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Contents

Review Articles

Review Article

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Volume 5 Number 1, January – June 2020

Cardiovascular Disease and its Diagnosis with Cardiac Markers

Gulshan Jagdish Karhade[1], Jopasana S Adkane[2], Sachin C Narwadiya[3]

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Abstract

Cardiovascular diseases (CVDs) are becoming major cause of deaths in India. Ischemic heart disease and stroke are the are major responsible among the deaths of CVDs. As per the Global Burden of Disease study the CVD death rate of 272 per 100000 populations in India is higher as compared to the global average of 235 per 100000 populations. The markers of various diseases always attract researchers for development of technologies. These technologies are then helpful for the early diagnosis of diseases. The markers of CVDs enable the doctor to diagnose the onset of disease and start its management. Diagnostics measures of Lactate dehydrogenase (LDH), creatine kinase (CK) or aspartate aminotransferase (ASAT) enzymatic activities are good indicator of acute myocardial infarction (AMI). Enzymatic assessment and myoglobin findings slowly replacing with assessment of cardiac troponins (I and T) and its high sensitivity versions are leading to help in acute myocardial infarction Diagnostics. Many tests were performed to assess the severity of the heart failure in case of recent onset of heart attack but more emphasis is on the development of markers which can be used in cardiovascular disease prevention and reduced risk of cardiovascular disease.[3]

The cardiac troponins is mostly used as cardiac markers for the diagnostics for Acute coronary syndrome and MI patient with elevated troponin levels but negative creatine kinase - MB (CK - MB) use in diagnosed in unstable angina or minor myocardial injury.[2]

Keywords: Cardiovascular disease; Lactate dehydrogenase (LDH); Creatine kinase (CK); Cardiac troponins (I and T)

Introduction

Cardiovascular disease is the one of the high death rate causing disease worldwide. Many people die annually from cardiovascular disease. Cardiovascular disease is a group of disorders of the heart and blood vessels.[6]

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First markers for cardiac disease diagnostics were described already in the late 1950 and early 1960. Since those days cardiac disease diagnostics has gone through a significant evolution. First improvement was development of immunological based test with the help of using polyclonal antibodies.[9]

Cardiac markers are of great importance in the timely accurate diagnosis and management of heart function. Cardiac markers helpful in early prediction or diagnosis of heart disease. Cardiac biomarkers are also a powerful tool for triaging.[5]

Table 1: Historical Perspectives of Cardiac Markers

S No	Year	Cardiac Marker
1	1954	serum glutamic-oxaloacetic transaminase-SGOT or aspartate aminotransferase-AST)
2	1955	Lactate dehydrogenase- LDH
3	1960	Creatine Kinase- CK
4	1972	Creatine Kinase- CK isoforms by electrophoresis
5	1975	Creatine Kinase-MB by immune-inhibition
6	1975	Myoglobin
7	1985	Creatine Kinase-MB by mass immunoassay
8	1989	Troponin T
9	1992	Troponin I

Ischemic Heart Disease

Definition- Ischemic heart disease is a condition of recurring chest pain or discomfort that occurs when a part of the heart does not receive enough blood supply.

It is a condition is term as an acute or chronic disease of the heart cause due to insufficient blood supply to the coronary artery. May be the coronary arteries are narrow, Functional disturbances, thrombosis involvement may occurs or combination of organic, functional or thrombosis also occurs.

Atherosclerosis of the coronary artery is the commonest cause of Ischemic Heart Disease. When plaque narrows the arterial diameter more than 70% it can cause the stenosis and then obstruction increases resulting into insufficient blood flow. The Ischaemic is formed obstruction and its outward symptoms will appear like Angina pectoris. Identification of Ischemia is involuntary contractions of a muscle typically harmless and temporary but can be painful, of the smooth muscle of the arterial wall. Mostly it's seen in a condition in which a endothelial inner lining of the small arteries fails to perform all of its important functions due to the external stimuli like cold, tobacco, smoking, physical inactivity, mental stress also including diabetes or metabolic syndrome, hypertension.[10]

Occurrence of the plague in arteries will rupture then subendothelial structures of the vessel wall. The wall then becomes exposed, and it leads to blood clotting due to platelet activity which may lead to coronary artery closure which is caused as acute coronary syndromes.

