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THE GUT-BRAIN AXIS AND ITS RELATION TO PARKINSON'S DISEASE: AN *AYURVEDIC* PERSPECTIVE

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ABSTRACT The Primary Neuropathological features of Parkinson's disease (PD) are loss of pigmented dopaminergic neurons mainly in the substantia nigra (SN) and the presence of Lewy bodies – eosnophilic cytoplasmic inclusions; found within the pigmented neurons, the primary structural component of which is alpha synuclein. Human Gut Microbiota (GM) has now been accepted as a potential modulator of cognition, learning, behaviour and can directly or indirectly modify brain neurochemistry. Gut microbiota can influence dopamine turnover, dopaminergic cell expression and striatal gene expression. The gut microbiota composition is altered in PD and this dysbiosis has been related to motor fluctuations. Dysregulation of the brain-gut-microbiota axis in PD may be associated with gastrointestinal manifestations frequently preceding motor symptoms, which supports the fact that the pathological process of PD is spread from the gut to the brain. In *Ayurveda* , the symptoms of PD can be correlated to *Kampavata*. The initial pathology of all *rogas* is stated to be *Mandagni.* The unwholesome diet and regime leads to the formation of *Aama* at *Jataragni* level in *kosta*. If it is not treated at *kosta* level, the *Apakwa Rasa Dhathu* gets circulated by *Vyana Vayu* and is driven by the vitiated *Apana, Udana* and *Prana vata* which finally undergoes *Stanasamsraya* in *Mastulunga Majja* which is already having a *khavaigunya*. The major aetiopathogenesis of PD can be considered as *Mala Sanchayam(Ama visham)* at *Mastulunga majja* which further leads to *Majjavritha Vata* and finally leads to *Dhathukshaya*. So the aim of treatment is *Amapachana* and *Agni deepana* at *kosta* and *Dhathu leve*l, *Avaranaharatva and Vatanulomana* followed by *Rasayana.* This in turn helps in improving the ADL,reducing the signs and symptoms of PD and improving the nonmotor functions.

KEYWORDS : *Amapachana, Agnideepana,* Gut microbiota, *Kampa vata*, Parkinsons disease, *Rasayana.*

INTRODUCTION

Parkinson's disease is the second commonest neurodegenerative disease, exceeded only by Alzheimer's disease (AD). It is estimated that the number of people with PD in the most populous nations worldwide was approximately 4 million in 2005, and this number is expected to more than double to approximately 9 million by the year 2030 based on the ageing of population [1] Usually the patient's clinical status progresses from a relatively modest limitation at diagnosis to an ever-increasing disability over 10 to 20 years [2]. Mean age of onset of PD is 60 years [3] . It is a type of movement disorder affecting the extrapyramidal system with principal lesion being in the basal ganglia. Clinically, PD is characterized by Rest tremor, Rigidity (stiffness), Bradykinesia (slowness of movement), and Gait dysfunction with Postural instability. These are known as cardinal features of the disease. Additional clinical features can include Freezing of gait, Speech difficulty, Swallowing impairment, Autonomic disturbances, and a series of non motor features that include Sensory alterations, Mood disorders, Sleep dysfunction and Cognitive impairment.

ROLE OF GUT MICROBIOTA IN THE PATHOGENESIS OF PD

Pathologically, the hall mark features of PD are the degeneration of dopaminergic neurons in the Substantia nigra pars compacta (Snc), reduced striatal dopamine, and intraneuronal protinaceous inclusions Known as Lewy bodies and Lewy neuritis that primarily contain the protein alpha synuclein. Recent theory suggests that Gut Microbiota composition is altered in PD and this dysbiosis has been related to motor fluctuations. So the Lewybody pathology can begin in the Peripheral autonomic nervous system, olfactory system, and dorsal motor nucleus of the Vagus nerve in the lower brain stem, and then spread in a predictable and sequential manner to affect the upper brain stem and cerebral hemispheres (Braak stage) [4] .These studies suggest that the degeneration of SNc dopamine neurons and the cardinal features of PD develop at a mid-stage of the disease. Indeed, epidemiologic studies also suggest that the clinical symptoms reflecting early involvement of non dopaminergic neurons such as constipation, anosmia, rapid eye movement, behaviour sleep disorder, and cardiac denervation can precede the onset of the classic motor features of PD[5]. Accumulating evidence suggests that the onset of non motor symptoms such as gastrointestinal manifestations, precede the onset of motor symptoms and disease diagnosis, giving support that the gut microbiome-gut-brain axis may play a vital role in the pathogenesis of PD.

