

A CASE STUDY ON TRITIYA PATALAGATA PITTAJA TIMIRA W.S.R TO AGE RELATED MACULAR DEGENERATION WITH CHOROIDAL NEOVASCULAR MEMBRANE

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ABSTRACT

Age-Related Macular Degeneration (ARMD) is a degenerative condition associated with aging, primarily affecting the macula and causing a gradual decline in central vision. It stands as the leading cause of vision impairment and blindness in developed nations, particularly among individuals aged 40 years and older. The pathology of ARMD involves the Retinal Pigment Epithelium (RPE) cells accumulate metabolic byproducts due to incomplete degradation of phagocytosed rod and cone membranes that supply oxygen and nutrients to the retina, leading to a deprivation of essential elements to the macula and ultimately resulting in progressive vision loss. Contemporary medical approaches typically involve offering zinc supplements, antioxidants, and vitamins in the early stages, and resorting to intravitreal injections (ranibizumab, bevacizumab) and laser photocoagulation in advanced cases. However, these interventions often prove insufficient in arresting the unyielding progression of vision loss. Ayurveda, on the other hand, presents a promising alternative with its emphasis on Shodhana therapy (purification treatments) and Kriyakalpa (therapeutic procedures). These modalities aim not only to alleviate symptoms but also to impede the advancement of the disease process. In a clinical scenario involving a diagnosed case of Wet ARMD, presenting with central vision loss in the left eye over the course of a year, the patient sought treatment at the outpatient division of the hospital. The management approach adopted included Shodhana therapy, Nasya, Aschyotana, Anjana, and Vasaguduchyadi Kashaya. Remarkably, significant improvement in vision was observed following the Ayurvedic intervention, indicative of a favourable treatment outcome. Furthermore, the progression of the disease was notably curtailed, underscoring the efficacy of Ayurvedic interventions in addressing the complexities of ARMD. These encouraging results highlight the potential of Ayurveda as a viable therapeutic option in the management of ARMD, offering hope for patients seeking alternatives to conventional treatment modalities.

INTRODUCTION

Age-Related Macular Degeneration (ARMD) stands as a prevalent ocular disorder globally, heralding significant morbidity, particularly in the aging population. In its advanced stages, ARMD culminates in irreversible visual impairment, impacting approximately 1.7% of individuals over 50 years of age and escalating to affect nearly 18% of those aged over 85 years. The pathogenesis of ARMD is multifactorial, influenced by a constellation of genetic predispositions and environmental exposures. Notable risk factors encompass hereditary predispositions, dietary constituents, tobacco consumption, systemic hypertension, phototoxicity from sunlight exposure, ocular anatomical features such as hyperopia and blue

irises, and ocular comorbidities like cataracts, with a specific emphasis on nuclear opacification.

Central to the pathology of ARMD is the degeneration of the macula, the specialized central region of the retina responsible for acute visual acuity. This intricate retinal structure, comprised of densely packed photoreceptor cells (rods and cones) and intricate neural circuitry, orchestrates the transformation of incident light stimuli into neuroelectric signals. These signals are then relayed via the optic nerve to higher visual processing centres within the brain, facilitating the perception and interpretation of visual stimuli. The hallmark of ARMD lies in the progressive degeneration and eventual demise of these light-sensitive photoreceptor cells within the

