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Safety and Efficacy of Intermittent Fasting in Type II Diabetes Mellitus Patients on Insulin Therapy

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Abstract: ***Objectives: To determine the safety and feasibility of 3 non-consecutive days intermittent fasting (IF) per week in type II diabetes patients already on insulin therapy. Methodology: Thirty patients each were randomized to an intermittent fasting group and control group. Dietary counseling along with continuous glucose monitoring was provided for all participants. Primary objective was to determine the change in HbA1c from baseline to 3months and secondary objective was to determine body weight reduction and reduction in daily insulin dose requirement. Results; The intermittent fasting group showed a significant reduction in HbA1c along with daily insulin dose requirement and bodyweight compared with the control group over 3months Study period (P < 0.01). No episodes of severe hypoglycemia were encountered during the study. Conclusions: Intermittent non-consecutive days fasting can be considered as a safe and reliable method to attain adequate glycemic control along with significant reduction in total daily insulin dose requirement and body weight in type II diabetes mellitus patients on insulin therapy.***

Keywords: Diabetes mellitus, insulin, intermittent fasting

1. Introduction

Considering the increasing number of patients with type II diabetes rising worldwide Dietary modifications may be considered as a safe and reliable alternative to attain an essential therapeutic control of blood glucose levels, bodyweight, and cardiovascular risk management [1, 2]. Intermittent fasting (IF) has now emerged as an alternative to the previous daily caloric reduction [3]. The approach to intermittent fasting includes limiting the food consumption to certain hours of the day to alternate-day fasting [4, 5]. People with type II diabetes mellitus on insulin therapy often struggles with weight gain [6], resulting in a vicious cycle of increasing the required dose of daily insulin to overcome the insulin resistance, which further contribute to weight gain, and ultimately resulting in cardiovascular complications [7]. A recent meta-analysis has shown that Intermittent fasting can be used as an appropriate diet strategy in people with type II diabetes; however, the risk of hypoglycaemia during state of fasting in individuals on insulin therapy remains a crucial barrier to adhere to diets demanding caloric restriction and further randomized controlled trials are required to verify the safety and feasibility in larger population [8].

2. Methodology

An open labelled, randomized controlled trial, to determine the safety and efficacy of intermittent fasting in patients with type II diabetes mellitus on insulin therapy, was conducted over a period of six months in department of general medicine VSSIMSAR BURLA after getting approval from by the institutional ethics committee (LNO:042-IST 21/22). This study included a total of 60 type II diabetes mellitus patients satisfying the inclusion criteria, aged between 35 and 65 years and having HbA1c>7, on insulin therapy and not on any oral sulphonyl urea drugs as volunteers. Thirty patients each were allocated to intermittent fasting (IF) and control groups respectively. The participants in the IF group practiced 3 days intermittent fasting every week, reducing their calories on these days by 70% (i.e., consuming only 30% of the normal regular caloric intake). Diet Ingestion was only allowed at breakfast and or during lunch time to maintain a minimum of 18-hour fasting. The participants were asked to strictly maintain a food intake diary to monitor the adherence to the study. On the remaining days of the week, the participants of the intermittent fasting group didn't have any caloric restrictions and were free to take normal diet. Also, there were no restrictions on the consumption of water, unsweetened tea or coffee without milk. On normal days, the participants were allowed to consume any type of regular dietary food or drinks without any caloric restriction. Both groups had to maintain a comparable number of interactions with the study staff. All the study group participants were switched to the same basal insulin (insulin glargine) prior to their randomization. The basal insulin was administered to subjects in the morning. During the fasting days, intermittent fasting group participants were asked to reduce the basal insulin by 20% and prandial insulin dose was only administered for glucose correctional reasons, in order to reduce the risk of hypoglycaemia during the intermittent fasting day. All regular oral non-sulfonylurea medication was continued even on fasting days [9].

