การเปลี่ยนแปลงของความดันลูกตาระหว่างและหลังการฟอกเลือดด้วยเครื่องไตเทียม

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Abstract: Changes in Intraocular Pressure during and after Hemodialysis

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Background: The effects of hemodialysis (HD) on intraocular pressure (IOP) have been investigated for almost 60 years since Sitprija et al. first reported IOP increases during HD in 1964. Subsequent studies have reported different results ranging from an acute increase in IOP to a decrease in IOP, as well as reporting no change at all. To our knowledge, high IOP is a significant factor in the development of glaucoma and glaucoma progression. Nevertheless, this issue is not really a significant concern for both ophthalmologists and nephrologists. Objective: To evaluate changes in intraocular pressure during and after HD and to identify abnormal ocular symptoms. Method: A cross-sectional observational study was conducted in Dialysis Unit 2 at Lerdsin Hospital from 4 February 2022 to 14 April 2022. Demographic data, age, gender, underlying diseases, duration of HD (in months), ultrafiltration volume, and abnormal eye symptoms were recorded. The IOP was measured with an iCare PRO tonometer three times: before HD (Pre-HD), two hours after starting HD (2-hr HD), and after HD (Post-HD). Results: 41 end-stage renal disease patients (41 eyes) who received HD were enrolled. None of the participants experienced abnormal ocular symptoms at the time of HD. The mean IOP recorded were as follows: 22.49±4.67 mmHg at pre-HD, 23.65±4.61 mmHg at 2-hr HD, and 24.92±4.42 mmHg immediately after HD. According to the multiple regression analysis, there was no relationship between ultrafiltration volume, pre-existing glaucoma, and IOP change after HD. Conclusions: IOP was found to be increased both during HD (2 hours) and immediately after HD. However, the statistical significance was found after HD only.

Keywords: End-stage renal disease, Hemodialysis, Intraocular pressure.

บทคัดย่อ

ภูมิหลัง: เป็นระยะเวลาเกือบ 60 ปีแล้วที่มีความสนใจเกี่ยวกับผลของการฟอกเลือดด้วยเครื่องไตเทียมต่อความดันลูกตา เริ่มจากการศึกษาแรก โดย Sitprija และคณะ ในปี ค.ศ. 1964 ที่รายงานความดันลูกตาที่สูงขึ้นในขณะฟอกเลือด จนถึงปัจจุบันมีการศึกษาเรื่อยมาซึ่งผลสรุปของแต่ละการศึกษาก็มีความหลากหลายมีทั้งที่รายงานว่าความดันลูกตาเพิ่มขึ้น ไม่เปลี่ยนแปลงและลดลง นอกจากนี้เป็นที่ทราบกันดีว่าความดันลูกตาสูงเป็นปัจจัยเสี่ยงสำคัญของการเกิดโรคต้อหิน และทำให้ต้อหินลุกลามมากขึ้นจนทำให้สูญเสียการมองเห็นได้ อย่างไรก็ตามผลของการฟอกเลือดด้วยเครื่องไตเทียมต่อการเปลี่ยนแปลงของความดันลูกตายังไม่ค่อยเป็นที่กล่าวถึงและให้ความสำคัญมากนักทั้งในจักษุแพทย์และอายุรแพทย์โรคไต วัตถุประสงค์: เพื่อศึกษาการเปลี่ยนแปลงของความดันลูกตาในขณะและหลังการฟอกเลือดด้วยเครื่องไตเทียม เทียบกับความดันลูกตาก่อนการฟอกเลือด และศึกษาอาการผิดปกติทางตาที่เกิดขึ้นขณะฟอกเลือดด้วยเครื่องไตเทียม วิธีการ: เป็นการศึกษาเชิงพรรณนาแบบตัดขวาง (cross-sectional descriptive study) ของการเปลี่ยนแปลงของความดันลูกตาในผู้ป่วยไตวายเรื้อรังระยะสุดท้ายที่มาฟอกเลือดด้วยเครื่องไตเทียม ที่ศูนย์ไตเทียม 2 โรงพยาบาลเลิดสิน ในช่วงวันที่ 4 กุมภาพันธ์ พ.ศ. 2565 ถึง 14 เมษายน พ.ศ. 2565 โดยบันทึกข้อมูลทั่วไปของผู้ป่วย และทำการวัดความดันลูกตาด้วยเครื่อง iCare PRO 3 ครั้ง คือ ก่อนการฟอก

