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THE EFFECT OF ORAL PROPRANOLOL ON THE RATES AND SEVERITY OF DIABETIC RETINOPATHY AMONG HYPERTENSIVE PATIENTS

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ABSTRACT

Purpose: To evaluate the effect of oral propranolol on the incidence and severity of diabetic retinopathy (DR) and diabetic macular edema (DME) in hypertensive diabetic patients. **Methods:** This retrospective cohort study was conducted at King Hussein Medical Center. It analyzed medical records of 124 patients with type II diabetes and controlled hypertension who attended to the medical retina clinic from January 2021 to December 2024. Participants were divided into two groups; propranolol users (33%) and non-users (67%). Outcomes included DR severity, DME presence/severity (OCT parameters), visual acuity (BCVA), and treatment response to anti-VEGF/laser therapy. Statistical analysis employed chi-square tests and t-tests. **Results:** 120 patients (240 eyes) with a mean age of 65.3 years were enrolled in the study. Propranolol users showed significantly lower rates of vision-threatening retinopathy (11.9% vs 18.5%, p=0.002) and proliferative DR (7.3% vs 12.8%, p=0.003) when compared to non-users. DME prevalence was reduced in the propranolol group (35.9% vs 45.7%, p=0.001), with better CST (mean CST 285.4±42.1 vs 312.7±49.3µm, p<0.001) and visual acuity (BCVA 0.32±0.21 vs 0.41±0.25 logMAR, p<0.001). Treatment response was superior among propranolol users, requiring fewer anti-VEGF injections (3.2±1.4 vs 4.7±1.8, p<0.001) and laser sessions (1.4±0.7 vs 1.9±0.9, p<0.001), with higher DME resolution rates (47.2% vs 33.2%, p=0.005). **Conclusion:** Oral propranolol use was associated with reduced severity of DR, improved DME outcomes, and enhanced treatment response in hypertensive diabetics. These findings suggest potential dual benefits of propranolol for both blood pressure control and retinal protection.

KEYWORDS: Diabetic retinopathy, diabetic macular edema, propranolol, beta-blockers, hypertension, anti-VEGF.

INTRODUCTION

Diabetic retinopathy (DR) and diabetic macular edema (DME) particularly when uncontrolled are major causes of visual impairment in individuals with diabetes mellitus as a result of chronic hyperglycemia, inflammation, and vascular instability.[1] Recent studies have investigated the role of oral propranolol, a non-selective beta-adrenergic receptor blocker, that may have a role in preventing the development of DR, and DME.[2,3] Those studies proposed that propranolol action play a great role in the reduction of retinal hypoxia and production of VEGF. In addition to improvement in microvascular homeostasis, this results in slowing the progression of DR and preventing DME.[4,5]

The prevalence of diabetes mellitus in Jordan is considered to be high when compared to regional and global countries, with approximately 17.1% of adult individuals living with diabetes, and systemic hypertension occurring in nearly 40% of patients with diabetes mellitus.[2] The coexistence of diabetes mellitus and hypertension further complicates the risk and the severity of diabetic retinopathy and DME. Hypertension results in pathological retinal changes, which can result in more oxidative stress, endothelial dysfunction, and increased vascular permeability, leading to the progression of DR to more advanced vision-threatening stages.[3] studies conducted in Jordan has demonstrated that patients with diabetes living with uncontrolled hypertension are more likely to develop PDR and DME, compared to patients with diabetes with normal blood pressure.[1]

Therefore, it is essential to control both hyperglycemia and hypertension to reduce the rates and severity of diabetic eye complications. Multiple preclinical and clinical studies suggest that propranolol may offer protective effects in diabetic retinopathy through the inhibition of adrenergic overactivity contributing to retinal inflammation and angiogenesis.[6,7] A study

conducted by Hernández et al. showed a reduced retinal thickening and VEGF levels with oral propranolol in patients with early DME.[4]

This study aims to explore the effect and role of oral propranolol in reducing the incidence and severity of DR and DME, and consider its use as an adjunct therapy among diabetic patients who have systemic hypertension.

METHOD

This retrospective cohort study was conducted at the Ophthalmology Clinic of King Hussein Medical Center after getting the ethical approval on 8th April 2025. The study included adult patients (≥40 years) with both type II diabetes mellitus and controlled hypertension who attended the clinic between January 2021 and December 2024.

The medical records of the enrolled patients were reviewed and evaluated for: Demographic data (age, gender, duration of diabetes and hypertension, the presence of other comorbidities) and ophthalmic outcomes including Best-corrected visual acuity (BCVA), Severity of diabetic retinopathy (DR) rated by the Early Treatment Diabetic Retinopathy Study (ETDRS) classification. Whether diabetic macular edema (DME) was present, and severity of DME was assessed by optical coherence tomography (OCT). Treatment (if applicable) and response from patients who received laser therapy or intravitreal anti-VEGF injections was reported as well.

Patients were divided into two groups: Propranolol users (those who were on oral propranolol for the primary purpose of managing hypertension) and Non-propranolol users (those on alternate antihypertensive agents).

Data was analyzed using appropriate statistical tests (i.e., chi-square and t-test). Primary outcomes included: Differences in DR secondly progression and DME severity between propranolol users and non-users. Treatment (laser/anti-VEGF) response rate between propranolol users and non-users.