The gradation of atherosclerosis is assessed depending on the percentage of arterial lumen narrowing, due to sclerotic plaques, when arterial lumen narrowing 25% then coronary. Atherosclerosis is in Grade I, when arterial lumen narrowing 50% then coronary atherosclerosis is in Grade II, when arterial lumen narrowing 75% then coronary atherosclerosis is in Grade III, when the arterial lumen narrowing above 75% then coronary atherosclerosis in Grade IV.[4]

Myocardial infarction, unstable angina pectoris, sudden cardiac death.[1]

Atherosclerosis

When denerative involvement of arterial walls characterized by the accumulation of lipid, inflammatory of the vessel wall and fibrous tissue proliferation is called as atherosclerosis

In simple language a disease of the arteries which is characterized by the deposition of fatty material on their inner wall.

Previously in the early practising atherosclerosis was considered as a mechanical process when lipid is accumulated in the wall of the vessels and afterwards calcium deposition.

Most important symptoms are seen in current practise, they are as follows

Mostly atherosclerosis caused by increased penetration and infiltration of artherogenic lipoproteins, inflammatory cells from the blood from endothelium, accumulation in the sub-endothelial space,

In the Grade III or Grade IV fibro productive processes may occur in depositing lipids and inflammatory infiltration of the vessels wall.

Acute Coronary Syndromes : It is a condition due to the sudden reduction or blockage of blood flow to the heart mostly due to plaque rupture or clot formation in the heart's artery.

Pathophysiology: like Grade III and IV that is 50% to 75% of arterial lumen narrowing.

Myocardial Infarction

Acute myocardial infarction is a medical terminology of heart attack in Lay man word it is called as heart attack. Causes for myocardial Infarction include atherosclerosis, coronary

occlusion secondary to vasculitis, ventricular hypertrophy and coronary artery. Myocardial Infarction is a condition with cardiac ischemia; necrosis assumes coagulative character, caused by high protein content.[13]

Cardiac Markers: In high probability cardiac Troponin I, Troponin T concentration of CK-MB concentration.

As the rapid onset of signs and symptoms, secondary to abnormal cardiac function. Cardiac dysfunction can be relates to systolic or diastolic dysfunction 13 abnormalities in cardiac rhythm or to preload and afterload mismatch.

In Acute heart failure sudden worsening of the heart function where the heart is unable to pump blood flow from venous circulation to the lungs, or from lungs to the arterial circulation which leads to congestion in some organs tissue oxygenation hypoxia.

Types of Heart Failure

Acute or chronic Failure can begin on either the left or right side of your heart or both sides may fail at the same time. The chambers where your blood is pumped out of the heart are called ventricles. If heart muscle is weak then ventricles can stretch out which causes failure to work efficiently.

Left Sided Heart Failure: It occurs when the left ventricle does not pump efficiently. When the heart pumps blood comes out and backs up into the lungs and due to that Shortness of breath is seen.

There are two types of two left sided heart failure:-

Systolic Heart Failure: it is mostly seen. It is the commonest cause for heart failure. It happens when heart muscle is weak or in case of cardiomegaly.

When systolic heart failure occurs, the heart left ventricle is unable to contract or shorten. It occurred that prevents blood from being pumped effectively out to the body.

Diastolic Heart Failure: In Diastolic heart Failure blood isn't able to properly fill the heart left ventricle which leads to heart pumps less blood to body as compared to normal. Low blood flow caused by the ventricular stiffening. Symptoms of Diastolic heart failure are not able to be identified as different or distinct from those of systolic heart failure. Right sided heart Failure:- This usually Occurs Simultaneously with left sided heart failure. Failure of the left ventricle results in increased pressure and subsequent damage to the right side heart from pumping efficiently. Right side heart is unable to pump correctly, fluid accumulates in veins. This may cause swelling over legs and feet.

Laboratory diagnostic test for myocardial infarction with use of cardiac markers.

Electrocardiogram

An electrocardiogram (ECG) is a recording of the electrical activity of the heart and its visible Recording.