เลือด, 2 ชั่วโมงหลังเริ่มฟอกเลือดและเมื่อสิ้นสุดฟอกเลือดทันที **ผล:** อาสาสมัครที่เป็นผู้ป่วยไตวายเรื้อรังระยะสุดท้ายที่มารับการฟอกเลือดจำนวนทั้งสิ้น 41 ราย (41 ตา) ได้เข้าร่วมโครงการวิจัย ไม่มีอาสาสมัครรายใดที่มีอาการผิดปกติทางตาระหว่างและหลังการฟอกเลือด ความดันลูกตาเฉลี่ยก่อนฟอกเลือด 22.49±4.67, ที่ 2 ชั่วโมงของการฟอกเลือด 23.65±4.61 และหลังการฟอกเลือด 24.92±4.42 มิลลิเมตรปรอท จากการศึกษาพบว่าปริมาตรน้ำที่ดึงในการฟอกเลือด (ultrafiltration volume) และโรคต้อหินที่ได้รับการวินิจฉัยอยู่ก่อนแล้วของอาสาสมัครไม่ได้มีผลต่อการเปลี่ยนแปลงของความดันลูกตา **สรุป:** ค่าเฉลี่ยของความดันลูกตาสูงขึ้นทั้งที่ 2 ชั่วโมงหลังเริ่มการฟอกเลือดและหลังฟอกเลือดทันที โดยนัยสำคัญทางสถิติพบที่หลังการฟอกเลือดทันที

คำสำคัญ: ไตวายเรื้อรังระยะสุดท้าย ฟอกเลือด ความดันลูกตา

Introduction

Elevated intraocular pressure (IOP) is generally accepted as a significant factor contributing to the development of glaucoma[1] and glaucoma progression[2] that may potentially cause irreversible blindness and affect the patients' qualities of life. IOP is determined by the aqueous humor dynamic and can be influenced by many conditions. One of these conditions is the effect of hemodialysis (HD), a process considered one of the main treatments for end-stage renal disease (ESRD) patients. As the author has found through practice, some glaucoma patients with end-stage renal disease complained of eye pain, decreased vision, and headache during HD. This relationship was first reported in the study of Sitprija et al. in 1964, which demonstrated a significant increase in IOP[3]. Nonetheless, the conclusions of the subsequent studies remain inconsistent. Some studies reported an increase in IOP during HD[4], some found that IOP did not change[5], and some revealed that IOP actually decreased[6]. There are two main hypotheses that attempt to explain the effects of HD on IOP: first, the rapid decrease in serum osmolarity compared to the stationary ocular osmolarity causes fluid shift from serum to the eye, resulting in IOP elevation[7]; second, the increased colloid osmotic pressure as a result of the removal of the excess fluid without the removal of albumin causes fluid influx from serum to the eye and a decrease in IOP.[8] However, the mechanism that cause HD to affect IOP is still unclear. Apart from the mentioned hypotheses, there are other unknown mechanisms of HD (external factors) as well as ocular risks (internal factors), both of which affect IOP.

According to the Thai renal replacement therapy committee, 114,262 Thai ERSD patients received hemodialysis in 2019.[9] As the primary treatment for ERSD, HD is usually done two to three times a week for about four hours at a time, and patients have to be administered HD lifelong. Therefore, this issue is very important to patients, and has significant implications on their lives. The adverse ocular effects of HD, such as increased IOP or glaucoma, should be further investigated in order to increase awareness during regular HD care. This study aimed to investigate the changes in IOP during and after HD, as well as to discover any abnormal ocular symptoms.

