ISSN: 0975-833X

Available online at http://www.journalcra.com

International Journal of Current Research
Vol. 15, Issue, 01, pp.23189-23191, January, 2023
DOI: https://doi.org/10.24941/ijcr.44262.01.2023

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

RESEARCH ARTICLE

IMPROVEMENT IN DIABETIC RETINOPATHY AND URINE FOR MICROALBUMINURIA WITH EMPAGLIFLOZIN VERSUS TENELIGLIPTIN. AN OPEN LABEL RANDOMIZED CONTROLLED TRIAL

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ARTICLE INFO

Article History:
Received 14th October, 2022
Received in revised form
12th November, 2022
Accepted 25th December, 2022
Published online 20th January, 2023

Key words:

Non Proliferative Diabetic Retinopathy, Macroalbuminuria, Empagliflozin, Teneligliptin.

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ABSTRACT

Aim & Objective: To compare the efficacy of empagliflozin versus teneligliptin on diabetic retinopathy and urine for microalbuminuria as add on therapy to metformin monotherapy in patients of uncontrolled T2DM. ***Material and Methods:*** The study was randomized, prospective, open label, comparative interventional study conducted at Dr RPGMC Tanda. Out of total 66 patients, 32 patients (Group A) received empagliflozin 25mg/day and 34 (Group B) received teneligliptin 20mg/day in addition to metformin 1000 mg BD. Total 18 patients, 9 in each group had mild to moderate non proliferative diabetic retinopathy (NPDR). Both the groups were evaluated after 6 months. ***Statistical Analysis:*** The data is presented as mean+/- SD. Student's t test was used for data analysis. The p value<0.05 is significant. ***Results:*** After 6 months, In group A only 1 patient had mild NPDR, In group B only 3 patients had mild NPDR. There was statistically significant decrease in urine for microalbuminuria in both groups at 6 months, when compared with baseline (both $p < 0.001$). ***Conclusion:*** Non proliferative diabetic retinopathy improved with both the drugs (empagliflozin > teneligliptin) which also proved their potential role in protection from microvascular complications. Both the drugs showed decrease in microalbuminuria by improving diabetic status.

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Citation: ***Dr. Shilpa Sharma, Dr. Dinesh Kansal, Dr. Dhiraj Kapoor and Dr. Atal Sood, D.*** **2023.** "Improvement in diabetic retinopathy and urine for microalbuminuria with empagliflozin versus teneligliptin. An Open Label Randomized Controlled Trial*". International Journal of Current Research*, 15, (01), 23189-23191.

INTRODUCTION

Diabetes mellitus (DM) refers to a group of common metabolic disorders that share the phenotype of hyperglycemia.[1] Diabetic retinopathy (DR) is one of the most serious complications of diabetic microangiopathy. DR has an early onset and is not easy to detect. When visual impairment occurs, the optimal period for therapy is often missed. Therefore, the prevention and treatment of DR should start from the early stage of diabetes.[1] Sodium-dependent glucose transporter 2 inhibitors (SGLT2i) are new antidiabetic drugs which are mainly used in clinical practice to control blood glucose of patients with type 2 diabetes prone to develop chronic heart failure. Recent studies have found that SGLT2 is also expressed in the human retina. Now, the prevention and treatment of diabetic retinopathy with SGLT2i while reducing blood sugar has become a new research field.[2]

Classification of diabetic retinopathy: The classification of DR development is related to the abnormalities of retinal microvascular system, including increased blood retinal barrier permeability, decreased vascular endothelial cells and pericytes and thickened vascular basement membrane

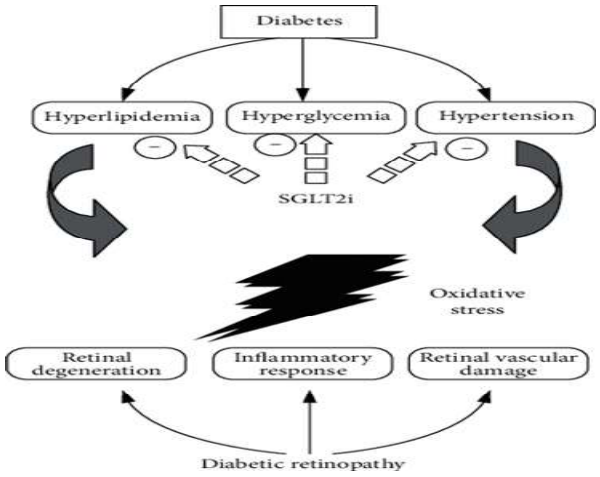
Therefore, DR is currently divided into non-proliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR).[2]