Characteristic changes in case of MI on the ECG, which seen that increase or decrease of ST segment is a secure diagnosis of heart attack can be made quickly in the emergency room and treatment can be started Immediately.[5]

Cardiac Markers

The various cardiac markers includes enzymes - CK-MB , SGOT, LDH, proteins - Troponin T, Troponin I, Myoglobin and inflammatory markers - CRP, Amyloid A.[6]

Cardiac Profile Test

Group 1 Test: Blood sugar F and Post Prandial-PP, Blood urea Nitrogen, Serum creatine, Serum electrolytes - Na and K

These tests are useful to find out the possibility of disturbed carbohydrate metabolism and existence of pre-renal condition of the patient.

Group 2 Tests: Total cholesterol Very low density Lipids and Low Density Lipids HDL- cholesterol,High Density Lipids- HDL cholesterol,Triglycerides - TG Cholesterol

Group 3 Test: Troponin, Myoglobin, SGOT, CPK – MB

Troponin

It is the contractile protein of the myofibril. Cardiac Markers currently available, cTnI and cTnT offers the highest degree of cardiac Specificity. In case of Myocardial Infarction-MI, the troponin is found to be

Quantitative and qualitative monoclonal anti-body based immunoassay can be done for cTnI in serum or plasma on whole blood. In addition to detecting an MI, elevations of either cTnI have

prognostic value and are associated with future adverse cardiac events.

Myoglobin

Myoglobin has low molecular weight protein that is about 18 KD. Skeletal and cardiac muscle and is involved in oxygen binding seen. Since myoglobin is found in most tissues, it has the least specificity to any of the cardiac markers. Due to its small size and cytoplasmic location, it appears in serum rapidly after release from injured muscle of either Skeletal or cardiac muscle.

SGOT (Serum Glutamate Oxaloacetate Transaminase)

The mitochondria of heart muscles are rich in SGOT and release on cell destruction. In MI, The SGOT is found initial rise in - 3 - 8 hours after onset of the attack and return normal in - 3 - 6 days.

CPK (Creatinine Phosphokinase) CK (Creatine Kinase)

CK Molecular weight 86 kilodaltons. Creatine kinase is an enzyme responsible for the conversion of creatine into phosphocreatine, the energy source for muscle contraction. CK is a dimer and 3 different forms of enzyme with varied tissue distribution. Since CK is found in all muscle tissue, elevations of the total activity of this enzyme are not specific for cardiac damage. Reference range-10-13 units/L

CKMM - Predominant is skeletal muscle:CKBB - Predominant in brain tissues while CKMB - In heart muscle makes up about 20% of the CK activity, in skeletal muscle CKMB is generally only about 1%.

In MI, CKMB is found to be, initial rise in – 3-8 hours than peak level in - 20- 24 hours and return to normal within- 2-3 days.

LDH (Lactate Dehydrogenases)

LDH molecular weight 135 kilodaltons and it is found in the cytoplasm of all cells. The highest activity of LDH is found in skeletal muscle, livers, heart, kidney and Red Blood Cells. The cardiac muscles are rich in LD1. The LD1 is clinically 90% sensitive at 24 hours Symptom onset. The Ratio of LD1/LD2 is normally < 1 but in case of MI LD1 increases over LD2 which is also called "Flipped LD pattern" (90% sensitive and 85% specific). There are 5 isoforms of LD, composed of 4 Subunits peptides of 2 distinct types designated M (for muscle) and H (for heart). LD1 - HHHH:- heart, kidney and RBC, LD2 - HHHM:- RBC, LD3 - HHMM:- Brain, LD4 - HMMM:- liver, LD5 - MMMM:- muscle. In case of MI, LD1 is found to be raised as and the initial rise occur in 6 -12 hours reaching to peak level 72-144 hours and returned back to normal within 8-14 days.[11,12,13]

Conclusion

The Myocardial infarction is critical situation for the patients. Management of the Myocardial infarction is depends on timely diagnosis of marker levels. The assessment of markers is indicative of the acuteness of the cause of infarction. Hence these Enzymes, Proteins are helpful for the physician to decide the line of treatment.