macular region, precipitating a cascade of functional deficits and culminating in a gradual decline in central visual acuity. ARMD encompasses two primary clinical subtypes: Non-exudative or atrophic ARMD, which represents the predominant form, accounting for approximately 90% of cases, and Exudative ARMD, also known as wet or neovascular ARMD, which constitutes the remaining 10% of cases. The distinction between these subtypes hinges on the underlying pathophysiological mechanisms governing disease progression, with non-exudative ARMD primarily characterized by the gradual accumulation of retinal pigmentary changes and drusen deposition, while exudative ARMD is typified by the aberrant growth of choroidal neovascularization and subsequent exudative complications. This scientific discourse elucidates the intricate interplay of genetic, environmental, and anatomical determinants underlying the pathogenesis of ARMD, laying the groundwork for comprehensive therapeutic interventions and preventive strategies aimed at mitigating the burden of this sight-threatening condition. It's postulated that senescent Retinal Pigment Epithelium (RPE) cells accumulate metabolic byproducts due to incomplete degradation of phagocytosed rod and cone membranes. Senescent RPE cells are believed to accumulate metabolic debris, remnants of incomplete degradation from phagocytosed rod and cone membranes. This progressive accumulation within RPE cells leads to the formation of drusen and further dysfunction of the remaining RPE. Age-related changes in the hydraulic conductivity of Bruch's membrane result in reduced water movement and metabolic exchange between the RPE and choriocapillaris, exacerbating the degenerative process. The thickening of Bruch's membrane, in conjunction with the presence of drusen, increases the likelihood of crack formation within the membrane. Notably, calcification and fragmentation of Bruch's membrane are more pronounced in eyes affected by exudative ARMD. It is believed that these structural defects in Bruch's membrane create a conducive environment for the development of choroidal neovascularization (CNV). In Ayurvedic perspective, AMD with CNVM can be correlated with Tiritiya Patalagata Pittaja Timira based on symptoms like "*Karnanasaakshiyuktani viparitani veekshat*" (central scotoma) "*Aadithyakhadyota pashyati*" (flashes of light) caused by the vitiation of Achakshushya and Tridoshakara aahara vihara affecting Rasa Rakta, Mamsa, Dhatu of Akshi. Modern treatments offer zinc supplements, antioxidants, and vitamins in the early stage and intravitreal injections (ranibizumab, bevacizumab) and laser photocoagulation in later stages, but they are not very effective in reversing the progression of vision loss. Ayurveda, with its emphasis on Shodhana and Kriyakalpa therapies, offers a viable solution and can aid in arresting the advancement of the disease.

PURPOSE OF THE STUDY

The purpose of conducting a study on the Ayurvedic management of ARMD with CNVM would be to generate scientific evidence highlighting the superiority of Ayurvedic interventions in effectively managing this specific subtype of the disease. By demonstrating the efficacy of Ayurvedic therapies, such as dietary modifications, lifestyle interventions, and specialized therapeutic procedures, the study aims to establish Ayurveda as a potent and reliable alternative to conventional approaches.

AIMS AND OBJECTIVES

By assessing patient satisfaction, quality of life improvements, and long-term outcomes, the study aims to underscore the overall superiority of Ayurvedic management in enhancing patient well-being and minimizing disease burden. Ultimately, the goal is to position Ayurveda as a leading integrative approach to eye health, offering patients with ARMD with CNVM a comprehensive and effective treatment option that complements or surpasses conventional other therapies.

MATERIALS AND METHODS

Various Ayurvedic classical texts like Brihatrayee, Laghutrayee were used as source materials. Apart from this, websites and contemporary textbooks, published journals were also searched for this study.

CASE REPORT

A 60 years old female patient who is a known case of hypertension since 3 years and using visual aid for both distant and near vision (for distant vision from 45 years and near vision from 4-5 years) presented with chief complaints of central vision loss since one year, along with she was experiencing flashes of light in her left eye and visualizing moving black dots in front of right eye. On October 2022 she noticed gradual blurriness of vision which hampered her daily routine activities but she ignored those symptoms, one day she felt visual discomfort while applying a tilak to her granddaughter that made her to consult an ophthalmologist. On 1/11/2022 she consulted at Aaradhana Netra mandira where she underwent an OCT examination and where she was diagnosed with age related macular degeneration (ARMD) in both eyes and a choroidal neovascular membrane (CNVM) in her left eye. She was initially prescribed Moxiblu eyedrop (1 drop QID), along with I-Site AF capsules (1 capsule at HS) and advised to undergo intraocular anti-VEGF injection therapy. She denied to undergo injection therapy and sought a second opinion at Modi Eye Care Hospital on November 3, 2022, where she was prescribed Nevanac eyedrop (1 drop twice daily) and recommended anti-VEGF injection therapy for her left eye. Patient was reluctant to undergo intraocular injection, so she sought a third opinion at Minto Ophthalmic Hospital again on November 4, 2022, where she received a reaffirmation of the diagnosis of ARMD in both eyes and CNVM in left eye. She revisited Narayana Netralaya for the same complaints, where she

underwent four sittings of anti-VEGF injection therapy for her left eye from the month of December 2022 to September 2023 along with post-injection eye drops (Gatifloxacin 0.5%) topically and I-SITE AF capsules for three months.

