Effect of low caloric diet in type-2 diabetes patients with different systems of medicines

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Abstract

Excessive nutritional state favors insulin resistance and inflammation; such inflammation leads to loss of islet integrity and causes metabolic disorders. Hence the current study was conducted with the objective to determine the effect of a low-calorie-diet on indices of plasma-glucose treated by medications of diverse systems. The study design was Cross-sectional; began in July-2019 and ended in June-2020. Two-hundred patients of Type–2 Diabetes were enrolled. Patients received any one treatment; Allopathic, Herbal or Combination. Primary end-points; Changes in Fasting-Blood-Glucose (FBG), Random-Blood-Glucose (RBG), %HbA1c with or without a low-calorie-diet. Study ethical approval was obtained with reference number; IBC KU 23. The SPSS-22 version analyzed the collected data. Interpretation of results revealed that Mean-FBG with low-caloric-diet; Allopathic: 168±73mg/dL, Herbal: 135±18mg/dL, combination 131±37mg/dL (p=0.004). Mean-FBG with regular diet; Allopathic: 183±89mg/dL, Herbal : 121±16 mg/dL, 121 Combination: 138±56mg/dL (p=0.006). Mean RBG with low-caloric-diet; Allopathic: 217±83mg/dL, Herbal: 201±49mg/dL, Combination: 228±102mg/dL (p=0.181). Mean-RBG with regular-diet; Allopathic: 244±95mg/dL, Herbal: 187±43mg/dL, Combination: 207±62mg/dL (p=0.022). Mean-HbA1c with low-caloric-diet; Allopathic: 8.50±2.0%, Herbal: 6.60±0.40%, Combination: 7.0±1.60% (p=0.0001). Mean-HbA1c with regular-diet; Allopathic: 8.80±2.10%, Herbal: 6.40±0.30%, Combination: 7.20±1.30% (p=0.0001). With low-caloric-diet multiple comparison, mean differences in FBG were significant; Allopathic-Herbal FBG (p=0.023), Allopathic-Combination FBG (p=0.008). With regular--diet multiple comparison, mean differences in FBG and RBG were significant; Allopathic-Herbal FBG (p=0.002) and RBG (p=0.01), Allopathic - Combination FBG (p=0.010) and RBG (p=0.049). Hence low calorie diet has better control on indices of plasma glucose par-ticularly in allopathic system. In mul-

tiple comparisons, herbal and combination treatments sigmi- ficantly achieved the target goals of FBG, RBG and HbA1c.

Keywords

Plasma-glucose; low-calorie, medications, blood glucose-fasting; blood glucose-random; HbA1c; medicines

1. INTRODUCTION

Impairment in production or body response to insulin can lead to Diabetes mellitus (DM).(Eizirik *et al.*, 2020) In different types of DM, the most dominating form is Type-2 DM.(Maffi *et al.*, 2017) Among all type of diabetes; type-2 DM prevails more than 90% (Roden *et al.*, 2019). Type-2 DM caused by two primary factors; defective insulin secretion by pancreatic beta cells and inability of insulin sensitive tissues to respond appropriately to insulin. (Roden *et al*., 2019). An evidence recently reported that dysfunction of beta islet of langerhan of pancreas in Type-2 DM is perhaps due to interaction between environment and different molecular pathways (Halban *et al*., 2014). Excessive nutritional state favors insulin resistance and inflammation; such inflammation leads to loss of islet integrity (Christensen *et al.*, 2019). Literature review shows that; significantly better glycemic control and even remission of T2DM were noted following a very low-calorie diet (VLCD) in people with type-2 diabetes (T2D) (Juray *et al.*, 2021). Very low-calorie diets (VLCD) are hypocaloric dietary regimes of 400–800 Cal./ day that results in 20–30 percent weight loss in 12–16 weeks (Juray *et al*., 2021). A study has shown that in the patients of T2DM blood glucose levels return to normal with the use of a very low-calorie diet (VLCD) (Steven *et al*., 2016). A well-established non-surgical method for weight loss of eH10% within three months is low-calorie diet (VLCDs) (Steven *et al*., 2016). In obese individuals; low caloric diet reversed the underlying pathology of T2D (Umphon sathien *et al., al.*, 2019). Risk factors are high that deteriorate vital organ functions in diabetes, while VLCDs are associated with rapidly reducing these risk factors (Baker *et al.*, 2009). The intermittent use of VLCD can enhance weight-loss and better blood glucose control; however, its clinical use is not justified yet because effects were relatively modest. Additional investigations are required to develop a best approach for lasting weight management in persons with diabetes (Wing *et al.*, 1994). Short-term treatment with a very low-caloric diet results in safe and effective weight loss in both obese persons with diabetes and without diabetes; but also normalize elevated glucose and lipid levels (Henry *et al.*, 1986).

