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Retrospective review of seven patients with obesity simultaneously treated with a combination of a glucagon-like peptide-1 receptor agonist and a meal replacement product

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ABSTRACT

Background: The use of meal replacement products (MRPs) to obtain a caloric deficit while maintaining micro- and macronutrient requirements, has a long tradition in obesity medicine. Limitations include low compliance, variability in efficacy, adverse events (related to acute changes in nutrient intake), and risk of weight regain when discontinued, and their popularity has declined after the emergence of potent GLP-1 receptor analogues (GLP1-RAs). However, GLP-1RAs have limitations, including dose-dependent risk for adverse events (AEs), high cost, as well as weight regain when discontinued. Although concomitant use of MRPs and GLP-1RAs could address some of the limitations, there is a scarcity of data reported on this. Herein we report real world clinical experience of such combined use.

Methods: This retrospective case evaluation involved people with obesity that concomitantly used MRPs (Optifast) and a GLP-1RA and were followed at one of three weight management centers in Australia or South Africa. Parameters collected were gender, age, co-morbidities, height, weight, frequency/amount of MRPs used, dose/type of GLP-1RA used, duration of combined use, and occurrence of AEs. Written informed consent for use of data was obtained from each individual, and the data were managed in an anonymized form and summarized descriptively.

Result: A total of seven (5 females) individuals (mean [min, max] age 49 [30,66] years, BMI 44.8 [30.7, 57.9] kg/m^2) initiated either semaglutide (n=4) or liraglutide (n=3) concomitantly with daily MRPs (starting number of servings/day 2.7 [1,6]) for a duration of 12 [4, 25] months. Change in weight/BMI/% TBW was -32.0 (-9.6, -77.8) kg/-10.3 (-3.4, -24.5) kg/m^2/-24.2 %. Five individuals experienced ≥1 GLP-1RA related AE (nausea, reflux, burping, diarrhea, constipation). One individual discontinued GLP-1RA, whereas two persons discontinued the use of MRPs.

Conclusions: MRPs can be initiated concomitantly with a GLP-1 RA for weight management. This might enhance weight-loss effectiveness, with potential additional benefits that should be elucidated in further and larger studies.

1. Introduction

Meal replacement products (MRPs) have been available for a long period [1], and offer a controlled and nutritionally balanced alternative to regular meals, for individuals to manage their caloric intake while ensuring they receive essential nutrients. These products are designed to be low in calories yet fortified and rich in protein, fiber, vitamins, and minerals. Adequate consumption of protein during weight loss may be of particular importance, as this support weight loss while preserving lean muscle mass [2]. Use of MRPs can facilitate a significant weight-loss (>10 % of body weight) as well as improvement in liver health and cardiovascular (CV) risk factors [3]. Their use in weight management have been adopted into several guidelines across the world [4,5] and the typical applications are either as part of a comprehensive total diet