Non-proliferative Diabetic Retinopathy (NPDR): NPDR occurs in the early stage of DR. The main pathophysiological basis is high glucose-induced retinal degeneration, including loss of capillary pericytes, thickening of the basement membrane, thinning of the blood vessel layer and destruction of the blood-retinal barrier and microvascular abnormalities in the retina and cotton wool spots (fluffy white plaques on the retina caused by local swelling of the retinal nerve fiber layer). However, in the NPDR stage, patients are usually asymptomatic and have normal vision. When visual impairment occurs, the best period of treatment is often missed. Therefore, it is necessary to prevent the occurrence of DR in the early stage of diabetes.[2]

Proliferative Diabetic Retinopathy (PDR): Studies have found that the prevalence of PDR is close to 50% after 25 years of diabetes diagnosis, and most patients with type 1 diabetes (T1DM) will develop PDR after about 10 years. At the PDR stage, the new blood vessels in the eye are continuously generated and often accompanied by the oozing and hyperplasia of the eye tissue, which can destroy the normal structure and function of the eye and ultimately lead to the

visual impairment of the patient. Compared with NPDR, PDR is more harmful to eyesight and could cause severe vision loss or even complete blindness.[2]

The Mechanism for Diabetic Retinopathy: The pathogenesis of DR is complex, and the mechanism has not yet been fully elucidated. The pathological mechanism hypotheses currently proposed mainly include the theory of chronic inflammation, retinal hemodynamic changes, oxidative stress, gene polymorphism, and neurodegenerative changes.[2]



Microalbuminuria, typically defined as urinary albumin excretion (UAE) of 30–300 mg in a 24-h urine sample, corresponds to a subclinical microvascular derangement in the glomerular filtration barrier that precedes overt diabetic nephropathy. It has been well-established that increased UAE, even below the threshold values usually considered for microalbuminuria, constitutes an early marker of microvascular damage and a potent predictor of cardiovascular morbidity and mortality.[3]

MATERIALS AND METHODS

Study design and setting: The study was randomized, prospective, open label, comparative interventional study. The study was conducted in the Department of Pharmacology and the Department of Medicine at Dr. R.P.G.M.C, Kangra at Tanda which is 700 bedded multispeciality tertiary health care center situated in the foothills of Dhauladhar mountain range, at altitude of 32.0986360N and longitude of 76.3003390 E, amidst the serene Kangra valley of Himachal Pradesh in India. IEC approval vide letter no. IEC/139/2019: dated 17/12/2019. CTRI registration no. (REF/2020/03/032516), Trial completed on 24/10/2021.

Study population: The study population was the consenting adult patients of T2DM of different socio-economic strata, from the Kangra and adjoining 5 districts of Himachal Pradesh. The patients were selected on an outpatient department basis.

Inclusion criteria:

- Willing to give written informed consent for the study.
- Adult patients of age more than 18 years of either sex.
- Ambulatory subjects who were suffering from type 2 diabetes mellitus and prescribed anti-diabetic drug at medicine OPD.

Exclusion criteria

- Subjects age less than 18 years.
- Subjects not willing to participate.
- Coexisting cardiac, renal, liver and CNS emergency conditions.
- Any condition resulting in severe learning disability (e.g. brain injury) or unable to comprehend for other reasons.
- Acute complications of diabetes mellitus such as hyperglycemic hyperosmolar state and diabetic ketoacidosis.
- Pregnancy and lactating mothers.
- Known hypersensitivity or contraindications to study drugs.
- Patients already on study drugs.

Study duration: The study stretched over a period of one year for the enrollment of patients and follow-up was done at the end of first, third and sixth month after initiating the treatment.

Study intervention: Detailed history of the patients with T2DM was elicited, clinical examination was done and hematological and biochemical investigations were carried out. Once diagnosed, the registered patients of T2DM were informed about the study through the patient information sheet and were allowed to understand thoroughly about the study and related aspects in their own language. After a written informed consent, the participants were assigned to either group either A or B, based on computer generated random numbers.

GROUP A Participants	Empagliflozin 25 mg/day + metformin 1000 mg twice a day with meals.
GROUP B Participants	Teneligliptin 20 mg/day + metformin 1000 mg twice a day with meals.

- Fundus examination for diabetic retinopathy at baseline and at 6 months.
- Urine for microalbuminuria at baseline and at 6 months.
- Patients were contacted telephonically on the next day of initiating the therapy and enquired for any adverse event..
- Randomization was computer generated.

Measurement of outcome

Efficacy
1. No. of patients with controlled diabetes. a) Without addition of new drug (per protocol). b) With addition of new drug (intent to treat).
2.No. of patient with uncontrolled diabetes even after addition of new drug.

Statistical analysis: The data were recorded on Microsoft excel spreadsheet. Statistical analysis was done using Microsoft excel and online SPSS software. Quantitative data was presented as mean ± SD. Categorical data was presented as frequency and percentage. Student's t-test was used for comparing continuous variables between the two groups. Chi square or Fisher's exact test was used for comparing the qualitative data between the two groups. An intention-to-treat analysis was done to compare the data. p value < 0.05 was considered significant.

