

The effects of hemodialysis on the eye

Olena Protsyk^{1,2}, Javier Lacorzana^{3,4}

The purpose of this study was to examine the effects of hemodialysis on the eye and its long-term consequences. Hemodialysis is a process that purifies the blood and maintains the balance of water, solutes, acid-base, and electrolytes. The eye, being primarily composed of fluid, has been speculated to be affected by this technique. To analyze these effects, a literature review was conducted, focusing on the anatomical structures, functions, and changes in the eye following hemodialysis. The search for relevant articles was carried out on PubMed, including studies published in English between 2000 and 2023. The results of the review showed that certain observations such as visual acuity, refraction, intraocular pressure, biometric parameters, and retinal nerve fiber layer did not show significant timing-related impacts, or there were conflicting findings. However, a connection was established between hemodialysis sessions and visual fields, parameters of visual-evoked potential, intraocular pressure in glaucoma, tear break-up time, Schirmer's test values, choroidal thickness, flow velocities of vessels, and ocular perfusion pressure values. In conclusion, it was determined that hemodialysis sessions can cause fluctuations that may complicate the assessment of eye health. To obtain a more accurate baseline evaluation, it is recommended to schedule ophthalmological examinations, a few hours after the hemodialysis session. Additionally, it is important to provide appropriate management for dry eyes and ocular hypertension, particularly during hemodialysis sessions. Coordination of these examinations with the timing of renal replacement therapy is advised to ensure optimal patient care.

Key words: Chronic kidney disease, eye, hemodialysis, intraocular pressure, ocular diseases, review

Hemodialysis (HD) is a medical procedure that extracorporeally replaces the kidney function by removing fluid and waste products from the blood. During HD, several metabolic, osmolar, and structural changes occur that affect body fluids, including ocular fluids. In addition, several diseases that affect the kidneys also affect the eyes (e.g., diabetes mellitus, arterial hypertension, Alport syndrome, tubulointerstitial nephritis, and uveitis); therefore, many HD patients also undergo ophthalmological assessment.

Although the effects of HD on systemic pathologies have been previously investigated, currently, no studies have analyzed in detail the effects of HD on the eye.^[1-3] Thus, we sought to assess the effects of HD on the eye to facilitate multidisciplinary management. Accordingly, we conducted a literature review to identify all articles discussing HD and the eye, investigate the pathophysiology that explains the effects of HD on the eyes, based on current scientific evidence, identify possible eye complications secondary to HD, investigate

factors that could affect the process, and investigate all therapeutic approaches to avoid complications. We focused our investigation on the different anatomical structures, functions, and alterations of the eye.

Literature research methodology

We searched PubMed using the key terms “haemodialysis” OR “hemodialysis” OR “dialysis” AND “eye” OR “ocular” NOT “dialysis peritoneal” for articles published in English from 2000 to March 28, 2023.

Synthesis of findings

Visual acuity and refraction

Both best-corrected visual acuity (BCVA) and refraction may be affected by post-HD physiological changes. Much of the volume of the eye is fluid; therefore, anatomical or functional changes after an HD session are plausible. However, most recent studies have not reported significant changes in BCVA or post-HD refraction.^[2-9]

Controversies remain regarding the long-term effects of renal replacement therapy or HD on BCVA. Hwang *et al.*^[10] found structural improvement in optical coherence tomography (OCT)

Access this article online

Website:

<https://journals.lww.com/ijo>

DOI:

10.4103/IJO.IJO_1450_23

Quick Response Code:



¹Department of Ophthalmology, Jaen University Hospital, Jaen, Spain,

²Doctoral Program in Clinical Medicine and Public Health, University of Granada, Granada, Spain, ³Cornea Unit, Moorfields Eye Hospital, London, UK, ⁴Department of Ophthalmology, Virgen del Rocío University Hospital, Seville, Spain

Correspondence to: Dr. Olena Protsyk, Department of Ophthalmology, Jaen University Hospital, Av. Del Ejército Español 10, 23007, Jaen, Spain. E-mail: olenaprotsyk@gmail.com

ORCID:

Olena Protsyk: <https://orcid.org/0000-0002-8287-3053>

Javier Lacorzana: <https://orcid.org/0000-0002-7625-7078>

Received: 04-Jun-2023

Revision: 04-Oct-2023

Accepted: 25-Feb-2025

Published: 24-Apr-2025

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Cite this article as: Protsyk O, Lacorzana J. The effects of hemodialysis on the eye. Indian J Ophthalmol 2025;73:648-55.

one month after starting HD in diabetic patients without previous ophthalmological treatment. Nonetheless, in the multicenter study by Takamura *et al.*,^[11] functional improvement in patients with diabetic retinopathy at 1 month and 1 year was reported only in patients whose initial BCVA was better than or equal to 20/50. Moreover, Sun *et al.*^[3] found that diabetic patients had a statistically significant improvement in BCVA after one HD session. Risovic *et al.*^[12] also noted significant changes after one session in near visual acuity. Other authors observed that half of their patients became hyperopic.^[4,5]

Ocular surface

Common symptoms of dialyzed patients include red and irritable eyes. Alterations in the tear break-up time (TBUT), Schirmer's test, and ocular surface disease index test may be present (60–70%, 20–40%, and 77% of the population, respectively).^[13–15] Aktas *et al.*^[14] reported similar results; however, they found no significant difference in Schirmer's test results between the study and control groups. Therefore, they do not recommend the exclusive use of this test to diagnose dry eye in HD patients, as it may underdiagnose dry eye. Using OCT, Kal *et al.*^[16] found decreased tear meniscus height, depth, and area in HD patients. These findings correlated with Schirmer's test and TBUT but not with the ocular surface disease index test. Zong *et al.*^[15] found differential proteins in the tears of HD patients compared to healthy controls. Thus, the possibility arises to identify biomarker candidates and to help improve the diagnosis and classification of dry eye disease.

It is unclear whether the differences found in previous studies between dialyzed patients and healthy controls are due to underlying chronic kidney disease (CKD) or HD. However, the effects of an HD session on the ocular surface have been widely studied, the results of which describe a decrease in TBUT and Schirmer's test values.^[2,5,7,17] Contrary to previous studies, Nakata *et al.*^[18] found an improvement in basal tear secretion in non-diabetic patients. An increase in the severity of corneal epitheliopathy, dry eye symptoms, and normalization of tear hyperosmolality due to the decrease in urea has also been reported after one HD session.^[2,5,7,19]

In patients with dry eyes, tear osmolality is increased mainly because of an increase in sodium. Nevertheless, in HD patients, in addition to the usual pathophysiology of dry eye, there is an increase in urea before HD sessions and a decrease in tear secretion. Urea has a protective effect on the ocular surface, so any epithelial defects that may occur are usually milder despite hyperosmolality.^[20]

One of the most frequent ophthalmological findings in HD patients is corneconjunctival calcium deposits.^[2,13,14,17,20,21] These are frequently located in the interpalpebral conjunctiva close to the limbus. Ismayilov *et al.*^[17] observed that after an HD session, patients with these lesions had lower TBUT and Schirmer's test results. However, Özdemir *et al.*^[22] found no such relationship. Regarding the length of time patients have been on dialysis, several authors found a relationship between this parameter and the amount of calcification.^[17,21] Moreover, Hsiao *et al.*^[23] found a statistically significant relationship between the severity of calcifications and 1-year mortality in dialysis patients.

Squamous metaplasia may also occur in patients with dry eyes. These cellular changes can be observed in impression cytology, and their alterations are very frequent in patients on sustained HD. Demir *et al.*^[24] observed a positive relationship

between the duration of CKD and the presence of metaplasia, with a higher degree of metaplasia in patients with longer disease duration. However, the actual impact of HD on these histological changes is unclear.

Balbaba *et al.*^[25] analyzed the conjunctival bacterial flora in dialysis patients and observed a positive relationship between the duration of HD and culture positivity. The most frequently detected microorganism in dialyzed patients was *Staphylococcus aureus*, followed by *Staphylococcus epidermidis*. In healthy controls, the *Staphylococcus epidermidis* remained stable; however, the prevalence of *Staphylococcus aureus* decreased markedly.