Post therapy patient was asymptomatic for 3 weeks later on the symptoms started resurfacing. Again, She experienced discomfort and difficulty in her daily routine. So, she consulted Narayana Netralaya where they refused to give further injections and advised her to manage her condition for the rest of her life and she was worried, seeking an alternative management, she consulted Shalakya OPD on 05/10/2023 with complaints of central vision loss, perception of flashes of light in left eye, visualizing moving black dots in front of her right eye.

EXAMINATION

GENERAL PHYSICAL EXAMINATION

Patient was fully conscious, cooperative and well oriented to time, place and person at the time of history taking. She had moderate built and appeared to be of her age. There was normal colour of skin without any hypo/hyper pigmentation. No skin lesion was present. There was no periorbital edema. Pupil: reactive to light bilaterally. The Ear, Nose, Throat and Paranasal sinus were clear from any discharge, collection, sign of infection and inflammation. Lips were pinkish in colour. Oral hygiene was well maintained.

Systemic examination of respiratory, cardiovascular, CNS and G.I.T systems revealed no abnormality.

LOCAL EXAMINATION

PARTS	EXAMINATION	RIGHT EYE	LEFT EYE
EYE BALL	POSITION VISUAL AXIS SIZE MOVEMENTS	PLACED SYMMETRICALLY NORMAL NORMAL NORMAL	PLACED SYMMETRICALLY NORMAL NORMAL NORMAL
EYELIDS	POSITION MOVEMENTS LID MARGIN	NORMAL NORMAL NORMAL	NORMAL NORMAL NORMAL
LACRIMAL APPARATUS	LACRIMAL SAC LACRIMAL PUNCTA	NORMAL NORMAL	NORMAL NORMAL
CONJUNCTIVA	CONGESTION FOREIGN BODY FOLLICLES PAPILLAE CONCRETIONS CYST	ABSENT ABSENT ABSENT ABSENT ABSENT ABSENT	ABSENT ABSENT ABSENT ABSENT ABSENT ABSENT

SLIT LAMP EXAMINATION

PART	EXAMINATION	RIGHT EYE	LEFT EYE
CONJUNCTIVA	CONGESTION FOREIGN BODY FOLLICLES PAPILLAE CONCRETIONS CYST	ABSENT ABSENT ABSENT ABSENT ABSENT ABSENT	ABSENT ABSENT ABSENT ABSENT ABSENT ABSENT
CORNEA	SIZE SHAPE SHEEN SURFACE	NORMAL NORMAL PRESENT REGULAR	NORMAL NORMAL PRESENT REGULAR
ANTERIOR CHAMBER	DEPTH	NORMAL	NORMAL
PUPIL		ROUND REGULAR REACTIVE	ROUND REGULAR REACTIVE
IRIS	COLOUR	NORMAL	NORMAL
LENS	TRANSPARENCY	VACUOLES	NS GRADE – I

FUNDUS EXAMINATION

PARTS	RIGHT EYE	LEFT EYE
MEDIA	CLEAR	CLEAR
GENERAL BACKGROUND	WNL DRUSENS PRESENT	DOT & BLOT HAEMORRHAGES DRUSENS PRESENT
OPTIC DISC	WNL	WNL
RETINAL VESSELS	ATTENUATED BLOOD VESSELS	ATTENUATED BLOOD VESSELS
MACULA LUTEA	DULL FOVEAL REFLEX	FOVEAL REFLEX ABSENT
CHOROID	WNL	CHOROIDAL NEOVASCULAR MEMBRANE PRESENT

