CHAPTER IV

AIMS & OBJECTIVES

4.1 Aim

- To study the effect of yoga on glucose excursions and glycemic variability in patients with uncontrolled type 2 diabetes (T2DM).

4.2 Objective of the study

- To study the effect of yoga practice on mean glucose levels in patients of type 2 diabetes.
- To study the effect of yoga on intraday variability in patients of type 2 diabetes through MAGE (Mean Amplitude of Glucose Excursions).
- To study the effect of yoga on interday variability in patients of type 2 diabetes through MODD (Mean of Daily Differences).
- To study the effect of yoga on risk of mortality in patients of type 2 diabetes measured through LI (Lability Index).
- To understand the effect of yoga in establishing homeostasis in glucose levels in type 2 diabetes.

4.3 Research Question

Does yoga have any influence on glycemic variability in patients of type 2 diabetes?

4.4 Hypothesis

Yoga helps in reduction of glycemic variability in Type 2 DM patients

4.5 Null Hypothesis

Yoga therapy does not have any effect on glycemic variability in patients with type 2 diabetes.

CHAPTER V

METHODOLOGY

5.1 Methodology

Studies on exercise, measuring glycemic variability (GV) often have an intervention period of 3-7 days for measuring the GV (Mikus et al., 2012; Figueira et al., 2013). As the current study being the first yoga study on GV, we were unsure of the duration of yoga required to have an impact on the GV. To know whether a seven day yoga intervention would be sufficient to bring about any change in the GV, we did a small pilot study with ten T2DM participants who were on oral glucose lowering agents with a minimum of one insulin secretagogue. The inclusion criterion of one insulin secretagogue was set because of the known adverse effect of insulin secretagogues in inducing hypoglycaemia (Gehlaut et al., 2015). Measurement was done using continuous glucose monitoring. Results of the pilot study showed that GV could be reduced through one week of yoga practise.

Three steps were taken to ensure that the changes were due to the intervention and not merely occurring as a chance or due to the influence of an external object-the glucose monitoring sensor. First, a control group was included in the main study. Second, participants were informed at baseline that the sensors would continuously monitor their glucose levels every 15 minutes and the patch would be removed after the end of the yoga sessions. Participants were requested to attend the one week yoga sessions on day 8 (intervention group) or day 15 (control group) from the day of sensor application. Exact information on how many days the sensor would be measuring glucose levels (i.e. 14 day)was not providedto participants of both the groups to simulate‘partial blinding’, wherein participants were not aware on whether they belong to intervention or control group. Thus, we also ensured that participants of both the groups had their one week yoga intervention at the end of 21 days. Third, no

intermediate data either as a graphical formor on the freestyle scanner was shown to participants of both groups till the end of the study period, to avoid introduction of any possible confounding factors in the middle of the study.

5.1.1 Ethical approval

Ethical approval was obtained from the Institutional Ethical committee (IEC) of S-VYASA University and at Narayana Health City, Bommasandra for the initial pilot study. Ethical approval was also obtained from the Ethical Committee of Madras Diabetes Research Foundation (MDRF), Chennai for the main study (Appendix 6). The trial was registered under clinical trial registry of India (CTRI) (CTRI no. CTRI/2017/11/010455).

5.1.2 Sample size

A reduction in the GV was observed in the pilot study. Sample size was calculated using the Mean of Daily Differences (MODD) value obtained from the pilot study, which had a correlation co-efficient of 0.85. Sample size of 23 per group was calculated with effect size 0.797, powered at 0.90 and statistical significance of $p < 0.05$. Accounting for possible dropouts, 30 participants were recruited in each group.

5.1.3 Study population

Participants were recruited from a private diabetes speciality centre in Chennai, India. T2DM patients of both genders, between 40-70 years of age, HbA1C between 7% - 8.5% and medication score above 1.5 were recruited for the study. In addition, taking at least one oral insulin secretagogue was a pre-requisite for recruitment.

Patients with HbA1C above 8.5% and/ or on insulin were excluded from the study. Patients with severe complications including proliferative diabetic retinopathy, diabetic nephropathy with CKD stage 4 and 5, active diabetic foot ulcer or any cardiovascular event requiring hospitalization in the last 6 months were not considered. Also, participants who were performing yoga or regular walking for 1 hour or more every day in the past 3 months were excluded from the study.