Anterior segment

Intraocular pressure

Intraocular pressure (IOP) is determined by the production and drainage of aqueous humor (AH). Changes in osmolality, oncotic pressure, and urea levels during HD may influence this balance.^[26] Theoretically, a series of processes occur during HD. (1) Solute elimination eliminates low molecular weight molecules by diffusion, thereby decreasing plasma osmolality and generating an osmolar gradient between compartments. These changes lead to an increase in AH production and a decrease in its drainage, thus increasing IOP.^[27] (2) Fluid clearance, achieved by ultrafiltration, leads to an increase in plasma oncotic pressure, a decrease in AH production, and an increase in drainage. Consequently, IOP is decreased. (3) A decrease in extracellular urea with no effect on intracellular urea results because both compartments tend to equalize their concentrations over time. This flow, called the urea rebound effect, may also influence IOP.^[28,29] Tovbin *et al.*^[30] observed that high post-dialysis urea rebound correlated positively with intra-dialysis changes in intraocular pressure.

CKD is associated with a higher IOP, independent of age, diabetes, and glaucoma.^[31] However, the influence of HD on the CKD-IOP relationship remained unclear, and it was unknown whether this IOP increase may also be affected by HD.^[27,32,33]

Most authors found no significant changes between pre- and post-HD values.^[1–3,10,26,34–47] Although some studies reported a statistically significant decrease in IOP with discrete values (maximum – 3 mmHg on average), the results may be clinically insignificant.^[5–8,17,28,48–55] However, two studies observed increased IOP after HD sessions.^[56,57] Possibly, these results can be explained by the fact that Hu *et al.* did not exclude glaucoma patients, and the measurement by Panagiotou *et al.* was obtained 24 h post-HD, unlike the other studies, which measured in the immediate hours after HD.

Over the years, IOP measurements between studies have not been standardized, making comparison difficult. Yet, Chen *et al.*,^[58] in a meta-analysis, showed that acetate HD increased IOP. As dialyzer switching from acetate to bicarbonate HD became more prevalent, HD ceased to significantly affect IOP and even lowered IOP.

It has been observed that mean and peak IOP, as well as its fluctuations, during HD days were higher than those during non-HD days.^[57] Furthermore, patients treated for a longer duration were more likely to have a higher IOP after their sessions.^[52] Such changes in IOP during HD have also been studied in patients with narrow angles, with controversial results.^[5,26]

Other cases with a tendency toward IOP peaks have been described. Their etiologies are variable; however, all show a decrease in AH drainage manifested by existing glaucoma,

narrow angles, neovascularization, pseudoexfoliation, and recent pars plana vitrectomy, among others.^[29,33,59–68] Chen *et al.*^[58] in a meta-analysis found that glaucoma was a significant moderator independent of the dialysate effect in bivariate meta-regression. Wang *et al.*^[69] concluded that IOP varies in relation to anterior chamber anatomy. Due to their comorbidities, the management of these patients with underlying ocular pathology can be complex and should be personalized. Treatment options include antihypertensive eye drops, oral acetazolamide, hypertonic solution with glycerol, intravenous mannitol or intravenous glucose, laser or glaucoma surgery, and modification of hemodialysis parameters or modality.^[27,29,36,59–61,63–68,70]

Corneal thickness

Changes in corneal thickness can influence IOP measurements obtained by Goldman tonometry, causing overestimation and underestimation in the cases of thickening and thinning, respectively. As the degree of corneal thickening is important when assessing refractive corneal surgery, special attention should be paid to candidates for these surgeries who are undergoing HD.