Persons with diabetes lose weight while on very low caloric diet; however, regain of weight is observed after sometimes. The five years, long term use of conventional diet with anti-diabetes medications also resulted in significant weight loss (Paisey *et al.*, 2002). In another study, patients of T2DM have taken a very low-caloric diet for more than eight years; the findings of study suggested that, a low-caloric diet has a 50% chance of keeping fasting glucose levels to normal range without anti-diabetes medicines (Paisey *et al*., 2002). In another study; the marked improvement in metabolic profile was observed after 7th day of VLCD in severely obese patients; primarily due to the amelioration of beta cell function; whereas no contribution of insulin sensitivity was shown (Malandrucco *et al.*, 2012). In a review article; significant weight loss, reduction of cardiovascular risks, lowering of plasma glucose indices, high tolerability and overall positive outcomes were reported while T2

DM patients were on VLCD (Sellahewa *et al.*, 2017). The studies included in this review were heterogeneous and had long-term outcomes; data for post VLCD is still required (Sellahewa *et al.*, 2017). Hence, current evidences suggest; low-caloric diet contributes in better glycemic control of T2D patients; however, no sound evidence exist in Pakistani population. Therefore, purpose of current research was to determine the effect of low-caloric diet in the T2DM patients using different systems of treatment on plasma glucose and glycated hemoglobin (HbA1c).

2. MATERIALS AND METHODS

Study Design and Settings: A cross-sectional, prospective, observational. Conducted in outpatient care centers of Karachi. The study began on July 2019 and ended on June 2020. The study enrolled two hundred (N=200) patients of Type–2 Diabetes (Fig-1). Average duration of a type 2 DM was 13 years. Based upon choice of patients; patients treated by anyone of the system of medicine; Allopathic, Herbal and Combination (Allopathic + Herbs) system (Fig- 1).

Study End Points: The primary end-points of the study were changes in the indices of blood glucose levels; Fasting-Blood-Glucose (FBG), Random-Blood-Glucose (RBG) in mg/dL with or without low-caloric diet. The secondary end-point was a change in Glycated Hemoglobin (HbA1c).
Low-caloric diet; 800 Calories/day.

Ethical Approval: Study ethical approval was sought from the Interactive Rsch. & Development, IRB-IRD # IRD_IRB_2017_03_018. Registration number IRB 00005148). Advanced Studies & Research Board of University of Karachi also approved the current study (Reference No. ASRB/03274/Pharm).
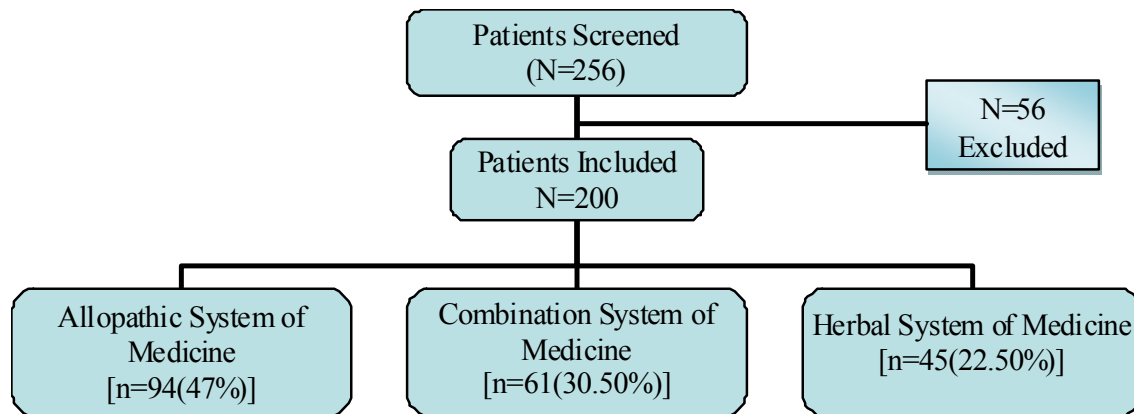
Fig- 1: Screening and inclusion of patients at different arms of treatment in study

