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CONCEPTUAL UNDERSTANDING OF MYASTHENIA GRAVIS ON THE BASIS OF VYANVAYU AND OTHER VYADHI GHATAK

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ABSTRACT

In Myasthenia gravis is a disease, where AChRs in the neuromuscular junction are destroyed by immune bodies which develop due to an autoimmune disease [1]. Treatment is use anticholine esterase drugs and immunosuppressive drugs (to suppress the immune bodies which destroy the AChRs). Myasthenia gravis has prevalence as high 200 in 100,000. It affects individuals in all age groups, but peak incidences occur in women in their twenties and thirties and in men in their fifties and sixties. Overall, women are affected more frequently than men, in a ratio of 3:2.

In MG, the fundamental defect is a decrease in the number of available AChRs at the postsynaptic muscle membrane. It presents with fluctuating skeletal muscle weakness and fatigue most commonly affecting the ocular muscles, although any muscle may be affected.

Ayurvedic therapies can give much more promising results. Comparison between myasthenia gravis and diseases explained in Ayurveda is difficult and exact correlation is not possible. But based on critical understanding of prakrut karma of vyan vayu and its vikrut karma and also included other vyadhighataka, a probable diagnosis can be made and treated accordingly.

In this article, attempt is made to understand the pathogenesis of myasthenia gravis by considering the concepts vitiated Dosha vyanvayu, Dushya- Aama, Agnimandya, and Srotovaigunya. For any disease pathology to begin, all components must be present. Pathogenesis of any disease will not occur without these elements.

Keywords: Myasthenia Gravis, Vyanvayu, Vyadhi Ghatak

INTRODUCTION:

It can be difficult to compare myasthenia gravis to diseases described in Ayurvedic medicine, and an accurate correlation is not possible. Aggravated Dosha may cause manifold diseases depending upon the various etiological factors and the sites of manifestations.

There are concepts in Ayurveda like Vatakshaya, Udanavrita Vyana, Prakrut lakshana of Vyanvayu, Aama and Mansa Kshaya etc; by means of these concepts we can able to understand the pathogenesis of myasthenia gravis. Understanding the Myasthenia gravis in Ayurveda involves the hypothetical understanding of the Vyadhighatak. As we look after prakrut karma of vyan vayu I just made a try to explain the pathophysiology of myasthenia gravis

Involvement of vyanvayu and related vyadhighatak into Pathogenesis of Myasthenia Gravis:Vyadhi Ghatak are the factors that contribute to the pathogenesis (Samprapti) of any disease. There are five elements: Dosha (vitiating Dosha), Dushya (vitiating Dushya), Aama, Agni, and Srotovaigunya. For any disease pathology to begin, all components must be present.

Pathogenesis of any disease will not occur without these elements.

Myo = muscle; asthenia = weakness; gravis short, this term means, grave weakness of the muscle. = grave. All muscles have one major common characteristic feature: they can contract. With (1) skeletal muscles, this causes external locomotion (e.g. flexion/extension of limbs, walking, movements of rib cage for respiration and so on [1]

(2) with heart muscle, this causes the movement of blood, while [1]

(3) with the smooth muscles this causes narrowing squeezing/relaxation of the various viscera eg. intestine/blood vessels/respiratory tubes/ urinary bladder and so on. All contractions lead to some form of movements, like external movement (skeletal muscle), movement of blood from the heart (cardiac muscle) or movement of the content (eg. intestine/urine/fetus from the uterus). Thus, muscles are the motors (= that which causes motion) of our body and nerves commanding them to contract are called motor nerves. The contraction of the muscles leads to maintenance of homeostasis [1].