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replacement (TDR) program (where these products represent the sole source of nutrition, typically intended to last for a specific period of time) or used in less intensive settings (e.g., taken one to three times daily in place of specific meals or snacks, or one to two days/week in combination with other foods and meals) as part of a weight maintenance phase. Challenges with the use of MRPs include long-term adherence, adverse events (related to acute changes in nutrient intake, in particular in the early phases when used as TDR), like risk for gastrointestinal side effects, fatigue, lightheadedness, gallstones, and potential dehydration. In case of incompliant use, nutrient deficiencies may also be experienced, although, if used adequately, typically micronutrient status improve due to the fortification [6]. Furthermore, there is also a risk for weight-regain when the products are discontinued [7,8], owing to the numerous biological adaptations that occur [9], such as increased hunger and enhanced perception of food palatability, reduced satiety and resting energy expenditure, and risk for "MRP" fatigue (e.g., taste, lack of variability) [1]. Over the past decade, there has been a rapid growth in use of glucagon-like peptide -1 (GLP-1) receptor analogues (GLP-1 RAs), a pharmaceutical medication also shown to deliver ≥10 % loss of bodyweight. GLP-1RAs predominantly act centrally and thereby reduce appetite and increases satiety [10,11], thus contribute to a reduced caloric intake, although the contribution of their direct effects on slowing gastric emptying should also be acknowledged [12]. GLP-1 RAs are associated with nausea, vomiting, diarrhea, and pancreatitis. Sometimes these effects can be severe [12,13]. Also reported have been injection site pain and a small to moderate increase in heart rate. When discontinuing GLP-1 RAs, many experience weight rebound [14]. The cost of this medication varies from market to market, but is relatively high, and in many markets, the medications are not reimbursed when prescribed for obesity. This has raised concerns around disparity in medication accessibility [15]. Combining a GLP-1RA with MRPs may represent a promising approach to weight management, as this combination could leverage the appetite-suppressing effects of GLP-1RAs alongside the convenience and nutritional control of meal replacements. This dual approach could also potentially lead to more significant and sustainable weight loss by addressing both physiological and behavioral aspects of eating. It can be particularly effective for individuals struggling with portion control, overeating, fatigue, or those who have difficulty adhering to traditional diet plans. However, there is a scarcity of data reported on this, and herein we report real world clinical experience of such combined use with a focus on 7 patients whose initial treatment included the concomitant use of a GLP-1 RA and a MRP. Additional information is provided regarding 2 patients treated with sequential use of a MRP followed by a GLP-1 RA, and 2 patients treated with a GLP-1 RA and a MRP used in conjunction with bariatric surgery.

2. Methods

2.1. Design

This was designed as a non-systematic retrospective chart review of data from individuals with obesity who were followed at a weight management center experienced in treating people with obesity (PwO), and who had received combined treatment with MRPs (as partial or full low or very low caloric MR diet [LCD, VLCD]) and a GLP-1RA indicated for obesity management, either concomitantly or sequentially, with the aim to generate a case series. The retrospective chart review was considered a quality practice evaluation and the MRPs in focus was Optifast (Nestlé Health Science, Vevey, Switzerland; Table 1). The report followed the CARE case report guidelines (care-statement.org).

2.2. Participants and parameter evaluation

The health care professionals (CB, TLS, SR) from each center (two in Australia, one in South Africa) involved in this quality evaluation, reviewed data from individuals ≥18 years living with obesity, that had received a combined treatment of MRPs and a GLP-1RA indicated for weight management, within the last 30 months prior to Feb 15, 2024 in one of the following constellations: 1) MRP use before starting a GLP-1RA, and continuing on a combined regimen, 2) initiation of MRPs and a GLP-1RA concomitantly, or 3) addition of MRPs to ongoing GLP-1RA treatment. Parameters collected and evaluated were sex, ethnicity, age, onset age of start of obesity, current presence of co-morbidities (atrial fibrillation [AF], gastrointestinal reflux disease [GERD], obstructive sleep apnoea [OSA], metabolic associated fatty liver disease [MAFLD], osteoarthritis [OA], type 2 diabetes [T2D], polycystic ovary syndrome [PCOS], atrial fibrillation [AF], heart failure [HF], or CV disease), smoking habits, height, weight, frequency and amount of MRPs used, dose and type of GLP-1RA used, duration of combined or sequential use, occurrence of AEs, and data on compliance. At the time when this evaluation was conducted, liraglutide (Novo Nordisk, Bagsværd, Denmark) and semaglutide (Novo Nordisk, Bagsværd, Denmark) had been approved for weight management in Australia, and liraglutide in South-Africa. All centers had experience in using the specific MRPs in focus as part of a partial or full LCD or VLCD. Written informed consent for use of data was obtained from each individual, and the data were managed in an anonymized form and summarized descriptively. Graphical displays were generated using GraphPad Prism 5 (GraphPad Software, Boston, MA, USA), and summary statistics were performed in Excel (Microsoft Office).

Table 1
Nutrient composition (non-exhaustive) of select MRPs used by participants (per serving).

