Author/s:
Cheng, J;Nolan, BJ;Sumithran, P

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Date:
2022-11-01

Citation:
Cheng, J., Nolan, B. J. & Sumithran, P. (2022). Retrospective analysis of an intensive medical weight loss program in adults with obesity and severe or end-stage chronic kidney disease. Journal of Nephrology, 35 (8), pp.2165-2167. https://doi.org/10.1007/s40620-022-01445-3.

Persistent Link:
https://hdl.handle.net/11343/332344

Retrospective analysis of an intensive medical weight loss program in adults with obesity and severe or end-stage chronic kidney disease

Jingyi Cheng[1], Brendan J. Nolan[2,3], Priya Sumithran[2,4*]

1. Melbourne Medical School, University of Melbourne, Parkville, Australia
2. Department of Endocrinology, Austin Health, Heidelberg, Australia
3. Department of Medicine (Austin), University of Melbourne, Heidelberg, Australia
4. Department of Medicine (St Vincent's), University of Melbourne, Fitzroy, Australia

Word count: 795

Correspondence:

Dr Priya Sumithran
Clinical Sciences Building, Level 4
St Vincent's Hospital
Fitzroy, Vic., 3065
Australia
priyas@unimelb.edu.au
+61 3 9231 2592

Keywords

Chronic kidney disease; obesity pharmacotherapy, very low energy diet, weight loss

Obesity is an independent risk factor for the development and progression of CKD [1]. There is a lack of data examining whether intensive medical obesity management, such as very low-energy diets (VLEDs) and obesity medications, are safe and efficacious in people with severe (glomerular filtration rate [GFR] <30 ml/min/1.73m^2) and end-stage (GFR <15 ml/min/1.73m^2 or dialysis-dependent) renal disease (ESRD). The use of such interventions is particularly challenging in this population, due to restrictions on the intake of protein and fluids, renal excretion of several obesity medications, and the risk of sarcopenia with rapid weight loss.

This retrospective evaluation reports clinical outcomes in people with severe CKD or ESRD who attended an outpatient obesity treatment service at a tertiary hospital in Melbourne, Australia between October 2018 and July 2021 and were prescribed a VLED and/or medications for obesity management. These medications included liraglutide, phentermine (approved in Australia for obesity management), topiramate and semaglutide (approved in Australia for indications other than obesity). Patients were reviewed every 6-8-weeks, and biochemical monitoring was done at the discretion of the treating specialist. Data were extracted from electronic medical records. For patients who underwent the same intervention more than once during follow-up, the attempt with the largest weight loss was used for weight outcomes and each attempt was considered separately for identification of adverse events.

Eighteen patients with severe or end-stage CKD attended the service during the study period, of whom 14 commenced an intensive medical intervention (supplementary Figure s1, Table s1). Median maximal weight loss was 15.9 kg (IQR, 5.0-22.3), or 13.5% (IQR 4.8-16.9), over a median of 34 weeks (range, 8-626). At last follow-up (median 120 weeks, range, 14-626), median weight loss was 7.7 kg (IQR, 4.7-20.2), or 7.1% (IQR 4.4-11.5).

Figure 1 shows the maximal weight loss for each patient using VLED and pharmacotherapy alone and in combination. Patients using VLED alone had a median maximal weight loss of 13.7 kg (IQR, 6.0-20.4) or 7.8% (IQR, 5.4-13.8) over median 18 weeks, and those who started with VLED alone and

subsequently added pharmacotherapy (n=3) lost an additional median 4 kg (range, 0.0-12.2), or 2.6% (range, 0.0-10.5). GLP-1 receptor agonists (GLP-1RA) were the most commonly prescribed agents as monotherapy, and were associated with weight loss of 3% (range, 2.1-4.3). Pharmacotherapy outcomes are shown in supplementary Table s2. Eleven adverse effects were reported in 5 patients (summarised in supplementary Table s3).

The main findings of this retrospective analysis of real-world clinical data are that VLEDs alone were associated with a median maximal weight loss of 7.8% over a median of 18 weeks with few adverse effects, and addition of obesity medications resulted in additional weight loss with a higher incidence of adverse effects. This weight loss is consistent with previous reports of VLED in patients on haemodialysis [2]. One participant in the present study discontinued the VLED due to hyperkalemia despite addition of an ion-exchange resin (Resonium). Hyperkalemia was also the most common adverse effect noted in the report by Woods et al [2].

To our knowledge, there are no published studies reporting on the use of centrally-acting medications approved for the treatment of obesity in people with stage 5 or dialysis-dependent ESRD. In our patient cohort, the ~3% weight loss associated with liraglutide (0.6 mg-2.4 mg daily) and semaglutide (0.25 mg-0.5 mg weekly), and predominance of transient gastrointestinal adverse events, are consistent with outcomes reported when these medications are used in the treatment of type 2 diabetes in people with stage 4 or 5 CKD [3].