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Review Article

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Evaluation of Diagnostic Significance of Novel Corona Virus

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Abstract

In the current scenario viral diseases continue to emerge a serious public health hazards. Viruses are parasite like molecules that cannot reproduce by itself, for the production of number of viruses it requires cell machinery. Coronaviruses (CoVs) (order Nidovirales, family Coronaviridae, and subfamily Coronavirinae) are a positive sense, single-stranded RNA genome of 26 to 32 kilobases (kb) in length, and enveloped viruses. It genomes is largest in RNA viruses. Many diagnostic tests for coronavirus disease 2019 (COVID-19) are available so far. An RT-PCR test is considered very reliable because it detects less number of virus particles in swabs. D-dimer one of the markers of inflammation, its levels were higher in COVID-19 patients. In this review we discuss about the various diagnostic test for corona virus and their reliability

Keywords: Coronaviruses; Diagnosis; RT-PCR; D-Dimer; Prognosis

Introduction

Corona viruses, belongs to the family Coronaviridae are a large family of viruses that cause "the common cold" or up to 30 percent of upper respiratory tract infections in adults, prevalent almost all part of the world. First described in detail in the 1960s, the coronaviruses single-stranded RNA viruses roughly 26,000 to 32,000 bases long that measure approximately 120 nm when visualized under an electron microscope it appear like a crown (coronam is the Latin term for crown) due to the presence of Club-shaped spike glycoproteins on the envelope. Four major types of these viruses exist. They're known by the Greek letters alpha, beta, delta and gamma. Alpha and beta infect mammals, including bats, pigs, cats, and humans. Gammacoronavirus commonly infects birds such as poultry, while Deltacoronavirus infects both birds and mammals.

In structurally complete viral particle, four major structural proteins: the spike (S) protein, nucleocapsid (N) protein, membrane (M) protein, and the envelope (E) protein, encoded by coronaviral genome play an important role.[1-3] The S protein play an important role in the attachment of the virus to the host cell surface receptors and help in the fusion between viral and host cell membranes to finally support the viral entry into the host cell.[4–6] N protein helps in the binding to the CoV RNA genome, making up the nucleocapsid.[7] N protein also involved in other aspects of

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the CoV replication cycle and the host cellular response to viral infection.[8] The N is localized into the endoplasmic reticulum (ER)-Golgi region has proposed a function for it in assembly and budding.[9,10] The diagnosis of corona virus largely varies from molecular biology to immunology. The real-time reverse transcription-PCR (RT-PCR) most preferred testing method.

Currently, virus nucleic acid Real Time-PCR (RTPCR), CT imaging and some hematology parameters are the primary tools for clinical diagnosis of the infection.[11] The virus nucleic acid RT-PCR test has become as the current standard diagnostic method for diagnosis of COVID-19. A real-time PCR test kit has certain limitations: 1) these tests have turnaround times is high and is complicated in operation; for the generation of results it takes on average over 2 to 3 hours. 2) The PCR equipment is expensive and trained technicians to operate. 3) In RT-PCR sometimes results are false negatives for COVID-19.[12] There are certain limitations that make RT-PCR unsuitable for use in the field for rapid and simple diagnosis and screening of patients. Therefore, there is an urgent need to develop a rapid, simple to use, sensitive, and accurate test to quickly identify of SARS-CoV-2 patients.

Testing of specific antibodies such as IgM and IgG of SARS-CoV-2 in patient blood is a good choice for rapid, simple, highly sensitive and it provides the first line of defense during viral infections, high affinity IgG responses play an important role for long term immunity and immunological memory[13] It was reported that after SARS infection, IgM antibody could be detected in patient blood after 3 - 6 days and IgG could be detected after 8 days.[14,15]

Currently, development of serological tests (i.e., blood tests for specific antibodies) is still going on.[16-18] Zhang et al. detected immunoglobulin G and M (IgG and IgM) from human serum of COVID-19 patients using an enzyme-linked immunosorbent assay (ELISA) which uses SARS-CoV-2 Rp3 nucleocapsid protein in which 90% amino acid sequence homology to other SARS-related viruses has been reported.[16] Xiang et al. also detected SARS-CoV-2 IgG and IgM antibodies in suspected cases.[17] For detection of COVID-19 some other protein or cellular markers are currently used. By Guan et al infected patients had elevated levels of C-reactive protein and D-dimer and in some pateints low levels of lymphocytes, leukocytes, and blood platelets are found.[19] The problem with these biomarkers is that they are also show abnormal in other illnesses. For the improvement of specificity a multiplex assay with both antibody and small molecule markers can be used.

