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ORIGINAL RESEARCH

Effect of Hemodialysis on Glaucoma Patients

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Purpose: Prospective study to determine if patients with glaucoma are at increased risk of intraocular pressure (IOP) fluctuation and changes in ocular perfusion pressure (OPP) during hemodialysis (HD) sessions when compared to patients without glaucoma.

Patients and Methods: Patients undergoing HD at the University of Iowa for end-stage renal disease were recruited. Enrollment was restricted to patients undergoing standard HD sessions for a minimum of three months. Hand-held slit lamp examination, IOP, blood pressure (BP), and central corneal thickness (CCT) measures were taken at the following three time points: the beginning of the session *(before*), at the half-way point *(middle)*, and at the conclusion of the session *(end)*. Ocular perfusion pressure was calculated using the formula: 2/3[diastolic BP + 1/3 (systolic BP – diastolic BP)] – IOP.

Results: Every eligible patient having dialysis was approached, and 105 eyes of 54 patients were recruited for the study. The glaucoma cohort included 19 eyes from 11 patients. The variability in IOP from the beginning to the end of HD (*end-before*) was 1.54 mmHg greater in the glaucoma group (p=0.005), with some glaucoma patients having IOP increases up to 25 mmHg. Ocular perfusion pressure decreased significantly more in glaucoma patients compared to controls at both *middle-before* (p=0.008), and *end-before* (p=0.01) time points.

Conclusion: Glaucoma patients may be more vulnerable to IOP swings and drops in OPP during HD sessions compared to controls. In all cases, these changes were asymptomatic, potentially placing glaucoma patients at increased risk for glaucomatous progression during each HD session. Our results suggest that HD may be an independent risk factor for glaucomatous progression, and may be especially worth investigating in patients with progression despite low to normal IOPs measured in clinic.

Keywords: ocular perfusion pressure, hemodialysis, dialysis, intraocular pressure fluctuation, glaucoma

Introduction

Chronic kidney disease (CKD) is a progressive condition affecting over 10% of the world's population (over 800 million people).[1,2] In the United States alone, more than 50 million hemodialysis (HD) treatments are performed each year.[3] Due to rapid solute and fluid shifts during HD sessions, the impact of HD on intraocular pressure (IOP) has been a topic of interest among researchers for decades.[4–11] Several studies have investigated the effect of HD on IOP in the general population with variable results, however the majority of studies demonstrated no significant change in IOP throughout the session.[4,5,9,10,12,13] To our knowledge, there have been no prospective studies evaluating changes in IOP during HD sessions in patients with known glaucoma. With individual case reports of significant IOP spikes in glaucomatous patients,[14–19] we hypothesized that IOP spikes or decreases in ocular perfusion pressure (OPP) may be more common than currently recognized in patients with glaucoma undergoing renal standard replacement therapy, and may be an unrecognized risk factor for glaucomatous progression despite low IOPs in clinic.

Materials and Methods

Study Design

This is a prospective study occurring during the course of a single HD treatment session in individuals with and without glaucoma.

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Patient Enrollment

The study was approved by the University of Iowa IRB and followed the tenets of the Declaration of Helsinki. Adults provided written informed consent. Patients did not receive a stipend or incentive to participate in the study.

Inclusion/Exclusion Criteria

All patients undergoing HD at the University of Iowa Hospitals and Clinics who met inclusion criteria were approached for this study. Enrollment was restricted to patients with end-stage renal disease (ESRD) undergoing chronic HD for at least three months. Exclusion criteria included patients with acute kidney injury and patients who irregularly attended HD sessions.

Subject Recruitment

Adults admitted to the dialysis unit for chronic HD were initially screened by the research team to determine eligibility using the electronic medical record. Patients meeting inclusion criteria were approached before starting treatment or within 5 minutes of the start of the HD session. Patients were only recruited on the HD days of Wednesday, Thursday, or Friday to avoid the influences of the extra weekend day in typical thrice weekly HD schedules (Monday-Wednesday-Friday or Tuesday-Thursday-Saturday).

