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Improvement of visual acuity in non-proliferative diabetic retinopathy with *Nimi Nirdishta Yoga*- A case report

Case Report

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Abstract

Ayurveda can serve in many disease conditions, whereas conventional systems face several limitations. Diabetic Retinopathy (DR) is among such conditions, where effective management is becoming a challenge. Diabetic Retinopathy leads to visual disability and is one of the major complications of Diabetes Mellitus (DM). Currently available conventional treatments for DR have certain limitations; considering this fact, options from alternative resources are being searched. In Ayurveda, retinal diseases can be included in *Drishtigata roga* (~eye sight disorder) and DR can be correlated with *Timir* (~a class of morbid affections of the coats of the eye), as pathology of *Timir* is secondary to systemic *Dosha Dushti* (~vitiation of body humor) and DR can be considered as *Pramehajanya Timir*. A male patient of 61 years visited the *Netra* (ophthalmic) OPD complaining of defective distant and near vision for two months. Based upon the history of diabetes and clinical signs and symptoms, he was diagnosed with Non-Proliferative Diabetic Retinopathy (NPDR) in both eyes. The indirect ophthalmoscopy investigation was used to confirm the diagnosis. *Nimi Nirdishta yoga* which contains *Triphala, Yashtimadhu* (*Glycyrrhiza glabra* Linn.), and *Ghrita* was administered for one month daily at night with honey. At the end of one month, there was improvement noted in distant vision without glasses from 6/18 to 6/12 in the right eye and 6/9 to 6/6p in the left eye while near vision from N/8 to N/6 in both eyes with glasses. Indirect ophthalmoscopy revealed a reduction in exudates and hemorrhages. The observations reveal that Ayurvedic approaches are helpful in managing Diabetic Retinopathy.

Keywords: *Ayurveda,* Diabetic Retinopathy, *Nimi Nirdishta yoga, Pramehajanya Timir*.

Introduction

Diabetic Retinopathy (DR) is a major complication of Diabetes Mellitus (DM), a leading cause of visual loss in the working-age population. (1, 2) DR is a target disease for VISION 2020. (3) DM, a lifestyle disorder, originates from improper dietary habits and a sedentary lifestyle, characterised by chronic hyperglycemia with disturbances in metabolism due to insulin defects. (4) DR is clinically divided into Non-Proliferative Diabetic Retinopathy (NPDR) and Proliferative Diabetic Retinopathy (PDR). (5) Laser photocoagulation manages advanced DR, halting leakage but not addressing root pathogenesis. Intravitreal pharmacotherapies revolutionise DME and PDR management but are costly and require regular application. Treatment limitations include excessive retinal tissue damage and macular oedema. (6) Addressing DR management is important for affordable medical care.

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DR and other diabetic ophthalmopathies are linked to *Prameha* (~DM) leading to *Timir* (~a class of morbid affections of the eye coats) (7). There was no direct terminology mentioned for DR in classical text. Hence we have considered it as *Pramehajanya Timira*. *Ayurvedic* approaches aim to nourish capillaries for self-maintenance. *Dosha, Saptadhatu* especially *Rakta Dhatu,*, and all four *Drishti Patala* are affected in different stages of the disease. (8) *Avarana* and *Dhatu kshaya* play roles in DR development due to prolonged hyperglycemia. *Timir* is considered "*Aushadha sadhya vyadhi*" (~curable by medicinal treatment) in Ayurvedic texts (9). *Ghrita* and *Triphala* are *Rasayana* drugs, beneficial for eye health (10, 11). *Nimi Nirdishta* yoga is recommended for *Timir* treatment in *Ashtang Hridaya* (12), hence considered for the present study. Since the formulation has been stated by Acharya *Nimi* in *Timira treatment* hence the name given as *Nimi Nirdishta Yoga*. The said formulation was described in the form of *Churna* (powder form), however for the palatability the formulation was converted into tablet form of 500mg. It was also stated to take the formulation with *Amalaki Swaras* but the *Swaras* cannot be available all the time so we have modifies it with impregnation of powder with *Amalaki Swaras* to prepare its tablet.