5.1.4 Randomisation

Participants were randomised either to the intervention group or the control group using a computer generated block randomisation, with six participants per block. Allocation concealment was carried out using sequentially numbered opaque sealed envelope (SNOSE), maintained by a person who was not directly involved in the project who handed over the sealed opaque envelopes to the participants.

5.1.5 Continuous glucose monitoring tool

Continuous glucose monitoring (CGM) was carried out using Flash glucose monitoring system, Freestyle Libre Pro (Abbott Diabetes Care Ltd., Oxon, UK), applied

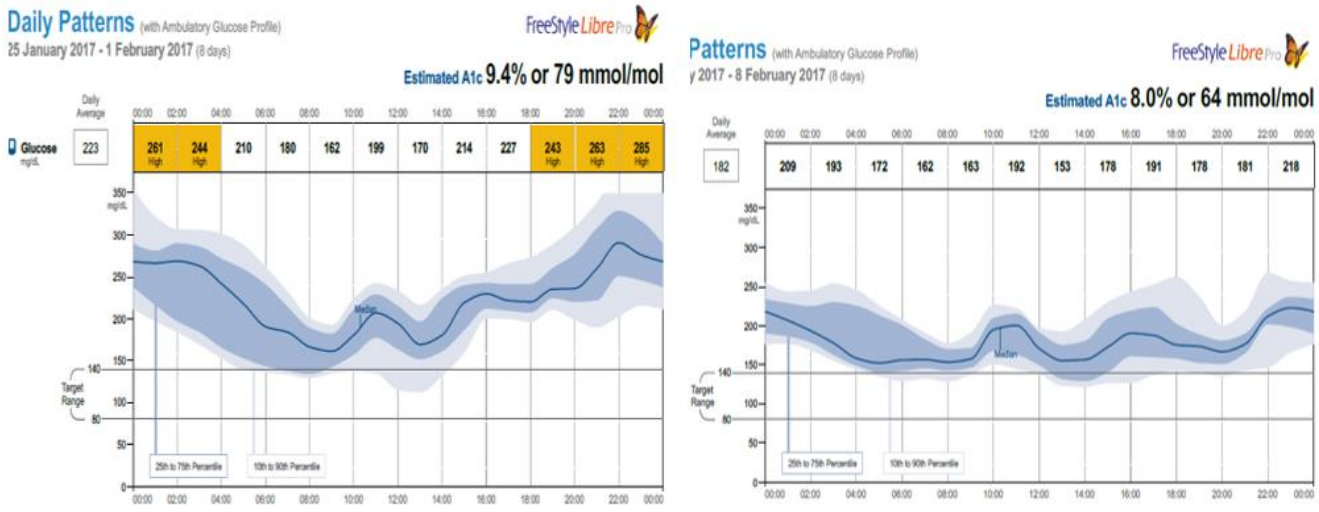

Fig 7: Graph capturing intraday & inter-day glycemic variability via CGM (Baseline vs post intervention)

on to the non-dominant backside upper arm of the participants after getting informed consent. Freestyle Libre Pro sensors are disposable continuous glucose monitoring sensors which measures blood glucose levels every fifteen minutes, for 14 days from the day of application. The first seven days were used to establish a baseline in the mean glucose levels and glycemic variability of the individual. In the following seven days, participants would be practising one hour of yoga or walking. Participants continued with their regular diet and lifestyle throughout the 14 day period and were requested not to modify.

5.1.6 Statistical analysis

Data analysis was done using statistical package for social sciences (SPSS)- version 24.0 and intention-to-treat (ITT) analysis was performed, using last observation carried forward (LOCF) method. Earlier, the glycemic variability was calculated using EasyGV software (version 9.0), for calculating the mean daily glucose, standard deviation (SD), mean amplitude of glucose excursions (MAGE), Lability index (LI), Mean of daily differences (MODD), using the data acquired from the CGM sensors. Normality of distribution was found using Shapiro Wilks test. Student's t-test (parametric) or Mann-Whitney U test/ Wilcoxon signed ranks (non-parametric) test is used wherever appropriate based on the normality of distribution.