Patients were divided into two groups based on ocular history: glaucoma and control. To be included in the glaucoma cohort, eyes had to have a diagnosis of open angle glaucoma, angle closure glaucoma (including a history of neovascular glaucoma), ocular hypertension, or be designated a glaucoma suspect. In the case of unilateral disease, only the eye with a diagnosis of glaucoma, glaucoma suspect, or ocular hypertension was included within the analysis. All glaucomatous eyes were included in the analysis regardless of surgical history (including glaucoma and phacoemulsification surgery).

Data Collection

All patients were asked about prior ocular and medical history, which was supplemented by review of the electronic medical record. A basic eye examination was performed before *(before)*, at the mid-point *(middle)*, and at the conclusion of the HD session *(end)*. The basic eye exam included central corneal thickness (CCT) with a hand-held ultrasonic pachymeter (Pachette 4, DGH Technology, Exton, PA) and IOP with a hand-held Tono-Pen Tonometer (Reichert Technologies, Depew, NY). At the time of enrollment, a hand-held slit lamp was used to evaluate anterior chamber depth. The CCT was measured once at each time point, while IOP was calculated by taking the mean of three IOP measures at each time point with the patient seated in an upright position. The HD sessions were not altered in any way for this study. Per standard HD protocol, each patient was weighed prior to starting and after the conclusion of the HD session, and blood pressure was taken every 30 minutes. Patients were asked to report any ocular symptoms experienced during the HD session.

For each patient, IOP, CCT, and BP were recorded at three time points: "before" as defined as before or within five minutes of starting dialysis, "middle" as defined as the half way point in the dialysis session, and "end" as defined by within five minutes of the conclusion of the dialysis session. In order to calculate the change in these measures from the "before" baseline, the following two differences were calculated: "middle-before" and "end-before." The subject's participation in the study ended at the completion of their dialysis session.

Statistical Analysis

The two patient groups (glaucoma vs control) were analyzed separately for the three separate time points (*before, middle, end*). A mixed effects model was used for the differences and absolute differences (variability) at different time points, and each subject has its own intercept. In cases where both eyes are included, right and left eyes from the same subject are not distinguished in the statistical analysis. The threshold of significance was set at $\alpha = 0.05$.

Ocular perfusion pressure was calculated by the following equation: OPP = 2/3[diastolic BP + 1/3 (systolic BP – diastolic BP)] – IOP.

Results

Patient Characteristics and Demographics

Every eligible patient having dialysis at the University of Iowa who fit the inclusion criteria was approached, and 105 eyes of 54 patients were recruited for the study. The average age of the glaucoma study participants was 67.6 years, while the average age of the control group was 60.3 years (see Table 1 for demographic information).

Glaucoma Cohort Details

Eleven patients (19 eyes) were included in the glaucoma cohort. Eight (42.1%) of the eyes classified in the glaucoma cohort had a diagnosis of POAG, 2 (10.5%) had a history of neovascular glaucoma, 2 (10.5%) had a history of pigmentary glaucoma, and 7 (36.8%) were either designated as glaucoma suspect or had a diagnosis of ocular hypertension (Table 2). Two (10.5%) eyes in the glaucoma group had prior glaucoma surgery: one eye had a trabeculectomy and one eye had an Ahmed seton implant (Table 3). Based on record review, only one patient was using glaucoma drops (brimonidine, dorzolamide-timolol in the right eye).

Table 1 Demographic Information for the Two Groups

	All	Glaucoma	Control
No. eyes (no. patients)	105 (54)	19 (11)	86 (43)
Age, mean±SD	61.8 ± 14.4	67.6 ± 15.7	60.3± 13.9
Sex, n (%)			
Male	28 (51.9)	1 (9.1)	27 (62.8)
Female	26 (48.1)	10 (90.9)	16 (37.2)
Race, n (%)			
White	38 (70.4)	6 (54.5)	32 (74.4)
Black	16 (29.6)	5 (45.5)	23 (53.5)
Ethnicity, n (%)			
White Hispanic	7 (12.9)	1 (9.1)	6 (14.0)
Non-White Hispanic	0 (0.0)	0 (0)	0 (0)
Asian	3 (5.6)	1 (9.1)	2 (4.7)

Notes: Race, ethnicity, and sex were based on self-report.
Abbreviations: N, number of patients; SD, standard deviation.