Thus: (1) contraction of gastro intestinal (GI) muscles → ultimately propulsion of food leading to absorption → maintenance of homeostasis,

(2) broncho- spasm, on being exposed to injurious fumes → non absorption of fumes → homeostasis,

(3) contraction of heart → circulation → feeding the vital organs; and so on. Contraction of skeletal muscles leads to external locomotion. They are supplied by somatic nerve and the muscle is called neuromuscular junction and acetyl choline- a neurotransmitter. MG is an autoimmune disorder most commonly caused by anti AChR antibodies.

The anti-AChR antibodies reduce the number of available AChRs at NMJs by three distinct mechanisms: [1]

(1) Cross-linking and rapid endocytosis of the receptors;

(2) Damage to the postsynaptic muscle membrane and

(3) Blockage of the active site of the AChR.

In MG, the postsynaptic folds are flattened. These changes result in decreased efficiency of neuromuscular transmission. Therefore, although ACh is released normally, it produces small end-plate potentials that may fail to trigger muscle action potentials. This will result in impair neuro muscular transmission at post synaptic membrane. The cardinal features are weakness and fatigability of muscles. The weakness

increases during repeated use (fatigue) or late in the day and may improve following rest or sleep. The cranial muscles, particularly the lids and extraocular muscles (EOMs), are typically involved early in the course of MG; diplopia and ptosis are common initial complaints. Facial weakness produces a “snarling” expression when the patient attempts to smile. Weakness in chewing is most noticeable after prolonged effort, Speech may have a nasal timbre caused by weakness of the palate or a dysarthric “mushy” quality due to tongue weakness. Difficulty in swallowing may occur as a result of weakness of the palate, tongue, or pharynx. The weakness becomes generalized affecting the limb muscles as well. If the weakness is limited to the extraocular muscles for three years, it is unlikely to become generalized, and these patients are termed to have ocular MG. In MG, limb weakness is frequently proximal and may be asymmetric. Deep tendon responses are retained despite muscular weakness. If ventilatory weakness becomes requires respiratory assistance, the patient is said to be in crisis.

AIMS AND OBJECTIVE:

1] To study the pathophysiology Myasthenia gravis of from Ayurvedic perspective.

2] To understand pathophysiology through prakrut and vikrut karma of vyanvayu and included other Vyadhi Ghatak -Dosha, Dushya, Aama, Agnimandya, and

Srotovaigunya concept mentioned in Ayurved

MATERIALS AND METHODS:

The Ayurvedic literature includes Brihatrayee. The number of published research, articles, and books on the subject are a testimony to importance of the topic.

All the available sources have been included as a source material for critical understanding of Myasthenia gravis on the basis of lakshana of vyanvayu and other Vyadhi Ghatak. For Myasthenia gravis detail included from Harrison's principles of Internal Medicine and other internate resources

DOSHA:Dosha is the one who does the Dushti of Mana and Shareera. Disease always requires the Vaishmya of the Dosha to emerge [2]. On the basis of symptoms in

myasthenia gravis, we can see the involvement of Vata Dosha. Here in this disease fatigue and weakness of skeletal muscle is the cardinal symptoms. Diplopia, ptosis, difficulty in chewing and swallowing, dysarthria, and dysphonia etc symptoms are present due to impaired neuro muscular transmission.

Among all the five types of Vata Dosha, especially Vyana Vayu is responsible for all actions like- Apkshepan, Utkshepan, Nimesh, Unmesh etc. [3] In myasthenia gravis, these activities are hampered due to impaired neuro muscular junction, so from ayurvedic perspective Vyan Vayu Dusti is responsible for the pathogenesis of the disease.

