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ORIGINAL RESEARCH

Impact of Partial Meal Replacement on Glycemic Levels and Body Weight in Indian Patients with Type 2 Diabetes (PRIDE): A Randomized Controlled Study

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ABSTRACT

Introduction: Partial meal replacement (PMR) offers potential glycemic and weight control benefits in type 2 diabetes mellitus (T2DM) patients. We evaluated the clinical impact of PMR (diabetes-specific nutritional supplement [DSNS]) in overweight/obese Indian patients with T2DM.

Methods: PRIDE, a 12-week, phase IV, open-label, multicenter study randomized (1:1) newly diagnosed T2DM patients (≤ 1 year) to either DSNS plus standard of care (SOC; diabetes treatment with dietary counseling) group (PMR) or SOC alone group (SOC). The primary endpoint was mean change in glycated hemoglobin (HbA1c) from baseline to week 12. Secondary endpoints were changes in glucose profiles, body weight, waist circumference, lipid profile, and factors impacting quality-of-life (QoL) at week 6 and 12 from baseline. Safety was assessed throughout the study.

Results: Of the 176 patients enrolled, 171 (n = 85 in PMR group; n = 86 in SOC group) were included in the modified intent-to-treat population. The mean reduction in HbA1c at week 12 from baseline in PMR group was significant compared to the SOC group (− 0.59 vs. − 0.21%, p = 0.002). At week 12, the PMR group showed significant reduction in mean body weight (− 2.19 vs. − 0.22 kg; p = 0.001) and waist circumference (− 2.34 vs. − 0.48 cm; p = 0.001) compared to SOC group. Mean fasting plasma glucose and post-prandial glucose significantly reduced from baseline at week 6 and 12 in each group ($p < 0.05$). No significant change was observed in lipid profile. QoL parameters (treatment adherence, general well-being, and energy fulfilment) in the PMR were significantly better than SOC group ($p < 0.05$). Patients were satisfied with the taste of DSNS. No serious adverse events were reported.

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Conclusions: DSNS is an encouraging option for PMR strategy, as it significantly improved HbA1c, body weight, waist circumference, and overall well-being among overweight/obese Indian T2DM patients.
Trial Identification No.: CTRI/2019/10/021595.

Keywords: Diabetes-specific nutritional supplement; Glycemic control; India; Partial meal replacement; Quality of life; Type 2 diabetes mellitus; Body weight

Key Summary Points

Why carry out this study?

Type 2 diabetes mellitus (T2DM) and obesity are strongly correlated. 74.2 million of India's population suffers from T2DM, and about 135 million of urban India's adult population is overweight/obese.

Clinical guidelines for managing T2DM recommend medical nutrition therapy and dietary counselling by registered dieticians in consultation with physicians to complement treatment for T2DM. In India, meal planning and diet adherence remain a major roadblock to effective management practices for T2DM.

Meal replacement strategies can effectively manage T2DM via glycemic and body weight control. In India, limited evidence exists regarding the effectiveness of the partial meal replacement (PMR) strategy in helping achieve glycemic control and its effect on anthropometric measurements in the overweight/obese T2DM population in conjunction with pharmacotherapy.

What did the study entail?

The study assessed the effect of PMR therapy on glycemic control and anthropometric measurements in the Indian overweight/obese T2DM population.

What was learned from the study?

PMR using a diabetes-specific nutritional supplement (DSNS), dietary counseling, and standard treatment helped improve glycemic control, achieve weight reduction, and improve factors impacting QoL in overweight/obese Indian patients with T2DM compared to standard care (diabetes treatment + standardized diet).

PMR using a DSNS can help improve glycemic levels, anthropometric measurements, and factors impacting QoL in Indian overweight/obese T2DM patients.

INTRODUCTION

The increasing prevalence of type 2 diabetes mellitus (T2DM) is associated with micro- and macrovascular complications resulting in increased healthcare costs, making it a potential public health burden worldwide, including India [1, 2]. Of the various challenges faced by T2DM patients, the primary challenge remains the achievement and maintenance of on-target glycemic control (glycated hemoglobin A [HbA1c] levels of $< 7.0\%$) [3].

A strong causal link has been suggested between inadequate glycemic control, defined as HbA1c levels of $\geq 7.0\%$, and increased risk of T2DM-related complications [4–6]. Despite the availability of diverse treatment options, real-world data suggest that globally, up to 60% of T2DM patients exhibit sub-optimal glycemic control [7]. According to the IMPACT study, T2DM patients in India had an average HbA1c of 8.56%, with FPG of 172 mg/dl, and a PPG of 253 mg/dl. Seventy-four percent of the patients had HbA1c $> 7\%$ and FPG > 130 mg/dl, whereas PPG > 160 mg/dl was observed in 83% of the patients [8]. The enhanced risk of developing T2DM among overweight/obese people [9], coupled with the high co-occurrence of both, often represents a combined pathological condition called "diabesity," which is purported to be mediated by the chronic inflammatory

response observed in obese individuals [10, 11]. The second National Health and Nutrition Survey found the prevalence of diabetes to be much higher in overweight individuals versus the general population [12, 13]. In India, 38% adults with diabetes were overweight, compared with the global average of 19% adults [14].

Balanced and well-structured nutrition plays a critical role in managing T2DM and achieving glycemic and weight control [15]. The Diabetes Prevention Program Research Group indicated that, over the long term, an intensive lifestyle intervention (low-calorie diet and modest physical exercise) resulting in weight reduction might reduce the incidence of T2DM in overweight/obese individuals and improvement in impaired glucose tolerance by 27–58% [16–18]. However, body weight reduction can be challenging due to usage of anti-diabetic agents that cause weight gain, and due to barriers to long-term lifestyle changes like poor dietary education, diminishing motivation to change, delays in scheduled medical follow-up, and lack of family support [19, 20]. In the multicenter DiabCare Asia-India study, only 4% of the 2269 patients followed a specified dietary regimen [21]. High fat consumption, particularly trans-fats and saturated fats, has been linked to insulin resistance, glucose intolerance, and poor diabetes control [22]. Managing T2DM with diet requires designing diet plans customized to meet individual patient needs, which remains an unmet need in India to a large extent.

Medical nutrition therapy is a fundamental component in the overall treatment plan for overweight/obese patients with T2DM, offering the flexibility to maximize treatment outcomes and improve general well-being [23, 24]. Furthermore, it is associated with up to 2.0% decrease in HbA1c [25]. According to the ADA, medical nutritional therapy comprises an essential component of the behavior change critical for achieving improved health outcomes in T2DM patients [26]. The Research Society for the Study of Diabetes in India recommends individualizing diet based on patient's health profile and cultural and economic background [25, 27, 28]. Meal replacements (partial or complete) are extended strategies of the medical nutrition therapy and used effectively in T2DM management [29–31]. A partial meal replacement (PMR) strategy involves one or two meal replacements with high-protein, low-carbohydrate beverage or food bars. Evidence suggests that PMRs are clinically efficacious in promoting weight loss in obese T2DM patients [32].

Aligned with the PMR strategy, Prohance-D® is a balanced and low glycemic index (GI) diabetes-specific nutritional supplement (DSNS). It provides an appropriate distribution of calories from proteins, mixed carbohydrates, fibers, and fats. Currently, limited evidence documents the glycemic and weight control benefits of PMR therapy for Indian patients with T2DM. PRIDE was one of the first studies in India to explore the impact of the low glycemic index PMR treatment strategy using DSNS (Prohance-D®) to reduce glycemic levels, manage body weight, and improve lipid profiles, as well as factors impacting QoL in overweight/obese patients with T2DM in India.

