Risk reduction of retinopathy in type II diabetes patients – A cross sectional survey

Mahmood Sheikh[1], *Sheikh Abdul Khaliq[2], Iqbal Azhar[1]

[1]Department of Pharmacognosy, Faculty of Pharmacy and Pharmaceutical Sciences, University of Karachi, Karachi – 75270, Pakistan
[2]Department of Pharmacy Practice, Faculty of Pharmacy, Hamdard University, Karachi 74600, Pakistan

Corresponding author: Sheikh Abdul Khaliq
Email address: drsheikh1974@gmail.com

Abstract

In diabetic patients; retinal neuropathy is common and a primary cause of blindness. The study was aimed to evaluate the effects of different therapeutic systems of medicines in reducing the risk of Diabetic-Retinopathy (DR) in type II diabetes (T2D) patients. The study design was cross-sectional, recruited two-hundred (N=200) patients suffering from T2D. Clinical settings were out-patient clinics in the mega city Karachi. Ethical approval has been obtained (Registration-number-IRB-00005148). Written informed consent was obtained from each study participant.The treatment arms of study were allopathic, herbal, homeopathic and/or combination. Standardized precision analysis technique was used for the determination of sample size of study. Collected data was evaluated by Number needed to treat (NNT) analysis and relative-risk-reduction (RRR) through SPSS 20 software. In different systems of medicine, RRR of DR in patients taking insulin; aallopathic v/s combination:6.28%, NNTH"-19.0; without-insulin allopathic v/s homeopathic:- 27.78%, NNTH"-7.0; v/s herbal:-63.82%, NNTH"-4.0; v/s combination:-34.16%, NNTH"-6.0. RRR of DR with-exercise allopathic v/s homeopathic:37.50%, NNTH" 3.0; v/s herbal:- 462%, NNTH"-2.0; v/s combination:-25%, NNTH"-8.0. RRR of DR without exercise allopathic v/s homoeopathic:-67.08%, NNTH"-3.0; v/s herbal:-57.32%, NNTH"-4.0; v/s combination:- 31.45%, NNTH"-6.0. RRR of DR with diet of low calorie allopathic v/s homoeopathic:- 46.66%, NNTH"-4.0; v/s herbal:- 46.66%, NNTH"-4.0; v/s combination:-14.57%, NNTH"-11.0. RRR of DR in diet without-low-calorie allopathic v/s homoeopathic:-48%, NNTH"-4.0; v/s herbal:-166%, NNTH"-2.0; v/s combination:- 48%, NNTH"-4.0. The high risk of DR was noted in the treatment of allopathic medicines compared to complementary and alternative medicines (homoeopathic, herbal and combination) in patients of T2D.

Keywords

Diabetes Mellitus; diabetic retinopathy, risk

assessment; risk; blood glucose; glycated hemoglobin A.

1. INTRODUCTION

Micro-vasculopathy leads to retinopathy; however; in diabetic patients retinal diabetic neuropathy is common and retinal damaging process is caused by high sugar levels which is a primary cause of blindness (Sohn *et al.*, 2016). Type II Diabetes Mellitus (T2DM) is a growing health related concern around the globe.(Zhou *et al.*, 2016) In long standing diseases like Diabetes Mellitus (DM); many complications are reported in literature and observed in clinical practice, one of such complications is retinopathy (Wan *et al.*, 2015). Diabetic Retinopathy (DR) is classified as Non proliferative Diabetic Retinopathy (NPDR) and Proliferative Diabetic Retinopathy (PDR) (Hammes, 2018). 11% patients every year leads to blindness due to DR and a major challenge for ophthalmologists (Wang *et al.*, 2017). The prevalence of DR and PDR in South Asian population was 46% and 1.7% respectively (Stolk *et al.*, 2008). According to another literature; prevalence of DR and PDR in India is 36.47% and 25.82% respectively (Huang *et al.*, 2015). These evidences are showing that PDR is rising in South Asian countries particularly in India and Pakistan; a neighboring country of an India.