Patient Information

A 61-year-old, male patient reported to the ophthalmic OPD on 19-05-2021 complaining of gradual

painless diminution of distance as well as a near vision for two months. He was a known diabetic on oral hypoglycemic medicines for twenty years. On his visit to the ophthalmic OPD, his glycemic control was 9.5 (HbA1c). He was on Tab. Switglim M 2/500 and Inj. Biphasic Isophane (Humstard 30) insulin U twice a day. There was no family history of DM or DR. Patient had a defective vision for distant and near objects and was diagnosed with a case of Non-Proliferative Diabetic Retinopathy (NPDR) of stage 1 in both eyes in March 2021. He visited the OPD enquiring about Ayurvedic solutions for his condition. Ayurvedic treatment was started on 19-05-2021 after taking his consent.

Clinical findings

The patient was afebrile with Pulse-78/min and blood pressure- 130/80mm of Hg. No abnormality was noticed in the functioning of the respiratory, circulatory, or digestive systems.

Visual examination

In both eyes, the distant visual acuity without glass on Snellen's chart was right eye 6/18 and left eye 6/9. The best corrected visual acuity in both eyes was 6/9. Correction for the right eye was +0.25 spherical and-1.50 cylindrical at 90 degrees. Correction for the left eye was -0.50 cylindrical at 80 degrees. Pinhole correction without spectacles is right eye 6/12 and left eye 6/9. Near vision with and without spectacles was N/ 8 in both eyes.

Ocular Examination

Eyelids, conjunctiva, sclera, cornea and anterior chamber were normal in both eyes. Pupils were of normal size and had a normal reaction to light. Both eyes had an intraocular lens in situ. Intraocular pressure (IOP) by Schiotz Tonometry was 14.6 mmHg in both eyes. Indirect ophthalmoscopy revealed Non-Proliferative Diabetic Retinopathy (NPDR) in both eyes.

***Dashavidha Pareeksha* (~tenfold examination)**

Prakriti of the patient was *Kaphapitta*. *Pitta* predominant *Tridosha vikruti* such as *Urdhwaga Raktapitta* (~intra-retinal hemorrhages) was observed during the examination. *Satwa* (~psyche) normal, *Sara* (~excellence of tissues) normal, *Samhanana* (~compactness of organs), *Ahara shakti* (~Power of food intake and digestive functions), *Vyayama shakti* (~power of performing exercises), *Satmya* (~suitability) and *Pramana* (~measurements of body organs) of the patient were of *Madhyama* (~moderate) level.

***Ashtavidha Pareeksha* (~eightfold examination)**

Nadi (~pulse) was *Pittapradhan*, *Mutra* (~urine) and *Shabda* (~voice) was *Sadharana (*~normal). Mala (~bowel habit) was regular, *Jihwa* (~tongue) was *Anupalepa* (~non-coated), *Sparsha* (~touch) was *Anushna Sheeta* (~normal temperature), *Akriti* (~body built) was *Madhyama*(~moderate) and *Drik* (vision) was *Heena* (~diminished vision).

***Sroto Pareeksha* (~examination of body channels)**

Raktavaha srotas (~blood circulating channels) is involved in this manifestation and the pathology is *Vimarga gamana* (~flowing abnormally or in opposite directions) that possibly manifested as haemorrhages on the retina.

Timeline

There was an improvement in distant and near visual acuity in both eyes noted on a follow-up which is further illustrated in figures 1, 2, and 3 for the right eye and left eye respectively.