METHODS

Study Design

PRIDE was a phase IV, open-label, randomized, controlled study performed in overweight/obese patients with T2DM between October 2019 and June 2020 across five centers in India. Patients were randomized (1:1) to receive either daily one serving (50 g) of the DSNS (Prohance-D® Vanilla flavored powder) along with standard of care (SOC) treatment (PMR group) or SOC alone (SOC group) for 12 weeks. The Standard of Care was defined as diabetes treatment with dietary counseling. Randomization was performed using centralized block randomization. The randomization code and dispensing products were placed in the clinical pharmacy under controlled access.

The study was conducted according to the principles and requirements of the Declaration of Helsinki and was consistent with the International Conference on Harmonization Good Clinical Practice (GCP) guidelines, the local regulatory requirements of GCP for Clinical Research in India, and the Indian Council for Medical Research guidelines (2017) for

Biomedical Research on Human Subjects. The study was reviewed and approved by the Institutional Ethics Committee of each participating center. All subjects provided informed consent to participate in this study. The study was explained in detail along with the potential benefits vs. risks to the patients and/or their families by the investigator. Patients and/or their families were given sufficient time to think and deliberate before consenting to participate in the study. Prior to study enrollment, duly signed and dated informed consent was obtained from each participant in the presence of a legally accepted representative or impartial witness.

The study was reviewed and approved by the Institutional Ethics Committee of each participating center. The study was registered on Clinical Trials Registry India using the identifier CTRI/2019/10/021595.

Study Population

Patients meeting the following criteria were deemed eligible for inclusion in the study: male and non-pregnant females aged 18–65 years, diagnosed with T2DM for at least 1 year preceding the study; and treated with a stable dose of oral anti-diabetic drugs (drugs permitted include: metformin, sulfonylureas, thiazolidinedione, dipeptidyl peptidase-IV inhibitors, glucagon-like peptide-1 agonists) for $\geq$ 1 month before screening.

Individuals with HbA1c levels between 6.5 and 10%, body mass index (BMI) of 23–34 kg/m^2 (according to the consensus statement for diagnosis of obesity in Asian Indians) and willingness to provide written informed consent were included in the study.

Patients were excluded if they were on basal or multiple prandial insulin injections, on nutritional food supplements or multivitamin supplements (specifically calcium/vitamin D supplements and B complex syrups) within 15 days before study initiation, on herbal/ayurvedic preparations that could affect blood glucose, or had a history of food allergies to one or more components of the study product. Detailed exclusion criteria are provided in online Supplementary Table S1.

Intervention, Monitoring, and Assessments

One serving of the DSNS was used as either a breakfast/evening snack replacement or before lunch/dinner as directed by the physician. Following dietary counseling, the physician assessed the patients based on a standard diet chart that they filled out after each visit. Based on the data obtained from this diet chart, the physician prescribed DSNS as either a breakfast/evening snack replacement or to be taken prior to a major meal like lunch or dinner. One serving of 50 g of DSNS provides 16.8% of the recommended daily allowance (RDA) of protein. The SOC included diabetes treatment, dietary counseling, and maintaining a diet chart. Diet counseling and standard diet charts were provided to participants in both groups at study enrollment.

The DSNS used was a balanced mix of high-quality protein, complex carbohydrates, healthy fats, and soluble fibers with vital vitamins and minerals, and low GI nutritional supplement by Sun Pharmaceutical Industries Limited, Mumbai, India. The powder contained 454 kcal energy, 20.2 g protein, 46.1 g carbohydrate, 0 g sugar, 8.1 g dietary fiber, 3.5 g fructooligosaccharide (FOS), 19.2 g fat, 2.3 g saturated fatty acids, 11.2 g monounsaturated fatty acids, 3.6 g polyunsaturated fatty acids, 3 g linoleic acid, 465 mg alpha-linolenic acid, 0 g trans fatty acids, and 0 mg cholesterol per 100 g powder. Key ingredients included FOS, inulin, vitamins, minerals, maltodextrin, sunflower seed oil, calcium caseinate, whey and soy protein isolate, isomaltulose, fructose, rapeseed oil, carnitine, and taurine.

Adherence to diet intervention was monitored at every study visit through patient diaries. Routine treatment for diabetes was to be continued during the study. Each participant recorded their daily food intake in a diet diary and serving size based on their diet chart and dietary counseling at each study visit by dietician/physician.

The study consisted of three visits: baseline, week 6, and week 12. At each study visit, general physical examinations such as height, weight, and waist circumference were carried out. Blood

samples were collected for scheduled laboratory evaluation to assess glycemic profile (fasting plasma glucose [FPG], postprandial glucose [PPG], and HbA1c), and lipid profiles (total cholesterol, high-density lipoprotein cholesterol [HDL-C], low-density lipoprotein cholesterol [LDL-C] and triglyceride [TG]), measured by the respective laboratory of each center. Factors impacting QoL were also assessed for both groups during this period.

Patients were followed up during the entire study period for any adverse event (AE), including hypoglycemia, adherence to diet restriction, and factors impacting QoL. For any severe AEs, adverse reaction, illness or injury, the subjects were informed to seek immediate treatment and instruct the clinical study sites.

Study Endpoints

The primary endpoint was the mean change in HbA1c from baseline to week 12 in PMR group versus SOC group. The secondary efficacy endpoints were mean changes in FPG, PPG, body weight, waist circumference, and lipid profile from baseline to weeks 6 and 12 within each group. The factors impacting QoL included the assessment of treatment adherence (never, often, sometimes, very seldom), energy fulfilment, satiety (all the time, never, often, sometimes, very seldom), and feeling of general well-being (moderately dissatisfied, moderately satisfied, neither, very dissatisfied, very satisfied). Additionally, in patients receiving PMR therapy, assessment of taste (moderately dissatisfied, moderately satisfied, neither, very dissatisfied, very satisfied) of DSNS was also recorded.

Safety was assessed by recording AEs and serious adverse events (SAEs) by the investigator. AEs were classified according to severity as mild (events that required minimal or no treatment and did not interfere with patient's daily activities), moderate (events that resulted in a low level of inconvenience or concern with therapeutic measures), and severe (events that interrupted a patient's usual daily activity and required systemic drug therapy). The relationship of the AE to the study product was assessed and categorized as unrelated (events that were not related), unlikely (events that were doubtfully related), possible (events that may be related), probable (events that were likely related) and definite (clearly related to the investigational agent, disease, concomitant medication, or other contributing cause).

Statistical Analysis

A sample size of 71 patients in each group was required to detect a difference of $\geq 0.5\%$ in mean HbA1c with 80% power, using a two-sample *t* test and assuming a (two-sided) α of 0.05 and a standard deviation (SD) of 1.5%.

Student's *t* test was performed for demographic data and efficacy parameters. The data were analyzed, and the mean, SD, and range were tabulated. Safety parameters were analyzed as percentages, and the group comparisons were evaluated using the chi-square test. The primary analysis group was the modified intention-to-treat (mITT) population (all randomized patients who completed at least one post-baseline visit), and the efficacy analysis results were reported for this population and the per-protocol (PP) population (all randomized patients who completed the study in accordance with the protocol without major deviations). Patient samples were supposed to be collected twice (fasting and postprandial) during each visit. However, due to COVID-19 disease-related restrictions, samples for either fasting or postprandial condition were not obtained in a few patients.

Safety findings were reported for the safety population, which included all randomized patients who received at least one dose of the study product.

The statistical analyses were performed using SPSS version 10.0 Statistical Package for Social Sciences.

Post Hoc Subgroup Analysis

A post hoc analysis was undertaken to identify if certain subgroups of patients with T2DM experienced better outcomes with DSNS. The post hoc analysis was performed on the following subgroups stratified based on metabolic relevance—BMI $\leq$ or >30 kg/m^2; waist

circumference ≤ or > 35 inches; FPG ≤ or > 150 mg/dl; PPG ≤ or > 204 mg/dl; and HbA1c % ≤ or > 8. This subgroup analysis was performed for exploratory purposes.