Gender wise distribution

51.7% (n=103) male and 48.3% (n=97) female. Mean age (male: 54 years; female: 52 years). Mean BMI (male: 26 kg/m^2; female: 31 kg/m^2).

Sample Size and Technique

The study registered two-hundred (N=200) patients of T2D, these patients were divided based upon their treatment choices of either allo-

pathic, herbal, and/or combination. According to precision analysis technique (Aparasu, 2020); at least 196 patients of T2D should be registered in the study to keep study power.

Inclusion Criteria: Patients with the confirmed diagnosis of T2DM.

Exclusion Criteria: Type 1 diabetes; Gestational diabetes; LADA (Latent Autoimmune Diabetes in Adults).

Data Collection Procedure:

Pre-designed and organized question-naires was used to obtain data. Before initiating the survey, each patient signed a written informed consent; objectives of the research were discussed with each patient. The data of the patients was ensured for confidentiality according to the Declaration of Helsinki (Shrestha *et al.*, 2019).

Assessment of Data:

Primary questionnaire was filled by the Pharmacists, Family Physicians and Hakims (A Herbal Practitioners). The collected data was tabulated and classified as continuous (Interval/Ratio). Based upon classification of data; it has been evaluated by the descriptive statistics [mean; standard deviation (SD); standard errors (SE)] & inferential statistics (One-Way ANOVA). The One-Way ANOVA was used to determine the significance between mean values of variables. These variables are FBG, RBG and HbA1C in between different therapeutic systems. For calculation of data; a software was used named Statistical Package for Social Sciences (SPSS version 22).

3. RESULTS AND DISCUSSION

Means and the standard deviations (S.D) of blood glucose on fasting (FBG), blood glucose ch-ecked randomly (RBG) and glycated hemoglobin (HbA1c) levels were compared in the patients who use diet of low calorie and who use regular diet (without low calorie) (Table 1). Significant differences in the means of FBG, RBG of the patients who used the low caloric diet in the different treatment types are also determined by keeping the p-value of significance at <0.05 (Table 2). Similarly, significant differences in the means of FBG, RBG of the patients who used regular diet (without low calorie) in the different types of treatments were also determined by keeping the p-value of significance at <0.05 (Table 3).

Optimistic effect on glycemic control by low caloric diet was studied by Thomas M S Wolever. (Wolever *et al.*, 1992) Similar effects were also noted in the current study; mean value of FBG (Fasting Blood Glucose) were 168±73mg/dL (diet with low calorie) and 183±89mg/dL (regular diet) in patients taken allopathic medications; the difference of FBG with and without low caloric diet was clinically significant i.e. 15mg/dL; hence, patients with low caloric diet have better control of FBG. In RBG; the mean of glucose levels were 217±83mg/dL, 244±95mg/dL; and HbA1c 8.5±2.0%, 8.8±2.1% with and without low caloric diet, respectively. These differences of RBG (Random Blood Glucose) and HbA1c (Glycated hemoglobin) are also significant from clinical perspective. Similar results were reported by Judy et al. in type 2 diabetes; use of low caloric diet on six months significantly reduced the HbA1c levels; however; their conclusions are made on the base of secondary data (Shiau *et al.*, 2018). The another literature mentioned that one third of patients did not use anti-diabetes medications for up to 12 months while on low caloric diet (Taylor *et al.*, 2021; Umphonsathien *et al.*, 2019).