Here what other acharya also mention about vyanvayu karma [3, 4, 5] :

Table A:

	A.H.	CH.S.	CHAKRAPANI	SU.S.	DALHAN	GAYADAS	AH.SANGRAH	BHEL.SAMHITA
Krutsnadehchari [movement all over body]	+			+			+	
Utkshepan- Apakshepan [upward movement- downward movement]	+	+			+		+	
Nimesh-Unmesh [opening and closing of eyelids]	+	+			+		+	+
Sarvakriya tasmin pratibaddha sharirinam [if vitiated cause generalised disease of whole body.	+	+						
Gati [gait movement]	+	+	+		+		+	+
Aakunchan [contraction]			+		+			
Prasaran [Flexion]		+	+		+		+	
Yugpata	+	+		+				

[circulation of Rasa dhatu all over the body simultaniously]								
Swed asruk stravan [sudation and haemorrhage]				+				+
Panchdha chesta api [5 body movements- extension, contraction, lowering, rasing and moving obliquely]				+	+			
Praspandan [movements of the body]				+	+			

Table B [6, 7, 8, 9]

	Charak samhita	Sushrut samhita	AshtangHridaya	Ashtangsangraha
Sthana (Location) Sthana (Location) Sthana (Location) Sthana [Location]	Vyana has swift movement and spreads all over the body	Vyana vayu occupies entire living body. It helps in circulation of rasa throughout the body	Vyana vayu located in hridaya and it travels along the whole body with very high velocity.	located in heart moves all over the body with great speed.
Karma [Function]	responsible for gait, flexion, extension, twinkling etc.	responsible for sweating, blood circulation, and five type of movement like expansion, contraction upward, downward and oblique movements along with blinking and opening of eyelids	All motor functions of the body such as mahajava (rapid movement), gati (movement), avakshepa (flexion), utkshepa (extension), nimesha (closure of eyelid/ being not responsive to movement), unmesha (opening eyelids/ staying responsive	Responsible for movement, expansion, contraction, upward movement, downward movement, opening and closing of eyelids, yawning, feeling the tastes of food, clearing of the channels, causing the flow of sweat and blood, bringing the male reproductive tissue into the uterus, separating the nutrient portion and waste portion of the food (after its digestion) and supplying nourishment to all the dhatu

Vyana is located in Hrudaya (heart), Krusnadehachara Gati (movement locomotion), Prasarana (expansion), Akunchana (contraction), Utkeshapa (upward movement), Avakshepa (downward movement), Nimesha Unmesha (opening and closing of the eyelids), Jrumbha (yawning), Annasvadana (feeling the tastes of food), Sroto Vishodhana (clearing of the channels), Swedasruka Sravanadi Kriya (causing the flow of sweat and blood),

Yonau ca Shukrapratipadano (bringing Shukra into the uterus), Vibhajya Annasya Kittatsara Tena Kramasha Dhatu tarpati (separating the nutrient portion and waste portion of the food and supplying nourishment to all the dha tus in proper order).

Bhela said that Sharira Cheshta, Nimesha & Unmesha are the functions of VyanaVayu.

In myasthenia gravis, these activities are hampered due to impaired neuro muscular

junction, so from ayurvedic perspective Vyan Vayu Dusti is responsible for the pathogenesis of the disease.

तत्र, वातक्षय मन्दचष्टताऽल्पवाक्त्वमप्रहषो
मढसञ्ज्ञता च [10]...

In condition of Vata Kshya there are some symptoms like- Manda Chestata, Alpavaktvam, Apraharsha, Mudhasangnyata are seen which can be correlate with symptoms of Myasthenia gravis.

In Udanvrita Vyana there are some symptoms like –Alpaagnita, Chestahani and Nimilinam which can also corelate with Myasthenia gravis.

Dushya:

This is the second element that is frequently linked to Doshas. Together, Saptadhatus and Malas form the Dushyas. Doshadushya Sammurchana is the initial stage of any Vyadhi, is the association of Dushta Dosha and Dooshita Dushyas.

Rasa Dhatu and mamsa dhatu are dushya which are responsible for the pathophysiology of myasthenia gravis. In Astang Hridaya Sutrasthan, Acharya explain Mansa Kshaya Lakshna -मास क्षीणऽक्षग्लापन, which correlate with ocular manifestation of disease. In Rasa Kshaya Lakshan, Acharya states that-रस रौक्ष्य श्रम शोषो ग्लापन शब्दासपहष्णता [11]. Here Glani and Shram represent as muscular fatigue which are cardinal symptoms of the myasthenia gravis.

