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# Measurement of foveal thickness by optical coherence tomography in adult haemodialysis patients with diabetic nephropathy

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## ABSTRACT

**Background:** Several studies have demonstrated the efficacy of hemodialysis (HD) on macular edema in diabetic patients. ***Objective:*** To study the effects of a HD session on foveal thickness by optical coherence tomography (OCT) in adult patients with type 2 diabetes mellitus with chronic renal failure (CRF) secondary to stage 5 diabetic nephropathy in HD. Patients and methods: We studied 25 eyes of 14 patients who underwent analytical studies and pre-HD and post-HD OCT. **Results:** As a group, the foveal thickness did not change after one session of HD in the 25 eyes studied (245.28±52.21 μ versus 240.40±40.25 μ) (p=0.428) (2% reduction) or correlated with any clinical or laboratory parameters analyzed. When comparing the subgroup of 13 eyes in which the foveal thickness did not change or decreased compared to the subgroup of 12 eyes in which the foveal thickness increased we found that in the first subgroup the bath temperature was significantly higher (37.00±0.00 versus 36.29 °C, p=0.008) and the conductivity was significantly lower (14.00±0.00 versus 14.29±0.10mS/cm, p=0.030). **Conclusion:** HD may modify the foveal retinal thickness as a function of changing parameters such as bath temperature and conductivity.

**Key words:** Optical coherence tomography. Foveolar thickness. Hemodialysis. Macular edema.

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## *Medida del grosor foveolar mediante tomografía de coherencia óptica en pacientes adultos con nefropatía diabética en hemodiálisis*

## *RESUMEN*

***Antecedentes:*** *Diversos estudios han demostrado la eficacia de la hemodiálisis (HD) sobre el edema macular de los pacientes diabéticos.* ***Objetivo:*** *Estudiar los efectos de una sesión de HD sobre el grosor foveolar, mediante tomografía de coherencia óptica (OCT), en pacientes adultos con diabetes mellitus tipo 2 con insuficiencia renal crónica (IRC) estadio 5 secundaria a nefropatía diabética en HD.* ***Pacientes y métodos:*** *Se estudiaron 25 ojos de 14 pacientes a los cuales se les realizó analítica y OCT pre-HD y post-HD.* ***Resultados:*** *Como grupo, el grosor foveolar no se modificaba tras una sesión de HD en los 25 ojos estudiados (245,28 ± 52,21 μ frente a 240,40 ± 40,25 μ) (p = 0,428) (2% de reducción) ni se correlacionaba con ninguno de los parámetros clínicos o analíticos analizados. Al comparar el subgrupo de 13 ojos en los que el grosor foveolar no se modificaba o disminuía respecto al subgrupo de 12 ojos en los que el grosor foveolar aumentaba se encontró que en el primer subgrupo la temperatura del baño era significativamente mayor (37,00 ± 0,00 frente a 36,29 °C, p = 0,008) y la conductividad significativamente menor (14,00 ± 0,00 frente a 14,29 ± 0,10 mS/cm, p = 0,030).* ***Conclusión:*** *La HD podría modificar el grosor foveolar retiniano en función de la modificación de parámetros como la temperatura del baño y la conductividad.*

***Palabras clave:*** *Tomografía de coherencia óptica. Grosor foveal. Hemodiálisis. Edema macular.*

## INTRODUCTION

Macular oedema in diabetic patients has been linked to the length of time patients have had diabetes, the level of control of hypertension, levels of glycosylated haemoglobin, the ex-

tent to which dyslipidaemia is controlled, smoking, the degree of renal failure? and hypoproteinaemia in patients with nephrotic syndrome? It has been reported that haemodialysis (HD) improves macular oedema in diabetic patients.[3,4] Thus, we studied the effect of an HD session on foveal thickness using pre-HD and post-HD optical coherence tomography (OCT) in 14 adult HD patients with type 2 *diabetes mellitus* and stage 5 chronic renal failure (CRF) secondary to diabetic nephropathy. In contrast to other types of tests which are used to evaluate retinal pathology, OCT enables foveal thickness to be quantitatively measured with minimal inter-observer variations.