Table 1. Comparison of FBG[a], RBG[b] and HbA1c[c] levels with diet of low calorie and diet without low calorie in different ttreatment systems

Patient's Diet Status	Blood (Plasma) Glucose Levels	Descriptive Statistics	Treatment Systems			Significance (p<0.05)
			Allopathic	Herbal	Combination	
Diet with Low calorie	FBG[a] (mg/dL)	Mean	168	135	131	0.004
		S.D[d]	±73	±18	±37	
	RBG[b] (mg/dL)	Mean	217	201	228	0.181
		S.D[d]	±83	±49	±102	
	HbA1c[c] (%)	Mean	8.5	6.6	7	0.0001
		S.D[d]	±2	±0.4	±1.6	
Diet without Low calorie	FBG[a] (mg/dL)	Mean	183	121	138	0.006
		S.D[d]	±89	±16	±56	
	RBG[b] (mg/dL)	Mean	244	187	207	0.022
		S.D[d]	±95	±43	±62	
	HbA1c[c] (%)	Mean	8.8	6.4	7.2	0.0001
		S.D[d]	±2.1	±0.3	±1.3	

[a] FBG=Fasting Blood Glucose, [b] RBG=Random Blood Glucose, [c] HbA1c=Glycated Hemoglobin, [d] S.D=Standard Deviation

Table 2. Multiple Comparison of FBG[a], RBG[b] (Diet with low calorie in different treatments)

Indices	Treatments (A)	Treatments (B)	Difference of means	S.E[c]	Significance (p<0.05)
FBG[a]	Allopathic	Herbal	33.14	±14.35	0.023
		Combination	37.81	±13.92	0.008
	Herbal	Combination	4.67	±16.39	0.776

RBG[b]	Allopathic	Herbal	15.17	±21.09	0.474
		Combination	-11.27	±20.45	0.583
	Herbal	Combination	-26.44	±24.08	0.275

[a] FBG=Fasting Blood Glucose, [b] RBG=Random Blood Glucose, [c] S.E=Standard Error

Table 3. Multiple Comparison of FBG[a], RBG[b] (Regular diet without low calorie in different treatments)

Indices	Treatments (A)	Treatment (B)	Difference of means	S.E[c]	Significance (p<0.05)
FBG[a]	Allopathic	Herbal	62.01	±19.81	0.002
		Combination	45.19	±17.23	0.010
	Herbal	Combination	-16.81	±21.87	0.444
RBG[b]	Allopathic	Herbal	56.78	±21.46	0.010
		Combination	37.14	±18.64	0.049
	Herbal	Combination	-19.63	±23.75	0.411

[a] FBG=Fasting Blood Glucose, [b] RBG=Random Blood Glucose, [c] S.E=Standard Error

Interestingly, the patients on the low caloric diet poorly controlled fasting blood glucose (135±18mg/dL) as compared to those who did not take low caloric diet (121±16mg/dL). Unfortunately, in herbal system of medicine; same observations were noted for random blood glucose levels and HbA1c. However, in another study; when effect of purslane seeds on FBG were evaluated; reduction in FBG was significant (p=0.017) compared with control group; the drawback of this study is that; most of the patients enrolled in this study were having metabolic syndrome (Gheflati *et al.*, 2019). Uswa Ahmed *et al.* conducted another study to detect the effects of aqueous extract of *Stevia rebaudiana* on FBG, RBG and HbA1c in albino rats, extract of the herb significantly (p<0.05) reduced the FBG, RBG and HbA1c; however; these results cannot be extrapolated on human because it was an animal study (Ahmad *et al.*, 2018). The present research compared the differences of FBG, RBG and HbA1c treated by diverse systems of medicine. It is noted that the mean differences of FBG were significant in all systems of medicine while the groups were taking diet with low calorie (p=0.004) and regular diet groups (p=0.006). On the other hand; mean differences of RBG were non-significant of all systems of medicine in low caloric diet groups (p=0.181) and significant in regular diet groups (p=0.022). Another important index of the blood glucose level is HbA1c; significant differences were noted for HbA1c in

the low (p=0.0001) and non-low caloric diet groups (p=0.0001). Although, the published data for such comparison is scarce; however, Bibi Marjan *et al*. reported that a herbal drug saffron (*Crocus sativus*) has shown efficacy in reducing metabolic syndrome or pre-diabetes condition, although primary end-point of her study was risk reduction of cardiovascular diseases (Razavi *et al.*, 2017).