All participants were monitored using continuous glucose monitoring system device for entire 3 months of the study and the data was collected. The data obtained was used to analyse the primary objective outcomes i.e., the difference in the change in HbA1c from baseline to 3months and secondary objectives of reduction in bodyweight and total dose of insulin required to maintain euglycemia. The continuous data of primary and secondary outcomes were analysed using unpaired t tests.

3. Results

A total of sixty subjects were screened in this study, of which (8 women and 22 men) were randomized to the intermittent fasting group (n=30) and30 to the control group. The mean age was 55.5 ± 4 years, diabetes duration was 11.2 ± 5 years, BMI was 29.2 ± 1.2kg/m2, HbA1c was 7.85 ±1.3%, and the mean total daily insulin dose was 56 ± 16 IU. The details of the baseline characteristics of study participants are given in Table 1.

Table 1: Baseline characteristics of participants

Variables	Intermittent fasting (n=30)	Control group (n=30)
Age	55±4 yrs.	56±4 yrs.
Duration of Diabetes	11.0±5.0 yrs.	11.4±5.0 yrs.
HbA1c	7.8±1.1 %	7.9±1.4 %
BMI	29.3±1.3 kg/m^2	29.1±1.1kg/m^2
Total Daily Insulin dose	54 ± 18 IU	58 ± 13 IU
Total Cholesterol	162 ± 51 mg/dl	164 ± 41 mg/dl
Resting Metabolic Rate (RMR)	2,250 ± 358 kcal	2,440 ± 376 kcal
Comorbidities:		
Dyslipidaemia	20 (66.7%)	21 (70%)
Hypertension	19 (63.3%)	17 (56.7%)
OHA's. Metformin	24 (80%)	26 (86.7%)

After 3 months, HbA1c in the IF group decreased by an average of 2.3± 0.4 % compared with an increase in the control group by 0.1 ±.2% (P = 0.011). The difference in the change in HbA1c between the control and IF group remained statistically significant (P = 0.007) after adjusting for age, sex, diabetes duration, and baseline HbA1c. The mean time above range over the entire 3 months was significantly lower in the IF group than in the control groups. The mean time in range was significantly higher in the IF group (76.7 ± 19.2%) compared with the control group (55.0 ± 16.0%, P = 0.029), while the mean time below range over 3 months were similar in the intermittent fasting and the control groups

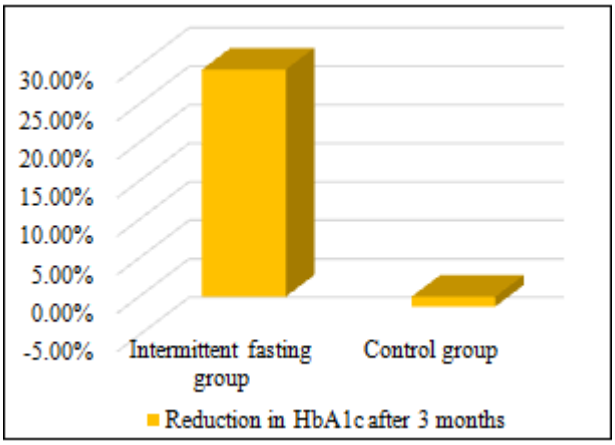

Figure 1: Average Reduction in HbA1c after 3months Study period

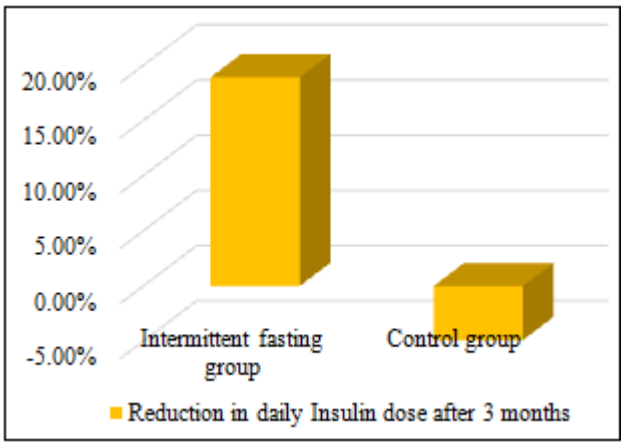

Figure 2: Average Reduction in daily Insulin dose requirement after 3 months study period.