Role of Agni in Improving Immunity:

Normal functioning of Agni leads to longevity. The condition of Agni in the body determines the quality of life, appearance, strength, health, sustenance, luster, Ojas, Teja (energy), and Prana (living energy). Here in this Shloka, Bala and Oja represents as immunity which is depends upon Agni [12].

Sahajabala may be correlated to innate immunity. The innate immune system allows for the quick induction of inflammatory reactions based on the identification of chemicals expressed by bacteria or molecules that serve as "danger signals" secreted by infected cells (either at the cell surface or within cells). These receptor interactions trigger signaling events that ultimately lead to inflammation. Innate immune responses encompass almost all cell lineages, not just immune cells, however myeloid cells, such as neutrophils and macrophages, play a significant role due to their phagocytic ability. Adaptive immune system and Yuktikritabala may be connected. An immune activation program is carried out by the adaptive immune system after clonal identification of antigens, which is followed by a sharp proliferation of cells that react to the antigen [13].

In myasthenia gravis, When the Agni becomes weak, due to improper digestion Ama produced in the body. Ama act as

antigen and modulate signaling at cellular levels leading to incompatible autoimmune response by producing auto-antibodies against Ach receptor. AChR availability is decreased by anti-AChR antibodies. This will result in impair neuro muscular transmission at post synaptic membrane.

Aama:

Ama is the prime cause for diseases. Some Acharya consider indigested and improperly formed Ahar Rasa as Ama, [14] while others assume it to be the accumulation of waste products in body (Mala) and few others consider it as early stage of Dosha vitiation (Dosha Dusti). Autoimmune diseases occur due to the harmful response of self-immune system when immune system started attacking of body tissue as anticipated response against antigen/toxins or Aama [15]. The inflammatory response occurs in autoimmune disorders triggered by Aama or antigen at cellular level. Antigens disrupt the immune system, which further destroys tissues by vitiating the Dosha. The Aama enters the circulation i.e., it impairs the Bhutagni due to its Gurvadi properties, and reduces its function. Due to Bhutagni impairment, the Vijatiya (heterogenous) Ahara rasa will not be able to become Sajatiya (homogenous) and act as antigen in circulation. Free radicals may also be considered as Ama substance in circulation as it does not undergo final change in configuration thereby causing damage to

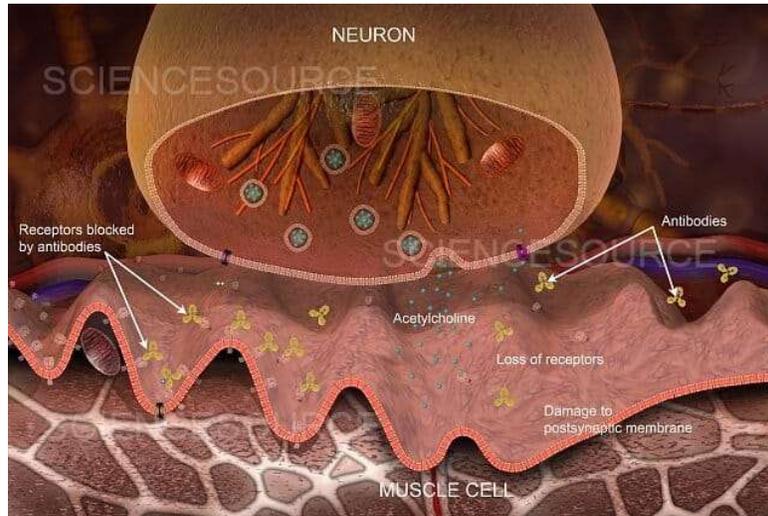
proteins, vitamins and lipids. So, most of the diseases like gastrointestinal disorders, allergic and auto-immune diseases, and various metabolic disorders have hypo functioning of Agni and Aama formation as primordial factor in their manifestation. In myasthenia gravis, there are two types of the auto antibodies produced against receptor at post synaptic membrane. In 85% of the patients have auto antibodies which produced against nicotinic AChRs and in remaining 15% of the patients having autoantibodies against muscle-specific kinase (MuSK). In this condition Ama act as antigen and that antigen/ Aama modulate signaling at cellular levels leading to incompatible autoimmune response and the auto antibodies produced against receptor at post synaptic membrane.