RESULTS

A total of 185 patients were screened of which 176 (88 each in the PMR and SOC groups) were eligible to be enrolled in the study (three patients in the PMR group and two patients in the SOC group were lost to follow up). Of these enrolled patients, 171 completed at least one post-baseline visit (85 in PMR and 86 in SOC group; mITT population). Of these, 19 patients were lost to follow-up and ten had protocol deviations. The protocol deviations observed in the study were due to the visit not being performed by the patients due to COVID-19 disease-related restrictions that prevented patients from visiting the site for the study related procedures. Hence, a total of 142 patients (71 each in the PMR and SOC group; PP population) completed the study in accordance with the protocol without major deviations.

The patient disposition flowchart is shown in Fig. 1. A total of 24 patients did not report for the scheduled follow-up visits on weeks 6 and 12. They were either unable to reach the study site due to COVID-19 disease-related restrictions or were lost to follow-up (no contact was established when the study was completed, resulting in insufficient information to determine their status at the last visit).

The results for HbA1c, weight, and waist circumference for mITT and PP population are presented below. For FPG, PPBG, lipid profile, and factors impacting quality-of-life, results for mITT population are presented below and the same for PP population are presented in the online supplementary material.

Demographics and Patient Baseline Characteristics

The demographic and baseline characteristics were comparable in the mITT patient population between the PMR and the SOC groups. A total of 41.2% of patients (n = 35) in the PMR group and 33.7% in the SOC group (n = 29) were females. The mean age was 50.44 ± 9.79 years

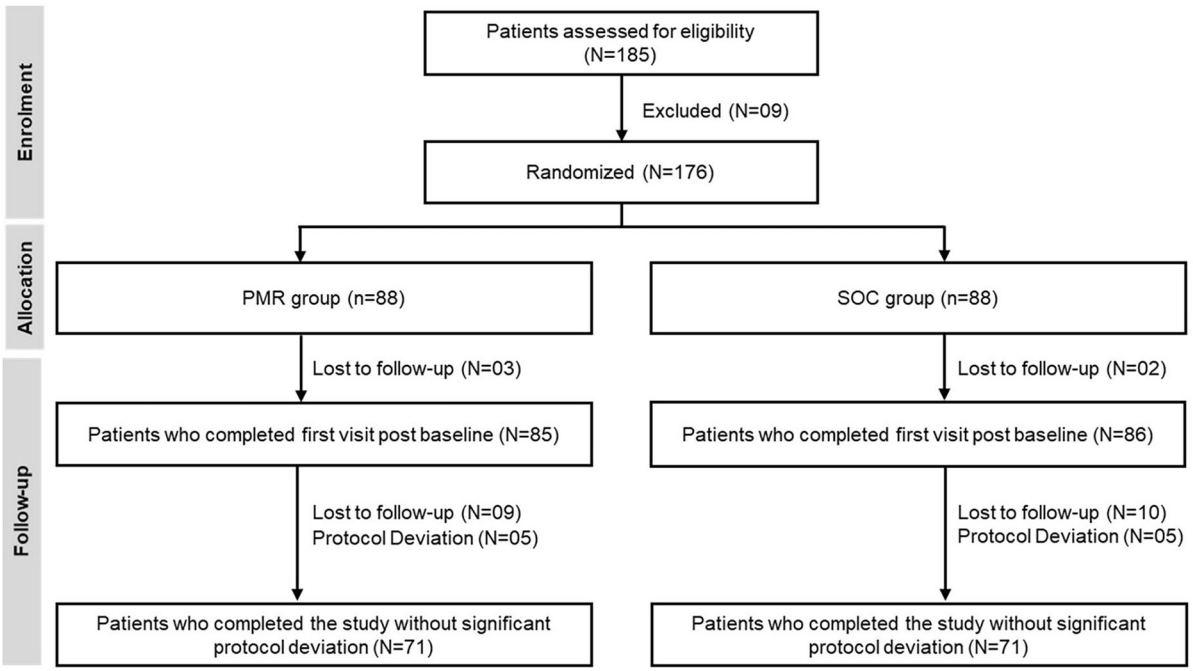


Fig. 1 Patient disposition flowchart. *N* total number of patients, *n* number of patients included in the specific category, *PMR* partial meal replacement, *SOC* standard of care

Table 1 Patient baseline demographics and disease characteristics

Parameters	PMR group (N = 85)	SOC group (N = 86)	p value
Age, years	50.44 ± 9.79	49.92 ± 10.39	0.736
Male, *n* (%)	50 (58.80)	57 (66.30)	0.313
Female, *n* (%)	35 (41.20)	29 (33.70)	
Height, cm	161.95 ± 7.40	163.55 ± 8.20	0.182
Weight, kg	70.05 ± 9.89	71.78 ± 7.49	0.199
BMI, kg/m^2	26.65 ± 2.92	26.81 ± 2.74	0.712
Waist circumference, cm	91.0 ± 9.91	92.84 ± 9.86	0.227
HbA1c, %	8.04 ± 0.81	7.92 ± 0.83	0.340
FPG, mg/dl	153.7 ± 47.04	151.67 ± 39.57	0.716
PPG, mg/dl	208.97 ± 60.95	203.76 ± 54.59	0.556
Total cholesterol, mg/dl	165.78 ± 32.64	167.47 ± 31.61	0.732
HDL-C, mg/dl	40.68 ± 8.53	41.73 ± 7.25	0.387
LDL-C, mg/dl	97.13 ± 24.03	101.85 ± 27.37	0.232
TG, mg/dl	151.98 ± 81.10	163.93 ± 126.37	0.462

All values are presented as mean ± SD

BMI body mass index, *FPG* fasting plasma glucose, *HbA1c* glycated hemoglobin, *HDL-C* high-density lipoprotein cholesterol, *LDL-C* low-density lipoprotein cholesterol, *N* number of patients in each group, *PMR* partial meal replacement, *PPG* post-prandial glucose, *SD* standard deviation, *SOC* standard of care, *TG* triglyceride

and 49.92 ± 10.39 years in the PMR and SOC groups, respectively (p = 0.736); mean BMI was 26.65 ± 2.92 kg/m^2 in the PMR group and 26.81 ± 2.74 kg/m^2 in the SOC group (p = 0.712), and mean waist circumference in the PMR and SOC groups was 91.01 ± 9.91 and 92.84 ± 9.86 cm, respectively (p = 0.227).

There was no significant difference in the demographics and baseline disease characteristics between the groups (Table 1).

PRIMARY ENDPOINT: GLYCEMIC PROFILE

Mean change in HbA1c

At week 12, the mean HbA1c reduced significantly from baseline by 0.59 ± 0.65% and 0.21 ± 0.92% in the mITT population in the PMR and SOC groups, respectively (p = 0.001 and p = 0.037) (Fig. 2a). The PMR group demonstrated a significantly greater reduction from baseline in mean HbA1c % compared to the SOC group at week 12 (p = 0.002).