Table 2 Types of Glaucoma or Glaucoma Suspects Within Glaucoma Group (n=19 Eyes) Based on Record Review

Type of Glaucoma	No. eyes (%)
Primary open angle glaucoma	8 (42.1)
Ocular hypertension	3 (15.8)
Neovascular glaucoma	2 (10.5)
Pigment dispersion glaucoma	2 (10.5)
Glaucoma suspect	4 (21.5)

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Table 3 Prior Ocular Surgeries Performed on Included Eyes Within Both Glaucoma and Control Groups

Prior Ocular Surgeries			
Glaucoma Cohort	**No. Eyes (%)**	**Control Cohort**	**No. Eyes (%)**
Phacoemulsification/IOL	17 (89.5)	Phacoemulsification/IOL	28 (32.6)
Trabeculectomy with mitomycin C	1 (5.3)	Orbital plate	1 (1.2)
Ahmed seton implant	1 (5.3)	Deep anterior lamellar keratoplasty (DALK)	1 (1.2)
Pars plana vitrectomy	6 (31.6)	Pars plana vitrectomy (PPV)	2 (2.3)

Abbreviation: IOL, intraocular lens.

Dialysis Measures

Patients had an average pre-dialysis weight of 88.9 kg and an average post-dialysis weight of 86.1kg, representing a 1.9 kg fluid loss on average during the HD session (Table 4). The mean pre-dialysis systolic blood pressure was 145.6 mmHg and mean diastolic blood pressure was 72.7 mmHg compared to the mean post-dialysis blood pressure of 141.1 mmHg and 72.8 mmHg systolic and diastolic values respectively (Table 4).

Intraocular Pressure Change

The change in IOP from the mid-dialysis reading (*middle – before*) and from the end reading (*end – before*) was not statistically significantly between the groups (p=0.098 for *middle – before*, p=0.892 for *end – before*). However, the variation from starting IOP (absolute change up or down) was 1.54 mmHg higher in the glaucoma group (SE=0.782, p=0.005) when comparing the end to the before readings (*end – before*) (Table 5). When looking at the breakdown of IOP swings, more glaucoma eyes had an increase in IOP of more than 10 mmHg during the dialysis session (4 total, 21.1%), and one eye had an IOP increase of more than 25 mmHg (Table 6). This patient has a history of pigmentary glaucoma and had an IOP that increased from a baseline of 8.3 mmHg at the beginning of the session to 33.3 mmHg mid-session. The IOP began to decrease by the end of the session, finishing with an IOP of 20.7 mmHg. This patient was pseudophakic and did not have a history of glaucoma surgery.

Both cohorts had patients who had a mild decrease in IOP (−5.0 to −10.0 mmHg) throughout the session. In the one eye with a prior trabeculectomy, the IOP dropped from a mean of 12.0 mmHg before dialysis to 4.0 mmHg mid-dialysis,

Table 4 Systemic Measures of Hemodialysis (HD), Including Blood Pressure (BP) and Weight

	All	**Glaucoma**	**Control**
No. eyes (no. patients)	105 (54)	19 (11)	86 (43)
Baseline weight	88.9 ± 23.5	86.0 ± 25.2	89.7 ± 23.3
Post-HD weight	86.9 ± 23.1	83.7 ± 24.8	87.8 ± 22.8
Baseline BP			
Systolic	145.6 ± 21.4	153.7 ± 21.0	143.4 ± 21.3
Diastolic	72.7 ± 15.8	66.5 ± 25.7	74.3 ± 11.8
Post-HD BP			
Systolic	141.3 ± 25.1	137.6 ± 29.4	142.3 ± 24.2
Diastolic	72.8 ± 14.2	66.6 ± 19.5	74.5 ± 12.2

Table 5 Intraocular Pressure (IOP), Ocular Perfusion Pressure (OPP) and Central Corneal Thickness (CCT) Changes Throughout Hemodialysis (HD) Session