VISUAL ACUITY

	DISTANT VISION	DV WITH AIDS	NEAR VISION	NV WITH AIDS
BOTH EYES	6/9 (p)	6/6	N-10	N-6
RIGHT EYE	6/18 (P)	6/9	N-10	N-6
LEFT EYE	CF from ½ meter	CF from ½ meter	N-36(P) from 25cm	N-36(P) from 25cm

CORRECTED VISUAL ACUITY

	SPH	CYL	AXIS	BCVA
RIGHT EYE	-1.50 D	-	-	6/9
LEFT EYE	-1.75 D	-	-	CF from ½ meter

	SPH	CYL	AXIS	BCVA
RIGHT EYE	+1.00 D	-	-	N-6
LEFT EYE	+ 1.50 D	-	-	N-36(P)



- ✓ Presence of drusenoid deposits in both the eyes.
- ✓ A choroidal neovascular membrane changes in left eye.

OCT FINDINGS IN LEFT EYE

- Minimal subretinal fluid +
- Large cystic spaces (IRF)
- Pigment epithelial detachment (PED)
- Increased central retinal height thickening (500 µm)

Choroidal neovascular membrane formation

MAJOR COMPONENTS FOR THE PATHOGENESIS OF TIMIRA

Dosha	Pitta pradhana tridosha
Dushya	Rasa, Rakta, mamsa, meda
Agni	<u>Jatharagni mandhya, Sthanika dhatwagni mandhya</u>
Ama	<u>Jatharagni Sthanika dhatwagni mandhyaa janya aama</u>
Srotas	<u>Rasavaha, Raktavaha, Mamsavaha, Medavaha</u>
Srotodusti prakara	<u>Ati pravruti, Sangha, Vimarga gamana</u>
Udbhava sthana	<u>Amashaya</u>

<u>Roga marga</u>	<u>Madhyama</u>
<u>Vyakta sthana</u>	<u>Netra</u>
<u>Sanchara sthana</u>	<u>Siras(microvasulature)</u>
<u>Adhisthana</u>	<u>Dristi(Retina)</u>
<u>Vyadhi swabhava</u>	<u>Chirakari</u>
<u>Sadhyasadyata</u>	<u>Yapya</u>

DIAGNOSIS: On the basis of signs and symptoms and ocular examination it was diagnosed as Tritiya Patalagata Pittaja Timira (Age related macular degeneration with choroid neovascular membrane in left eye)

THERAPEUTIC INTERVENTION: The treatment was devised with a two-dimensional approach, considering the specific nature of the disease.

* The first course of treatment was given from 05/10/2023 to 14/10/2023. Patient was scheduled for Virechana with Trivrut lehya (Table. 1)

* Second course of treatment was given from 16/10/2023 to 02/11/2023. Patient was given Vasaguduchyadi Kashaya internally along with Sthanika upakarmas like aschyotana with Elneeru khuzumbu. (Table.2)

* In Third course of treatment from 15/11/2023 to 22/11/23 patient was prescribed with Gudanagara nasya along with vasaguduchyadi kashaya. (Table.3)

* In fourth course of treatment from 05/12/2023 to 12/12/2023 patient was prescribed with Darvyadi Anjana and Vasaguduchyadi Kashaya

TABLE: 1 first course of treatment.

DATE	TREATMENT	OUTCOME
05/10/2023 – 07/10/23	Tab. Liv 52 DS (2 TID) B/F	
08/10/2023 – 14/10/2023	1. Snehapana with mahatriphaladi ghrita in aarohana matra for 3 days. 2. Vishramakala (Sarvanga abhyanga with moorchita tila taila f/b Sarvanga bashpa sweda) for 3 days 3. Virechana with trivrut lehya (60gms) 4. Samsarjana karma for 3 days	DV: B.E - 6/9 R.E – 6/9 L.E – 3/60

Table 2: Second Course of Treatment.