This dysbiosis of the Gut microbiome, associated with an abundance of potentially detrimental bacteria, can compromise the gut barrier integrity through bacterial production of endotoxins which are capable of altering the immune response, initiating the proinflammatory pathways and directly damaging the intestinal epithelial cells. Several studies have explored the potential connection between alpha-syn nuclein-related pathology and GI symptoms of PD. While alpha synuclein is found abundantly in the brain, it is also found in the Enteric Nervous System (ENS) and is produced by the enteric neurons to mediate neurotransmitter release and uptake .In individuals with PD, Pathological alpha synuclein aggregates found in GI tissue biopsy reveals that PD pathology could be initiated in the ENS [6].

Discovery of gut brain link in PD reveals it as a contributory factor in PD pathogenesis where Vagus nerve acts as a highway for the aggregated alpha synuclein to transmit from gastrointestinal tract to the lower brain stem. Several studies in animal model have shown that vagotomy potentially reduce the risk of developing PD.

AYURVEDIC PERSPECTIVE

In Ayurveda the clinical signs and symptoms of Parkinson's disease can be correlated to *Kampavata*. In *Charaka Samhita*,*Vepathu* has been included under *Nanatmaja* disorder of *Vata*[7]. Even though the *Stanasamsraya* of *kampavata* is in *Mastulunga majja*, the pathology starts in the *kosta*. The dysbiosis of the micro biome can compromise gut barrier integrity and can initiate pro inflammatory pathways which inturn can damage intestinal epithelial cells further leading to the accumulation of alpha synuclein. These can be considered as a *Stanika pitha dusthi* which promotes the inflammatory process .The main *Dosa* in PD are *Vata* and *kapha* in the initial stage associated with *Pitha. Vata Prakopa* and *kapha Prakopa ahara viharas* and *Manasika bhavas* can vitiate the *kostagata Samanavata* and *kledaka kapha* along with *Pachakapitha*. Along with this *kalavishesha* has an important role. In *Jeerna vaya Acharya Charaka* explained that *Grahana, Dhaarana,Poursha Virya* etc gradually decreases and the patient becomes more *Vata Pradhana*. The aggregation of age-related somatic damage combined with a failure of compensatory mechanisms may lead to an acceleration of PD with age. *Vepathu* is the long term complication of *Dooshivisha*[8]. Environmental toxins, pesticides, herbicides can be included under the concept of *Dooshivisha*. By all this nidana the *Chala, Ruksha guna* of *Vata* and *Guru Manda guna* of *kapha* will increase in *kosta* which constitute the *Chaya Avastha*.The *vridhi* of *Samavata* may promote the *Pachaka Pitha* and there by increasing the inflammatory process. The next stage is the accumulation of Alpha synuclein which can be taken as *Amavisha. Amavisha* which act as *Visha lakshna* and *Mahaghoram* in nature.The *Chalatva* is the *atmaguna* of *vata.*The *Amavisha* which enters the

Rasavaha srothas and circulated by *Vyana vata* do *Margaavarana* by the vitiated *Apana,Udana* and *Prana vata*[9]. In PD pathogenesis Vagus nerve act as a highway for aggregated alpha synuclein to transmit from gastrointestinal tract to the lower brain stem[10] .By the *Dosa dusya samurchana* the circulated *Ama visha* takes *stana samsraya* in *Mastulunga Majja* were there is already a *Khavaigunya*. Further it leads to *Majjavritha vata* along with *Stanika snayu pradosham*. According to *kasyapa samhita Snayu* is referred to as *Mastulunga moola*[11]. The last stage of PD is the degeneration of dopaminergic neurons which can be related to *Dhathukshya* due to the persistant *Avarana.*

Clinical Features

Table. No. 1: Clinical Features Of Parkinson's Disease

CARDINAL MOTOR FEATURES	OTHER MOTOR FEATURES	NOMOTOR FEATURES
Bradykinesia Rest tremor Rigidity Postural instability	Micrographia Masked facies Reduced eye blinking Drooling Hypophonia Freezing	Anosmia Sensory disturbances(eg: pain Mood disorders (eg; depression) Sleep disturbances Autonomic disturbances Orthostatic hypotension Genito urinal disturbances Sexual dysfunction Cognitive impairment/ Dementia

