation of in vitro diagnostic device for self-testing

7.1 Parkinson's disease

Tyrosine can generate dopa in the adrenal medulla and nerve tissue under the action of tyrosine hydroxylase, and then decarboxylate to generate dopamine. After hydroxylation to generate norepinephrine, and then through methylation to generate epinephrine, it becomes Neurotransmitter or hormone, decreased dopamine production in brain tissue can lead to Parkinson's disease.

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7.2 Mild depression

Tyrosine is a neurotransmitter-the precursor of norepinephrine and dopamine, these two transmitters can regulate mood and play other roles. Tyrosine is an emotional stimulant. Lack of enough tyrosine can cause a lack of norepinephrine in the brain, causing some mood disorders, such as mild depression.

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7.3 Albinism

Tyrosine is catalyzed by tyrosinase to produce dopa in melanocytes, and then through oxidation, decarboxylation, and other reactions, melanin is finally produced. Congenital deficiency of tyrosinase causes albinism.

Albinism is a hereditary leukoplakia caused by a lack of melanin in the skin and accessory organs or a synthesis disorder caused by tyrosinase deficiency or hypofunction. The disease is a family hereditary disease, mainly autosomal recessive inheritance. The main clinical manifestations are the lack or reduction of melanin in the skin, hair and eyes of the whole body, the skin and body hair are white or yellow-white, the retina is unpigmented, and the iris and pupils are pale pink and photophobia. According to the different tissues invaded, albinism can be divided into oculocutaneous albinism (OCA), where the lesions are limited to the skin and eyes, and ocular albinism (OA), where the lesions are limited to the eyes. The incidence of albinism in the population is about 5 to 10 per 100,000. It can occur in all races without gender differences, and it is more likely to occur in people who are married to close relatives.

Tyrosinase can convert tyrosine into melanin. Type I patients have mutations in the tyrosinase gene that cause lack of tyrosinase activity (type IA), decreased activity (type IB, I-MP), or lower enzyme activity. Decreased at higher temperatures (I-TS type), tyrosinase is a key enzyme in the melanin biosynthesis pathway, and its lack or decrease in activity can lead to reduction or loss of skin pigmentation. Type II patients have P gene deletion or mutation, resulting in loss of P protein function. P protein is related to the transport of melanin precursor tyrosine into the melanosome membrane and is a protein necessary for the production of melanin. Loss of P protein function can lead to Melanin synthesis disorder. Type III patients are mainly caused by mutations in the gene encoding tyrosine-related protein 1 (TYRP1).

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7.4 Pigment disorders (freckles, brown spots) and malignant melanoma tumors

Tyrosinase (EC 1.14. The occurrence of melanoma tumors is related to treatment.

Tyrosinase is mainly involved in two reaction processes: it catalyzes the hydroxylation of L 2 tyrosine into L 2 dopa and oxidizes L 2 dopa to form dopaquinone. After a series of reactions, dopaquinone forms melanin. Tyrosine Acid enzyme has an important physiological function in the organism. At the same time, it is also related to the occurrence of diseases such as excessive deposition of melanin such as freckles and brown spots in the human body.

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7.5 Phenylketonuria

Tyrosine can also be catalyzed by transaminase to produce p-hydroxyphenylpyruvate, which is transformed into fumaric acid and acetoacetic acid through intermediate products such as homogentisic acid. Therefore, phenylalanine and tyrosine are sugar-producing and ketogenic amino acids. Homogenic acid catabolism enzymes are congenital defects, and homogentisic aciduria can occur.

In the absence of phenylalanine hydroxylase, phenylalanine cannot be converted into tyrosine, phenylalanine accumulates, and a large amount of phenylpyruvate is generated by transamination, which is further converted into phenylacetic acid. At this time, a large amount of metabolites such as phenylpyruvate appear in the urine, which is called phenylketonuria.

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7.6 Tyrosinemia

Tyrosinemia is a rare autosomal recessive genetic metabolic disease. Due to tyrosine degradation, it causes damage to multiple organs such as brain, liver, kidney, and bone. The prognosis is poor, and the rate of death and disability high. Different types of patients have different clinical manifestations. Low-tyrosine diet and drug therapy are the main intervention methods, and liver transplantation is necessary if necessary. According to different defective enzymes, tyrosinemia is divided into three types:

1) Tyrosinemia type I is due to FAH gene mutations leading to defects in the terminal enzyme fumaryl acetoacetate hydrolase in the tyrosine metabolism process, tyrosine and its metabolites succinylacetone, 4-hydroxyphenyllactic acid and 4 -Accumulation of hydroxyphenylpyruvate, etc.
2) Tyrosinemia type Ⅱ is due to the lack of tyrosine aminotransferase caused by tyrosine decomposition disorder.
3) Tyrosinemia type III is caused by the deficiency of 4-hydroxyphenylpyruvate dioxide.