DATE	TREATMENT	OUTCOME
16/10/2023-02/11/2023	1. Vasaguduchyadi kashaya 15 ml with equal quantity of warm water twice a day in empty stomach. 2. Elneer khuzumbu (1°/1°) in each eye once in a day in morning.	DV: B.E - 6/6(P) R.E – 6/9 L.E – 6/60 • Flashes of lights was present (occasionally) • Floaters are reduced

Table 3: Third and Fourth Course of Treatment.

DATE	TREATMENT	OUTCOME
15/11/23 - 22/11/23	1. Nasya with Gudanagara (6°/6°) in each nostril Mukha abhyanga with moorchita tila taila 2. Vasaguduchyadi kashayam (15 ml) with equal quantity of warm water twice a day in empty stomach	DV: B.E - 6/6(P) R.E – 6/6(P) L.E – 6/60 • Flashes of lights was present (occasionally) • Floaters are reduced
05/12/23 - 12/12/2023	1. Vasaguduchyadi kashayam (15 ml) with equal quantity of warm water twice a day in empty stomach 2. Darvyadi anajana daily once in morning in each eye	DV: B.E - 6/6 NV: BE- N-6 R.E – 6/6 RE- N-8 L.E – 6/36(p) LE- N-18 • Flashes of light absent • Floaters absent • Central Scotoma getting fader

- **PATHYAS TO BE FOLLOWED:** Purana Ghrita, Lohita Shali, Yava, Mudga, Purnarnava, Patola, Vartaka, Karavellaka, Draksha, Saindhava, Madhu
- **APATHYAS TO BE AVOIDED:** Shuktaaranala nishavana, Kulatha, Masha, Vega vinigraha, Ati

yaana, Ati madhyapaana, Prasakta samrodhana, Kopa-Shoka, Klesha, Abhighata

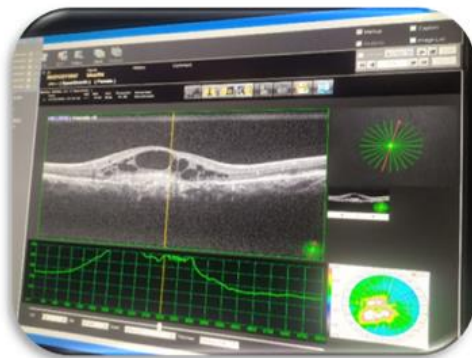
OBSERVATIONS

Patient was experiencing symptomatically better as she was noticing the changes in her overall symptoms like

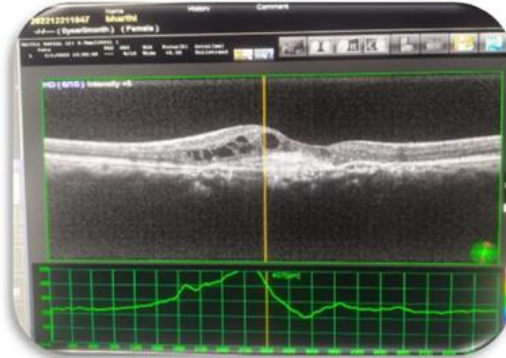
the central scotoma was getting fader and she can make out her nose, eyes and ears as he was not able to identify before the treatment.

CRITERIA	BEFORE TREATMENT	AFTER TREATMENT
Visual acuity	DV: BE- 6/9(P) RE- 6/18(P) LE- CF from ½ meters NV: BE: N-10 RE: N-10 LE: N-36(P)	DV: BE- 6/6 RE- 6/6 LE- 6/36(P) NV: BE: N-6 RE: N-8 LE: N-18
Central scotoma	Present	Getting fader
Flashes of light	Present	Absent
Floaters	Present	Absent
Drusens	Present	Significantly Reduced
Macular oedema	Present	Significantly reduced
Dot & Blot haemorrhages	Present	Absent

