PERSPECTIVE

Flirting with Fire: The Fight against Fat and Fate

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Obesity or more simply put, fatness, has become a global epidemic. Changes in our environment, lifestyle and diet, have led to modifications in our barophenotype, and our health. To counteract these unwanted consequences, we now have a widening variety of glucagon-like peptide-1 receptor agonist (GLP-1RA) drugs. Earlier limited to monopeptide agonists, this class now includes dual and triple peptide agonists. Currently available drugs such as liraglutide, semaglutide, and tirzepatide, are characterized by enviable efficacy, strong safety signals, and a track record of tolerability. Data is available regarding their sustainable action, cardio-renovascular benefits and long-term beneficence[1].

In spite of this, concerns have been raised regarding their usage and utility. Health economists bemoan the burgeoning costs of medicare, celebrity nutritionists and exercise enthusiasts decry the lack of self-discipline, while pharmacovigilance experts point to unexpected adverse events such as acute ischemic optic neuritis (AION)[2,3]. These cautionary messages, which may be valid for particular persons, in specific situations, tend to get amplified and generalized. For those who are unable to interpret the correct science, it may seem as if every GLP-1RA, and all obesity medications, are harmful for each and every individual.

This, however, is untrue. Obesity treatment is expensive, but the management of obesity and its related complications is even more unaffordable. Data show that obesity contributes to a significant health expenditure worldwide[4]. This cost is not because of obesity *per se*. Rather, it is incurred due to the cardiometabolic, musculoskeletal, mechanical, and other complications of obesity. GLP-1RAs are never used alone. They are prescribed along with behavioral therapy, lifestyle modification, exercise, and a 500 kcal-deficit balanced diet. Thus, they enhance, rather than obviate the need for self-discipline. In fact, GLP-1RA support disciplined eating habits by reducing the levels of "hungry" (orexigenic hormones), increasing "houseful" (anorexic) signals, and restoring neuroendocrine homeostasis[5]. This baro-balancing act may be associated with nausea and vomiting, but these are usually mild and transient. Reports of iatrogenic effects are worrisome, and these must be analyzed carefully for causality versus association[2,3].

Pessimists prophecy a Cassandran picture of potential negative effects, and suggest that the use of GLP-1RAs in modern medicine is flirting with fire, and that obesity should be managed purely with inefficient, unsustainable methods such as dietary restriction and physical activity. This, however, is untrue. Various studies, the Look AHEAD trial among them, have demonstrated the inability of lifestyle measures to reduce weight[6]. A large reservoir of research also highlights the relationship of obesity with multiple negative health outcomes[7].

It is not treating obesity that should be termed as flirting with fire; rather, treatment inertia in obesity is the equivalent of fire-flirting. Obesity prevention and management strategies should be instituted in a timely manner, as soon as possible. Pharmacotherapy and surgical interventions must be offered if they are indicated. The person living with obesity should be supported in choosing the right therapy, through person-centered informed decision-making[8,9]. Not doing so should be viewed as an unprofessional act, as we have clear cut evidence that weight loss improves long-term outcomes.

While obesity prevention represents the primordial and primary levels of prevention of health, timely obesity treatment is equivalent to secondary and tertiary levels of preventive intervention. Equal emphasis is required however, on the quaternary and quinary levels of prevention. Quaternary prevention reminds physicians to avoid overdiagnosis, overinvestigation, and overtreatment[9]. This is important in obesity. Establishment norms for identification and evaluation of inherited

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(syndromic) and endocrine obesity must be followed. Thresholds for diagnosis, pharmacological prescription and surgical intervention must be respected as well.

Pharmacovigilance programs should be strengthened to include anti-obesity medications. GLP-1RA prescription does not always present a Pollyanna-like picture. Drug tolerability can be enhanced by following a "start low, go slow" dosage approach, introducing the idea of gastrointestinal (GI)-friendly comfort foods beverages and spices, and helping identify GI-discomforting foods as well. These culinary tips and tricks, covering food procurement, preparation, patterns, presentation, and preservation, help fight the fire of fatness, by improving the efficacy of GLP-1RA[10].

Quinary prevention tasks us with preventing misinformation, and promoting accurate, appropriate messaging that is advantageous to health. This should be done at all possible platforms, at every offered opportunity, by each evidence-based obesity care professional. Intersectoral, pan-disciplinary cross-connections must be built, to ensure effective and efficient team-based obesity care[11]. Obesity medicine should be introduced at all levels of health curricula, across basic, investigative, and interventional sciences.

If we do not fight fat, we will actually be flirting with fire, and tempting fate. We need to fight fat, and fate, with firmness and fortitude. We need to fight now.

REFERENCES

1. Sidrak WR, Kalra S, Kalhan A. Approved and emerging hormone-based anti-obesity medications: a review article. Indian J Endocrinol Metab. 2024;28(5):445-60.
2. Kim JA, Yoo HJ. Exploring the side effects of GLP-1 receptor agonist: to ensure its optimal positioning. Diabetes Metab J. 2025;49(4):525-41.
3. Wang L, Volkow ND, Kaelber DC, Xu R. Semaglutide or tirzepatide and optic nerve and visual pathway disorders in type 2 diabetes. JAMA Netw Open. 2025;8(8):e2526327.
4. Nagi MA, Ahmed H, Rezq MAA, Sangroongruangsri S, Chaikledkaew U, Almalki Z, et al. Economic costs of obesity: a systematic review. Int J Obes (Lond). 2024;48(1): 33-43.
5. Kalra S, Verma M, Kapoor N. The 4BE quinqunx: a model for obesity pathogenesis. J Pak Med Assoc. 2025;75(6): 1002-3.
6. Pi-Sunyer X. The look AHEAD trial: a review and discussion of its outcomes. Curr Nutr Rep. 2014;3(4):387-91.
7. Kalra S, Kapoor N, Verma M, Shaikh S, Das S, Jacob J, et al. Defining and diagnosing obesity in India: a call for advocacy and action. J Obes. 2023;2023:4178121.
8. Garcha SC, Kalra S. Person centered approach and challenges in the management of obesity. In: Garcha SC, Kalra S (Eds.). Drugs for Medical Management of Obesity: A Machine-Generated Literature Overview. Singapore: Springer; 2025. pp. 155-82.
9. Madhu SV, Kapoor N, Das S, Raizada N, Kalra S; Endocrine Society of India. ESI clinical practice guidelines for the evaluation and management of obesity in India. Indian J Endocrinol Metab. 2022;26(4):295-318.
10. Kalra S, Kalhan A, Berard L. Oral glucagon-like peptide-receptor agonists (GLP1RA) counseling: comparison with insulin counseling. Postgrad Med. 2020;132(8):663-6.
11. Shrestha D, Kalra S, Somasundaram N, Dhakal GP, Selim S, Naseri MW, et al. The Kathmandu Declaration–Obesity in the south Asian region: an exigency statement. Clin Epidemiol Glob Health. 2023;22:101315.