In epidemic areas Chest CT may be considered as a primary tool for the current COVID-19 detection. Chest CT outperformed lab testing in the diagnosis of 2019 novel coronavirus disease (COVID-19). The recent study found that CT should be used as the primary screening tool for COVID-19. CT has limited sensitivity and specificity for COVID-19 than RT-PCR testing. Chest CT should be considered a supplemental diagnostic tool, particularly for patients who show symptoms. Chest CT is a conventional, noninvasive imaging modality with high accuracy and speed. On the basis of available data reported in recent literature, most of the patients with COVID-19 had characteristic CT features of the disease[20-22], such as different degrees of ground-glass opacities with and/or without crazy-paving sign, multifocal organizing pneumonia, and architectural distortion in a peripheral distribution. Initially Chest CT showed patchy ground-glass opacity, and it rapidly progressed to segmental mixed consolidation and ground-glass opacity, and it resolved in left upper lobe, but showed multifocal ground-glass opacities after few days, and they resolved after some time. The RT-PCR test also shows positive results. By CT findings alone it is difficult to distinguish COVID-19 pneumonia from other viral pneumonia; however, the utility of chest CT increases to detect early change of COVID-19 in cases which RT-PCR tests show negative results.

After COVID-19 outbreaks, the risk of thrombosis and bleeding has attracted much attention. D-dimer is a fibrin (relatively small protein) fragment degradation product that is often used to measure and assess clot formation by fibrinolysis. The liver produces several important proteins involved in the coagulation process, one of which includes fibrinogen. A single fibrinogen molecule is a symmetrical dimer that is made up of three pairs of three different polypeptide chains, which include α, β and γ, each of the intertwined polypeptide chains that comprise a single fibrinogen molecule is held together by disulfide bonds. D-dimer elevations were seen in 3.75–68.0% of the COVID-19 patients.[23-25] D-dimer level is higher in severe cases and may be used as a prognostic biomarker for the community-acquired pneumonia (CAP) and chronic obstructive pulmonary disease (COPD) patients[26-28], and D-dimer > 1 µg/ml is one of the risk factors for mortality in adult in patients with COVID-19. However, the role of D-dimer in

COVID-19 patients requires further investigation. A D-dimer concentration is a sensitive test for the diagnosis of thrombotic states, including pulmonary embolism and DIC.[29] Therefore, increase in D-dimer levels in COVID-19 patients' play an important role in disease severity, pulmonary complications, and risk of venous thromboembolism in the setting of a pro-thrombotic state. This would assist with risk stratification and therapeutic intervention that might reduce COVID-19 related morbidity and mortality.

Conclusion

Identification of the rapid and early laboratory diagnosis is critical to diagnose novel corona virus, control the pandemic, and reduce the economic impact of COVID-19 worldwide. RT-PCR test is gold standard for SARS-CoV-2 identification, which uses conserved regions of the viral genome and the reduced rate of false-negative results are due to a large number of genetic variations, mismatches between primers, probes, and target. IgM and IgG antibody detection of SARS-CoV-2 is a supportive molecular diagnostic tool. The immunological and molecular tests are not suitable for point-of-care diagnosis due to time-consuming, kits and equipment are expensive. Typical CT findings can help early screening of suspected cases and diagnosis of COVID-19. D-dimer levels increases in case of inflammation in COVID-19 patients and have limited predictive value for thrombosis, so in the treatment of COVID-19 patients, so the value of D-dimer levels should be observed dynamically.

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Review Article

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Myasthenia Gravis: an Autoimmune Neuromuscular Disorder

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Abstract

Myasthenia gravis (MG) is an autoimmune disease which is caused by impaired transmission of signals at neuromuscular junction and results in problem with muscle contraction. At neuromuscular junction neurotransmitter acetylcholine is released by nerve ends which binds to the receptor at surface of muscle cells. The patients with MG the acetylcholine receptors are blocked or destroyed or altered by its own antibodies and interrupts the communication between nerve cells and muscle cells. MG includes symptoms like weaken muscles, tiredness by any regular work e.g. chopping vegetables, movement of eye, drooping of eyelids and double vision. MG is classified in five types out of which the two main forms are ocular and generalized myasthenia gravis. Diagnosis and treatment of MG can be done by various process. MG preferably affects young women on their20s and 30s and old men after their 60s.