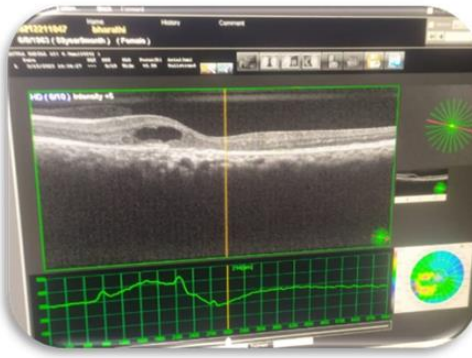
BEFORE TREATMENT OCT FINDINGS DURING ANTI- VEGF THERAPY IN LEFT EYE



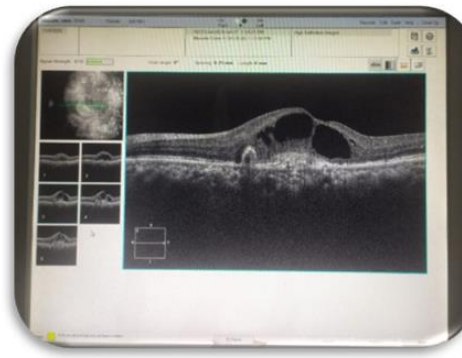
11/09/22



23/12/22



08/02/23



11/09/23

AFTER TREATMENT OCT FINDING



Marked reduction in the macular oedema and Neovascularization

DISCUSSION

- Causative factors for exudative ARMD according to Ayurveda are the pathological increase of Vata and Pitta due to indulge in Achakshushya and Tridoshaka aahara and vihara. The vitiated Vata disrupts both nutrition and excretion processes, resulting in the accumulation of Ama (undigested toxic metabolites) specifically at the macula. This deposition occurs due to compromised nutritional delivery and waste removal mechanisms, exacerbating the condition of exudative ARMD,

which in turn caused Srotorodha (obstruction of the Srotas), leading to compromised nutrition. This results in impaired function of Alocaka Pitta, which is responsible for vision. The impaired nutrition, subsequent obstruction of Srotas, and the increase of deranged Pitta results in hypoxia to the macula, leading to choroidal neovascularization. Neovascularization was due to Vimarga Gamana (diversion of flow to improper channels) of the Raktavaha Srotas (metabolic channels carrying blood), which was caused by increased Pitta due to the Asraya-Asrayi Bhava (homologous relationship) between Pitta and Rakta. Acharyas have explained Chikista sutras for Timira as according to doshas Snehapana, Raktamokshana, Nasya, Anjana, Shirovasti, Basti kriya, Tarpana, Lepa, Seka.

• PROBABLE MODE OF ACTION OF DRUGS

◊ VIRECHANA

Virechana yoga because of its Vyavayi Guna gets absorbed quickly and due to its Virya, it reaches to Hridaya, Dhammani and all of the macro and micro channels of the body. Its Vikasi Guna causes softening and loosening of the bond by Dhatu Shaithilya Karma. Ushna guna causes liquifications of Dosha Sanghata. It breaks the Mala and Doshas in micro form due to its Tikshana Guna. Due to Sukshma Guna by reaching in micro channels, disintegrates endogenic toxins, which are then excreted through micro channels. Virechana occurs mainly due to Prabhava, Prithvi and Jala constitution and presence of Sara Guna. Trivrut is having properties like katu, tikta rasa, laghu, ruksha, tikshna guna, katu vipaka and ushna virya which promotes metabolism and assimilation by stimulating the dhatwagni while simultaneously eliminates metabolic waste products especially pitta dosha and removes Ama and according to Acharya Bhavaprakasha suggests the use of Trivrut for its potential in mitigating the vata and pitta doshas which are in manifestations of exudative ARMD and it is shothaapaha (reduces the oedema) helps in reduction of macular oedema significantly.