	VLCD Shake, 53g[a] (Australia)	Cereal bar, 65g[b] (Australia)	VLCD Shake[c], 53 g (South-Africa)
Energy	250 Cal	210 Cal	201 Cal
Protein	28 g	19.2 g	20 g
Fat total	5.6 g	5.2 g	4.5 g
Saturated fat	0.8 g	1.0 g	0.9 g
Carbohydrate	20 g	22.1 g	18.2 g
Sugars	1.9 g	5.2 g	10.1 g
Dietary fibre	3.6 g	5.9 g	3.6 g
Sodium	270 mg	405 mg	220 mg
Vit A	320 ugRE	338 ugRE	345 ugRE
Thiamin	0.60 mg	0.46 mg	0.58 mg
Vit B6	1.2 mg	0.9 mg	1.0 mg
Vit B12	1.5 ug	1.4 ug	1.1 ug
Vit C	40 mg	46 mg	40 mg
Vit D	3.4 ug	2.6 ug	3.7 ug
Vit E	7.0 mgTE	5.6 mgTE	7.4 mgTE
Vit K	36 ug	31 ug	32 ug
Zn	4.5 mg	5.1 mg	4.2 mg

[a] Coffee flavour.
[b] With cranberry.
[c] : strawberry flavour.

3. Results

3.1. Characteristics of cases

A total of 11 individuals (Table 2) were included in this chart review. There were seven individuals (5 females, mean [min, max] age 49 [30,66] years, BMI 44.8 [30.7, 57.9] kg/m^2) that had MRPs and GLP-1RA (three with semaglutide and four with liraglutide) initiated at the same time, whereas two (both females, age and BMI 57 and 59 years, and 34.9 and 47.3 kg/m^2, respectively) had a one month lead-in phase with MRPs, before receiving GLP-1RA (liraglutide and semaglutide, respectively). Two individuals (one male [age 34, BMI 64.2 kg/m^2], one female [age 25, BMI 49.9 kg/m^2]), had pre-bariatric surgery use of GLP-1RA, where MRPs were added on top of this as part of a pre—and perioperative strategy to reduce liver fat, or to generally prepare for

Table 2
Baseline demographics of all individuals receiving intervention with Optifast meal replacement products (MRPs) or a GLP-1 receptor analogue sequentially or concomitantly. Summary row depicts n (%) for categorical variables or mean (SD) for continuous variables.

	Sex	Ethnicity	Age, yrs	Age at onset of obesity, yrs	Height, cm	BMI, kg/m^2	Comorbidities					
							GERD	OSA	MAFLD	OA	T2D	Other(s)
Concomitant use: MRPs and GLP-1RA												
#1	M	White	63	16	168	36.7	Y	Y	N	Y	Y	HT
#2	F	White	30	25	164	30.7	N	N	N	N	N	Fibromyalgia, Fatigue
#3	M	White	53	5	189	57.9	Y	Y	Y	N	N	HT, binge eating,. dyslipidaemia
#4	F	White	67	52	166	38.5	N	N	Y	Y	Y	Anxiety
#6	F	White	50	46	160	40.9	N	N	N	Y	N	NR
#8	M	White	42	NR	175	56.5	N	N	Y	N	N	NR
#9	F	White	40	29	165	52.5	N	N	Y	N	N	Hypothyroidism
Summary	F: 4/7 (57 %)	White: 7/7 (100 %)	49 (13)	28 (18)	171 (9)	44.8 (10.7)	Y: 2/7 (29 %)	Y: 2/7 (29 %)	Y: 4/7 (57 %)	Y; 3/7 (43 %)	Y: 2/7 (29 %)	N/A
Sequential use: MRPs followed by MRPs and GLP-1RA												
#5	F	White	59	50	148	34.9	N	Y	N	N	N	NR
#7	F	White	57	20	169	47.3	N	N	N	N	N	NR
Summary	F:2/2 (100 %)	White: 2/2 (100 %)	58 (2)	35 (21)	159 (15)	40.1 (10.1)	Y: 0/2 (0 %)	Y: 1/2 (50 %)	Y: 0/2 (0 %)	Y; 0/2 (0 %)	Y: 0/2 (0 %)	N/A
MRPs and GLP-1RA used in conjunction with bariatric surgery												
#10	M	Black	34	23	168	64.2	N	Y	Y	N	N	HT
#11	F	White	25	8	166	49.9	Y	N	Y	N	N	Dyslipidaemia, hyperuricemia
Summary	F: ½ (50 %)	White: 1/2 (50 %)	29.5 (6.4)	15.5 (10.6)	167 (1)	57.1 (10.1)	Y: 1/2 (50 %)	Y: 1/2 (50 %)	Y: 2/2 (100 %	Y: 0/2 (0 %)	Y: 0/2 (0 %)	N/A