Strotovaigunya:

The term "Kha Vaigunya" refers to a defect in the channels of transmission and transformation [16]. The phenomenon known as Kha Vaigunya helps Ayurvedic practitioners to recognize changes in microtissues that contribute to disease. While these changes alone do not cause a disease, they do contribute to create the basis for potential diseases that may arise in the near future. They could be caused by faults from prior treatment, untreated toxins in the tissues, hereditary defects, microcellular defects, persistent inflammation in the tissues, or defects at the cellular level. The

six-stage pathophysiology of disease progression (Shatkriyakala) includes Kha Vaigunya as a significant milestone. The

defective body system is where the vitiated Dosha is localized, resulting in disease to develop.



In myasthenia gravis we can assume that Khavaigunyata is found in post synaptic cleft. In MG, the fundamental defect is a decrease in the number of available AChRs at the postsynaptic muscle membrane due to antibody production against Ach receptor [17]. The effectiveness of neuromuscular transmission is diminished as a result of these modifications. Therefore, although ACh is released normally, it produces small

end-plate potentials that may fail to trigger muscle action potentials. Muscle contraction becomes weak as a result of transmission failure.

DISCUSSION:

Myasthenia gravis (MG) is an autoimmune neuromuscular junction (NMJ) disorder characterized by weakness and fatigability of skeletal muscles.

Nidansevan



Agnimandhya



Aama enters in the circulation (Act as antigen that modulate signaling at cellular levels leading to incompatible autoimmune response)



Aama further vitiate Vata Dosha (Vyana Vayu) and Dhatu (Rasa Dhatu & Mansa Dhatu)



Vitiated Dosha and Dhatu gets obstructed where there is Khavaigunya (post synaptic cleft)



Decreased number of AChrs at post synaptic fold and eventually these folds are flattened (due to Aama)



Impaired function of Vyana Vayu and Mansa Dhatu (impaired neuromuscular transmission)



Weakness in muscle contraction



Myasthenia gravis

Vyadhi ghatak: understanding of Vyadhighatakas in Myasthenia Gravis Dosha

Vata Kshya: Manda Chestata (weakness and fatigability of muscles), Alpavaktvam (dysarthria, and dysphonia), Mudhasangnyata (“snarling” expression)

Vyana Vayu Karma Dusti: unable to do normal functions like; Apkshepan (downward movement), Utkshepan (elevation), Nimesh- Unmesh (eyelid movements) results into Diplopia, ptosis, difficulty in chewing and swallowing, weakness and fatigability of muscles.

Udanvrita Vyana:- Chestahani (weakness and fatigability of muscle) and Nimilinam

(Diplopia, ptosis) Dushya Mansa Kshaya Lakshna -Akshiglani (Diplopia, ptosis)

Rasa Kshaya:- Glani and Shram (muscular fatigue and weakness)

Agni Ama: Agnimandyata Aama enters in the circulation and act as antigen that modulate signalling at cellular levels leading to incompatible autoimmune response.

Strotovaigunya: Khavaigunya is found in post synaptic cleft.

CONCLUSION:

There is no definite cure for autoimmune diseases in contemporary sciences. In Ayurveda, we can play a vital role in management of the symptoms without further derangement of the body by applying

the concepts mentioned. This may help in the overall health status of such patients.

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