In last few decades; some important developments were observed regarding epidemiology of DR, retardation of its progression, clinical assessment and management; early screening, detection and management may prevent the vision loss due to DR (Ting *et al.*, 2016). It is an old saying that prevention is better than cure; unfortunately there is no cure exists so far for DM. Prevention from DR can be possible by optimal control of blood sugar, blood pressure, accomplishing lipid goals, and avoidance from smoking (Jennifer D, 2021). Eye dilated exam should be conducted five years after the diagnosis of DM and then annually thereafter (Jennifer D, 2021). In order to reduce severe vision loss; PDR can be treated by pan-retinal photocoagulation and vitrectomy techniques (Jennifer D, 2021). According to one study; conducted on 37894 Type II Diabetic (T2D) patients in Taiwan; use of statins significantly reduces the prevalence and progression of DR.(Kang *et al.*, 2019). Omega 3 fatty acids also inhibit the retinal angiogenesis and prevents neuronal loss; thus averting retinal degeneration (Behl *et al.*, 2017b). Many Chinese herbs have also shown promising effects in reducing the risk of DR in T2D patients by eliciting anti-inflammatory, anti-oxidant, anti-angiogenetic, anti-apoptotic and by many other complex mechanisms (Behl *et al.*, 2017a). *Puerariae lobata, Panax notoginseng, Lycium barbarum, Salvia miltiorrhiza, Anisodus tanguticus, Astragalus membranaceus, Ginkgo biloba, Scrophularia ningpoensis* are examples of some Chinese herbs reported to have effects in reducing the risk of DR in T2D patients (Behl *et* al., 2017a). Alternative and complementary medicine (ACM) is a main focus of research now a days; the major reason behind this focus is that majority of global population are now developing more trust on ACM for their health related disorders (Sen *et al.*, 2017). Since decade, Pakistan strongly established tradition for utilization of natural/unani medicines for cure of diseases and perfection of health, therefore; Pakistan is not having different trends compare to the rest of the world regarding use of ACM; one of the evidence mentioned that ACM is preferred by almost 50% of Pakistani population (homoeopathy, her-bal, combinations) (Bukhsh *et al.*, 2018). Relative ri-

sk reduction (RRR) is a risk reduction of one treatment compare to another treatment for any bad outcome while number needed to treat (NNT) analysis is a determination that how many patients should be treated by one treatment compare to another treatment to reduce one bad outcome; some tools e.g. RRR and NNT are standardized by Evidences Based Medical Practices (EBM); these tools are useful for comparison of outcomes of different therapeutic systems for their efficacy or safety (Aparasu *et al.*, 2020).

Due to high prevalence of DR in South Asian countries; the main objective of current study was to evaluate first time in the South Asian region especially in Karachi, Pakistan, the risk reduction of DR by different therapeutic systems commonly utilize in South Asian countries. Risk reduction was calculated and compared by determining RRR and NNT of treatments in patients of type II diabetes.

2. MATERIALS AND METHODS

Study Design

Cross-sectional survey duration of study: Started from July-2020 and ended by January-2022.

Study Objective

Evaluate comparative effectiveness of risk reduction of DR by ACM and allopathic medicines (oral hypoglycemic) in patients of T2D, place of study was outpatient care-centers of Karachi.

Sample Size

The study registered two hundred (N=200) patients of T2D, thesepatients were divided based upon their treatment choices of either allopathic, herbal,homeopathic and/or combination. According to precision analysis technique (Aparasu, 2020); at least 196 patients of a T2D should be registered in the study to keep study power.

Study End-Point

Occurrence or report of Diabetic Retinopathy (DR).

Ethical Approvals

Ethical approvals for study were obtained by two institutions, IBC (Institutional Bioethics Committee), University of Karachi (Reference-number IBC-KU-23); another approval was obtained from Interactive Rsch. & Development (Registration-number-IRB-00005148).

Data Collection Method

An organized questionnaire was designed for the collection of primary data. Prior to initiating the study; each participant was acquainted with the objectives, risks and benefits of study; participants signed the written informed consent. Researchers ensured the maintenance of confidential information of patients as per Declaration of Helsinki (Shrestha *et al.*, 2019).

Data Assessment

Questionnaire of the study was filled by clinicians. For the purpose of determination of risk reduction of DR; absolute risk reduction (ARR), RRR, relative risk and NNT were calculated. In order to compare safety or efficacy of treatments or drugs, they are an important indicators in EBM (Kim *et al.*, 2017). In current study, RRR is the relative differences in event rates of DR in between treatment groups, while NNT is that how many number of patients should receive the treatment to reduce one expected outcome (Aparasu *et al*., 2020). The whole data was evaluated by a software of SPSS (Statistical Package for Social Sciences) 22nd version.