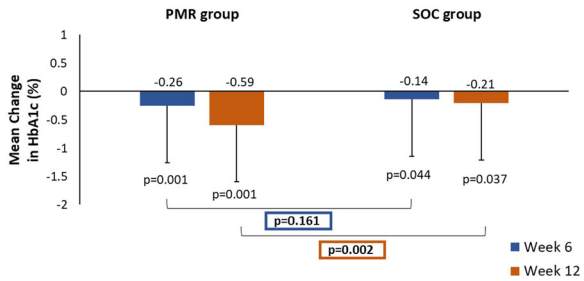


Fig. 2 Mean change in HbA1C (%) from baseline to week 6 and week 12 (mITT population). All values are presented as mean ± SD. p value: calculated using Student's t test. *HbA1c* glycated hemoglobin, *mITT* modified intention-to-treat, *PMR* partial meal replacement, *SD* standard deviation, *SOC* standard of care. The mITT population consisted of all enrolled patients who completed at least one post-baseline visit

Table 2 Mean change in HbA1C (%) from baseline to week 6 and week 12 (PP population)

	Mean change in HbA1c (%) (mean ± SD)	
	PMR group (*N* = 71)	**SOC group (*N* = 71)**
Baseline	8.05 ± 0.82	7.88 ± 0.85
Visit 2 (week 6)	7.78 ± 0.76	7.77 ± 0.97
Mean difference	− 0.26 ± 0.48	− 0.10 ± 0.67
p value	(0.001)	(0.215)
p value	**0.106***	
Visit 3 (week 12)	7.42 ± 0.68	7.72 ± 1.15
Mean difference	− 0.62 ± 0.65	− 0.16 ± 0.98
p value	(0.001)	(0.173)
p value	**0.001****	

All values are presented as mean ± SD. *p* value: calculated using Student's *t* test. *p values for within group comparison; **p value for between group comparison

HbA1c glycated hemoglobin, *PMR* partial meal replacement, *PP* per-protocol, *SD* standard deviation, *SOC* standard of care

The PP population consisted of all enrolled patients who had completed the study as per the protocol without major protocol deviation

The bold values indicate statistical significance

At week 12, the mean HbA1c decreased significantly ($p = 0.001$) from baseline by 0.62 ± 0.65% in the PP population in the PMR group. However, the decrease reported in the PP population in the SOC group (0.16 ± 0.98%) was not significant ($p = 0.173$) (Table 2). When compared between the two treatment groups, the mean HbA1c (%) reduction from baseline was significantly greater in the PP population in the PMR group compared to the PP population in the SOC group at week 12 ($p = 0.001$).

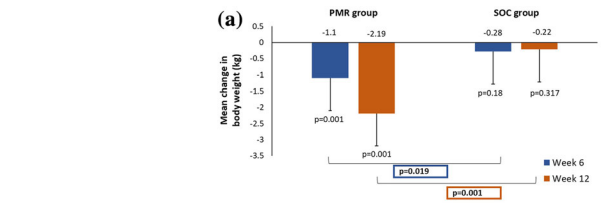
SECONDARY ENDPOINTS

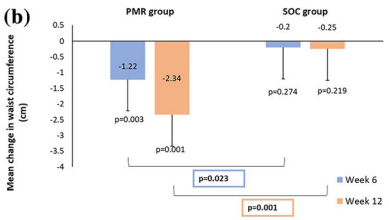
Mean Changes in Body Weight and Waist Circumference

At weeks 6 and 12, the mean body weight decreased significantly from baseline by 1.10 ± 2.57 kg and 2.19 ± 3.14 kg in the mITT population in the PMR group ($p = 0.001$ for both). However, the reductions were not significant in the SOC group at both week 6 (0.28 ± 1.91 kg; $p = 0.180$) and week 12 (0.22 ± 2.03 kg; $p = 0.317$). Moreover, the reduction in mean weight between the groups was significantly greater in the PMR vs. the SOC group, both at week 6 ($p = 0.019$) and at week 12 ($p = 0.001$) (Fig. 3a).

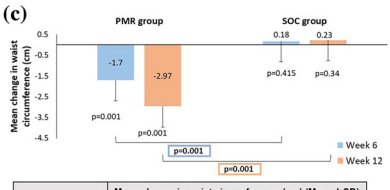
At weeks 6 and 12, the mean body weight decreased significantly from baseline by 1.40 ± 1.82 and 2.70 ± 2.42 kg in the PP population in the PMR group ($p = 0.001$ for both). In the SOC group, the change in the mean body weight from baseline was not reported to be significant at either week 6 (0.36 ± 1.72 kg; $p = 0.082$) or week 12 (0.26 ± 1.84 kg; $p = 0.237$) (Table 3). Between the two treatment groups, the reduction in the mean body weight from baseline significantly favored PP population in the PMR group over the SOC group at both week 6 and week 12 ($p = 0.001$ for both).

At weeks 6 and 12, the mean waist circumference showed a significant reduction from baseline by 1.22 ± 3.71 cm and 2.34 ± 4.57 cm in the mITT population in the PMR group ($p = 0.003$ and $p = 0.001$, respectively). However, patients in the SOC group did not report a significant change in the mean waist circumference at either week 6 (0.20 ± 1.70 cm; $p = 0.274$)





	Mean change in waist circumference (cm) (Mean ± SD)	
	PMR group (N=85)	SOC group (N=86)
Baseline	91.01 ± 9.91	92.84 ± 9.86
Visit 2 (Week 6)	89.71 ± 11.53	92.71 ± 9.86
Mean Difference P value	-1.22 ± 3.71 (0.003)	-0.20 ± 1.70 (0.274)
P value	0.023	
Visit 3 (Week 12)	88.67 ± 11.96	92.61 ± 9.73
Mean Difference P value	-2.34 ± 4.57 (0.001)	-0.25 ± 1.91 (0.219)
P value	0.001	



	Mean change in waist circumference (cm) (Mean ± SD)	
	PMR group (N=71)	SOC group (N=71)
Baseline	90.42 ± 9.75	91.72 ± 9.58
Visit 2 (Week 6)	88.72 ± 11.40	91.54 ± 9.63
Mean Difference P value	-1.70 ± 3.43 (0.001)	0.18 ± 1.83 (0.415)
P value	0.001	
Visit 3 (Week 12)	87.43 ± 11.84	91.49 ± 9.55
Mean Difference P value	-2.97 ± 4.37 (0.001)	0.23 ± 2.01 (0.340)
P value	0.001	

Fig. 3 **a** Mean change in body weight (kg) from baseline to week 6 and week 12 (mITT population). All values are presented as mean ± SD. *p* value: calculated using Student's *t* test. *BW* bodyweight, *mITT* modified intention-to-treat, *N* total number of patients with results for the specified timepoint, *PMR* partial meal replacement, *SD* standard deviation, *SOC* standard of care. The mITT population consisted of all enrolled patients who completed at least one post-baseline visit. **b** Mean change in waist circumference (cm) from baseline to week 6 and week 12 (mITT population). All values are presented as mean ± SD. *p* value: calculated using Student's *t* test. *mITT* modified intention-to-treat, *N* total number of patients with results for the specified timepoint, *PMR* partial meal replacement, *SD* standard deviation, *SOC* standard of care, *WC* waist circumference. The PP population consisted of all enrolled patients who had completed the study as per the protocol without major protocol deviation. **c** Mean change in waist circumference (cm) from baseline to week 6 and week 12 (PP population). All values are presented as mean ± SD. *p* value: calculated using Student's *t* test. *N* total number of patients with results for the specified timepoint, *PMR* partial meal replacement, *PP* per-protocol, *SD* standard deviation, *SOC* standard of care, *WC* waist circumference. The PP population consisted of all enrolled patients who had completed the study as per the protocol without major protocol deviation

or week 12 (0.25 ± 1.91 cm; $p = 0.219$). When compared between groups, patients in the PMR group showed a significantly greater reduction in the mean waist circumference from baseline compared to those in the SOC group at week 6 ($p = 0.023$) and week 12 ($p = 0.001$) (Fig. 3b).

At weeks 6 and 12, patients in the PP population in the PMR group showed a significant reduction in the mean waist circumference from baseline by 1.70 ± 3.43 cm and 2.97 ± 4.37 cm, respectively ($p = 0.001$ for both). However, patients in the SOC group did not report a significant change in the mean waist circumference from baseline at either week 6 (0.18 ± 1.83 cm; $p = 0.415$) or week 12 (0.23 ± 2.01 cm; $p = 0.340$). Furthermore, the reduction in mean waist circumference from baseline was significantly greater in the PMR group than SOC group at both week 6 and week 12 ($p = 0.001$ for both) (Fig. 3c).