Figure 1. Follow up timeline

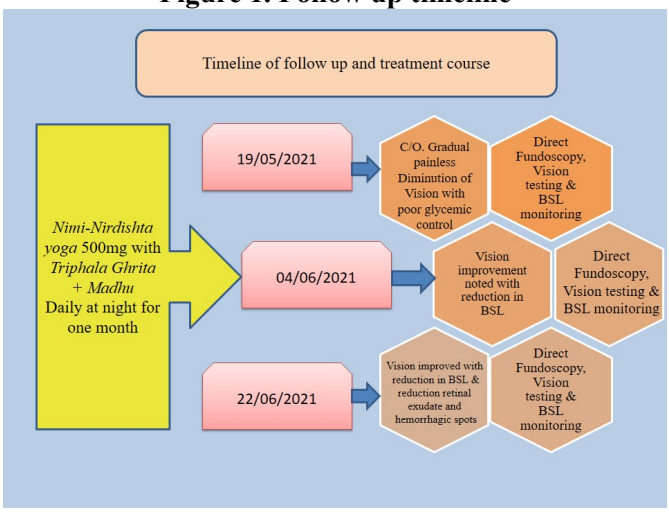


Figure 2. Vision improvement in right eye

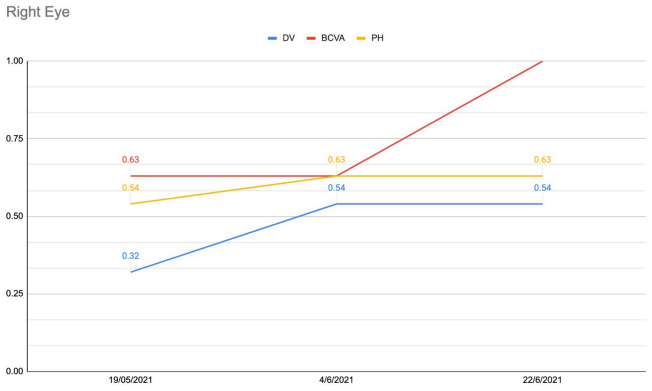
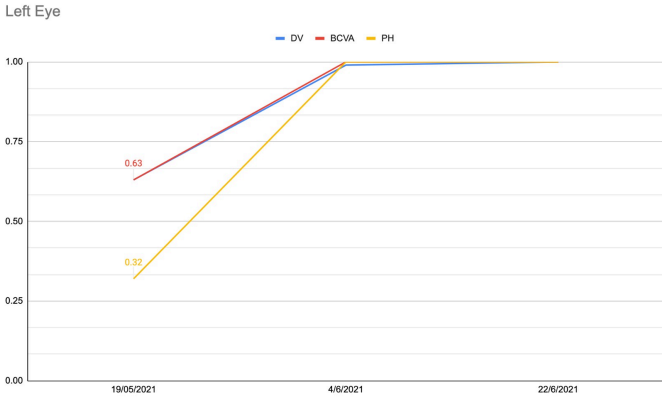


Figure 3. Vision improvement in left eye



Diagnostic assessment

Fasting blood sugar level dated 20/5/2021 was 298.16mg/dl, postprandial blood sugar level (PPBSL) was 399.62 mpg/dl and HbA1C was 9.96. Urine examination showed the presence of Sugar. Other hematological findings were within normal limits. A direct ophthalmoscopy examination was done that confirmed the diagnosis of NPDR in both eyes.

Therapeutic intervention

When the patient consulted in OPD on the same day itself he was diagnosed with NPDR due to its presenting symptoms as gradually diminishing vision with tiny hemorrhagic spots and mild exudates on the retina. Internal medicinal treatment was started on 19/05/2021 which includes *Nimi Nirdishta yoga* at night with *Anupana* (~compliant) as *Triphala ghrita* and honey is explained as follows:

Route of administration - *Abhyantar Aushadi Yoga* (~internal medication)
Drug (Pharmacological intervention) - *Nimi Nirdishta Yoga*
Dose - 500 mg 1 tablet daily at *Nishakale* (~night time)
Duration - 1 month
Compliant - 10ml *Triphala Ghrita +Madhu* (5ml)

While a detailed description of drugs is given in Table 1. No changes were made to in patient's diabetes control regime. After 15 days improvement was noted in distant and near visual acuity in both eyes. The patient continued the same treatment for the next 15 days with follow-up.