3. RESULTS AND DISCUSSION

Mean of glycated hemoglobin (HbA1c), fasting blood sugar (FBS), random blood sugar (RBS) and other baselines characteristics of T2D retinopathy in between different treatments compared to diet with low calories (Table 4). patients (Table 1). RRR, ARR and NNT of diabetic retinopathy in different treatments versus insulin use (Table 2). RRR, ARR and NNT of diabetic retinopathy in between different treatments compared to physical activity of patient (Table 3). RRR, ARR and NNT of diabetic

Table 1. Baseline Characteristics of Patients

Treatment Type	Mean HbA1c[a] (%)	Mean FBS[b] (mg/dL)	Mean RBS[c] (mg/dL)	Male : Female (Ratio)	Mean Age (Years)
Allopathic	8.67	176	231	1 : 2.28	55
Homeopathic	6.40	117	161	3 : 1	52
Herbal	6.53	129	195	2.9 : 1	48
Combination	7.13	135	217	2.06 : 1	52

[a] Glycosylated hemoglobin; [b] Fasting-Blood-Sugar; [c] Random-Blood-Sugar

Table 2. Insulin status, relative risk, RRR[a], ARR[b] and NNT[c] in different treatments compared allopathic treatment

Insulin Status	% Incidences of Diabetic Retinopathy in treatments				Relative Risk	RRR[a]	ARR[b]	NNT[c]
	Allopathic	Homeopathic	Herbal	Combination				
With Insulin	79.66%	--------	--------	85.0%	0.93	6.28%	5.34%	18.72 ~ 19.0
Without Insulin	63.89%	50.0%	--------	--------	-1.27	-27.78 %	-13.89%	-7.19 ~ -7.0
		--------	39.0%	--------	-1.63	-63.82 %	-24.89%	-4.01 ~ -4.0
		--------	--------	47.62%	-1.34	-34.16 %	-16.27%	-6.14 ~ -6.0

[a] relative risk reduction; [b] absolute risk reduction; [c] number needed to treat

Table 3. Exercise / Physical activity statue, relative risk, RRR[a], ARR[b] and NNT[c] in different treatments compared to allopathic treatment

Exercise / Physical Activity	% Incidences of Diabetic Retinopathy in treatments				Relative Risk	RRR[a]	ARR[b]	NNT[c]
	Allopathic	Homeopathic	Herbal	Combination				
Physical Activity	62.50%	100%	----------	--------	0.62	37.50%	37.50%	2.66 ~ 3.0
		--------	11.11%	--------	-5.62	-462%	-51.39%	-1.94 ~ -2.0
		--------	----------	50.0%	-1.25	-25%	-12.50%	-8.00
No Physical Activity	75.94%	45.45%	----------	--------	-1.67	-67.08%	-30.49%	-3.27 ~ -3.0
		--------	48.27%	--------	-1.57	-57.32%	-27.67%	-3.61 ~ -4.0
		--------	----------	57.77%	-1.31	-31.45%	-18.17%	-5.50 ~ -6.0

[a] relative risk reduction; [b] absolute risk reduction; [c] number needed to treat

Table 4. Diet status, relative risk, RRR[a], ARR[b] and NNT[c] in different treatments compared to allopathic treatment

Low Caloric Diet Status	% Incidences of Diabetic Retinopathy in treatments				Relative Risk	RRR[a]	ARR[b]	NNT[c]
	Allopathic	Homeopathic	Herbal	Combination				
Low Caloric Diet	73.33%	50.0%	-------	--------	-1.46	-46.66%	-23.33%	-4.28 ~ -4.0
		--------	50.0%	--------	-1.46	-46.66%	-23.33%	-4.28 ~ -4.0
		--------	-------	64.0%	-1.14	-14.57%	-9.33%	-10.71 ~ -11.0
Without Low Caloric Diet	74.0%	50.0%	-------	--------	-1.48	-48.0%	-.24.0%	-4.16 ~ -4.0
		--------	27.77%	--------	-2.66	-166%	-46.23%	-2.16 ~ -2.0
		--------	-------	50.0%	-1.48	-48.0%	-24.0%	-4.16 ~ -4.0

[a] relative risk reduction; [b] absolute risk reduction; [c] number needed to treat

Retinopathy related to micro-vascular complications is 25 times more common in T2D patients (Jennifer D, 2021). In United States; diabetes is a leading cause of blindness; most commonly due to retinal detachment and vitreal hemorrhage (Jennifer D, 2021). Circumstances are not different in Pakistan; according to one systematic review; prevalence of diabetic retinopathy (DR) in Pakistan is 28.78% (Mumtaz *et al.*, 2018). It seems that prevalence of DR are increasing in Pakistan; because, another study conducted in 1991; reported the prevalence of 26% (Khan, 1991). Keeping these scenarios under consideration; current study was conducted to compare different treatment systems for reduction of risk of DR in patients of T2D. These systems of medicine are commonly practiced in Pakistan. Baseline characteristics of enrolled patients (Table 1) were not having significant differences in therapeutic arms (Allopathic, homeopathic, herbal and combination).