After 3 months, 23 participants (76.7%) in the intermittent fasting group achieved both the primary and secondary objectives compared with none of the participants in the control group (at least 6% weight loss, at least 10% reduction in HbA1c, and at least 10% insulin dose reduction). (P < 0.04) After 3 months of intervention, the Intermittent fasting group showed a significant reduction in average body weight of 12.25% when compared to 3.5% among the participants in control group.

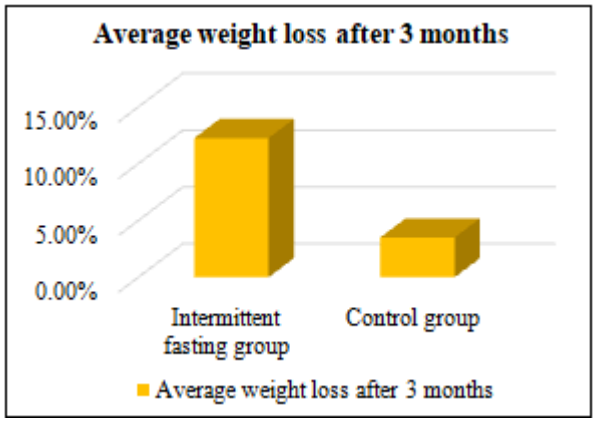

Figure 3: Average weight loss after 3 months study period

The resting metabolic rate (RMR) was not different between IF and control group, both at baseline (IF: 2,250 ± 358 kcal, control: 2,440 ± 376 kcal) and after 3 months (IF: 2,242 ± 334 kcal, control: 2,428 ± 388 kcal). No difference was observed in the change of the RMR from baseline to 3months between the two groups (P = 0.712). Likewise, no difference was observed in the change of the physical activity levels between the groups (P =0.621). The mean total daily dose of insulin at baseline was 54 ± 18 IU in the IF group and 58 ± 13 IU in the control group. At 3 months, the IF group had an insulin dose of 44 ± 17 IU while the control group had an insulin dose of 61 ± 35 IU, resulting in a total daily insulin dose reduction in the IF group over 3months by 10 ± 0.1 IU as opposed to the control group with an increase by 3 ± 0.12 IU (P = 0.008). Of the 30 participants in the IF group, 28 (93.3%) achieved >90% adherence to the given fasting protocol. During the study period, no adverse events leading to hospitalization were reported.

4. Discussion

This study demonstrates that 3 days of non-consecutive intermittent fasting per week over a period of 3 months significantly improved the HbA1c levels, reduced body weight, and resulted in a reduction of total daily insulin dose requirement in type II diabetes patients. The present data are in line with previous studies proving that intermittent fasting was effective for reduction of HbA1c inpatients with type II diabetes[11]. Li et al. [12]. Hence, our study has shown to provide beneficial effects in controlling body weight and achieving glycaemic control among patients with type II diabetes treated with insulin. Recent studies suggest that prolonged fasting may provide additional beneficial metabolic effects, independent of weight loss, by switching the metabolism to fatty acid mobilization and enhancing ketone body production [14]. For some individuals, intermittent fasting appears as an easy to apply dietary intervention without the need for continuous caloric reductions [15,16]. As mentioned in this study, the risk of hypoglycaemic episodes during intermittent fasting can be minimised by reducing the insulin dose on fasting days.

5. Conclusion

This study demonstrates that 3 days of non-consecutive intermittent fasting over a period of 3months in patients of type II diabetes mellitus on insulin therapy is a safe and reliable method which helps in significantly reducing HbA1clevels along with significant reduction in bodyweight and total daily insulin dose requirement compared to a control group, while RMR and the physical activity levels remaining unchanged.

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