Table 1: Ingredient of *Nimi Nirdishta yoga* and its Pharmacological properties as per Ayurveda

Drug Name	Latin Name	Family	*Rasa*	*Guna*	*Veerya*	*Vipak*	*Karma*
Amalaki (Phala)	*Emblica Officinalis*	Euphorbiaceae	*Pancharasa*	*Guru, Ruksha, Shita*	*Shita*	*Madhur*	*Tridoshhar, Rasayan*
Haritaki (Phala)	*Terminalia Chebula* Retz.	Combretaceae	*Pancharasa (except Lavan Kashaya Rasa*	*Laghu, Ruksha*	*Ushna*	*Madhur*	*Chakshushya, Rasayan, Tridoshhar*
Bibhitaki (Phala)	*Terminalia bellirica*	Combertaceae	*Kashaya*	*Ruksha, Laghu*	*Ushna*	*Madhur*	*KaphaPittahara, Chakshushya*
Yashtimadhu (Mula)	*Glycyrrhiza Glabra* Linn.	Leguminasae	*Madhur*	*Guru, Snigadha*	*Shita*	*Madhur*	*Tridoshhar, Rasayan,*
Ghrita	*Butyrum*	-	*Madhur*	*Guru, Snigdha,*	*Shita*	*Madhur*	*Chakshushya,*
Madhu	*Mal*	-	*Madhur*	*Ruksha,Grahi*	*Shita*	*Madhur*	*Chakshushya*

Follow-up and Outcome

Fundus examination revealed a reduction in exudates and haemorrhages in both eyes. Visual acuity was maintained during the follow-up period shown in Table 2. Scaling down of raised blood sugar levels was observed during and after the course of treatment. Changes in blood sugar level along with the report date are stated in Table 3.

Table 2: Follow-up and outcome: Improvement in vision

	Right eye			Left eye		
	Without Specs 19/5/2021	Without Specs 4/6/2021	Without Specs 22/6/2021	Without Specs 19/5/2021	Without Specs 4/6/2021	Without Specs 22/6/2021
DV	6/18	6/12p	6/12p	6/9	6/6(P)	6/6(P)
BCVA	6/9	6/9	6/6(P)	6/9	6/6(P)	6/6(P)
PH	6/12	6/9p	6/9	6/12	6/6(P)	6/6(P)
NV	N/8	N/6	N/6	N/8	N/6	N/6

DV- Distant Vision, **BCVA-** Best Corrected Visual Acuity, **PH-** Pin Hole Correction, **NV-** Near Vision, **P**-Partial

Table 3: Changes observed in blood sugar profile

	Changes in blood sugar profiles		
Date	20/05/2021	03/06/2021	21/06/2021
Fasting BSL	298.16 mg/dl	269.30 mg/dl	114.1 mg/dl
Post Prandial BSL	399.62 mg/dl	344.51 mg/dl	319.6 mg/dl

Discussion

Prameha, one of the eight major disorders in *Charaka Samhita*, underscores its significance according to ancient seers. (13) Diabetics face a 20-25 times higher risk of blindness development compared to the general population. The prevalence rates of Diabetic Retinopathy (34.6%), proliferative diabetic retinopathy (7%), diabetic macular oedema (6.8%), and vision-threatening Diabetic retinopathy (10.2%) are alarming, prompting a modern pathogenic analysis based on Ayurvedic texts. (14) *Acharyas* collectively categorise diseases affecting vision under *Drishtigataroga*. In diabetic retinopathy, gradual vision loss is prominent, akin to *Drishtiroga*, which describes progressive vision loss based on *Patala* involvement. *Timir*, analogous to DR stages, prognosis is linked to *Patala* involvement,

delineated by the functional composition of *Dhatu* and *Drishti*. *Doshas* affecting *Dhatu* manifest vision symptoms, establishing a probable correlation between *Timir* symptoms and diabetic retinopathy stages (14). Reviews suggest the first *Patala* corresponds to cornea and aqueous humor, the second to iris and uveal tract, the third to the cortical lens and vitreous humor, and the fourth to the nuclear lens (15).