It is noted in the current study that DR is a big challenge among T2D patients. Incidences of DR were compared among different types of therapy or treatments. Current study revealed that those patients who were taking insulin with combination of treatments, they had highest incidences of DR (85.0%); while second highest incidences were in allopathic system of medicine (79.66%) with the use of insulin. (Table 2) Based upon these findings; RRR of DR and NNT were 6.28% and H"19 respectively by allopathic system compared to combination system; therefore it can be concluded that risk reduction of DR is better in allopathic system compared to combination system. Without use of insulin; observations were opposite for allopathic system compared with ACM (homeopathic, herbal and combination). RRR of DR and NNT in allopathic treatment were -27.28%, H"-7.0, -63.82%; H"-4.0 and -34.16%; H"-6.0 compared to homoeopathic, herbal and combination systems respectively. (Table 1) Interestingly, patients who were taking ACM without insulin, they had less incidences of DR; the incidences were homoeopathic (50%), herbal (39%) and combination system (47.62%). (Table 2). Research findings of current study are highlighting this fact that ACM is superior relative to allopathic treatment for the risk reduction of DR in patients of T2D; however, home remedies and junk food was not considered in this evaluation because that was not the end-point of current study. Despite all these findings; compare to all other systems of medicine particularly herbal and homeopathic, anti-diabetic efficacy of allopathic drugs are superior (Andreadis *et al.*, 2018; Cape-

horn *et al.*, 2020; Philis Tsimikas *et al.*, 2019).

In patients of T2D to control blood glucose levels, exercises and physical activities are essential non-pharmacological interventions. American Diabetes Association (ADA) also mentioned in their guidelines; the better glycemic control in patients of diabetes can be accomplish by exercise and physical activities.(Colberg *et al.*, 2016) The focus of current study was also to compare risk reduction of DR in two groups of patients; these groups were divided based upon physical activities, it means exercise groups and no exercise group while on different systems of medicine.(Table 3) In group of patients engaged in physical activity; incidences of DR in different arms of study were allopathic (62.50%), homeopathic (100%), herbal (11.11%) and combination treatment (50%). Based upon these incidences RRR of DR and NNT were 37.50%, H"3.0, -462%, H"-2.0, -25% and H"-8.0 by allopathic treatment compared to treatments of homeopathic, herbal and combination respectively. Current findings are revealing that regarding risk reduction of DR homeopathic system of medicine is inferior compare to allopathic system. However; findings were different in other arms of study and herbal and combination medicines were better than allopathic medicine for reduction of DR risk. In contrast; the arms of the study where group of patients were not doing physical activity; allopathic treatment of medicine had lowest risk reduction of DR relative to all other types of treatments (homeopathic, herbal and combination). RRR of DR and NNT were -67.08%, H"-3.0, -57.32%, H"-4.0, -31.45% and H"-6.0 by allopathic treatment compared to ACM (homoeopathic, herbal and combination). Nutritional management with the support of diet having low calories; regulation of blood glucose is better in T2D patients (Russell *et al.*, 2016). Therefore, T2D patients were also divided in current study in two groups; one group was taking diet having low calorie and another group was taking regular diet; both groups were further divided into the groups taking either allopathic treatment or any ACM. The end point was risk reduction of DR. (Table 4) The incidences of DR in group having diet with low calorie; allopathic (73.33%), homoeopathic (50%), herbal (50%) and combination (64%). Similarly, incidences of DR in groups were taking regular diet; allopathic (74%), homoeopathic (50%), herbal (27.77%) and combination (50%). These results about incidences of DR are clearly indicating that in both groups (diet with low calorie and regular diet) risk of DR is greater in allopathic treatment groups relative to all other types of ACM (Table 4). Regarding RRR of DR and NNT (in group taking diet with low calorie), RRR were (homeopathic: -46.66%, herbal: -46.66%, Combination: -14.57%) compared to allopathic treatment system; while NNT (homeopathic: H"-4.0, herbal: H"-4.0, Combination: H"-11.0) compared with allopathic treatment. Similarly; in group taking regular diet; RRR were (homeopathic: -48, herbal: -166%, Combination: -48%) compared to allopathic treatment and NNT were (homeopathic: H"-4.0, herbal: H"-2.0, Combination: H"-4.0) compared to allopathic system of treatment.

4. CONCLUSION

To conclude; risk of diabetic retinopathy was noted greater in the patients of type-II diabetes when treated with allopathic treatment compared to all types of alternative and complementary medicine. Among systems of medicines; combination system with the use of in-

sulin and homeopathic system with physical activity have shown higher incidences of DR compared to allopathic system.

Conflict of Interests

None.

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