In Ayurveda, the *lakshna* of PD are similar to those explained in *Kaphavrita vyana*, *Kaphavrita udana*, *Majjavrita vata*, *Udanavrita vyana* , *Snayuprodhasa lakshna* and *kampavata*. No single *Avarana* or disease pathology can clearly explain *Kampa Vata*. The pathology starts in the *kosta* level.In the *Sanchaya avastha* of *dosa* in *kosta* level patient may show symptoms such as *Stabda kostam*, *Mandagni, Alasyam* and *Gourava* etc.In the proinflammatory pathways in gut wall patient may show *Stanika pitha dusti lakshana* .The alphasynuclein can be seen initially in the Enteric Nervous System and autonomic nervous system. At that stage the patient may show symptoms such as *Vibanda ,mutrakrichram*, *Aharshanam, Klaibyam* etc due to the *Apana vata vaigunya*. In the next stage the Ama visha is driven by *Pratiloma vayu* which undergoes *Stanasamsraya* in *Mastulunga majja*. Before manifesting the *lakshana* the patient may show *Poorvarupa* such as *Gandanjana*. In PD the alpha synuclein initially accumulates in the olfactory nuclei before it reaches the Substantia nigra. Due to the persistent *Margavarana* the patient gradually shows *kapha avruta vata lakshnas* such as *Skalitha gati*, *Vak swaragraham ,Tandra, Angeshu guruta, Stabthata, Smrithikshaya* [12] etc which resembles those symptoms which manifests in PD such as Bradykinesia, Hypophonia, Myalgia. Heaviness, Stiffness of body, Dementia etc. *Vishada* is another main *lakshna* which can be seen in PD patients. In PD patients the mesolimbic dopaminergic pathway may upper hand the striatonigral pathway. While taking *Stanasamsraya* in *Mastulunga majja* the patient may show the *Majjavritha vata lakshna* such as *Vinamanam* [13](stooping).Along with this, *Stanika snayu pradosha lakshana* such as *Stambha* [14](freezing,rigidity) etc will manifest. Finally it leads to *Dhathukshaya* which leads to the degeneration of Dopaminergic neurons shows symptoms of *Kampa vata* mentioned in *Basavarajeeyam* as *karapadatala kampa*(asymmetrical rest tremor), *Deha bhramam*(giddiness), *Nidrabhangam*(reduced sleep), *Ksheenamathi*(dementia) which is close resemblance with the motor and nonmotor functions of PD.

Scope of *Ayurvedic* intervention

The signs and symptoms of PD comes under *Vatavyadhi* which is included under the *Maharogas* which are difficult to treat generally. The disease affecting the *Madhyama Rogamarga* especially the *Shiromarma* are very difficult to manage. The aim of the treatment is to improve the ADL, reducing the signs and symptoms and improving the nonmotor functions. Since the prodromal symptoms of PD shows the vitiation of *Pachaka pitha* and *Apana vataviagunya*. The *Oushada* should aim at *Vatanulomana, Agni deepana, Amapachana* which is *Pitha kapha avirodi* should be done at *kosta* level. Next the treatment should aim at *Avaranaharatvwa* followed by *kevalavatika chikitsa*. For a *Kaphaavritha vata avastha Udwartana,Teekshana virechana* and *Niruha vasti* etc can be adopted. Even though the disease manifest in *kosta* , the *Asraya stana* is in *Shiras*. The *Amavisha* will do *Stanasamasraya* in *Mastulunga majja* will further leads to *Majjavritha vata*. The insufficiency of *Dhatwagni* will lead to the deposition of unwanted proteins in *Mastulunga majja*. Considering the persistence of *Dhatwagni mandya* and *Ama visha* in *Mastulunga majja* the drugs chosen should be acting at *Dhathu level*. The drugs having *Teekshana,Ushna ,Vyayayi ,Vikasi guna* and should act in the *Sookshma* level which also has a property of *kapha vata chedana* should be chosen.The drugs suchs as *chitraka,bhallathaka*, etc will have the above property acts as *Amavishahara* and *Agni deepana* .*Ghritha* is the best suitable drug which can be chosen as a vehicle for the administration of above drugs. In *Susrutha samhita Dalhana* commentary it is mentioned that *Mastishka majja* is *Ardhavilina ghrithaakara*(partially melted ghee)[15]. *Vasthi* is the main *Shodhana chikitsa* for *vata dosa*. Since *Dhatukshaya* predominates the pathology *of PD*, *Yapana vasthi* having *Rasayana* and *Dhathu vridhikara* properties will provide better results. In tremor predominant PD,*Nasya* has a definite action. *Oushada* having *Vatahara,Brihmana* and *Rasayana* properties can be chosen a drug of choice. *Dhatukshaya* is the hallmark of Parkinson's disease and so *Rasayana* has an important role. *Atmagupta* or *Kapikachu* is proven to contain natural levodopa and is tolerated better than the synthetic version[16].Withania Sominfera or *Aswagandha* is also a proven drug in opposing the oxidative damage and decline the catecholamine level in Parkinson's disease [17]. *Brahma Rasayana* has also shown improvements in the level of neurotransmitters like serotonin, dopamine, adrenaline, noradrenaline in animal models [18].