The magnitude of weight loss achieved with intensive medical interventions in this cohort has demonstrated clinical benefits [4]. However, it is worth noting that the 15 of the 18 patients were referred for the purpose of reaching BMI $\leq$35 kg/m^2, a widely-used criterion for eligibility for deceased donor kidney transplantation, and only 4 patients attained this goal. Until highly effective medications demonstrate safety and efficacy in this population, bariatric surgery is likely to be the treatment of

choice for this purpose, although whether the application of BMI targets in eligibility criteria improves the outcomes of kidney transplantation is a separate question that remains unanswered [5].

The major limitations of this study are that the data are drawn retrospectively from clinical practice, clinical information and biochemical testing was collected and documented at irregular follow-up times in a non-standardised way, and body composition data were not available. Nonetheless, to our knowledge this is the largest cohort of patients with ESRD in whom the use of medication for obesity management has been reported, and as such, provides important information on weight outcomes and adverse effects. Future clinical trials in people with ESRD should examine effects of weight loss on fluid and electrolyte balance and body composition, due to the particularly high risk of sarcopenia in this population.

Disclosures: B.J.N. reports fees from iNova pharmaceuticals for lectures unrelated to the submitted work. P.S. reports fees from Novo Nordisk for a lecture on obesity unrelated to the submitted work. J.C. has no conflicts of interest to declare.

Ethical approvals: This analysis was approved by Austin Health Office for Research as an audit. Individual consent was not obtained from participants.

Acknowledgements: This work received no specific funding. B.J.N. is supported by a Postgraduate Scholarship (2003939) from the National Health and Medical Research Council (NHMRC). P.S. is supported by an Investigator Grant (1178482) from the NHMRC.

Data availability: The data underlying this article are available in the article

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Figure 1: Percentage weight change associated with different interventions

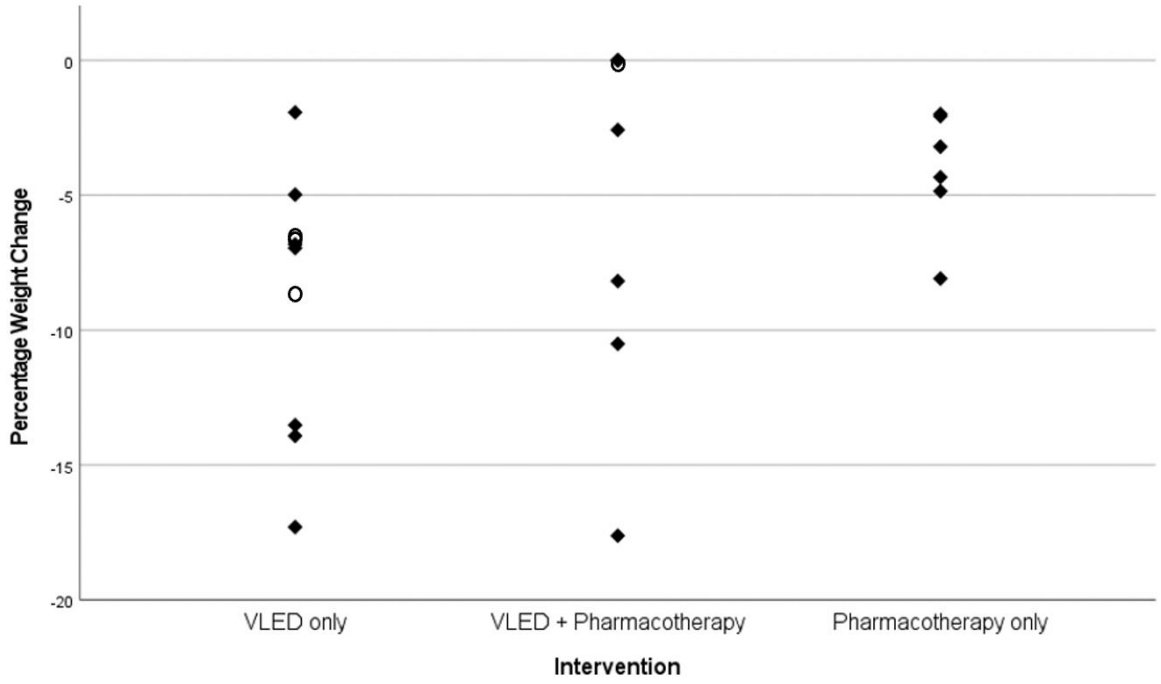

Fig. 1 Dot plot representing the maximal percentage weight change associated with VLED only, VLED and concurrent pharmacotherapy, and pharmacotherapy only. Diamonds indicate individuals with dialysis-dependent CKD (*n*=11) and circles indicate individuals with ESKD (*n*=3). Percentage weight change was calculated at maximal weight loss (nadir weight) with each intervention. Pharmacotherapy used with VLED included liraglutide monotherapy (*n*=2), liraglutide and topiramate (*n*=2) and phentermine-topiramate (*n*=2); pharmacotherapy only refers to semaglutide (*n*=1), topiramate (*n*=1), liraglutide monotherapy (*n*=2) and liraglutide and topiramate (*n*=1).