After one HD session, most authors found no change in central corneal thickness.^[1,2,9,39,42,47–49,51] Moreover, in studies wherein a significant decrease was detected, it was less than 15 µm on average.^[5,7,13,50,54]

Diaz-Couchoud *et al.*^[20] and Ulaş *et al.*^[48] found no difference in corneal thickness between dialyzed patients and patients without renal pathology at a 4-year follow-up. However, Sati *et al.* found greater corneal thickness in dialyzed CKD patients than in non-dialyzed CKD patients, with non-dialyzed CKD patients having greater corneal thickness than patients without renal pathology.^[71]

Corneal endothelium

Diaz-Couchoud *et al.*^[20] compared dialyzed patients with those without renal pathology and observed decreased endothelial density in the first group. However, they found no differences in polymegathism (coefficient of variation) or polymorphism (hexagonality). This confirms that endothelial cell density decreases in patients with a longer duration of HD treatments. Sati *et al.*^[71] compared dialyzed CKD patients and non-dialyzed CKD patients with those without renal pathology, and their results were compatible with those of Diaz-Couchoud *et al.* Endothelial density was lower in dialyzed CKD patients than in non-dialyzed CKD patients and lower in patients without renal pathology than in non-dialyzed CKD patients. There were no significant differences between the three groups in polymegathism and polymorphism.^[71] In contrast, Kanawa *et al.*^[72] found no significant differences in endothelial density, but they did find changes in polymegathism and pleomorphism while comparing hemodialyzed CKD patients, non-hemodialyzed CKD patients, and healthy controls. Chen *et al.*^[2] analyzed this relationship acutely and found no changes in the endothelium after one HD session.

Anterior chamber depth, axial length, iridocorneal angle, and biometry

The decrease in anterior chamber depth and axial length after an HD session is concerning not only because of possible changes in biometry but also because of hypothetical secondary angle-closure glaucoma. Overall, most authors found no statistically significant differences concerning pre- and post-HD anterior chamber depth, although Ismayilov *et al.*^[17] ($n = 71$) observed an increase in post-HD anterior chamber depth.^[8,37,39,42,54]

There seems to be more agreement on axial length; however, the measurement methods varied. Studies reported either no change or a discrete increase of approximately 0.04 mm on average.^[8,17,37–39,42] Kalayci *et al.*^[7] found a decrease in axial length of approximately 0.26 mm in their study of 112 eyes.

Elbay *et al.*^[11] analyzed the iridocorneal angle by OCT and found no change in its width.

Overall, the HD session did not significantly change the intraocular lens calculation.^[39]

Lens

Cataracts are common ophthalmological findings in HD patients (50–60%).^[17,21] Wang *et al.*^[37] ($n = 52$) found an increase in lenticular thickness following an HD session; they hypothesized that at the time of measurement, the lens had a higher urea concentration than the AH, generating a water gradient toward its interior. However, Chen *et al.*^[2] ($n = 45$) observed a decrease in thickness, and Caliskan *et al.*^[39] ($n = 40$) and Mayali *et al.*^[42] ($n = 22$) found no change. Thus, the effect of an HD session on the lens is not yet clear.

Posterior segment

OCT has enabled a major advancement in the study of the retina. This test provides quantitative information for patients undergoing HD treatment. When examining the variations caused by HD in the retinal nerve fiber layer (RNFL), retinal thickness, and choroidal thickness, the statements were very variable. It is almost impossible to draw a singular conclusion as all published studies to date used different OCT and even different software.

Retinal nerve fiber layer

RNFL thickness is important in optic neuropathies; therefore, in these patients, the effect of this variable on follow-up or therapeutic decisions is of interest. It has been observed that patients undergoing HD have a lower RNFL thickness than healthy patients.^[73,74]

Regarding the impact of an HD session on the RNFL and ganglion cell layer, different authors found no statistically significant differences.^[49–51,55,73,75] However, some authors found changes only in certain quadrants.^[2,41,74]

Retinal thickness

Retinal thickness can be measured using OCT. To date, studies on the effect of HD sessions on retinal thickness have not reached a clear conclusion. Most studies found no change in retinal thickness after HD sessions, whereas some found a significant increase, and others found a decrease.^[2,3,6,8,34,37,41,45,46,48,51,55,74–77]

Diabetic patients require special consideration as they have an impaired blood-retinal barrier; therefore, hemodynamic changes can significantly impact the retina's condition. The impact of an HD session on macular thickness in patients with diabetes is controversial. Some authors found no difference; however, others found a decrease, whereas one study reported an increase.^[2,3,6,8,45,46,76,78–80] However, the differences observed are smaller in diabetic patients with macular edema than in those without macular edema.^[2,79]