Keywords: Acetylcholine; Autoimmune disease; Myasthenia gravis; Neuromuscular junction.

Introduction

Immune system of human body protect it from foreign invaders or antigens e.g. bacteria, virus. Immune system fights with these antigens and provides immunity to body.[1]

The body has immune tolerance and is normally able to distinguish its own self-antigens from foreign non-self antigens and does not mount an immunologic attack against itself. At times the body loses tolerance and mounts an abnormal immune attack, either with antibodies or T cells, against a person's own self antigens.[1]

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Autoimmune disease results from the activation of self-reactive T and B cells that, following stimulation by genetic or environmental triggers, cause actual tissue damage. Examples include rheumatoid arthritis, Myasthenia gravis and Type I diabetes mellitus.[1]

An autoimmune disease Myasthenia gravis is a neuromuscular disorder which happens when tissues of human body are attacked by its own immune system and breaks the connection or linkage between nerve and muscle cells- the neuromuscular junction, resulting in muscle weakness. Myasthenia gravis is a Latin word which means "grave muscle weakness".[2]

Myasthenia gravis preferentially affects young women under fourth's and old men above sixty's.[6]

The first reported case of MG is likely to be that of the Native American Chief Opechancanough, who died in 1664.[7]

People living with myasthenia gravis might get weak and tired, sometimes getting weaker from repetitive movements like chopping vegetables.[6]

Symptoms

In myasthenia gravis degree of muscle weakness varies greatly among individuals. MG mostly affects muscles which are responsible for movement of eye and eyelids, facial muscles and swallowing, major symptoms include drooping of one or both eyelids (ptosis), blurred or double vision (diplopia) due to weakness of the muscles that control eye movements, a change in facial expression, difficulty swallowing, shortness of breath, impaired speech (dysarthria), weakness in the arms, hands, fingers, legs, and neck. Sometimes MG gets severe and affect muscles which are responsible for breathing-myasthenia crisis.[2]

Causes

Nerve cells communicate and control muscle cells at neuromuscular junction. When this processes in interrupted and transmission of nerve impulses to muscles are blocked, contraction of the muscles actively is compromised and causes myasthenia gravis.

At NMJ, nerve cell's endreleasesa chemical named acetylcholine which binds to acetylcholine receptors on the surface of muscle cells and activates muscle contraction.[5]

In individuals with MG antibodies are released and blocks or destroy the acetylcholine receptors on the surface of muscle cells at NMJ. This process blocks the transmission and results in problem with muscle contraction.

Main cause of myasthenia gravis is self-antibodies impairing signal transmission at NMJ but in some cases muscle-specific kinase antibodies are also responsible for this.

Thymus gland plays an important role in development of immune system and controls the immune function. Research shows that about ten to fifteen percent individuals with MG have thymomas-most often harmless but can become cancerous and others have more than usual number of cells in thymus. However thymus gland considered related to the myasthenia gravis but its exact function is unknown.

MG is an autoimmune disease but in about three to five percent of patients congenital myasthenia gravis is seen but inheritance pattern is unknown.[2]

Classification

Typically divided into five types: congenital myasthenia gravis, generalized myasthenia gravis, ocular myasthenia gravis, transient neonatal myasthenia gravis, and juvenile myasthenia gravis, depending on time of disease onset, the cause of the neuromuscular dysfunction, and the muscle groups affected.[3]

Congenital Myasthenia Gravis

Congenital disease is the defect caused by having a particular trait from birth or inherited by parents or family. Congenital myasthenia gravis is a genetic defect rather than autoimmune disease which is the cause of other types of this disease.

In this disease communication between nerve and muscle cells at neuromuscular junction interrupted by transformation in normal genetic order- gene order. For e.g. acetylcholine receptor encoding genes affected. The various types of congenital myasthenia gravis are defined by the location and type of genetic defect that causes poor neuromuscular signaling.

Ocular Myasthenia Gravis

Ocular means connected with eye or vision. Ocular myasthenia gravis is related with weakness and fatigue of the muscles linked with eye and eyelids, drooping eyelids and double vision are mostly occurred symptoms. Ocular myasthenia gravis is limited to muscles of these area and do not spread to other region.