Materials and Methods

This cross-sectional descriptive study was conducted in Dialysis Unit 2 at Lerdsin Hospital from 4 February 2022 to 14 April 2022. Ethical approval was obtained from the Ethics Committee of Lerdsin Hospital. The inclusion criteria consisted of end-stage renal disease patients who were undergoing maintenance hemodialysis in Dialysis Unit 2 at Lerdsin Hospital, and were 18 years or older. The exclusion criteria were keratitis, conjunctivitis, blepharitis, and those with any suspicion of eye infection, corneal scar, or phthisis bulbi. A total of 41 eyes of 41 participants were enrolled in the study. Informed consent was obtained from all individual participants. Only the right eye of each participant was selected. The demographic data were collected, and then IOP was measured by an iCare PRO tonometer (iCare Finland, Helsinki), a portable equipment that can measure IOP in a supine position without topical anesthesia. The accuracy of the iCare PRO tonometer is comparable to that of the Goldmann Applanation Tonometer[10], the gold standard for IOP measurement. IOP of each participant was measured at least three times: (1) before HD (Pre-HD), (2) two hours after starting HD (2-hr HD), and (3) immediately after HD (Post-HD). If the participant reported any abnormal symptoms such as eye pain, blurred vision, or a headache, an additional IOP measurement would be performed to determine IOP at that moment. The measurement did not interrupt the routine process of

HD regarding the position of participants. Hemodialysis was done for about four hours per session with the same type of machine (FRESENIUS 4008S). At the end of the HD session, participants were asked about the abnormal ocular symptoms that were suspected to have increased IOP, such as eye pain or blurry vision during and after HD. In the statistical analysis, continuous data were performed as mean and standard deviation, and categorical variables were expressed as numbers and percentages. The paired t-test was the selected method used to compare the two groups of continuous data. Multiple linear regression analysis was used to determine correlations among ultrafiltration volume (cc), pre-existing glaucoma, and the change in IOP Post-HD compared to Pre-HD.

Results

There were a total of 41 participants (41 eyes) with a mean age of 61.34 ± 14.21 years old, 43.9% of the participants were males and the total duration of HD was 33.7 ± 36.72 months. The main underlying systemic condition was hypertension (82.93%). Moreover, there were three participants who had pre-existing glaucoma. The demographic data are shown in Table 1.

Table 1. Demographic Data of 41 Participants

Characteristics	No (%)
Age, mean ± SD [range], year	61.34 ± 14.21 [32-84]
Gender	
Male	18(43.9)
Female	23(56.1)
Underlying disease	
Diabetes mullitus	18(43.9)
Hypertension	34(82.93)
Heart diseases	7(17.5)
Others	7(17.5)
Pre-existing glaucoma	3(7.5)
Duration of HD, mean ± SD [range], Month	33.7 ± 36.72 [0.5-168]
Ultrafiltration volume, mean ± SD [range], cc	2,968.29 ± 825.06 [1500-5000]

SD = standard deviation

We found that none of the participants experienced any abnormal symptoms that can be caused by increased IOP, such as eye pain, blurred vision, or headache during and after HD. The mean IOP increased from 22.49 mmHg Pre-HD to 23.65 mmHg at the 2-hr HD and 24.92 mmHg Post-HD, as demonstrated in Table 2. However, a statistically significant increase was found at Post-HD only (p-value = .0011), as shown in Table 2.

Table 2. Change in IOP during, after HD and effect of HD on IOP

IOP (mmHg)	Mean ± SD	Min	Max	95% CI		p-value
				Lower	Upper	
Pre-HD and 2 hr-HD						
Pre-HD	22.49 ± 4.67	11	30	21.02	23.67	.1852
2 hr-HD	23.65 ± 4.61	13	33	22.19	25.12	
Pre-HD and Post-HD						
Pre-HD	22.49 ± 4.67	11	30	21.02	23.67	.0011*
Post-HD	24.92 ± 4.42	15.5	33.2	23.52	26.31	

*Statistical significance

The author also studied the effects of ultrafiltration volume (cc) and pre-existing glaucoma on IOP change between Pre-HD and Post-HD with multiple regression analysis. The p-values of the results were .079 for ultrafiltration volume and .875 for pre-existing glaucoma, as shown in Table 3. Thus, there was no relationship between both factors and IOP change.