Regarding the longer-term effect of HD on retinal thickness, in 2000, Tokuyama *et al.*^[81] found no change in diabetic macular edema in patients analyzed using angiography 1 month after the initiation of therapy. However, Matsuo observed the disappearance

of exudates in a diabetic patient after starting HD, hypothesizing a “drying of the retina” due to HD.^[82] Furthermore, Hwang *et al.*^[10] found a decrease in both central retinal thickness and the incidence of diabetic macular edema in diabetic patients without prior ophthalmological treatment. The results of a retrospective multicenter study are similar: A decrease in thickness was maintained up to 1 year after the start of HD with an improvement in BCVA.^[11] Suryakanth *et al.*^[83] even found a decrease in a short term of 30 days. The results of these observations and the fact that the changes between the right and left eyes are parallel support the theory of a systemic influence on diabetic macular edema, with nephropathy itself being an independent risk factor for edema.^[11]

Choroidal thickness

Choroidal tissue is of great importance in supplying blood flow to the photoreceptors and impacts the creation and drainage of AH through the uveoscleral pathway, affecting IOP.

Almost all authors agree that choroidal thickness decreases after HD in the macular and peripapillary areas.^[1–3,8,10,35,37,40–42,45,46,48,49,55,77,84] This could be due to the direct effect of fluid depletion generated during HD or the sympathetic vasoconstrictor response of the choroid as an autoregulatory mechanism after hypotension. Jung *et al.*^[44] were the only ones to observe an increase in thickness post-HD; this was probably due to the manual measurement technique using spectral domain OCT without the enhanced depth imaging mode. Zhang *et al.*^[34] found no significant changes in subfoveal choroidal thickness or choriocapillary vascular density with OCT-angiography. In diabetic patients, this decrease in choroidal thickness is similar or even more marked than in non-diabetic patients.^[8,35,40,45,46,49]

Vascularization

Retrobulbar blood flow

Tosun *et al.*^[85] analyzed the effects of an HD session on retrobulbar blood circulation. They found a decrease in the systolic and diastolic flow velocities of vessels in both eyes, including the ophthalmic artery, central retinal artery, central retinal vein, and posterior ciliary arteries.

Ocular perfusion pressure

Ocular perfusion pressure is estimated by the difference between two-thirds of the mean arterial pressure and IOP. Except for Barbosa *et al.*,^[43] who found no significant differences, a decrease in its values was found after HD sessions.^[8,34,37,45,56]

Retinal blood flow

Nagaoka *et al.*^[86] observed an increase in retinal vascular diameter after an HD session. Their findings are congruent with Sun *et al.*^[3] Zhang *et al.*^[34] detected a decrease in vascular density in the outer retinal layer rather than the superficial and deep capillary plexuses. In contrast, Coppolino *et al.*^[84] observed a significant decrease in foveal vascular density in the superficial and deep capillary plexuses.

Neuro-ophthalmology

Neurological toxicity, caused by the accumulation of substances not excreted by the diseased kidney, requires further study, and visual-evoked potentials (VEPs) can help us in this regard. VEPs provide objective information on the functional integrity of central nervous system structures. Derici *et al.*^[87] found prolongation of P100 latency in 33% of their patients in HD, of whom 75% returned to normal at the time of the session. This suggests a neurotoxic effect of the accumulated substances. Seymen *et al.*^[88] and Güzey

Aras *et al.*^[89] observed changes in VEP in HD patients compared to healthy controls. Moreover, in a blink reflex study conducted by Resende *et al.*,^[90] a similar phenomenon was observed, and differences were found when compared with healthy participants.