◊ VASAGUDUCHYADI KASHAYA

वासगुडूचीत्रिफलाकट्वीभूनिम्बनिम्बजः ।

क्वाथः क्षौद्रयुतो हन्ति पाण्डुपित्तास्रकामलाः ॥

- * GUDUCHI : Tikta, Kashaya and Madhura vipaka does pittashamana and it is chakshushya and sangrahi helps in prevention of neovascular membrane formation.
- Chemical composition: Octacosanol, Heptacosanol, Tinosporin alkaloids inhibits the proliferation of endothelial cells and neovascularization induced by angiogenic factors and are antioxidant.
- * VASA: Tikta Kashaya, laghu ruksha guna, sheeta veerya and does the raktapittahara
- Chemical composition: Kaempferol is an anti-VEGF
- * NIMBA: Is having properties like tikta Kashaya, laghu ruksha guna, sheeta veerya and is a netrya as well as pittashamaka.

- Chemical composition: Kaempferol is an anti-VEGF, β – Sitosterol is an antioxidant.
- * KATUKI: Tikta, laghu ruksha guna and sheeta veerya, indicated in raktavikaras
- Chemical compositions: Iridoid glycoside, d-mannitol, phenol glucosides, apocyanin are immunomodulating, anti-inflammatory and anti-oxidant in activities.
- * BHUNIMBA: Is having Tikta, laghu, Madhura Vipaka and Rakta pittahara properties.
- Chemical composition: Andrographolide, diterpene lactones are anti-oxidant which reverse the cellular damage by inhibiting the excessive oxidative stress to the cells due to excess of free radicles.
- * TRIPHALA: It is a tridoshic rasayana and agrya for netrarogas as well as tridosha shamaka.
- Chemical composition: Tannin, polyphenols, flavonoids which have thrombotic action helps in controlling haemorrhage. It increases activities of anti-oxidant enzymes like superoxide dismutase, catalase, glutathione transeferase and glutathione peroxidase. It is a good anti-inflammatory effect as it decreases inflammatory markers.
- ◊ ELANEERU KHUZHAMBU: Karpura, darvi, triphala, yastimadhu, saindhava lavana, madhu, narikela jala and mainly indicated in pittajanetrarogas. as having anti-inflammatory, anti-oxidant and its soothing affects it is used.
- ◊ GUDANAGAR NASYA: It is a shodhana nasya, having properties like shophara, lekhana, graahi, srotoshodhana. anti-inflammatory and anti-oxidant Thus, effective in regression of macular oedema.
- ◊ DARVYADI ANJANA: Daruharidra, Patola, Yastimadhu, Nimba, Padmaka, Utpala, Prapaundrika. Almost all the drugs in the formulation have Chakshushya properties i.e they are beneficial for eyes and improves eyesight. Daruharidra, the chief component of the formulation has been as “Netrakarnaasyaroganut” i.e pacifies the disease of eyes, ear and mouth. Yastimadhu is also a content of the formulation which apart from having rasayan properties has also been called Chakshushya, Shothahara by Acharya Bhavaprakash. Patola and Nimba are antioxidants, and Nimba also possesses anti-VEGF properties, thus aiding in the management of Age-Related Macular Degeneration and macular oedema.

CONCLUSION

Exploring Ayurveda's role in disease management is an engaging pursuit, prompting a thorough examination of both traditional wisdom and modern perspectives. Adopting an impartial approach, we delve into the significance of Ayurveda with a receptive mindset. The integrative approach of utilizing Virechana, Nasya, Darvyadi Anjana, and Vasaguduchyadi Kashaya in the treatment of Age-Related Macular Degeneration (ARMD) with Choroidal Neovascularization (CNVM) has yielded promising results. By addressing both systemic imbalances and localized ocular pathology, this

holistic treatment regimen aims to not only alleviate symptoms but also target the underlying causes of the condition. Through purificatory therapies like Virechana and localized interventions such as Nasya and Darvyadi Anjana, the aim is to rebalance doshas, reduce inflammation, and promote tissue healing. Additionally, the administration of Vasaguduchyadi Kashaya provides targeted natural anti-VEGF support to address the specific pathology of CNVM. Overall, this comprehensive approach underscores the potential of Ayurveda in offering effective and personalized care for ARMD with CNVM, highlighting the importance of integrative medicine in optimizing patient outcomes and quality of life.

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