VIEWPOINT

DAWN (Drug-Assisted Weight Normalization): Normalizing the Pursuit for Health

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ABSTRACT

Obesity is accepted as a disease by professional organizations across the world. The rise in its prevalence has been matched by enhanced understanding of its causation, clinical trajectory as well as complications. Endocrinologists are now able to treat obesity with a variety of interventions, including behavioral, dietary, oral, injectable, invasive, and surgical therapies. In this manuscript, we describe highly effective antiobesity medications available for weight loss.

Keywords: Antiobesity medications, GLP-1 receptor agonists, incretin therapy, medical management of obesity

Endocrinologists are now able to treat obesity with a variety of interventions, including behavioral, dietary, oral, injectable, invasive, and surgical therapies[1]. While intensive behavioral therapy and calorie restriction remain the cornerstone of chronic weight management, drug treatment is increasingly becoming standard of care[2]. Drug-assisted weight normalization (DAWN) is used as a first-line treatment option, as an add-on in persons who do not respond to nonpharmacological means, as a strategy to optimize weight prior to bariatric surgery, and as an adjuvant after bariatric surgery as well. DAWN aims not only at reduction of weight, but also at correction of associated comorbidities, including blood pressure and hyperglycemia[3].

INDICATIONS AND INCENTIVES

The rapid adoption of DAWN has been fueled by multiple factors. Physicians understand the importance of weight management in obesity, and are able to counsel their patients more effectively. The currently available and upcoming drugs for the management of obesity are summarized in Table 1. Social awareness of obesity as a disease is improving as well, thereby creating a market for DAWN[4]. Availability of effective, well-tolerated drugs, such as semaglutide and tirzepatide, is spreading across the globe. Certain South Asian countries manufacture low-cost generic version of these products, thus making them more affordable.

ISSUES AND IRRITANTS

There do remain significant barriers to the widespread adoption of DAWN. While long-term cardiovascular outcome trials have been reported for both semaglutide and tirzepatide[5,6], these drugs have not been used in the real-world for more than a few years. Hence, long-term real-world data and evidence on their safety is lacking. The need to take these medicines indefinitely is another barrier for some. The relatively high cost of treatment, and lack of insurance coverage in most markets are other challenges. Misconceptions and myths regarding their usage also abound, thus creating uncertainty in the minds of users[7]. This is true not only for members of the public, but for many non-specialist health care professionals as well.

INITIATIVE AND IMPETUS

A concerted effort, by all concerned stakeholders, can make DAWN a ray of hope for all persons living with obesity and its complications. Continued pharmacovigilance should help demonstrate the long-term safety and sustainability of DAWN. Hopefully, newer drugs being developed will offer more effective choices

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Table 1. Current and Upcoming Highly Effective Antiobesity Medications

Antiobesity medication	Drug class	Trial status	% of weight loss	Population achieving ≥10%
Cagrisema	Amylin Analog & GLP-1RA	Phase 2 in T2DM with BMI ≥27 kg/m^2	15.6%	Cagrisema - 71%; Cagrilintide - 14%; Semaglutide - 23%
Survodutide	GCGR and GLP-1RA	Phase 2 in people with BMI ≥27 kg/m^2	19%	Not available
Orforglipron	Nonpeptide GLP-1RA	Phase 2 in people with BMI ≥30 kg/m^2 or ≥27 kg/m^2 with one weight-related condition	14%	Orforglipron - 75%; Placebo - 9%
Ecnoglutide	GLP-1RA	Phase 2 in people with BMI ≥30 kg/m^2 or ≤40 kg/m^2	14.7%	Not available
Retatrutide	GIP/GLP-1/GCG	Phase 2 in people with BMI ≥30 kg/m^2 or ≥27 kg/m^2 with one weight related condition	24.2%	Retatrutide - 93%; Placebo - 9%
Tirzepatide	GIP/GLP-1RA	Phase 3	14.7%	Tirzepatide - 65%; Placebo - 9%
Oral Semaglutide 25/50 mg	GLP-1RA	Phase 3 in people with BMI ≥30 kg/m^2 or at least 27 kg/m^2 with one weight-related complications	17.8%	Oral Semaglutide - 75%; Placebo - 12%

GLP-1RA = Glucagon-like peptide 1 receptor agonist; T2DM = Type 2 diabetes mellitus; BMI = Body mass index; GCGR = Glucagon receptor; GIP: Gastric inhibitory polypeptide.

in the near future. As experience increases, flexible prescription patterns, using lower doses, or reduced frequencies of administration, will improve the cost effectively of the existing molecules. The approval and development of biosimilar versions of semaglutide in India and other South Asian countries is an effort in this direction, too.

The most important limiting factor, however, is awareness. Continued campaigns about obesity, its prevention and management are required to ensure an equitable DAWN for all. All health care professionals should be made aware of the various options available. The indications, contraindications, and caveats of use should be known to endocrinologists and internists, who are qualified to use these medications. Quaternary and quinary prevention are equally important: one must avoid over usage or inappropriate usage of weight loss therapies, and at the same time ensure that all those with indications are offered DAWN[8].

INSIGHT

The word DAWN stands for a fresh beginning, for hope, for optimism. While the sun rises every day, no one can take the next day's DAWN for granted. DAWN offers hope for a healthier weight and healthier future. At the same time, weight management is a chronic, life long journey, where weight maintenance may be as challenging as weight loss. Long-term DAWN is the way to sustainable health in persons living with obesity.

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