RESULTS

Table 1. Baseline sociodemographic characterstics

BASELINE CHARACTERISTICS	GROUPA(n=32)	GROUP B(n=34)	p value
Age (years) 30-40	2(6%)	3(9%)	0.812
40-50	8(25%)	6(18%)	
50-60	15(47%)	15(44%)	
>60	7(22%)	10(29%)	
Gender			1.000
Male	16(50%)	17(50%)	
Female	16(50%)	17(50%)	
%Age of Hypertensives	16(50%)	15(44%)	0.632
%Age of family history of diabetes	18(56%)	18(53%)	0.787
%Age of smokers	13(41%)	12(35%)	0.635
%Age of incidence of alcohol intake	10(31%)	11(32%)	0.585
BMI	27.04±2.82	26.67±2.83	0.713

Improvement in fundus for diabetic retinopathy: There was progressive improvement in fundus for diabetic retinopathy over 6 months.

Baseline: Total 18 patients, 9 in each group had mild to moderate non proliferative diabetic retinopathy (NPDR).

Table 2. Improvement in fundus for diabetic retinopathy

	Fundus for diabetic retinopathy	Group A (n=32)	Group B (n=34)	p-value#
Baseline	Mild-Moderate NPDR	9 (28%)	9 (26%)	0.880
	Normal	23 (72%)	25 (74%)	
6-months	Mild-NPDR	1 (3%)	3 (9%)	0.806
	Normal	31 (97%)	31 (91%)	

After 6 months

Group A – only 1 had mild NPDR.
Group B- only 3 had mild NPDR.
Both the groups were comparable at baseline (p value = 0.880) and 6 months (p = 0.806).

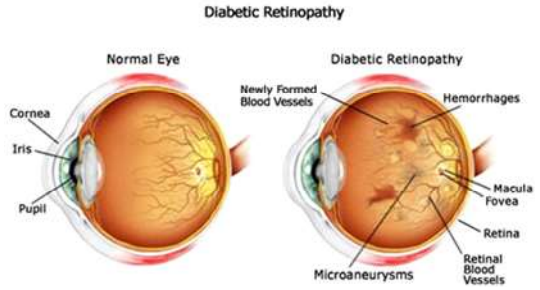


Figure 3. Comparison of urine for microalbuminuria in both groups

Comparison of urine for microalbuminuria in both groups: There was statistically significant decrease in urine for microalbuminuria in both groups when compared with baseline to 6 months (both p < 0.001).

Table 3. Comparison of urine for microalbuminuria in both groups

Urine for microalbuminuria	Group A (n=32)	Group B (n=34)	p-value#
Baseline	34.3 ± 4	22.9 ± 8	0.133
6-Months	17..2 ± 3***	17.1 ± 4***	0.927
p value	***<0.001 (Baseline vs. 6-month)	***<0.001 (Baseline vs. 6-month)	

DISCUSSION AND CONCLUSION

Both the drugs showed decrease in microalbuminuria by improving diabetic status. NPDR also improved with both the drugs (empagliflozin > teneligliptin) which proved their potential role in protection from microvascular complications.

LIMITATIONS: Being post graduate thesis, the follow-up could not be extended beyond 6 months. Follow-up for longer duration would have added more evidence about safety and efficacy of our study drugs.

FINANCIAL DISCLOSURE

No unnecessary financial burden was put on the patient for the treatment and investigations at any point of time throughout the study period. I did not get any financial benefit from any pharmaceutical company or any other source for this study.

CONFLICT OF INTEREST: No conflict of interest pertaining to any part of the study.

REFERENCES

1. Powers Alvin C, Niswender Kevin D.R, Molina Carmella Evans. Diabetes Mellitus: Diagnosis, Classification, and Pathophysiology. In: Jameson J. Larry, Kasper Dennis L, Longo Dan L, Fauci Anthony S, Hauser Stephen L, Loscalzo Joseph, Editors. Harrison Principles of Internal Medicine. 20th ED. McGraw-Hill Education. 2018; p. 2850.
2. Sha W, Wen S, Chen L, Xu B, Lei T, Zhou L. The role of SGLT2 inhibitor on the treatment of diabetic retinopathy. Journal of Diabetes Research. 2020 Nov 12;2020.
3. Nikolaidou B, Gkaliagkousi E, Anyfanti P, Gavriilaki E, Lazaridis A, Triantafyllou A, Zografou I, Douma S. The impact of hyperglycemia on urinary albumin excretion in recent onset diabetes mellitus type II. BMC nephrology. 2020 Dec;21(1):1-6.

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