Measure	Time	Glaucoma	Range	Control	Range	p-value
IOP	*Middle-before*	1.7 ± 7.8	−9.0–25.0	0.7 ± 3.8	−7.3–11.3	p=0.067
	End-before	−0.7 ± 4.9	−12.7–9.0	0.2 ± 3.1	−8.0–7.0	p=0.252
IOP (absolute, up or down)	*Middle-before*	4.6 ± 6.4	0.0–25.0	2.9 ± 2.5	0.0–11.3	p=0.085
	End-before	3.2 ± 3.6	0.0–12.7	2.3 ± 2.0	0.0–8.0	***p=0.049***
OPP	*Middle-before*	−6.4 ± 12.5	−24.6–22.2	−3.7 ± 8.4	−21.2–15.4	***p=0.006***
	End-before	−4.4 ± 15.2	−29.0–29.2	−1.1 ± 9.7	−20.9–28.8	***p=0.009***
CCT	*Middle-before*	16.8 ± 15.9	−18.0–46.0	7.3 ± 19.1	−40.0–102.0	p=0.908
	End-before	15.2 ± 11.4	−5.0–38.0	6.7 ± 18.0	−49.0–43.0	p=0.891

Notes: Before refers to the measurements obtained prior to or within the first 5 minutes of the HD session. Middle refers to the mid-HD measurements. End refers to the readings at the conclusion or within 5 minutes of the HD session. Bold/italic font indicates statistical significance (p<0.05).

Table 6 The Number and Percentage of Patients in Each Cohort Who Had Moderate to Severe IOP Increases (+) or Decreases (-) During the Hemodialysis Session (Middle – Before and End – Before)

IOP Change (mmHg)	Middle – Before		End – Before	
	Glaucoma N (%)	Glaucoma N Control N (%)	Glaucoma N Glaucoma N (%)	Glaucoma N Control N (%)
+ 20.0 or more	1 (4.5)	0 (0.0	0 (0.0)	0 (0.0)
+ 10.0–20.0	3 (14.6)	1 (1.2)	0 (0.0)	0 (0.0)
+ 5.0–10.0	0 (0.0)	9 (10.5)	2 (9.1)	4 (4.7)
− 5.0 - −10.0	3 (13.6)	9 (10.5)	3 (13.6)	5 (5.8)
−10.0 - −20.0	0 (0.0)	0 (0.0)	1 (4.5)	0 (0.0)
−20.0 or less	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

and increased again to 12.7 mmHg at the end of the session. In the eye with a prior Ahmed valve, the IOP remained stable at 27.3 mmHg before dialysis, 26.3 mmHg mid-dialysis, and 29.0 mmHg at the end of the session.

Of note, no patients reported any symptoms to indicate IOP rise or hypotony, including blurred vision or eye pain.

Pachymetry

The average CCT in the glaucoma cohort was 544.9 ± 46.2 mm, while the average CCT in the control cohort was 585.3 ± 50.3 mm. The CCT was not found to change significantly during the dialysis session, and the changes were not different between the two groups (*middle-before*, p=0.10; *end-before*, p=0.89) (Table 5).

Ocular Perfusion Pressure

The glaucoma cohort started at an average OPP of 49.4 mmHg, decreased to 43.0 mmHg mid-dialysis and 45.0 mmHg at the end of the dialysis session. The control group started at a similar OPP of 49.8 mmHg, but remained more stable throughout the session (46.0 mmHg mid-dialysis, 48.7mmHg at the end of dialysis). The change in OPP was significantly different between the groups for both the *middle-before* (p=0.008) and *end-before* (p=0.01) time points,

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with the glaucoma group having a more significant drop in OPP throughout the session (Table 5). In the glaucoma cohort, 75% of patients had an OPP that dipped below 50 mmHg compared to 58% of controls.

Discussion

The effect of HD on IOP in the general population has produced variable results, with the majority of studies demonstrating no significant change in IOP throughout the session.[4,5,9,10,12,13] To our knowledge, this is the first prospective study evaluating IOP and OPP changes during HD sessions in patients with glaucoma compared to a control population. Glaucoma patients appear to be more vulnerable to large IOP increases and OPP decreases during HD sessions compared to controls. Over 20% of eyes with glaucoma had IOP increases of more than 10 mmHg, including one with an IOP increase of 25 mmHg, all occurring asymptomatically within a single HD session. Significant drops in OPP in patients with glaucoma may additionally contribute to HD-driven glaucomatous changes. Given the frequency and regularity of HD sessions in patients with ESRD, clinicians need to be keenly aware of the impacts of these sessions on the progression of glaucoma, potentially necessitating medication changes or earlier incisional surgery. Our results suggest that HD may be an unrecognized risk factor in progressing glaucoma patients, and should be considered alongside other risk factors in normal tension glaucoma, such as Raynaud's phenomenon, nocturnal hypotension, and migraine headaches.[20]