Abbreviations: F - Female, M−male; yrs – years, NR – not reported, Y – yes, N -no, HT – hypertension, GERD – gastroesophageal reflux disease, OSA – obstructive sleep apnoea, MAFLD – metabolic fatty liver disease, OA – osteoarthritits, T2D – type 2 diabetes, N/A – not applicable.

surgery with liquid meals, as aligned with some recommendations [16]. Across these use-case series, most were "never-smokers" (82 % [9/11]), and comorbidities were relatively prevalent (27 % [3/11] reported GERD, 36 % (4/11) OSA, 55 % (6/11) MAFLD, 18 % (2/11) OA, and 18 % (2/11) T2D). None had AF or HF, but one individual had a previous CV event, and one female had PCOS. Age of onset of obesity varied overall, with mean (min, max) age 27 (5,52) years. Two had onset in childhood (respectively, 5 and 8 years).

3.2. Interventional details and outcome evaluation of sequential or concomitant use of MRP and GLP-1RA

The seven individuals that used either semaglutide (n=4) or liraglutide (n=3) in combination with daily MRPs (mean [min, max] starting number of servings/day 2.7 [1,6]), used this for a mean duration of 12 [4, 25] months (Table 3). The two GLP-1RAs were dose-titrated according to recommendations, and number of MRPs consumed per day, generally declined over the period. After initiation and until end of observation, change in weight/BMI was -32.0 (-9.6, -77.8) kg/-10.3 (-3.4, -24.5) kg/m^2 (Figs. 1 and 2). This represents an average reduction of -24.2 % in body weight. Owing to a higher baseline weight in men, we observed a difference in total amount of weight reduction across genders (females: -14.3 (4.6) kg/- 5.1 (1.6) kg/m^2; males: 76.5 (1.9) kg/– 23.2 (1.9) kg/m^2). A total of 71.2 % (5/7) of individuals experienced ≥1 GLP-1RA related AE (nausea, reflux, burping, diarrhea, constipation), but only one individual discontinued GLP-1RA, and two MRPs (Table 3). The discontinuation of GLP-1RA was due to financial constraints, and the discontinuation of MRPs financial constraints and taste-fatigue. Noteworthy individual observations include Case #1, who had an improvement in HbA1c (7.0 to 5.3 %) as well as in lipid- and renal parameters, and in knee pain. Case #2 also observed improvements in lipid parameters, and reported a high satisfaction with the use of MRPs given that fatigue was a comorbidity. Case #3 had meaningful improvements in blood pressure, as well as in OSA symptoms. Amongst the two individuals that used MRPs as a one-month lead-in before initiating GLP-1RA, weight reduction was meaningful during the first month (-4.2, and – 5.1 kg, respectively), but were >10 kg during the combined use phase, with observation periods of 10 months for case #5, and 4 months for case #7. One of these individuals (case #5) continued the combined use and had no notable AEs, whereas one discontinued GLP-1RA due to intolerable nausea, and continued only on MRPs. The third category of use cases involve two individuals (case #10 and #11) who were deemed candidates for bariatric surgery, that where recommended treatment with GLP-1RA ahead of surgery. Case #10 used GLP-1RA for a period of 7 months ahead of surgery, where the two last month included a combination with MRPs with the intent to reduce MAFLD burden. For this individual, GLP-1RA was discontinued prior to surgery, whereas MRPs were continued for another month as part of a liquid diet introduction. During all these phases, there were meaningful weight reductions, that was magnified post-surgery (Table 3). Case #11 used a GLP-1RA for 12 months prior to surgery, and MRPs were added as a part of the perioperative regimen, with initiation 14 days before surgery, that continued 2 months after. None of these individuals continued either product, and also did not report any AEs.