Sudden vision loss

Cases of sudden vision loss in patients with CKD have been described that have been associated with multiple factors, such as uremia, episodes of hypotension, anemia, and a previous history of anterior ischemic optic neuropathy (AION). However, these patients already have more cardiovascular risk factors (diabetes, hypertension, and dyslipidaemia); therefore, the loss of BCVA could not be directly attributed to their renal disease. Winkelmayer *et al.*^[91] suggested the following classification of possible causes:

- Uremic optic neuropathy: Cases of vision loss in patients with conditions of high uremia that fully or partially improve with HD and/or corticosteroids. This group has been proposed to resemble peripheral uremic neuropathy and uremic encephalopathy.^[91]
- Ischemic optic neuropathy (anterior and/or posterior): The main risk factors are thought to be anemia and hypotension, although some generalized hypoxia may also play a role. Loss of vision during HD is a rare, but described event. The most common complication during HD is hypotension, and therefore, the etiology of this acute BCVA loss is possibly ischemic. This theory is supported by the findings described in the section on vascularization: decreased flow velocity in the retrobulbar blood circulation detected by Doppler ultrasound and decreased ocular perfusion pressure after the HD session. Different authors have suggested a series of recommendations in patients with AION, including empirical corticosteroid therapy, 24 h blood pressure monitoring, avoiding eating and sleeping during the HD session, lowering the temperature of the dialysis solution (35.5°C), blood transfusion if anemia occurs, erythropoietin, antiplatelet therapy, vasoconstrictors, and reducing the duration of sessions and increasing their frequency.
- Cerebral infarction.
- Intracranial hypertension.
- Associated with drugs, brain infections, etc.

Optic disc swelling with preserved visual function

Chang *et al.*^[92] described the case of a patient undergoing HD who presented with papilledema due to intracranial venous hypertension. On examination, coexistent stenosis of the brachiocephalic vein was observed. Thus, much of the arterial flow is diverted through the shunt to the brain rather than the heart.

Motivated by this case, Taban *et al.*^[93] studied a series ($n = 44$) of HD patients; however, none of them had papillary edema, headache, vision loss, or visual events. Therefore, the authors suggest routine ophthalmological examinations in asymptomatic patients as uncensored.

Visual field

Costagliola *et al.*^[94] followed up the visual field of HD patients for 5 years without finding significant changes. Pelit *et al.*^[95] compared pre- and post-HD visual fields and observed an improvement in the mean deviation. Compared with healthy controls, they found differences in pre-HD values rather than post-HD values. Therefore, they recommend performing visual field tests for patients following HD sessions.

Pahor conducted an observational study comparing HD patients and healthy controls.^[96] He found differences in sensitivity that were unrelated to the duration of HD and may be linked to CKD rather than HD. This supports the hypothesis of uremic neuropathy, that is, the existence of neurological toxicity caused by uremia or the chronic accumulation of other toxic substances that are not excreted.

Ocular motility

Risovic *et al.*^[12] analyzed binocular vision disorders. They observed significant differences after the HD session in convergence, near BCVA, a worsening of binocular correspondence (Maddox rod and Worth test) and TNO test. However, no differences were found in Lang's stereo test, Cover's test or motility.

Following the same theory as that of ischemic optic neuropathy described above, Komine *et al.*^[97] presented a series of three cases of oculomotor palsy after HD.

Endophthalmitis

Hemodialysis patients have a higher prevalence of endogenous endophthalmitis. In the case series of Kuo *et al.*,^[98] almost all patients developed pain and periocular edema; however, only 50% had blurred vision. The predominant microorganisms identified included various strains of *Staphylococcus*, *Klebsiella pneumoniae*, and notably, *Pseudomonas aeruginosa*, a distinction compared to the control cohort. Consequently, due consideration ought to be extended toward *Pseudomonas aeruginosa* when instituting empirical therapeutic measures for endogenous endophthalmitis in hemodialysis recipients. Although the higher prevalence is probably due to the fact that these patients have several vascular access routes, they did not discover a definite connection to the vascular access infection. The higher number of dialysis patients with diabetic retinopathy before the eye infection might be why their vision the unfavorable visual outcomes witnessed in dialysis-afflicted subjects.

Discussion

Many researchers have studied the effects of HD on the body. However, to date, no studies have assessed the possible effects on the physiology of the eye. This is possibly due to the high complexity of such an analysis, the diversity of variables to be studied, and the great inter-measuring device variability. Our review aimed to elucidate and contrast the literature results to provide reliable and cogent information to answer the question: How is the eye affected by hemodialysis?