Mean Changes in FPG and PPG

At weeks 6 and 12, the mean FPG decreased significantly from baseline by 9.25 ± 27.02 mg/dl and 15.58 ± 37.12 mg/dl in the mITT population in the PMR group ($p = 0.003$ and $p = 0.001$, respectively) and by 6.74 ± 30.46 mg/dl

Table 3 Mean change in body weight (kg) from baseline to week 6 and week 12 (PP population)

	Mean change in body weight (kg) (mean ± SD)	
	PMR group (*N* = 71)	**SOC group (*N* = 71)**
Baseline	70.17 ± 9.93	71.56 ± 7.66
Visit 2 (week 6)	68.77 ± 9.74	71.21 ± 7.31
Mean difference	− 1.40 ± 1.82	− 0.36 ± 1.72
p value	(0.001)	(0.082)
p value	**0.001***	
Visit 3 (week 12)	67.47 ± 9.80	71.3 ± 7.36
Mean difference	− 2.70 ± 2.42	− 0.26 ± 1.84
p value	(0.001)	(0.237)
p value	**0.001****	

All values are presented as mean ± SD. *p* value: calculated using Student's *t* test. **p* values for within group comparison; ***p* value for between group comparison

The PP population consisted of all enrolled patients who had completed the study as per the protocol without major protocol deviation

BW bodyweight, *N* total number of patients with results for the specified timepoint, *PMR* partial meal replacement, *PP* per-protocol, *SD* standard deviation, *SOC* standard of care

The bold values indicate statistical significance

and 11.26 ± 27.98 mg/dl in the SOC group, respectively ($p = 0.047$ and $p = 0.001$, respectively) (online Supplementary Table S2). This change was not significantly different between treatment groups at week 6 and week 12 ($p = 0.579$ for both). The results of the PP population were similar to that observed in the mITT population (online Supplementary section 1 and Supplementary Table S3)

At weeks 6 and 12, the mean PPG significantly decreased from baseline by 13.25 ± 44.78 and 23.64 ± 48.85 mg/dl in the mITT population in the PMR group ($p = 0.008$ and $p = 0.001$, respectively) and by 17.20 ± 52.20 and 24.52 ± 55.47 mg/dl in the mITT population in the SOC group, respectively ($p = 0.003$ and $p = 0.001$, respectively) (online Supplementary Table S4). This change was not significantly different between treatment groups at week 6 and week 12 ($p = 0.603$ and $p = 0.912$ respectively).

The results obtained for FPG and PPG in the PP population were similar to that observed in the mITT population and are presented in online Supplementary Section 1 (online Supplementary Table S3 and Supplementary Table S5).

Mean Changes in Lipid Profile: Total Cholesterol, HDL-C, LDL-C, and TG

The mean total cholesterol, HDL-C, LDL-C, and TG within groups and between the groups at weeks 6 and 12 was non-significant (online Supplementary Table S6, S7, S8, S9).

The results of the PP population are presented in online Supplementary Section 2 (online Supplementary Table S10, S11, S12, S13).

Assessment of Factors Impacting QoL: Treatment Adherence, Satiety, Energy Fulfilment, Taste, and Well-Being

Factors impacting QoL as treatment adherence, satiety, energy fulfilment, and feeling of well-being were evaluated at baseline, week 6, and week 12 for both groups. Additionally, the taste of DSNS was assessed for the PMR group. In the mITT population, from baseline to week 12,

72.4% of patients reported never missing their treatment in the PMR group compared with 56.6% in the SOC group (within group and PMR vs. SOC, $p < 0.05$; Fig. 4a), 55.3% of patients never felt hungry in the mITT population in the PMR group compared to 44.8% in mITT population in the SOC group ($p < 0.05$ from baseline to week 12 for both groups; Fig. 4b), 64.5% of patients never felt lethargic in the PMR group compared with 42.1% in the SOC group (within group and PMR group vs. SOC group, $p < 0.05$; Fig. 4c), 73.7% of patients were satisfied with their general well-being in the PMR group compared with 46.1% in the SOC group (within group and PMR group vs. SOC group, $p < 0.05$; Fig. 4d). Taste was evaluated only in the mITT population in the PMR group, and at week 12, 57.9% reported to be "very satisfied" with the taste of the product in the PMR group, and no patients reported to be "very dissatisfied." (Fig. 4e). These results collectively indicate that a higher proportion of patients in the mITT population in the PMR group adhered to the treatment regimen and felt energetic and better compared to those in the SOC group.

The observations for factors impacting QoL were similar in the PP population (Fig. 4f–j) as observed for mITT population.

Safety

Overall, six AEs were reported among four patients (4.54%) in the PMR group, and seven AEs were reported among five patients (5.68%) in the SOC group. Most of the AEs were of mild intensity; 66.67% in the PMR group and 57.14% in the SOC group (n = 4 each) (online Supplementary Table S14). No AEs of severe intensity were reported.

The reported AEs in the PMR group were loss of appetite, stomach bloating, peripheral leg edema, burning micturition, and urinary retention. Loss of appetite, peripheral leg edema, burning micturition and urinary retention were assessed as being possibly or probably related to study intervention by the investigator. No patient in either study group reported hypoglycemia. No SAEs were observed during the study.

POST HOC SUBGROUP ANALYSIS

The findings of the post hoc analyses are described below.

Mean Changes in HbA1c

Consistent HbA1c reduction was observed from baseline to week 12 in patients across glycemic strata, BMI profiles, and waist circumference values in the PMR group (online Supplementary Figure S1). Furthermore, across subgroups like BMI ≤ 30 kg/m^2, waist circumference ≤ 35 inches, FPG ≤ 150 mg/dl, PPG ≤ 204 mg/dl, and HbA1c $\leq 8\%$, PMR group was associated with significantly greater reduction in HbA1c from baseline to week 12 when compared with SOC group. Reduction in HbA1c with PMR group for most subgroups was between 0.35% and 0.7% from baseline to week 12 and was statistically significant. Highest reduction of 0.96% was observed in PMR group in those with HbA1c $> 8\%$.