4. Discussion

This retrospective review illustrate that a sequential or concomitant use of two evidence based medicine principles for weight management, i.e., a medical nutrition therapy approach using MRPs (i.e., here a nutrient-fortified formulation that can adequately meet recommended vitamin, mineral and protein intakes for many adults) to facilitate a caloric deficit, and GLP-1RAs is feasible in real-life, and that this combination might offer potential advantages. An average reduction of -24.2 % in body weight as seen in this report is typically larger than what is seen with each modality individually [3,17]. There also do not appear

Table 3
Interventional details and outcome evaluations of all individuals receiving intervention with Optifast meal replacement products (MRPs) or a GLP-1 receptor analogue sequentially or concomitantly. Summary row depicts n (%) for categorical variables or mean (SD) for continuous variables.

	Weight at start, kg	BMI at start, kg/m^2	#MRPs at start, n	GLP-1RA and starting dose	Duration of use, months	Weight change at end of observation, kg	BMI change at end of observation, kg/m^2	AE, description	Regimen cont? Yes, No, Description
Concomitant use: MRPs and GLP-1RA									
#1	103.5	36.7	2	Sema/ 0.25 mg QW	4	−18.2	−6.4	Nausea Diarrhea	Yes
#2	82.5	30.7	2	Sema/ 0.25 mg QW	4	−9.6	−3.6	Nausae Burping	Yes
#3	206.8	57.9	3	Sema/ 0.25 mg QW	24	−77.8	−21.8	Reflux worsened	Only GLP-1
#4	106.0	38.5	1	Lira/ 0.6 mg OD	13	−9.5	−3.4	Constipation	Yes
#6	110.0	40.9	2	Lira/ 0.6 mg OD	7	−14.9	−5.5	No	Yes
#8	173.0	56.5	3	Lira/ 0.6 mg OD	25	−75.1	−24.5	No	No
N/A#9	148.3	52.5	6	Lira/ 0.6 mg OD	6	−19.1	−6.8	Nausea	Yes
Summary, all	132.8 (44.6)	44.8 (10.7)	2.7 (1.6)	N/A	12 (9)	−32 (30)	−10.3 (8.9)	Any AE: 5/7 (71 %)	Y: 5/7 (71 %)
Sequential use: MRPs followed by MRPs and GLP-1RA									
#5	76.4	34.9	2	Lira/ 0.6 mg OD[a]	10 (1 month MRP alone; 9 months combined)	−12.4 (-4.2 (MRP alone; additonal −8.2 (combined)	−5.7 (-1.9 MRP alone; additional -3.7 combined)	No	Yes
#7	135.0	47.3	4	Sema/ 0.25 mg QW	4 (1 month MRP alone; 3 months combined)	−12.9 (-5.1 MRP alone; additional -7.8 combined)	−4.5 (-1.8 MRP alone; additional -2.7 combined)	Nausea	Only MRP
Summary, all	105.7 (41.4)	41.1 (8.8)	3 (1)	N/A	7 (4)	−12.7 (0.3)	−5.1 (0.8)	Ane AE: 1/2 (50 %)	Y: 1/2 (50 %)
MRPs and GLP-1RA in conjunction with bariatric surgery									
#10 GLP-1 RA run in	181.1	64.2	N/A	Lira/ 0.6 mg OD	5 (prior surgery)	−15.6	−5.5	No	No
#10 MRPs to reduce MAFLD	165.5	58.6	3 for 1st month 1 for 2nd month	Lira/ 3.0 mg OD	2 (prior surgery)	−4.4	−1.6	No	No
#10 Post surgery	161.1 (on day of surgery)	57.1	2	N/A	1 (post surgery)	−11.5	−4.1	Taste alteration	No
#11 GLP-1 RA run-in	137.6	49.9	N/A	Lira/ 0.6 mg OD	12	−10.6	−3.8	No	No
#11 MRPs peri-operative (-14 days-2 months)	127.0	46.1	1	N/A	2	−10.5	−3.8	No	No

