Obesity Diagnosis and Treatment

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Glucagon-like peptide-1: The Current Trend in Obesity Treatment

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Editorial

As defined by the World Health Organization, adult obesity is a person having body mass index equal to or above 30. It is a condition generally known to be linked to a lack of physical activity and long-term consumption of high calorie diet. However, the treatment of obesity is not as straightforward as it appears to, i.e by changing one's lifestyle. Obesity is a metabolic disorder culminating from multiple factors and causes that are indicated by several biomarkers. As we advance to gaining better understanding of the development of obesity, these biomarkers range from those in the brain to liver and visceral organs, suggesting an effective treatment with sustained weight loss a challenging task.

The approval of liraglutide, a glucagon-like peptide-1 (GLP1) mimetic by the Food and Drug Administration in late 2014 for use in obesity treatment brought new hope to morbidly obese patients who considered bariatric surgery as their only option to overcome obesity. Liraglutide was originally developed to treat type-2 diabetes [1]. But its recent approval as an anti-obesity agent was not a new development. GLP1 was first reported to have a role in feeding way back in 1996, and 6 years later, Zander and co-workers found that GLP1 reduced the body weight of diabetic patients [2]. Hence, it has taken at least two decades before GLP1 and its mimetic are recognized as therapeutics for obesity [3].

GLP1 is secreted from the small intestinal L cells and entered the systemic circulation via intestinal capillaries that drained into the hepatic portal vein, and produces a systemic effect. In healthy individuals, GLP1 stimulates insulin secretion after meal, and subsequently lowers the post-prandial glucose level. Compared to its effect on pancreas, the physiological function of GLP1 in reducing appetite received lesser attention possibly due to the appetite-regulating centre being less accessible than the digestive system. The appetite-regulating centre is situated in the arcuate nucleus (ARC) of the hypothalamus. The ARC contains two sets of neuronal circuitry – the neuropeptide Y (NPY) and Agouti-related peptide (AgRP), which promotes food intake, and the anorexic pro-opiomelanocortin (POMC) and cocaine- and amphetamine-regulated transcript (CART). GLP1 acts by suppressing the expression of NPY and AgRP, and up-regulating the expression of POMC, and CART [4].

Most of the clinical trials have shown that GLP1 receptor agonists have better efficacy and lesser side effects than other classes of anti-obesity agents [5], implying that increased appetite is one of the main factors that contributes to obesity. Liraglutide is indicated to be administered together with other treatment regimens such as reduced calorie intake and increase in physical activity, which together suggests that effective weight management requires appetite regulation and balance in energy expenditure. GLP1 receptor agonists have the potential of preventing cardiovascular disease [6], and liraglutide is being assessed for its long-term cardiovascular outcomes [7]. Another advantage of GLP1 receptor agonist is that it prevents weight gain via mechanisms in the brain as well as those in the peripheral organs [8].

In comparison to its effects on pancreas and brown adipose tissues, the central effect of GLP1 has a greater physiological impact, including the general well-being and the reproductive system. Besides the appetite-regulating neurons, the ARC also contains another group of neuron – the kisspeptin neurons, which project to gonadotrophin-releasing hormone (GnRH) neurons in the preoptic area of the hypothalamus. GnRH induces gonadotrophin stimulation at the pituitary leading to gonadal hormone secretion. Importantly, kisspeptin was found to innervate and excite POMC cells while inhibit the NPY cells [9]. The relationship between the appetite-regulating peptide neurons and kisspeptin neurons was much more complex than it is presented here, but it basically suggests that obesity increases the risk of infertility. It is well known that stress suppresses GnRH secretion. With the complex interaction between kisspeptin, POMC and GnRH neurons, GLP1 may interfere with the effect of stress on body weight gain as well as the reproductive system.

In summary, GLP1 receptor agonist is a trend in obesity treatment for a number of reasons – it is comparable or superior to other classes of agents in inducing weight loss; gives tolerable adverse effects, which are only observed at higher doses; increases thermogenesis that further enhances its appetite suppressant effect. Interestingly, GLP1 acting centrally affects the reproductive system, which is now known to be regulated by the brain. More studies are being carried out to investigate the long-term safety profile of liraglutide and how it may reduce risk factors that lead to metabolic syndrome. But as liraglutide is administered subcutaneously, an orally administered GLP1 mimetic should be developed to improve patient compliance and the clinical outcome of the mimetic.

References

1. Garber AJ. Long-acting glucagon-like peptide 1 receptor agonists. Diabetes Care. 2011; 34: S279-S284.
2. Zander M, Madsbad S, Madsen JL, Holst JJ. Effect of 6-week course of glucagon-like peptide 1 on glycaemic control, insulin sensitivity, and B-cell function in type 2 diabetes: a parallel-group study. The Lancet. 2002; 359: 824-830.
3. Turton MD, O'Shea D, Gunn I, Beak SA, Edwards CMB, et al. A role for glucagon-like peptide-1 in the central regulation of feeding. Nature. 1996; 379: 69-72.
4. Seo S, Ju S, Chung H, Lee D, Park S. Acute effects of glucagon-like peptide-1 on hypothalamic neuropeptide and amp activated kinase expression in fasted rats. Endocr J. 2008; 55: 867-874.
5. Isaacs D, Prasad-Reddy L, Srivastava SB. Role of glu-

cagon-like peptide 1 receptor agonists in management of obesity. Am J Health-Syst Pharm. 2016; 73: e535-e549.

6. Monami M, Dicembrini I, Nardini C, Fiordelli I, Mannucci E. Effects of glucagon-like peptide-1 receptor agonists on cardiovascular risk: a meta-analysis of randomized clinical trials. Diabetes Obes Metab. 2014; 16: 38-47.

7. Prasad-Reddy L, Isaacs D. A clinical review of GLP-1 receptor agonists: efficacy and safety in diabetes and beyond. Drugs Context. 2015; 4: 212283.

8. Heppner KM, Perez-Tilve D. GLP-1 based therapeutics: simultaneously combating T2DM and obesity. Front Neurosci. 2015; 9: 92.

9. Fu L, van den Pol AN. Kisspeptin directly excites anorexigenic proopiomelanocortin neurons but inhibits orexigenic neuropeptide Y cells by an indirect synaptic mechanism. J Neurosci. 2010; 30: 10205-10219.