Pathogenesis of DR

The activation of a number of interconnecting pathways occurs due to prolonged DM. Hyperglycemia causes the increase of oxidative stress which cause the overproduction of superoxide known to act as a stressor link between all pathways. This complex pathology progressively reaches the stage of proliferative diabetic retinopathy and diabetic macular oedema. (16)

In *Prameha* main etiological factor is the vitiation of *Kapha* which is caused by *Kapha* predominant diet and lifestyle. The ophthalmic complications begin to manifest when most of the etiological factors are *Achakshushya* (~not beneficial to eyes as a sense organ). According to the Ayurvedic anatomy of the eye, the functioning of the eyes depends upon *Vatavaha, Raktavaha, Kaphavaha,* and *Pittavaha sira* (~any tubular vessel of the body). Vitiated *Dosha* circulated in upward directions (i.e. *Urdhva jatrubhaga*) through *Sira,* reaches the *Patala* of eyes, and produces the disease, *Timir*. The *Sira* having synonyms as *Srotasa* gets *Avruta* (~covered) by *Kapha Dosha* leads to *Srotas avarodha* (~obstructive pathology occurring in channels). (17)

The function of normal *Kapha* is *Sandhibandhana* (~joint stability). Pre capillaries, arterioles, capillaries, and venules are the types of vessels that are made up of tissue, elastic fibers, and smooth muscle cells. These all factors are intact together because of the character of joint stability.(18) Vitiation *of Kapha Dosha* leads to impeding normal functioning of *Kapha Dosha* that causes *Sandibandhana vikruti* (~deformity in joints) means capillary endothelial cell damage and loss of capillary pericytes. *Prithvi* (~earth) and *Jala* (~water) *Mahabhutas* are predominant in *Kapha*. Hence increase in *Prithvi* and *Jala mahabhuta* causes the thickening of the capillary basement membrane. In *Dushya* (~vitiated tissues) *Sangraha* of *Prameha*, *Meda* (~adipose tissue) is the foremost factor. The normal function of *Meda* is *Snehan* (~oleation). *Sira* is *Mrudu paka* (~soft transformation) of *Meda* and *Updhatu* (~the minor structural components that stabilize and sustain the body) of *Meda*, so *Sira* is also affected in *Meda vikruti* (~abnormal fat tissue).

As the chronicity of *Prameha* increases, symptoms like *Indreeya dourbalya* (~impairment of sense organs) occur. The eyes are the prime sense organ also it has been mentioned in the classic "*Hrinnetra jihwa saravangopadeha"* which states about the involvement of vital organs like an eye in *Prameha* pathogenesis. (19) Eyes are one of the *Bahya srotas* (~external body channel), its *Srotas dushti lakshana* (~vitiation of body channels) which are grossly mentioned by *Charaka* in *Viman sthana* can be correlated with signs of diabetic retinopathy as follow-

Atipravrutti (~increase or overflow of the content in the body) refers to an excessive formation of capillaries that leads to neovascularization. Neovascularization is the excessive growth of new blood vessels in an area where there is a lack of adequate blood supply. This condition can lead to vision loss.

Sanga/Siravarodha (~obstruction in tubular body vessels) by *Kapha* is another condition caused by an imbalance in the *Kapha*. It refers to retinal vessel occlusion leading to hypoxia-related ischemia. This condition is characterized by blockages in the retinal vessels which disrupt the blood supply to the eye leading to reduced oxygenation and an insufficient supply of nutrients.

Sira granthi (~occurrence of nodular growth in the body channels) refers to microaneurysms, which are small bulges in the walls of blood vessels. These aneurysms can be found in the eyes and can cause vision problems if they rupture or become blocked.