CONCLUSION

PD is one of the most common neurologic disorders worldwide . Because of the crippling nature and non-availability of curative treatment the disease remained as a great problem in the ageing society. Early diagnosis and intervention in the premonitory stage effectively improve quality of life, decrease the disease fatality and morbidity. The gut brain axis plays a major role in the pathogenesis of PD. Along with early intervention, a proper diet can also contribute a marked effect in treatment. In *Ayurveda* PD can be understood by *Jataragni* and *Dhathuwagnimandya* followed by *Amavisha* which leads to *Avarana* pathology and finally end up with *Dhathukshya* in *Mastulunga majja*. So a proper *Deepana pachana ,Avarana haratva* and *Vatanulomana* can helps to improve the motor and nonmotor functions in PD. Since it is a neurodegenerative disorder *Rasayana* plays an important role. Selection of an appropriate *Rasayana* will arrest further degeneration and improves the quality of life.

REFERENCES

1. Loscalzo J, Fauci A, Kasper D, Hauser S, Longo D, Jameson J. Harrison's principles of internal medicine. 19th ed. p.2609
2. Srinivasan, J., Scott, B., Chaves, C., Small, J. and Netter, F., n.d. Netter's neurology =. 2nd ed. 2012 p.287.
3. Loscalzo J, Fauci A, Kasper D, Hauser S, Longo D, Jameson J. Harrison's principles of internal medicine. 19th ed. p.2609
4. Srinivasan, J., Scott, B., Chaves, C., Small, J. and Netter, F., n.d. Netter's neurology =. 2nd ed. 2012 p.287.
5. Loscalzo J, Fauci A, Kasper D, Hauser S, Longo D, Jameson J. Harrison's principles of internal medicine. 19th ed. p.2609
6. Mulak A. Brain-gut-microbiota axis in Parkinson's disease. World Journal of Gastroenterology. 2015;21(37):10609. https://doi.org/10.3748/wjg.v21.i37.10609
7. Bhagwan Dash R. caraka samhitha sutra stana chapter 20. varanasi: Chowkamba Sanskrit Series Office,Varanasi; 2015.
8. Susrutha Samhitha,kalpastana 2nd chapter. varanasi: Chaukhambha orientalia; 2010.
9. Bhagwan Dash R. caraka samhitha chikitsa stana 15th chapter. varanasi: Chowkhamba sanskrit Series Office; 2012.
10. Mulak A. Brain-gut-microbiota axis in Parkinson's disease. World Journal of Gastroenterology. 2015;21(37):10609. https://doi.org/10.3748/wjg.v21.i37.10609
11. sharma d.Description of Snayu Sharira:A Review Article. 2022;
12. Murthy P. Vagbhatas's Ashtanga Hridayam nidana stanam 16th chapter. varanasi: Choukamba Krishnadas Academy,Varanasi; 2012.
13. Murthy P. Vagbhatas's Ashtanga Hridayam nidana stanam 16th chapter. varanasi: Choukamba Krishnadas Academy,Varanasi; 2012.
14. Bhagwan Dash R. caraka samhitha sutra stana 28th chapter. varanasi: Chowkhamba sanskrit Series Office; 2012
15. Sushruta Samhita sutrastana Dalhana Commentary. Varanasi: Chaukhamba Surbharati Prakashan; 2012, p 413
16. Katzenschlager R, Evans A, Manson A, et al.Mucuna pruriens in Parkinson's disease: a double blind clinical and pharmacological study Journal of Neurology, Neurosurgery & Psychiatry 2004;75:1672-1677.
17. Dar NJ, MuzamilAhmad. Neurodegenerative diseases and Withania somnifera (L.): An update. J Ethnopharmacol. 2020 Jun 28;256:112769. doi: 10.1016/j.jep.2020.112769. Epub 2020 Mar 30. PMID: 32240781.
18. Scientific Evaluation of Brahma Rasayana as a Cognitive Enhancer in D-Galactose Induced Cognitive Impairment in Mice - EPrints@Tamil Nadu Dr MGR Medical University [Internet]. Repository-tnmgrmu.ac.in. 2022 [cited 21 April 2022]. Available from: http://repository-tnmgrmu.ac.in/id/eprint/6398