Table 3. The effect of ultrafiltration volume and pre-existing glaucoma on IOP change between Pre-HD and Post-HD

Independent variable	β	Std. error	t-ratio	p-value
Ultrafiltration volume	0.002	0.281	1.803	.079
Pre-existing glaucoma	0.261	0.025	0.158	.875
Constant	-2.113		-0.808	.424

R= 0.281 R^2= 0.079 F-ratio= 1.629 p-value= .209 n= 41

Discussion

The effects of HD on IOP have been investigated worldwide through the decades, and conclusions have ranged from unchanging to a decrease in IOP to a significant increase in IOP. These studies lack uniformity in terms of the IOP measurement technique, measurement time, patients' statuses, presence of glaucoma, and outflow facility. The meta-analysis study by Chen SH, et al. found that in recent years (after 2005), the use of bicarbonate dialysate substitute for acetate dialysate showed that IOP tends to decrease.[11] Nonetheless, this study found that mean IOP increased both during and after HD, and statistical significance was only shown after HD. Therefore, there was no evidence for a significant acute IOP increase that would have caused symptoms in this study.

Overall mean IOP in our study was slightly high due to the participants' positions, mostly lying on their backs in a supine position with a different head of bed (HOB). Previous studies have shown a significant increase in IOP when in a supine position compared to when in a sitting position[12] (the regular position in our routine practice). Regarding the participants' preferences, some participants preferred a flat HOB, and some preferred the elevation of HOB to be 30 degrees, 45 degrees, or 60 degrees. All of them remained in the same position throughout the whole HD session; thus, the measurements of IOP were done in the same HOB position for each participant. Additionally, the Singapore Malay Eye Study reported that IOP level in chronic kidney patients are higher independent of age, presence of diabetes, blood pressure, and corneal thickness. However, there was no association between chronic kidney disease and glaucoma.[13]

This study documented three participants who have already been diagnosed with glaucoma. It found that in one of them, IOP increased from 17.6 mmHg pre-HD to 24.4 mmHg post-HD, while the IOP of the other two participants did not change. Thus, the overall result of the regression analysis showed no relationship between pre-existing glaucoma and IOP change. This might have been due to the small number of participants with glaucoma in this study and the variation of the ocular outflow facility in each eye. The previous study by Tawara A, et al. reported that an impaired aqueous outflow would play a significant role in increasing IOP during HD.[14] However there was no information on aqueous outflow facility in this study. Further investigations will be needed to observe this correlation.

During HD, water is removed from blood circulation, waste product is filtered out, and then the rest of the fluid returns to the blood system. The difference between the pre-dialysis weight and the patient's dry weight determines the volume of ultrafiltration, or the amount of water removed in each HD session. The study also investigated the effects of ultrafiltration volume using regression analysis, but revealed no relationship with IOP change. The relation between the effects of hemodialysis volume and IOP change has not been found in previous studies as well.

This study had the advantage of being Thailand's first study to evaluate IOP and abnormal ocular symptoms during HD with IOP measurements done in the regular supine position. The author attempted not to interfere with the routine HD process because changing positions from supine to seated could have altered blood pressure levels which can in turn affect IOP.

However, this study had three main limitations: The first limitation concerns the observational design of this study; second, there is no information on ocular conditions such as an outflow facility in this study, and further investigations should be done in the future; third, there is a small number of glaucoma patients in this study, and the glaucoma diagnoses were based on history and medical records which were inadequate to provide information in a high-risk group. Therefore, by multiple regression analysis, the results showed no association between pre-existing glaucoma factor and IOP change.

As a chronic progressive disease, glaucoma requires long-term follow up and management. Nevertheless, this study only explored the transient effects of HD on IOP; hence, long-term research would be advantageous for future studies. Furthermore, the retrospective population-based cohort study reported that the dialysis group was more susceptible to angle closure compared to the non-dialysis group, and that the impaired outflow facility was confirmed to be an important factor.[15] Besides the effects on IOP and glaucoma, HD can cause other ocular abnormalities such as cataracts, exudative retinal detachment, and band keratopathy, all of which should be concerns for an HD patient.[16,17] This points to the fact that ocular health in HD patients is challenging for ophthalmologists and nephrologists to diagnose and manage properly to potentially prevent visual loss. Ocular examinations in high-risk groups like those with narrow-angle, are beneficial. We hope and expect that this study will encourage collaboration between all related healthcare workers and will ultimately lead to a clinical practice guideline for Thailand.

Conclusion

IOP elevation during and after HD was demonstrated in this study. However, more randomized controlled trial studies in the future will be needed to ensure the result. In clinical practice in Thailand, we do not devote much attention to the effects of HD on ocular health. Therefore, the author sincerely hopes to emphasize the importance of this topic.

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