There are several postulated theories for the mechanism behind changes in IOP intradialytically, including the stimulation of aqueous humor production by the rapid drop in plasma osmolality,[21] an osmotic disequilibrium causing the pull of water into the aqueous humor and vitreous cavity,[16,22] and the mechanical anterior shift of the lens/iris diaphragm resulting in decreased outflow.[17] While an eye without glaucoma may be able to accommodate this influx of fluid, it is postulated that this fluid shift may be enough to overwhelm the outflow system of a glaucomatous eye and subsequently tip the eye out of pressure equilibrium.

The combination of an increase in IOP and drop in BP (the latter inherent to dialysis treatment) results in a dangerous drop in OPP in these fragile eyes. Although most patients are vulnerable to nocturnal BP drops,[23] HD patients are uniquely vulnerable to BP fluctuations throughout the HD session with intradialytic hypotension occurring in up to 40%.[24] Mean OPP of <42-50mmHg has been demonstrated to be an independent risk factor for glaucomatous progression.[25,26] In the glaucoma cohort, 75% had OPP dips below this level compared to 58% of controls.

One main limitation of the study is its size. Although study size is sufficiently powered to detect significant changes within the IOP and OPP, it is not powered for further subgroup analysis including the evaluation of the impact of glaucoma type, lens status, topical glaucoma medications, or prior glaucoma surgery. Furthermore, due to the limited number of patients undergoing dialysis at the University, glaucoma suspects and all types of glaucoma patients were grouped together for analysis, which may account for why the prevalence of glaucoma in this population exceeds the expected prevalence of glaucoma in the general population.[27] The glaucomatous diagnosis was based on chart review and not from a full clinic evaluation of the patient. While supporting records were available for most but not all patients with glaucoma, we did not have enough information to sufficiently narrow glaucoma categories. However, we suspect that widely broadening our glaucoma group to include suspects weaken our results rather than run the risk of exaggerating the effect of glaucoma on IOP and OPP. Another potential weakness is that data were only collected during one HD session, and may not be representative of every HD session.

The current data is insufficient to evaluate what changes can be made to mitigate the risk of IOP fluctuation and OPP, including incisional glaucoma surgery and HD session alterations. Our study had only one patient with a prior trabeculectomy, who interestingly had a drop in her IOP throughout HD from 12 mmHg pre-dialysis, to 4 mmHg mid-dialysis, and increased back to 12.7 mmHg post-dialysis. One patient had a prior Ahmed, whose IOP stayed stable throughout (27.3 mmHg pre-dialysis, 26.3 mmHg mid-dialysis, 29 mmHg post-dialysis). These individual cases introduce the question of whether incisional surgery, especially a trabeculectomy, may be protective. It is also possible that changes to the HD session may help to blunt some of these ocular findings, but the effect of HD parameters were not evaluated in this study, and additional research would be warranted to investigate this further.

Conclusion

Chronic kidney disease and HD is common, and each HD session may be putting glaucomatous eyes at increased risk of progression by causing both IOP fluctuation and decreases of OPP. Perhaps most concerning is that no patient with IOP spikes (with IOP increases up to 25 mmHg) or drops in OPP experienced any ocular symptoms. With the regularity of HD sessions, these IOP and OPP changes may have a profound and deleterious impact on glaucoma patients undergoing HD. Furthermore, these significant ocular fluctuations occur outside of the clinic setting which potentially could result in chronic undertreatment. Our results suggest HD may be an unrecognized yet significant risk factor for glaucomatous progression. Alongside known non-IOP risk factors in normal tension glaucoma like nocturnal hypotension, Raynaud's phenomenon, and migraine headaches,[20] the impact of HD should be assessed and considered in the evaluation and treatment of glaucoma patients who progress despite having apparently well controlled IOPs during their ophthalmology clinic visits.

Abbreviations

BP, Blood pressure; CCT, Central corneal thickness; CKD, Chronic kidney disease; HD, Hemodialysis; IOP, Intraocular pressure; OPP, Ocular perfusion pressure; OCT, Optical coherence tomography.

Disclosure

The authors have no conflicts of interest in this work.

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