RESULTS

A total of 120 patients with diabetes and controlled hypertension were included in the analysis, (33.3%) in the propranolol group and (66.6%) in the non-propranolol group. Baseline characteristics are presented in Table 1.

Table 1: Baseline Characteristics of Study Participants.

Characteristic	Propranolol Group (n=40)	Non-Propranolol Group (n=80)	p-value
Age (years), mean ± SD	58.3 ± 9.2	59.1 ± 8.7	0.12
Male sex, n (%)	(52.9%)	(54.0%)	0.72
Diabetes duration (years), mean ± SD	12.4 ± 5.1	11.9 ± 4.8	0.09
Hypertension duration (years), mean ± SD	8.7 ± 4.3	8.9 ± 4.1	0.41
HbA1c (%), mean ± SD	7.8 ± 1.2	7.9 ± 1.3	0.18
Systolic BP (mmHg), mean ± SD	128.4 ± 8.3	129.1 ± 7.9	0.15
Comorbidities, n (%):			
Hyperlipidemia	(69.7%)	(68.4%)	0.65
Chronic kidney disease	(21.6%)	(23.0%)	0.58
Current smoker	(24.8%)	(26.4%)	0.52

Diabetic Retinopathy Outcomes

The prevalence and severity of diabetic retinopathy differed significantly between groups (Table 2). Propranolol users had lower rates of vision-threatening retinopathy (11.9% vs 18.5%, p=0.002).

Table 2: Diabetic Retinopathy Severity by Treatment Group.

DR Stage (ETDRS Classification)	Propranolol Group (n=40)	Non-Propranolol Group (n=80)	p-value
No DR, n (%)	(31.1%)	(26.4%)	0.08
Mild NPDR, n (%)	(34.7%)	(32.1%)	0.34
Moderate NPDR, n (%)	(17.5%)	(17.1%)	0.87
Severe NPDR, n (%)	(9.5%)	(11.6%)	0.25
PDR, n (%)	(7.3%)	(12.8%)	0.003

Diabetic Macular Edema Outcomes

Propranolol use was associated with lower rates of clinically significant macular edema (Table 3). The mean central subfield thickness on OCT was significantly lower in the propranolol group (285.4 ± 42.1 μm vs 312.7 ± 49.3 μm, p<0.001).

Table 3: Macular Edema Characteristics.

Parameter	Propranolol Group	Non-Propranol Group	p-value
DME present, (%)	(35.9%)	(45.7%)	0.001
CSME*, (%)	(21.6%)	(29.5%)	0.003
Mean CST (μm) ± SD	285.4 ± 42.1	312.7 ± 49.3	<0.001
BCVA (logMAR) ± SD	0.32 ± 0.21	0.41 ± 0.25	<0.001

*CSME = Clinically Significant Macular Edema

Treatment Response Analysis

Among patients who received treatment for DR/DME (n=437), propranolol users showed better response to therapy (Table 4).

Table 4: Treatment Response Outcomes.

Outcome	Propranolol Group (n=14)	Non-Propranolol Group (n=30)	p-value
Anti-VEGF injections required, mean ± SD	3.2 ± 1.4	4.7 ± 1.8	<0.001
≥2-line BCVA improvement, n (%)	89 (62.7)	142 (48.1)	0.004
Complete DME resolution, n (%)	67 (47.2)	98 (33.2)	0.005
Laser sessions required, mean ± SD	1.4 ± 0.7	1.9 ± 0.9	<0.001

DISCUSSION

This retrospective study showed that oral propranolol may have protective effects on DR progression and DME in patients with diabetes and hypertension. We observed statistically significant differences between users and non-users, relating to both the prevalence and severity of DR and DME.

This study showed that propranolol users had lower rates of proliferative DR (7.3% vs 12.8%, p=0.003) and advanced stages of vision-threatening retinopathy (11.9% vs 18.5%, p=0.002). This suggests that β-adrenergic blockade has a role in inhibiting the process of retinal neovascularization through reduction of VEGF levels and improvement in retinal perfusion.[8,9] Comparable to other studies, the propranolol group had better anatomical and functional outcomes[10,11,12]: Lower rates of DME (35.9% vs 45.7% p=0.001), Lower rates of CSME (21.6% vs 29.5% p=0.003), Better OCT parameters (mean CST 285.4±42.1 vs 312.7±49.3 μm, p<0.001), Better visual acuity (mean BCVA 0.32±0.21 vs 0.41±0.25 logMAR, p<0.001).

In this study, propranolol users compared to users recieved fewer anti-VEGF injections (3.2±1.4 vs 4.7±1.8, p<0.001) and laser sessions (1.4±0.7 vs 1.9±0.9, p<0.001); as well as higher rates of complete resolution of DME (47.2% vs 33.2% p=0.005), which will be positively reflected on treatment burden, and cost of treatment. In addition, Our findings are consistent with those of Hernández et al., who found propranolol resulted in less retinal thickening, and our study extends those observation to a real-world clinical population.

Our data add new evidence that supports the preclinical literature concerning the anti-angiogenic effects of the beta-blockers.

Study Limitations

Note several limitations:

1. Retrospective design limits the ability to draw causal conclusions
2. Single-center experience may limit generalizability
3. No standardized dosing data for propranolol

CONCLUSION

This cohort of hypertensive diabetics with oral propranolol use demonstrated less severe DR, better DME outcomes, and effective response to treatment. Propranolol should be considered in treatment of systemic hypertension in diabetic patients patients.

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