Clinical manifestations

The condition of patients is different, and there are significant individual differences. Most untreated patients die before the age of 10, and the prognosis of early detection and treatment can be greatly improved.

Tyrosinemia type I
According to the age of onset, it is divided into acute type, subacute type and chronic type.
(1) Acute type
The child develops symptoms within a few days to a few weeks after birth. The main clinical manifestations are acute liver failure, jaundice, anorexia, bleeding tendency, vomiting, pale skin, slow growth, hepatomegaly, and rapid progress of the disease. If no treatment is given, Most die within 1 year of age.
(2) Subacute and chronic type
The onset usually occurs between 6 months and 2 years of age, liver, kidney, and nerve damage. Some children have rickets, reflexes, etc., and the children often cry because of severe pain. If untreated, it can develop into hepatocellular carcinoma.
The onset usually occurs between 6 months and 2 years of age, liver, kidney, and nerve damage. Some children have rickets, reflexes, etc., and the children often cry because of severe pain. If untreated, it can develop into hepatocellular carcinoma.

Tyrosinemia type II
The child is mainly characterized by ocular symptoms. A few months after birth, symptoms such as tearing, photophobia, and conjunctival congestion appear, followed by corneal ulcers and opacity, nystagmus, etc., and blisters, ulcers and hyperkeratosis on the palms and soles of the hands. 1 Intellectual and developmental disabilities after age.

Tyrosinemia type III
Children are generally asymptomatic. Mild mental retardation, cramps, and ataxia may also occur.

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7.7 Malignant tumors
Mainly include digestive tract malignant tumors (gastric cancer, bowel cancer), liver cancer, nasopharyngeal cancer, lymphoma, breast cancer, gynecological malignant tumors, lung cancer, etc.

Increased level of monohydroxyphenol metabolites (tyrosine) in urine is mainly related with the detection of abnormal amino acid metabolism in patients with malignant tumors, and it has appeared in the early stage of tumor. At this time, protein decomposition is enhanced, and amino acid catabolism is weakened. Amino acids are reused in tumor cell protein synthesis, and excess unusable amino acids are excreted.
A large number of experimental studies have found that the tyrosine content in the urine of almost all patients with malignant tumors increases significantly, reaching 50% to 150%, far exceeding normal people. If we can simply detect the content of tyrosine in human urine, thereby judging the metabolic activity of malignant tumor cells in the human body, conducting risk assessment, and achieving the purpose of early assistance in tumor screening.
Studies have confirmed that the positive detection rate of urine tyrosine test in patients with malignant tumors is significantly higher than that of normal health people and patients with benign tumors. The difference is statistically significant, and in different types of malignant tumors such as gastrointestinal malignancies (gastric cancer, bowel cancer), liver cancer, nasopharyngeal cancer, lymphoma, breast cancer, gynecological malignancies, lung cancer, etc. all have a high level of tyrosine content.
When the level of monohydroxyphenol metabolites (tyrosine) in urine is higher than average, it only indicates that there is abnormal tyrosine metabolism in the human body and cannot diagnose malignant tumors. Other detection methods need to be combined to rule out and diagnose. However, due to the above-mentioned characteristics, it can be used as a means of early tumor screening in clinical practice, and it has more important significance for the early diagnosis of tumors.

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8. Literature research conclusion

According to the above literature review, diseases that can cause low levels of tyrosine in urine include Parkinson's disease, depression (tyrosine deficiency), Albinism (genetic disorder), Phenylketonuria (PKU), Tyrosinemia (metabolic hereditary disorders).
Diseases that can cause high levels of tyrosine in urine are malignant tumors, mainly include digestive tract malignant tumors (gastric cancer, bowel cancer), liver cancer, nasopharyngeal cancer, lymphoma, breast cancer, gynecological malignant tumors, lung cancer, etc.
Diseases that probably increase tyrosine in the urine are pigment disorders (freckles, brown spots), diabeteses, stomach ulcers and gastritis.

9. User manual recommendation

When this reagent is used for testing, patients with pigment disorders (freckles, brown spots), gastritis and gastric ulcers who are accompanied by Helicobacter pylori infection, as well as patients with diabetes, are not suitable for this test.

10, References and list of documents

References have been made in each of the above sections.