Generalized Myasthenia Gravis

Generalized myasthenia gravis is a types in which muscle weakness and fatigue also spreads to the facial muscles and limbs not only to the muscles of eye and eyelid regions.

In some patients it leads to the myasthenia crisis which is a life-threatening disorder characterized by worsening of muscle weakness, resulting in respiratory failure that requires intubation and mechanical ventilation.

Transient Neonatal Myasthenia Gravis

Infants from Mothers who are suffering from myasthenia gravis are likely to develop myasthenia gravis after birth and shows symptoms like impaired sucking and swallowing, a weak cry, and respiratory insufficiency.

Juvenile Myasthenia Gravis

Juvenile myasthenia gravis is not very common and shows the symptoms before the onset of puberty. In patients with juvenile MG symptoms include limited eye muscles movement, trouble in swallowing and tiredness.

Diagnosis

Physical and Neurological Examination

Reviewing an individual's medical history, physical and neurological examination is first step to diagnose MG which further includes testing muscle weakness and fatigue by checking reflexes, muscle strength and tone, coordination, sense of touch, and look for impairment in eye movements.[4]

Endrophoniumtest

In this test to check ocular muscles weakness, injection of edrophonium chloride is provided to the patients of MG which reduces muscle weakness and temporarily cause active muscle contraction by blocking the enzyme responsible for breakdown of acetylcholine which leads to increase in acetylcholine at NMJ.[4]

Blood Test

Occurrence of abnormal antibodies that disrupts acetylcholine receptor at muscle sell surface is detected by blood test along with detection of another type of antibody called muscle specific kinase antibody associated with non-specific process of alteration and damage of nerve-muscle transmission. In some individual neither of these antibodies are detected-seronegativemyasthenia.[4]

Electromyography

In this test fine wire electrodes are inserted into muscles. These electrodes electrically stimulate single muscle fibers and measure the electrical activity traveling between the brain and the muscle.[4]

Imaging

Patients with thymoma have some abnormality in thymus gland which is detected by A computerized tomography (CT) scan or a magnetic resonance imaging (MRI) scan.[4]

Treatment

MG can be controlled by several therapies that improve muscle weakness.

Thymectomy.

In Patients with thymoma in some cases removal of thymus gland is a good way for rebalancing of immune system.

Anticholinesterase Medications

Anticholinesterase agents reduce the muscle weakness and improve the neuromuscular transmission process of breakdown of acetylcholine at the neuromuscular junction.[2]

Immunosuppressive Drugs

These drugs reduce the production of abnormal antibodies. E.g. prednisone, azathioprine.[2]

Plasmapheresis and Intravenous Immunoglobulin

These therapies eradicate the destructive antibodies, but their effect usually only lasts for a few weeks to months.

Plasmapheresis - In this process substitution of harmful antibodies in plasma is done.

Intravenous immunoglobulin - This process leads to temporarily change in the immune system by injecting concentrated antibodies which binds with MG causing antibodies and remove them.[2]

Yingzhe Cui et al in year 2019 published a research paper conforming that the metformin drug widely used for type 2 diabetes has anti-inflammatory functions. The drug functions via activating AMP-activated protein kinase (AMPK). As the circulating autoantibodies and disequilibrium of helper T cells and regulatory T cells are pathological indications of myasthenia gravis (MG). The drug has effect on the imbalance of different T cell populations.

Epidemiology

The study performed by B. S. Singhal et.al in 2008 on the 841 patients, they observed that 836 (611 males and 225 females) had acquired myasthenia (myasthenia gravis). The median age of onset was 48 years (males 53 years and females 34 years). Two hundred and twenty-two (26.31%) patients had ocular and 616 (73.68%) had generalized myasthenia. Serological studies were done in 281 patients with myasthenia gravis for Acetylcholine receptor (AchR) antibodies of which 238 (84.70%) were seropositive.

Conclusion

In case of Myasthenia Gravis epidemiological study at nation level in India is less covered. The disease

needs more attention and in depth research for its prevention, therapeutics is needed. The work done by Yingzhe Cui et al is remarkable in the treatment of Myasthenia Gravis. The anticholinesterase agents reduce the muscle weakness and improve the neuromuscular transmission can be used as therapeutics with other suggested treatment. The naturopathy ayurved also can be studied in detail for the possible diagnosis and treatment of Myasthenia Gravis.

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