Differences of mean FBG and RBG were also compared in between different systems of medicine, while the patients were on low caloric diet (Table 2). It is revealed that the mean difference of FBG of allopathic system of medicine is statistically significant with herbal system (33.14±14.35mg/dL, p=0.023); and combination (37.81±13.92mg/dL, p=0.008) system. It seems that the allopathic system of medicine is significantly better for mean control of FBG while patient is on low caloric diet compared with other systems of medicine. For mean differences of RBG, all systems of medicines have shown non-significant differences while patients were on low caloric diet. From current experimental evidence; it can be assumed that although allopathic system is significantly better compared to all other systems of treatment for controlling FBG; but control of RBG is similar in almost all systems of medicine. A review paper on alternative medicine *Cephalandra indica* reported as anti hyperglycemic agent and found that *Cephalandra indica* in highly diluted form provides anti-hyperglycemic effect (Wakte *et al.*, 2019).

Similarly, differences of mean FBG and RBG were also compared in between different systems of medicine; while patients were not on low caloric diet (Table 3). In this comparison; it is noted that mean differences were significant of FBG in between allopathic and herbal (62.01±19.81mg/dL, p=0.002); allopathic and com-

bination (45.19±17.23mg/dL, p=0.01) systems of medicines. It seems that allopathic system of medicine is significantly better for mean control of FBG compared to all other systems of medicines. Without low caloric diet; significant differences of RBG were noted in between allopathic and herbal systems of medicine (p=0.01); allopathic and combination systems of medicines (p=0.049). Current experimental evidence is revealing again that allopathic system of medicine is significantly better for controlling FBG and RBG compared with all other systems of medicine regardless of diet status, however; it is assumed that improvement is possible in healthcare by integration of different treatment systems; however, evidence based literature is still required on alternative medicines for correct clinical decision making (Sen *et al.*, 2015, 2017). It can also be assumed that non significant differences among mean RBG of different systems of medicine direct the healthcare providers to prefer to prescribe alternative medicine in population belongs to low socioeconomic class (Adler *et al.*, 2016). because evidences are available for the use of different herbs; e.g. iron wood tree (*Memecylon umbellatum*), root bark of *Lycium barbarum,* bitter melon (*Momordica charantia*), extracts of *Astragalus membranaceus*, *Lonicera japonica* and *Coptis chinensis*.(Pang *et al.*, 2019).

Strengths and limitations of study

Current study is the first evidence in Pakistan which provides comparison of allopathic treatment with the systems of herbal and combination treatments in type 2 diabetes patients. Study compared indices of blood glucose levels; FBG, RBG and HbA1c. Utility of study may be high for General Physicians and Pharmacists in Pakistan; they practice all types of medicines in

their clinics or pharmacy. Despite these strengths of study; some areas still need further research; e.g. study compared the effects on FBG, RBG and HbA1c in different treatment systems but not compared medications of each system. Further research is also required to determine the effects of drugs of each system at molecular levels and homeopathic system of medicine with sufficient sample size.

4. CONCLUSION

Hence low-calorie-diet has better control on indices of plasma-glucose particularly in allopathic system of medicine. In multiple comparisons, Herbal and combination treatments significantly achieved the target goals of FBG, RBG and HbA1c.

List of Abbreviations

DM = Diabetes Mellitus; FBG = Fasting Blood Glucose; RBG = Random Blood Glucose; HbA1c = Glycated Hemoglobin; IBC = Institutional Bioethics Committee; IRD = Interactive Research & Development; IRB = Investigational Review Board; SPSS = Statistical Package of Social Sciences; VLCD = Very Low Calorie Diet; T2D = Type 2 Diabetes; T2DM = Type 2 Diabetes Mellitus; ASRB = Advanced Studies and Research Board; BMI = Body Mass Index; LADA = Latent Autoimmune Diabetes in Adults; ANOVA = Analysis of Variance.

Conflict of Interests
None.

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