Mean Changes in Body Weight, Waist Circumference, and BMI

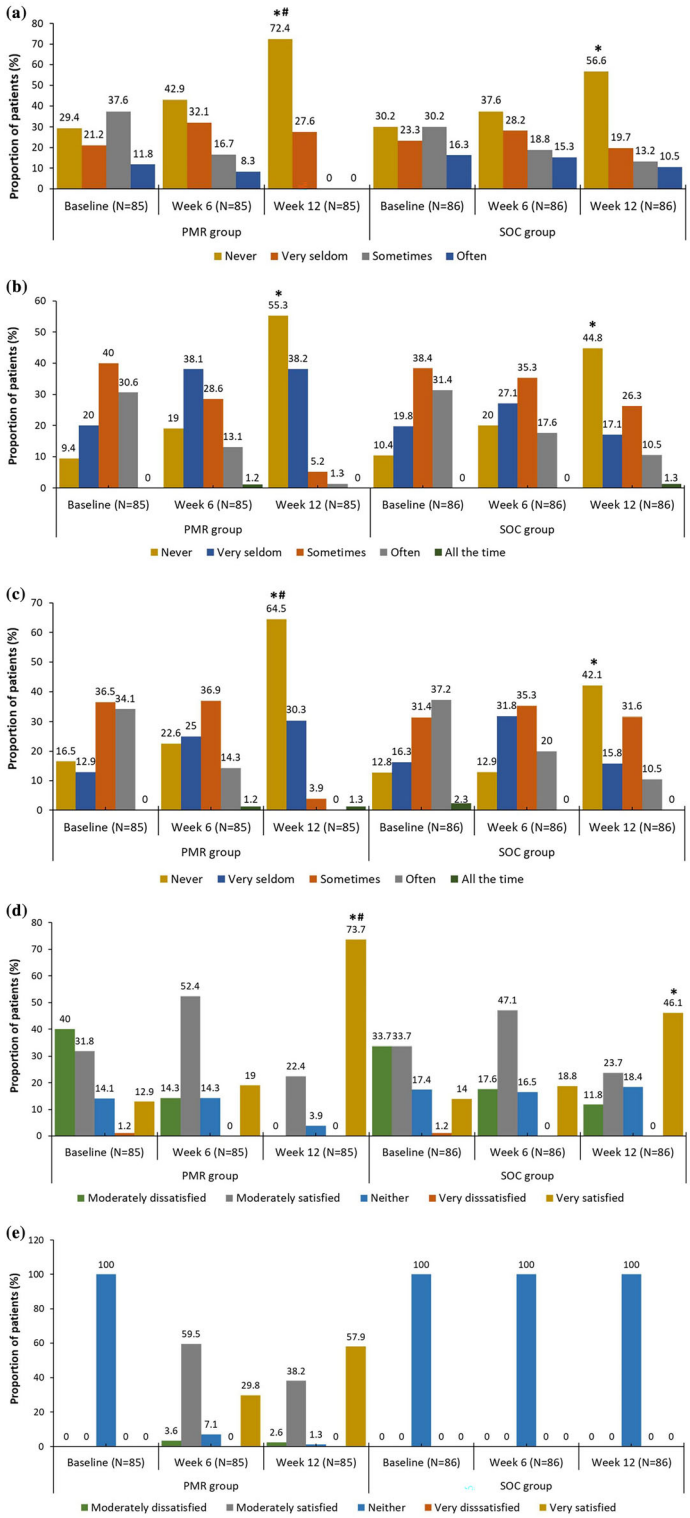
Significant weight reduction ranging from 1.71 to 2.62 kg was observed at week 12 in PMR group across the various subgroups defined by baseline HbA1c, PPG, FPG, and waist circumference. The reduction in weight was significantly higher in the PMR group compared to the SOC group in all the subgroups (online Supplementary Figure S2). Consistent reduction in waist circumference in the PMR group was noted at 12 weeks in patients with various glycemic profiles and abdominal obesity (online Supplementary Figure S3). The mean reductions in these subgroups ranged from 1.17 to 5.23 cm and were significantly higher than the reductions in the corresponding SOC subgroups. The highest reductions were observed in those with BMI > 76.2 and waist circumference ≤ 88.9 cm. At week 12, significant BMI reduction was observed in the PMR group compared to baseline, and to the reduction observed in the SOC group. In the PMR group, individuals with BMI > 30 had mean BMI reduction of 1.28 kg/m^2,

Fig. 4 **a** Factors impacting QoL assessment on how often patients miss their diabetes treatment (mITT population). *p* value: calculated using chi-square test. *Significant difference within group from baseline to week 12 ($p < 0.05$); #significant difference in PMR group compared to SOC group at week 12 ($p < 0.05$). *mITT* modified-intention-to-treat, *N* total number of patients, *PMR* partial meal replacement, *QoL* quality of life, *SOC* standard of care. The mITT population consisted of all enrolled patients who completed at least one post-baseline visit. **b** Factors impacting QoL assessment on how often patients feel hungry (mITT population). *p* value: calculated using chi-square test. *Significant difference within group from baseline to week 12 ($p < 0.05$). *mITT* modified-intention-to-treat, *N* total number of patients, *PMR* partial meal replacement, *QoL* quality of life, *SOC* standard of care. The mITT population consisted of all enrolled patients who completed at least one post-baseline visit. **c** Factors impacting QoL assessment on how often patients feel lethargic (mITT population). *p* value: calculated using chi-square test. *Significant difference within group from baseline to week 12 ($p < 0.05$); #significant difference in PMR group compared to SOC group at week 12 ($p < 0.05$). *mITT* modified-intention-to-treat, *N* total number of patients, *PMR* partial meal replacement, *QoL* quality of life, *SOC* standard of care. The mITT population consisted of all enrolled patients who completed at least one post-baseline visit. **d** Factors impacting QoL assessment on patient satisfaction with their general well-being (mITT population). *p* value: calculated using chi-square test. *Significant difference within group from baseline to week 12 ($p < 0.05$); #significant difference in PMR group compared to SOC group at week 12 ($p < 0.05$). *mITT* modified-intention-to-treat, *N* total number of patients, *PMR* partial meal replacement, *QoL* quality of life, *SOC* standard of care. The mITT population consisted of all enrolled patients who completed at least one post-baseline visit. **e** Factors impacting QoL assessment on patient satisfaction with the taste of Prohance-D® (mITT population). *mITT* modified-intention-to-treat, *N* total number of patients, *PMR* partial meal replacement, *QoL* quality of life, *SOC* standard of care. The mITT population consisted of all enrolled patients who completed at least one post-baseline visit. **f** Factors impacting QoL assessment on how often patients miss their diabetes treatment (PP population). *p* value: ▶ calculated using chi-square test. *Significant difference within group from baseline to week 12 ($p < 0.05$); #significant difference in PMR group compared to SOC group at week 12 ($p < 0.05$). *N* total number of patients, *PMR* partial meal replacement, *PP* per-protocol, *QoL* quality of life, *SOC* standard of care. The PP population consisted of all enrolled patients who had completed the study as per the protocol without major protocol deviation. **g** Factors impacting QoL assessment on how often patients feel hungry (PP population). *p* value: calculated using chi-square test. *Significant difference within group from baseline to week 12 ($p < 0.05$). *N* total number of patients, *PMR* partial meal replacement, *PP* per-protocol, *QoL* quality of life, *SOC* standard of care. The PP population consisted of all enrolled patients who had completed the study as per the protocol without major protocol deviation. **h** Factors impacting QoL assessment on how often patients feel lethargic (PP population). *p* value: calculated using chi-square test. *Significant difference within group from baseline to week 12 ($p < 0.05$); #significant difference in PMR group compared to SOC group at week 12 ($p < 0.05$). *N* total number of patients, *PMR* partial meal replacement, *PP* per-protocol, *QoL* quality of life, *SOC* standard of care. The PP population consisted of all enrolled patients who had completed the study as per the protocol without major protocol deviation. **i** Factors impacting QoL assessment on patient satisfaction with their general well-being (PP population). *p* value: calculated using chi-square test. *Significant difference within group from baseline to week 12 ($p < 0.05$); #significant difference in PMR group compared to SOC group at week 12 ($p < 0.05$). *N* total number of patients, PMR partial meal replacement, *PP* per-protocol, *QoL* quality of life, *SOC* standard of care. The PP population consisted of all enrolled patients who had completed the study as per the protocol without major protocol deviation. **j** Factors impacting QoL assessment on patient satisfaction with the taste of Prohance-D® (PP population). *N* total number of patients, *PMR* partial meal replacement, *PP* per-protocol, *QoL* quality of life, *SOC* standard of care. The PP population consisted of all enrolled patients who had completed the study as per the protocol without major protocol deviation

while those with BMI < 30 had mean BMI reduction of 0.75 kg/m^2 (online Supplementary Figure S4).