[a] Swapped to semaglutide approximately 3 months into treatment due to supply issues with liraglutide, N/A – not applicable; Lira – liraglutide, Sema – semaglutide, QW, once weekly, OD – once daily.

to be an increased rate of AEs compared to what is reported from GLP-1RAs as a class [12,13]. There are several reports from randomized controlled clinical trials (RCTs) that support a combinatory approach, however, most of these are short-term. For example, the use of MRPs to induce weight reduction and then subsequently use a GLP-1RA for weight maintenance has been reported in the SCALE Maintenance study (n=422), where a 6 % weight reduction achieved with the LCD was better maintained, or enhanced, with 3.0 mg liraglutide compared with placebo at week 56 [18]. Another smaller RCT (n=52), where weight reduction was -12 % after 8 weeks with MRP, suggested that a low-dose of liraglutide (i.e. 1.2 mg) was efficacious to maintain this weight loss over 1 year [19]. Some RCTs that illustrate concomitant initiation include STEP-3 (n=611), where it was observed that the weight reducing efficacy of 2.4 mg semaglutide at week 8 was enhanced when combined with a MR strategy (1000-1200 kcal/d as liquid shakes, meal bars, portion-controlled meals) compared to MRs alone [20]. Unfortunately, this combinatory approach was stopped at week 8, and there is no solid data on the potential long-term benefits of such a combined approach, although a slightly longer (12 weeks) but much smaller RCT (n=19) involving people with T2D with BMI >27 kg m^2, also support such benefit of an initial combination. This RCT had three interventions: semaglutide 1 mg (n=7), 800 kilocalorie/day VLCD (n=7), or a combination of semaglutide and VLCD (n=5), and although all groups demonstrated weight reduction, the largest reduction was seen with the combination of VLCD and semaglutide (-14.9 kg vs- 6.4 kg with semaglutide alone, p<0.01) [21]. Illustration of weight effects from RCTs that assess effects of adding MRPs to ongoing GLP-1RAs are found in a US-study (n=150) that evaluated whether 12-weeks with MRPs, when added during weeks 4-16 to an intensive behavioral therapy (IBT) program plus liraglutide (3.0 mg) could provide an incremental weight loss to either IBT alone or IBT plus liraglutide alone, found a weight loss at week 24 of 12.2 % when the MRP component was considered, compared with 10.1 % for the IBT + GLP-1 RA [22]. There is a limited amount of data reported on any constellations of combined use of GLP-1RAs and

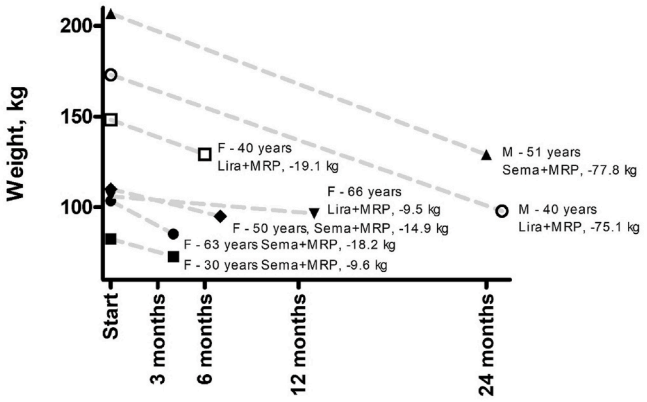

Fig. 1. Weight trajectories (kg) of individuals starting Optifast MRPs and GLP-1 concomitantly
AbbreviationsF – female, M−male, Lira – liraglutide, Sema – semaglutide, MRPs – meal replacement products.

