

Editorial

Weight Loss Drugs: Striking the Balance Between Benefits and Risks

Raja D

Professor, Department of Community Medicine, Chettinad Hospital & Research Institute, Chettinad Academy of Research & Education, Kelambakkam, Chengalpattu District, Tamil Nadu, India.

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I N F O

E-mail Id:

rajanasekaran@gmail.com

Orcid Id:

<https://orcid.org/0000-0002-4571-0407>

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E D I T O R I A L

Obesity is a complex and chronic condition with significant health implications, including an increased risk of cardiovascular diseases, type 2 diabetes, and certain cancers. The rising prevalence of obesity necessitates effective treatment strategies. While lifestyle modifications like diet and exercise remain foundational, pharmacotherapy has emerged as a crucial adjunctive treatment.¹ This article explores the balance between efficacy and safety in the pharmacotherapy of obesity.

Efficacy of Weight Loss Medications

The efficacy of weight loss medications is primarily measured by their ability to achieve and maintain clinically significant weight loss, typically defined as a reduction of 5–10% of initial body weight. Several classes of medications have been approved for obesity treatment, each with varying mechanisms of action and efficacy profiles.

- 1. GLP-1 Receptor Agonists:** Glucagon-like peptide-1 (GLP-1) receptor agonists, such as liraglutide and semaglutide, have shown substantial efficacy in weight reduction. In clinical trials, patients treated with semaglutide achieved an average weight loss of around 15% of their initial body weight. GLP-1 receptor agonists enhance satiety and reduce appetite, contributing to their effectiveness.²
- 2. Lipase Inhibitors:** Orlistat, a lipase inhibitor, reduces dietary fat absorption by approximately 30%. While effective in promoting modest weight loss (5–7% of body weight), its gastrointestinal side effects, such as steatorrhea and flatulence, can limit its long-term use.³
- 3. Sympathomimetic Agents:** Phentermine, a sympathomimetic amine, has been used for short-term weight management. It acts as an appetite suppressant, leading to a weight loss of 5–10% of body weight over a few months. However, its potential for abuse and cardiovascular side effects necessitate careful monitoring.⁴
- 4. Combination Therapies:** Combining medications can enhance weight loss efficacy, for example, phentermine/ topiramate ER combines an appetite suppressant with an antiepileptic agent,

resulting in greater weight loss than either drug alone. In trials, patients achieved an average weight loss of up to 10–12% of their initial body weight.⁵

Safety Considerations

The safety of weight loss medications is a paramount concern, as the benefits of weight reduction must be weighed against potential adverse effects. Long-term safety data are essential for ensuring that these medications do not pose significant health risks.

- 1. Cardiovascular Risks:** Cardiovascular safety is a critical consideration for weight loss medications, particularly those with sympathomimetic properties. Medications like phentermine can increase heart rate and blood pressure, necessitating monitoring and caution in patients with pre-existing cardiovascular conditions.⁴ The drug agencies mandate cardiovascular outcomes trials for new obesity drugs to ensure they do not increase the risk of major adverse cardiovascular events.
- 2. Gastrointestinal Side Effects:** Medications such as orlistat can cause significant gastrointestinal discomfort, leading to poor adherence. Managing these side effects with dietary adjustments can help improve tolerability and adherence.³
- 3. Psychiatric Effects:** Some weight loss medications have been associated with psychiatric side effects, including mood changes, anxiety, and insomnia, for instance, phentermine/topiramate ER has been linked to cognitive and mood disturbances, highlighting the need for patient education and monitoring.⁵
- 4. Endocrine Effects:** GLP-1 receptor agonists, while effective, can cause endocrine side effects such as pancreatitis and thyroid C-cell tumours in rodents. Human studies have not conclusively shown an increased risk of these conditions, but ongoing surveillance is necessary.²

Balancing Efficacy and Safety

Achieving a balance between efficacy and safety in obesity pharmacotherapy involves several strategies:

- 1. Personalised Treatment Plans:** Tailoring treatment plans to individual patient profiles can optimise efficacy while minimising risks. Factors such as baseline cardiovascular risk, comorbid conditions, and potential for medication interactions must be considered.
- 2. Comprehensive Monitoring:** Regular monitoring of patients on weight loss medications is crucial. This includes tracking weight loss progress, assessing for adverse effects, and making necessary adjustments to the treatment regimen.

- 3. Patient Education:** Educating patients about the potential side effects of weight loss medications and the importance of adherence to prescribed therapies is vital for achieving desired outcomes. Patients should be informed about the signs and symptoms of serious adverse effects and when to seek medical attention.
- 4. Combination Therapy Approaches:** Utilising combination therapies can enhance efficacy while potentially reducing the dosage and side effects of individual medications, for instance, combining lower doses of phentermine with topiramate can achieve substantial weight loss with a potentially lower risk of adverse effects compared to higher doses of monotherapy.⁵
- 5. Post-Marketing Surveillance:** Continuous post-marketing surveillance and reporting of adverse events contribute to a better understanding of the long-term safety profiles of weight loss medications. Regulatory agencies like the Food and Drug Administration (FDA) play a crucial role in monitoring and addressing safety concerns as they arise.

Conclusion

Pharmacotherapy for obesity offers a valuable tool in the management of this complex condition, complementing lifestyle interventions. While the efficacy of weight loss medications has been demonstrated in clinical trials, their safety profiles require careful consideration and monitoring. A balanced approach, incorporating personalised treatment plans, comprehensive monitoring, patient education, and post-marketing surveillance, is essential to maximise the benefits and minimise the risks of obesity pharmacotherapy. Ongoing research and development of new medications will continue to enhance our ability to treat obesity effectively and safely.

Conflict of Interest: None

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