DISCUSSION

PRIDE is the first study in India to evaluate the effect of PMR using the DSNS, Prohance-D®,


(a)
Proportion of patients (%)
Baseline (N=85)
Week 6 (N=85)
Week 12 (N=85)
Baseline (N=86)
Week 6 (N=86)
Week 12 (N=86)
PMR group
SOC group
Never
Very seldom
Sometimes
Often
(b)
All the time
(c)
(d)
Moderately dissatisfied
Moderately satisfied
Neither
Very disssatisfied
Very satisfied
(e)

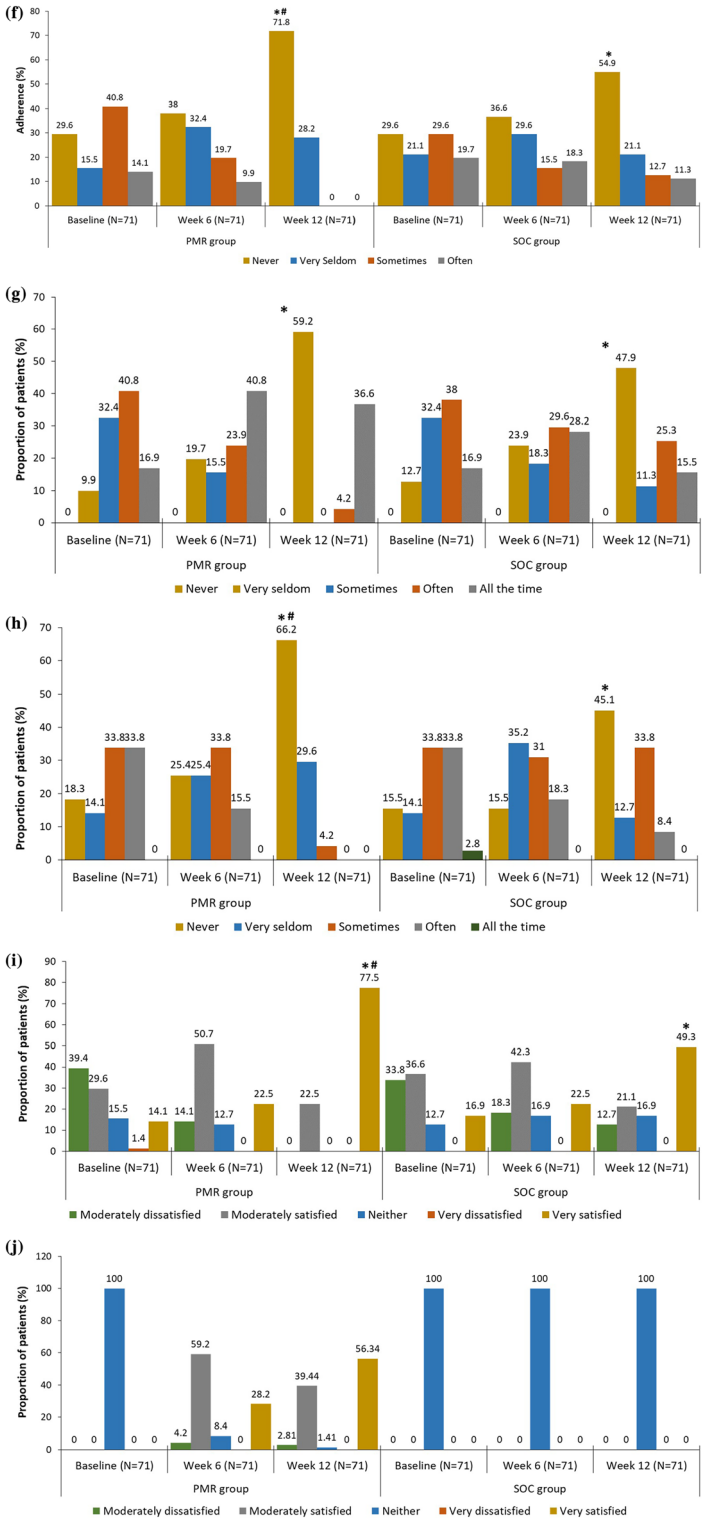


Fig. 4 continued

together with dietary counseling and standard treatment on improving glycemic and lipid parameters and factors impacting QoL in the overweight/obese patients with T2DM. International treatment guidelines by the ADA and AACE/ACE and the ICMR guidelines on managing T2DM emphasize the need to achieve good glycemic control and recommend an HbA1c target of $< 7.0\%$ [33–35]. Over the 12-week duration of this study, participants in the PMR group achieved a significantly greater mean reduction in HbA1c, body weight, and waist circumference. Although patients on GLP-1 agonists were not excluded from the study, it was seen that none of the patients had received GLP-1 receptor agonists. SGLT2i and its combinations were uniformly distributed between the PMR and SOC groups (12.51% in the PMR group and 13.65% in the SOC group). (online Supplementary Table S15) This indicates that the reduction in HbA1c levels observed in this study could have been due to the effect of the PMR.

Statistically significant improvements were observed in FPG and PPG levels in the PMR group at weeks 6 and 12 from baseline although the between group change in FPG and PPG was not significant. The factors impacting QoL such as treatment adherence, satiety, energy fulfilment, taste, and well-being in comparison to SOC group demonstrated that the patients in PMR groups were significantly more energetic, felt better, and were more adherent to the treatment. However, no statistically significant difference was observed in any lipid parameters between the groups. Most AEs were mild in intensity; no SAEs were reported, making the DSNS well tolerated in the study population. Thus, the findings indicated that a PMR strategy consisting of SOC with DSNS could be more effective than SOC alone in Indian patients with T2DM in managing blood glucose, and anthropometric measurements.

In patients with diabetes, meal replacement treatments are clinically successful and therefore recommended in clinical nutrition guidelines [36]. PMR therapies, low in calories and GI, may induce weight loss and promote glycemic control by increasing satiety levels [37, 38]. Consequently, PMRs may be promising non-pharmacologic interventions in managing patients with T2DM. Furthermore, when compared with very low calorie diets (calorie-controlled, vitamin/mineral fortified, liquid meal replacements), PMRs may be better suited to promote gradual weight loss [32]. The DSNS, Prohance-D®, used in PRIDE, is formulated with suitable and adequate macronutrient proportions for glycemic and metabolic control—the sources of carbohydrate being FOS and isomaltulose. Isomaltulose is a low GI index, slow and sustained-release carbohydrate, which improves fat-oxidation during physical activity [39]. Maltodextrin added as a dietary fiber source can help lower FPG levels [40]. Isomaltulose and maltodextrin have demonstrated reductions in the glucose-uptake rate, glucose, and insulin levels stability, and avoiding glucose spikes [41]. Whey protein isolate can help lower PPG, and soy protein isolate can help manage cholesterol levels [42–44]. Positive effects of the PMR strategy have been documented extensively in patients with T2DM and discussed in the ADA guidelines [27]. In line with this, introducing such a strategy as part of clinical practice guidelines to manage obese/overweight T2DM patients in India can significantly benefit disease management.

In India, managing patients with T2DM is more challenging due to a reduced level of disease awareness, a high rate of undetected illness [45], and scarcity of time available to healthcare professionals to offer guidance/support, integrating medical nutritional therapy in general management practices [46]. Considerations in managing diabetes amongst Indian T2DM patients with diet should be reviewed carefully considering regional influence, personal, culture, lifestyle, culinary, and economic diversity, to improve acceptance [47]. The Indian dietary guidelines for managing T2DM recommend 50–60% energy from carbohydrates, 10–15% from protein, and $< 30\%$ from fat [48]. However, India has the lowest (< 48 g/day) average protein consumption [49] and the highest carbohydrate consumption [50, 51].