Vimarga gamana (~diversion to the flow of the content to the improper channels) is another condition that refers to the presence of hemorrhages, hard and soft exudates, Intra Retinal Microvascular Abnormalities (IRMA), and Neovascularization of Disc (NVD). Hemorrhages are bleeds on the retina, exudates are deposits of fatty material, and IRMA refers to abnormal blood vessels in the retina. NVD refers to new blood vessels growing on the optic disc, which can lead to vision loss.

Therapeutic intervention i.e. *Nimi Nirdishta yoga* possesses predominance of *Madhur* (~sweet in taste) *Kashaya rasa* (~astringent), *Ruksha gunas* (~unctuous), *Sheeta virya* (~cold potency), *Madhur vipaka* (~sweet biotransformation), hence acts as *Tridosha shamana* (~alleviates all three *Dosha*).

With the help of earlier mentioned symptoms of vitiation of body channels, probable *Samprapti Vighatana* (~breakdown of etiopathogenesis) would be as follow:

- **Action on *Atipravrutti*-** *Prameha* is *Kapha* predominant *Tridoshaja vyadhi*, along with mainly tissue involved *Meda, Mamsa* (~muscular tissue), *Nimi Nirdishta yoga* acts on *Tridosha* along with specifically *Kapha Dosha.*
- **Action on *Sanga/Sira avrodha- Sira avrodha*** (obstruction of tubular body vessels) occurs due to *Kapha Dosha*. Here *Mruduvirechan* (~mild laxative) property of *Amalaki* (20), *Bibhitaki's Bhedya* (~therapeutic carving/dissection) character (21), *Haritaki's Anuloman* (~purgative) (22) property helps in removing of *Sira avrodha* (~capillary occlusion), reduce the thickening of capillary walls. *Shamana of Vata Dosha* which is vitiated by *Sira Avrodha* is occurred by *Amla, Madhur Rasa* of *Amalaki, Madhur Vipaka* of *Haritaki,* and *Madhur Rasa* and *Vipak* of *Yashtimadhu.*
- *Dhatu* like *Rasa, Mamsa, Meda,* and *Upadhatu Dushti* occurs by *Kledak Kapha* in *Prameha* and is treated by *Kaphakledhara, Rasasrukmansamedoj Doshahara* property of *Bibhitaki*.
- ***Sira granthi-*** *Sandhibandhaniya vikruti* treated as *Yashtimadhu* is one of the herbs mentioned in *Sandhaniya gana* by *Acharya Charaka*. (23) Also, *Amalaki's Sthambaniya* (~styptic action) and *Haritaki's*

Varnya property is helpful to prevent the loss of pericytes and strengthen capillary walls by repairing these vessels.

- ***Vimarga gamana*** (Hard exudates, dot and blot hemorrhages)- may be reducible as *Vatahara, Rasayana* (~rejuvenating), *Shodhaniya* (~detoxifying), *Lekhaniya* (~therapeutic scraping) and anti-inflammatory properties of *Triphala Churna.*

Direct and Indirect ophthalmoscopy has been done and findings were recorded before and after treatment.

No new exudative or hemorrhagic spots are seen i.e. cessation of disease progression was occurred due to the breakdown of pathogenesis which ultimately stopped the development of *Timir*, i.e. Diabetic retinopathy. Since the facility of fundus photograph is not available at center hence not able to perform it. However improvement in vision is evident and had been shown as before and after treatment.

- **Improvement of *Drishti* (vision)** - Etiological factors of *Prameha* are mainly *Achakshushya* (~non-beneficial to eyes) factors that cause *Kleda Utpatti* along with *Kapha* leading to *Chakshu Vaisheshika Alochaka Pitta Dushti* (~vitiation of one of the types of *Alochak Pitta*). Reduction of *Kleda* by *Ruksha, Laghu Guna* will ease *Kapha* along with the absorption of *Kleda*. Due to this along with the *Chakshushya* property of *Triphala Churna, Alochaka Pitta* gets normalized leading to the improvement of vision.