## PATIENTS AND METHOD

We examined 14 patients (9 males and 5 females) with an average age of 70.64±7.01 years, who had diabetes for 22.86±8.98 years and had received HD for 21.14±16.83 months. Their pre-HD systolic blood pressure was 136.54±24.55mm Hg and their pre-HD diastolic blood pressure was 65.85±8.68mm Hg. Thirteen patients had a past or current history of smoking. The average time of the HD session was 3.58±0.42 hours. Ultrafiltration rate was 2,042.31±1,134.28ml, bath temperature 36.46±0.19 ºC, conductivity 14.23±0.26mS/cm, blood flow 261.54±29.96ml/min and KT 37.43±6.59. The characteristics of the HD session were as follows: conventional HD, consisting of a schedule of three HD sessions per week using a Hospal Integra monitor, using a dialyser with a $2m^2$ polyarylethersulfone membrane (kUF 27.1ml/h/mm Hg, Qd 500ml/min with a composition of: sodium 140, calcium 3 mg 0.75 and K 1.5 mEq/l). Eight patients received an initial dose of 20mg of enoxaparin and 6 patients received 40mg. UF, sodium and temperature profiles were not recorded and there were no blood transfusions. Eight patients were subjected to dialysis using a Hickman catheter and 6 patients via an arteriovenous fistula. Eleven patients had less than 7% $A_{1C}$ glycosylated haemoglobin. Ten patients were being treated with insulin, two with insulin and oral anti-diabetic drugs and two by diet alone. Their average values were as follows: haemoglobin 11.07±0.85mg/dl, haematocrit 33.03±3.50%, intact PTH 374.1±278.33pg/ml, calcium-phosphorus product 33.3±15.19, total cholesterol 143.53±33.07mg/dl, triglycerides 165.46±61.94mg/dl and the average dose of intravenous beta erythropoietin was 5,642.8±3,045.51 units after each HD session. Nine eyes had received argon laser treatment prior to initiating HD and six showed evidence of active diabetic retinopathy when they were examined. Diabetic macular oedema was only found in one patient. HD patients with stage 5 CRF secondary to diabetic nephropathy and with corneal pathology or cataract affecting optical clarity, optical neuropathy or amaurosis were excluded. Patients who could not come to the centre for complementary ophthalmological tests were also excluded. Twenty-five eyes corresponding to 14 patients were selected. All the patients underwent haemogram, urea, creatinine, sodium, potassium, calcium, bicarbonate, osmolarity and total protein tests, and pre-HD and post-HD OCT following drug-induced mydriasis, which involved taking third-generation 3D TOPCON OCT-1000 radial macular images. OCT was used to calculate whether the criteria for defining increased, unchanged or decreased foveal thickness were met, according to a normalisation scale that included variables such as age, sex and race. Foveal thickness was determined in micras and after haemodialysis any value above or below the baseline value was regarded as increased or decreased thickness. All the patients underwent pre-HD visual acuity tests. Both visual acuity tests and foveal thickness measurement were performed by the same ophthalmologist.

Categorical variables were expressed as percentages and numerical variables as mean values plus standard deviation. Proportions were compared by means of the chi-square test of independence or Fisher's exact test and the Student t test was employed for continuous variables. Findings which confirmed or contradicted our hypothesis were considered statistically significant when the corresponding *P* value was less than .05. The SPSS statistical package was used (version 17.0). Patients were divided into 2 subgroups, depending on their foveal thickness measurements: "increased" and "unchanged/decreased". Each of the variables was analysed in both subgroups using the statistical test indicated, depending on whether they were quantitative or qualitative.

## RESULTS

With respect to the data obtained using OCT, average foveal thickness shows a tendency to decrease (from 245.28±52.21µ to 240.40±30.09µ), but this finding was not statistically significant (*P*=.428). At baseline foveal thickness was found to be increased in one patient, but this was not related to any of the clinical or analytical parameters which were analysed. Twelve of the eyes which were examined showed an increase in foveal thickness, three remained unchanged and 10 showed a decrease. With respect to visual acuity, six of the eyes that were analysed showed a visual acuity of less than 0.05; in seven eyes it was less than 0.5 but greater than 0.05 and in 12 eyes it was greater than 0.5. Changes in OCT (in the two subgroups which were studied) failed to correlate with individual visual acuity (*P*=.414) or visual acuity divided into subgroups (*P*=.663). For the group as a whole the changes in foveal thickness were unrelated to demographic data, the laboratory parameters analysed, previous argon laser treatment, the existence of active diabetic retinopathy or the dose of erythropoietin that was administered (Table 1). However, when the subgroup of 13 eyes in which foveal thickness showed no change or decreased after HD was compared to the subgroup of 12 eyes in which there was an increase, it was found that in the former subgroup the bath temperature was significantly higher (37.00±0.00 compared to 36.29ºC, *P*=.008) and conductivity was significantly lower (14.00±0.00 compared