In general, disparate ideas were found in some sections, limited by the aforementioned difficulties. However, when analyzed by section, we found ideas that could change the ophthalmological management of these patients.

Visual acuity and refraction

No significant changes in visual acuity or refraction were found in dialyzed patients. However, some authors^[4,5] suggest a small tendency for hyperopia between sessions, possibly due to a decrease in axial length secondary to volume loss.^[4,5] Therefore, further studies are needed to confirm this and, if it exists, to clarify its duration to adapt a refractive solution and better meet the fluctuating needs of this population. A progressive spectacle that would allow the patient to see as the hyperopic effects of HD disappear, as mentioned above, could be developed. Long-term BCVA in the dialyzed diabetic population is more controversial.

Ocular surface

HD patients have worse ocular surface parameters (TBUT, Schirmer's test, ocular surface disease index test, and lacrimal meniscus) and a higher prevalence of corneconjunctival calcium deposits and squamous metaplasia than the healthy population. High serum calcium levels and increased pH at the ocular surface (secondary to the loss of carbon dioxide to atmospheric air) could facilitate their precipitation. Calcifications could worsen tear stability, generate more inflammation, and promote further calcium precipitation. In addition, session-related fluctuations have been observed. These changes should be considered when personalizing treatment for dry eye syndrome, possibly aggravated by the COVID-19 pandemic.

The relationship between the number of calcifications and mortality is very interesting; this aspect could be studied in greater depth for screening purposes, wherein the ophthalmologist could anticipate complications to facilitate prevention or determine the patient's prognosis.^[23]

Meibomian gland dysfunction is quite prevalent in HD patients as changes in TBUT have been observed. Accordingly, future studies could analyze the function and structure of these glands using meibography and interferometry.

The HD population has a different bacterial flora than that of the healthy population, which is more typical of hospital environments. Therefore, this should be considered in empirical treatments for infectious pathologies because of the possibility of resistance.

Anterior segment

Due to improvements in HD techniques, no clinically relevant changes in IOP were observed after the sessions. Specifically, in patients with glaucoma or alterations in drainage, it would be interesting to know more about IOP fluctuations because of their greater clinical relevance.

Circadian fluctuations in IOP differ from those in the healthy population. On HD session days, the mean IOP was higher, with a peak occurring during the sessions; therefore, the timing of prostaglandin eye drops should be targeted to these peaks.^[57] This could be achieved by applying them at another time of day, not necessarily at night, or by reinforcing the predictable peaks of the sessions with another compound. Furthermore, these fluctuations have been studied in a non-glaucomatous population; thus, in at-risk patients, they could be more aggressive, and it may even be necessary to modify the surgical indication for greater control.

Regarding corneal thickness, HD does not seem to influence corneal thickness; however, there is controversy about endothelial cell density, polymorphism, and pleomorphism. This could be more relevant in populations with pathological endothelium, such as Fuchs endothelial dystrophy.

For the intraocular lens calculation, HD does not appear to have a clinically significant influence on biometric parameters.^[39] This evidence improves our confidence in performing biometry in these patients. However, only a time window very close to the session has been studied, and HDs influence after several hours or even the following day remains unknown. For future studies, we can also consider the hypothesis that the results of vitrectomized

patients, without vitreous support might be different. In these studies, HD sessions may generate differences in IOP and biometry.

No changes in the iridocorneal angle have been observed, and lenticular thickening after the sessions remains debatable.^[1,2,37,39] Therefore, it is necessary to study the effects of HD on the iridian curvature, angle width, and degree of lens protrusion (lens vault) using OCT, especially in hyperopic patients or those with narrow angles, with a possible relative pupillary blockage.