Ghrita which has *Chakshushya, Rasayana,* and *Sanskarasyaanuvartanam* property is given as media to reach the targeted sight i.e. eye. *Ghrita* also contains vitamins A, D, E, and K. Vitamin A and E are well known for their anti-oxidant properties and are helpful in the prevention of various oxidative process which causes loss of pericytes of the capillaries wall. (24)

Triphala exerts hypoglycemic effects. Patients with type 2 diabetes are likely to have high postprandial blood glucose levels, especially after consuming carbohydrates. Elevated blood glucose results from the breakdown of carbohydrates by the digestive enzymes, alpha-amylase and alpha-glucosidase, and reduced ability of cells to take in glucose from the blood. *Triphala* may exert actions similar to diabetic pharmaceutical drugs by inhibiting digestive enzymes and may decrease glucose absorption by inhibiting glycolytic enzymes, thereby reducing blood glucose levels. *Triphala*, including ellagitannins and gallotannins, also enhance PPAR-alpha and –gamma signaling, increasing insulin responsiveness and glucose uptake without inducing adipogenesis. These polyphenols may also promote decreased blood glucose and insulin levels in diabetic patients. Elevated BSL can cause severe damage through glycation, in which sugar molecules compromise protein molecules in the body, which may lead to nerve damage or blindness. The tannins in the *Triphala* effectively inhibit protein glycation in vitro. (25)

Yashtimadhu (*Glycyrrhiza glabra* Linn.) plant contains different phytocompounds, such as glycyrrhizin, 18B-glycyrrhetinic acid, glabrin A and B, and isoflavones, that have demonstrated various pharmacological activities. Pharmacological experiments have demonstrated that different extracts and pure compounds from this species exhibit a broad range of biological properties, including antibacterial, anti-inflammatory, antiviral, antioxidant, and antidiabetic activities. (26)

In the early stage of diabetic retinopathy i.e. up to the NPDR stage, available options are periodic ophthalmic examination, good glycemic control, and antioxidants medications. Considering the above factors, the NPDR case was treated with Ayurvedic medicines to regain or maintain visual acuity and restrict the further progression of disease.

Conclusion

With the help of available literature in Ayurveda and modern medicine, diabetic retinopathy can be considered as *Pramehajanya Timir*. This shows that in the management of NPDR by medicine *Nimi Nirdishta yoga* is as effective. The disease process is not reversed but can be controlled up to a certain extent. *Ayurveda* classics mentioned the duration of administration as one month of *Nimi Nirdishta yoga* for the improvement of vision in various diseases and showed the result in the short time span in the case of NPDR. However, this clinical study's results can substantiate with more clinical trials. Thus, it can be concluded that Ayurvedic approaches are helpful in managing complications like Diabetic Retinopathy.

Scope for further study

Diabetic Retinopathy is a vision-threatening complication and can be studied on a molecular level with the help of Ayurvedic medicines. The Anti-VEGF (vascular endothelial growth factor) medicines/herbs in Ayurveda can be identified and tested on such chronic ailments of the eye where modern medication has limitations.

Declaration of patient's consent

Authors certify that they have obtained patient consent form, where the patient/caregiver has given his/her consent for reporting the case along with the images and other clinical information in the journal. The patient/ caregiver understands that his/her name and initials will not be published and due efforts will be made to conceal his/her identity, but anonymity cannot be guaranteed.

Patient's perspective

"I have been diagnosed with diabetes 20 years back and recently I noticed that my vision was becoming blurry, even with glasses. During my visit to the outpatient department, I came to know that my diabetes had caused changes on my retina and was diagnosed as non-proliferative diabetic retinopathy. However, after starting an Ayurvedic treatment, I was pleasantly surprised to see an improvement in my vision and a decrease in my blood sugar levels in a short span of time. I am now feeling confident about the effectiveness of Ayurveda medicines and will continue further to avoid such complications."

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Conflicts of interests: NIL

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