**Table 1.** Data of patients and haemodialysis session

| | |
|---|---|
| Sex (male/female) | 5/9 |
| Age (years) | 70.64 ± 7.01 |
| Duration type 2 diabetes (years) | 22.86 ± 8.98 |
| Time on HD (months) | 21.14 ± 16.83 |
| Intact PTH (pg/ml) | 374.14 ± 278.33 |
| HD session time (hrs) | 3.58 ± 0.42 |
| Pre-HD SAP (mm Hg) | 136.54 ± 24.55 |
| Pre-HD DAP (mm Hg) | 65.85 ± 8.68 |
| HD bath Temp. (ºC) | 36.46 ± 0.19 |
| Conductivity (mS/cm) | 14.23 ± 0.26 |

to 14.29±0.10mS/cm, *P*=.030) (Table 2). Six of the eyes that we examined showed evidence of active diabetic retinopathy and the remainder showed none. Four eyes were affected by non-atrophic non-exudative age-related macular degeneration and another 4 eyes had epiretinal membranes which failed to meet criteria for surgical treatment.

## DISCUSSION

Numerous treatments are used to control diabetic retinopathy. The most widely used of these include photocoagulation[5-8] or vitrectomy,[9-10] with intravitreal injections becoming increasingly popular. Diabetic macular oedema in non-dialysis patients with stage 5 CRF has been linked to systemic factors[11-13] such as increased volaemia, hypertension and anaemia. Thus, in addition to treating diabetic retinopathy, it is recommended that these patients also receive renal function replacement therapy, which would improve the above mentioned factors. An improvement in macular oedema, together with a reduction in blood pressure and volaemia values, has been reported one month after the start of peritoneal dialysis[3] or HD.[4] Similar results have been reported 6.5 months after initiating HD.[14] An improvement has also been demonstrated in thick macular exudates a year after starting HD.[2] However, in a fluorescein angiography no improvement in macular permeability was demonstrated 4 weeks after initiating HD.[15] All the above mentioned studies were performed by angiography or ophthalmoscopy. The only published study using OCT[16] compared the retinal thickness of healthy people and HD patients and it found that HD patients showed a significant reduction in retinal thickness with respect to healthy controls. This reduction was significant in all the quadrants which were analysed and it correlated with the age of the HD patients. In this study no differences were found in foveal thickness between haemodialysis patients and healthy controls. In the literature we did not find any comparative studies on the effect of an HD session on foveal thickness measured by OCT in type 2 diabetes patients. In our study foveal thickness tended to decrease after a session of HD, although this tendency was not statistically significant, as only 13 out of the 25 eyes which were examined showed a decrease or remained unchanged. These findings could be related to the time our patients had been receiving dialysis, as the previous studies were conducted during periods which were closer to the start of HD. The finding that the subgroup of eyes in which foveal thickness decreased or failed to change had been dialysed using a higher bath temperature could be linked to the dilation of retinal capillaries. The fact that this subgroup of eyes had been dialysed with a lower level of conductivity compared to the subgroup in which foveal thickness increased following HD, without any differences in ultrafiltration in the two subgroups, could be related to a tendency towards the extravasation of osmotically active substances. Only 6 out of the 23 eyes which were examined showed signs of active diabetic retinopathy, which indicates a beneficial effect of HD on diabetic retinopathy, bearing in mind that only 9 eyes had been subjected to argon laser treatment prior to starting HD and that none had received this therapy after starting HD. Lastly, it has been published that the administration of erythropoietin to HD patients improves macular permeability evaluated by angiography.[17] Our study found no correlation between changes in foveal thickness measured by

**Table 2.** Haemodialysis session parameters and changes in foveal thickness measured by optical coherence tomography

| Haemodialysis session parameters | Subgroup of eyes with unchanged or decreased foveal thickness after haemodialysis (n=13) | Subgroup of eyes with increased Foveal thickness after haemodialysis (n=12) |
|---|---|---|
| Conductivity (mS/cm) | 14.00 (0.00) | 14.29 (0.10[a]) |
| Bath temperature (ºC) | 37.00 (0.00) | 36.28 (0.18[a]) |
| Blood flow (ml/min) | 275.00 (14.43) | 250.00 (10.91) |
| Ultrafiltration (ml) | 887.50 (653.95) | 1814.28 (412.56) |

[a] P<0.005

pre-HD and post-HD OCT and the dose of erythropoietin that was administered so we have not ruled out the possibility that, at least partially, the beneficial effect of HD on diabetic retinopathy may be due to the fact that all the patients studied were being treated with erythropoietin.

To summarise, this study suggests that the use of HD as an adjuvant to ophthalmological treatment may modify retinal capillary regulation, depending on parameters such as bath temperature and conductivity. New studies with larger sample sizes that involve the analysis of a greater number of HD sessions would be needed to corroborate this hypothesis.

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