Posterior segment

The posterior pole has been extensively studied since the advent and generalization of OCT. However, the high inter-measuring device variability makes it difficult to strictly compare the results. Knowledge of the behavior of RNFL is of interest, especially for glaucomatous patients, because doubts arise as to the best time to perform the test during follow-up or if RNFL influences the long term to discern between disease progression due to a lack of IOP control or systemic changes. No significant changes were observed in the thickness of the RNFL after the sessions; however, the hemodialyzed population had less thickness than the healthy population. Therefore, these patients are disadvantaged from the onset, and more aggressive care may be needed for their remaining fibers.

Regarding the retinal thickness, no or minimal changes were observed, both in the long term and after the sessions. Special mention should be made of diabetic patients since the state of the blood-retinal barrier, affected by the underlying disease itself, may have an impact. In these patients, HD sessions do not seem to have a significant influence; however, there is controversy. However, a decrease in thickness was observed over the long term.

Because of the emergence and popularization of intravitreal treatments, diabetic patients should not be the only ones receiving special consideration when studying the retina in the dialyzed population. Neovascular membranes, as in the very common age-related macular degeneration, may also change their behavior in the context of HD, which could impact the follow-up and treatment of those patients.

A decrease in choroidal thickness has been observed after HD sessions and may be even more pronounced in the diabetic population. Decreased peripapillary choroidal thickness could influence the optic disc, especially in glaucoma. Caution should be exercised in interpreting these changes since their thickness may vary due to circadian cycles, processes affecting vascular permeability, and interobserver measurements.^[99]

Vascularization

The changes in the vascular tissue, as described in the previous paragraph, are congruent with the decrease in retrobulbar blood circulation and perfusion pressure. This suggests a tendency toward ocular ischemia after each session, which may aggravate or promote neuropathies, vascular obstructions, or proliferative retinopathies. OCT-angiography may be useful for predicting the risk of hypotensive episodes during HD sessions. From a systemic perspective, in addition to the hypotension that could be related to these findings, these patients usually present with anemia and a certain degree of generalized hypoxia

Neuro-ophthalmology

The literature suggests worse visual field, RNFL, and VEP

parameters in patients with HD than in healthy individuals. This difference is probably due to nephropathy rather than the HD technique, tipping the balance toward the belief that neurological toxicity stems from substances not excreted by the diseased kidney.

Ocular motility

A few studies have examined the effects of HD on ocular motility. Therefore, not much can be highlighted, except for the lack of differences before and after an HD session in the Cover Test, motility, and Lang's test.

Endophthalmitis

Due to the blood access routes required for HD, there is an increased risk of endogenous endophthalmitis. Hence, ophthalmologists should investigate at the slightest suspicion of endophthalmitis in HD patients, considering that endophthalmitis usually manifests as pain and periocular edema in these patients and is not always characterized by blurred vision.

Conclusion

To summarize the literature, HD sessions cause fluctuations that can be a confounding factor in an ophthalmological assessment, especially in relation to visual fields, IOP in glaucoma patients, and VEP parameters. Therefore, to obtain a more accurate baseline status, the ideal time for these examinations should be a few hours after the HD session. In addition, a connection was found between hemodialysis sessions and intraocular pressure in glaucoma, TBUT, Schirmer's test values, choroidal thickness, vessel flow velocities, and ocular perfusion pressure values. For the other examinations, either no significant impact in timing was observed, or there was controversy. The most prudent approach is to schedule patients simultaneously with respect to renal replacement therapy. Patients may need reinforcement of their dry eye or ocular hypertension treatments, mainly during HD sessions.

The incorporation of studies with very different designs and study variables, as well as the inter-measuring device variability in some studies, was limitations of our review. However, to the best of our knowledge, this is the first study to attempt to unify the published literature regarding the effects of HD on the eye. Thus, the study's main strength is related to its limitation.

Most of the studies reviewed were prospective observational studies with relatively small sample sizes; therefore, larger studies are needed. Although it may be particularly difficult, it would be of great clinical interest to study the influence of HD in patients with ophthalmological pathology, where its effects could be relevant enough to change the therapeutic plan.

Acknowledgments

The authors are grateful to the Andalusian Society of Ophthalmology for their support of this project.

Financial support and sponsorship: This study has received funding from the Andalusian Society of Ophthalmology to support its translation and editing.

Conflicts of interest: There are no conflicts of interest.

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