The efficacy of meal replacement therapy has been established across studies. Evidence collectively demonstrates that in patients with T2DM, meal replacement is associated with better glycemic control and weight loss

[32, 52–56]. Achieving an optimum HbA1c level is critical for T2DM therapy since it is linked to reducing microvascular complications [57]. Diabetic patients who followed a low GI diet had approximately a 0.4% reduction in their HbA1c levels within 10 weeks [58]. Moreover, the Diabetes Remission Clinical Trial (DiRECT) reported that a strict calorie-restricted formula led to significant improvement in the HbA1c levels (− 0.9%) [52]. The DSNS used in our study resulted in a significant reduction in HbA1c levels ($p = 0.001$), in concurrence with DiRECT study results. Although our assumption of 0.5% difference between the groups in HbA1c was not achieved, the observed difference of 0.38% was found to be clinically meaningful. It has been observed that a 0.1% or more decline in HbA1c significantly reduced fatal/nonfatal CHD (39%), fatal/nonfatal CVD (37%), and total mortality (46%) ($p < 0.001$) in patients with a mean baseline HbA1c levels of 7.8% [59].

Maintaining the FPG and PPG levels is another critical treatment target in the successful management of T2DM. In a 3-month randomized controlled trial that assessed the effect of a low GI meal replacement in T2DM patients, patients who took the meal replacement exhibited a stronger ability to regulate 2-h PPG versus those who did not [60]. A recent study in India investigated the effectiveness of medical nutrition therapy in T2DM patients. Over 6 months, significant reductions from baseline were noted for HbA1c and FPG [46]. These findings are consistent with the findings of PRIDE—showing a significant reduction in FPG and PPG ($p = 0.001$ for each) over a 12-week period, implying that PMR strategy utilizing DSNS could be beneficial in achieving enhanced glycemic control in T2DM patients in India.

Obesity is an established risk factor for the development or progression of T2DM [61]. Evidence from real-world studies suggests that as high as 85.9% of patients with T2DM fall under the category of overweight or obese [62]. Moreover, the risk of T2DM has been reported to be up to sevenfold higher among people who remain obese for > 25 years [63]. Furthermore, it has been reported that the mean BMI of patients with T2DM is frequently ≥ 30 kg/m^2, the threshold for classifying individuals as obese [64, 65]. Improvements in glycemic control are linked directly with the weight loss of an individual with T2DM [66, 67]. In India, for every 100 overweight adults ≥ 20 years old, there were 38 with diabetes vs. the global average of 19 adults [14]. Meal replacement therapies have demonstrated effectiveness in reducing body weight, waist circumference, and fat mass previously [68–70]. The ADA recommends using meal replacement options to substitute for breakfast or lunch in people trying to lose weight [53]. A prospective, randomized clinical study evaluating the safety and feasibility of meal replacement therapies in obese T2DM patients observed greater weight loss and significant weight reduction ($p = 0.012$) in a similar group [32]. Another prospective controlled study that compared the efficacy of a portion-controlled meal replacement diet to a standard ADA recommended diet in overweight/obese T2DM patients reported significantly greater initial weight loss and less regain after 1 year of maintenance in the meal replacement group [68]. Similar results were observed in improving obesity-related risk factors in our study using PMR. A significant decrease in the body weight and waist circumference in T2DM patients who received the DSNS versus those who did not indicates that future PMR strategies should become a part of the clinical guidelines for managing Indian patients with T2DM.

Previous studies have suggested that meal replacement may be associated with weight loss and improvements in lipid profiles in patients with T2DM [71, 72]. However, the mean changes in lipid profile in the PRIDE study were not significant for any studied parameters.

Consistent with the overall patient population, significant reduction in HbA1c, weight, BMI, and waist circumference was observed in patients who received PMR for 12 weeks across various subgroups defined by BMI, waist circumference, FPG, PPG, and HbA1c in the post hoc analysis. These subgroups capture a large spectrum of the patients with T2DM. Furthermore, the reductions from baseline at week 12 for PMR group were significantly higher versus the corresponding subgroups that received SOC. Although critical, these findings are based on post hoc subgroup analyses. Since the PRIDE

study was not sufficiently powered for these analyses and multiple comparisons were undertaken, these results must be considered with caution while interpreting the statistical significance of some of these analyses.

The strength of PRIDE is that it is the first study to evaluate the effect of PMR using DSNS, Prohance–D®, on glycemic parameters and factors impacting QoL in Indian overweight/obese T2DM patients. The PMR improved clinical endpoints such as glycemic control, anthropometric measurements, and factors impacting QoL. Moreover, the multicenter nature of the study ensured that dietary patterns could be studied in a relatively large sample size, lending credibility to the potential generalizability of the results. However, the study was limited by a lack of blinding between the study groups, which could have contributed to potential bias. Besides, the study aimed to observe a minimum of 0.5% difference in HbA1c between the test and control groups. However, as the group difference observed was 0.38%, it was found to be statistically significant ($p = 0.002$). Additionally, the inclusion criterion of patients on stable dose of non-insulin antidiabetics > 1 month was used considering the real-world nature of the study. Although this could have an impact on the effect of PMR on HbA1c, the total number of patients on stable oral antidiabetics for less than 3 months was only $\sim 10\%$ and was uniformly distributed among both groups; 8/88 in PMR and 9/88 in SOC group. This should be taken into consideration in planning future studies with DSNS and should include patients on stable OADs for at least 3 months, at study initiation. The QoL parameters were assessed using a non-standardized questionnaire and hence, additional validation is required to understand the impact of the DSNS on these parameters. Also, a long-term and controlled study would have further helped to understand the sustained benefits of PMR in this diabetic population. Although the results are encouraging in this population, long-term studies in the future could be performed to evaluate the benefits of the current PMR strategy.

CONCLUSIONS

PMR strategy utilizing DSNS accompanied by dietary counseling over 12 weeks helped improve glycemic levels, and anthropometric measurements in Indian overweight/obese T2DM patients compared to standard medical care. Overall, it was noteworthy to ascertain that most patients were very satisfied with the taste, well-being, and energy provided by DSNS, which possibly could have contributed to better treatment adherence. Attempts should be made to conduct future long-term, real-life clinical research to complement present findings and incorporate PMR strategy with DSNS into clinical guidelines in India for managing T2DM.

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Authorship Contributions. Dr. Mala Dharmalingam contributed to the study conception and design. Dr. Mala Dharmalingam, Dr. Rupam Das, Dr. Sandeep Jain, Dr. Sachin Gupta, and Dr. Manoj Gupta were the study investigators and contributed to data acquisition. Dr. Suyog Mehta, Dr. Deepak Bachani, Dr. Vinay Kudrigikar, and Dr. Sadhna Joglekar, contributed to data analysis and interpretation. All authors had full access to the data, critically reviewed the manuscript, and approved the final submitted version.

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Compliance with Ethics Guidelines. The study was conducted according to the principles and requirements of the Declaration of Helsinki and was consistent with the International Conference on Harmonization Good Clinical Practice (GCP) guidelines, the local regulatory requirements of GCP for Clinical Research in India, and the Indian Council for Medical Research guidelines (2017) for Biomedical Research on Human Subjects. The study was reviewed and approved by the Institutional Ethics Committee of each participating center. The details of ethics committees are provided in online Supplementary Table S16. All subjects provided informed consent to participate in this study. The study was explained in detail along with the potential benefits vs. risks to the patients and/or their families by the investigator. Patients and/or their families were given sufficient time to think and deliberate before consenting to participate in the study. Prior to study enrollment, duly signed and dated informed consent was obtained from each participant, in the presence of a legally accepted representative or an impartial witness.

Prior Presentation. The study was presented at the following conferences: e-poster presentation at the Diabetes India conference 11–13 June 2021. Oral presentations at: Conference of the Integrated Diabetes and Endocrine Academy—IDEACON Virtual meeting 2 July 2021. Annual Conference of Endocrine Society of India, ESICON, Bengaluru, 11th Dec 2021. International Diabetes Expert Conclave, IDEC Virtual conference, 4th Sept 2021.

Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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