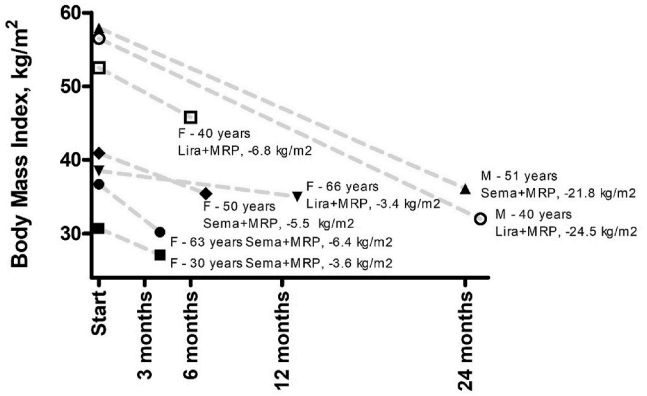

Fig. 2. BMI trajectories (kg/m^2) of individuals starting Optifast MRPs and GLP-1 concomitantly
Abbreviations: F – female, M−male, Lira – liraglutide, Sema – semaglutide, MRPs – meal replacement products.

MRP in real life, however, one recent US study reported on MRPs combined with GLP-1RAs, suggested that this combination (n=28) could help to reduce risk of weight regain over 18 months compared to using MRPs alone (n=139) [23]. Thus, there appear to be several opportunities for a combinatory approach in weight management. Future research, of which some are ongoing, should 1) include evaluation of potential long-term effectiveness (>6 months), including assessment of weight stability, and whether 2) the relatively high protein content (as well as other micro/macro nutrients) typically found in the MRPs maintain lean mass better, 3) there could be potential synergistic or additive benefits on CV risk factors, and 4) this combinatory approach could lead to lower required dose of GLP-1 RA, which could have implications for compliance, cost and access to, and risk for GLP-1RA related AEs. Studies should also evaluate if weight reduction induced with GLP-1RAs, could be maintained in the long-term with MRPs.

5. Limitations

This assessment was based on a very limited number of cases, and interpretation needs caution. Importantly, duration of intervention was highly variable, and there was a lack of information on confounding parameters of importance (e.g., nutritional habits, details on amount of MRPs consumed, exercise habits, psychological behavioral support). Such a retrospective case evaluation involving a small sample size, with predominantly white women, thus provides a low degree of reassurance [24], however, we believe it provides some useful insights for practitioners and future studies.

6. Conclusion

MRPs can be initiated concomitantly with a GLP-1 RA for weight management. This might enhance weight-loss effectiveness, with potential additional benefits of improving long-term adherence. Further and larger studies are needed.

Key takeaways.

- MRPs can be initiated concomitantly with a GLP-1 RA for weight management.
- A combinatory approach might enhance weight-loss effectiveness, with potential impact on long-term adherence for both modalities
- Future research should address long-term effectiveness and compliance (incl adverse events, optimal dose of GLP-1 RA and frequency of MRPs use), impact on body composition, and potential synergistic or additive benefits on CV risk factors

CRediT author statement

The concept of this submission was by OEJ. Data curation was performed by CB, TLS and SR. First draft writing was by OEJ and all reviewed, edited subsequent versions, and approved the final submission.

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This study was funded by NHSc and CB, TLS, and SR received standard fees to compensate for the time it took to collect the data. NHSc had no influence on the selection of the interventions, or clinical considerations, for the individuals.

Ethics review

The was a retrospective case evaluation with the intent to review quality of services. Written informed consent for use of data was obtained from each individual, and the data were managed in an anonymized fashion.

Declaration of artificial intelligence (AI) and AI-assisted technologies

No AI or AI-assisted technologies were used for this submission.

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