With Severe Psychiatric Disorders New Role for GLP-1 Drugs to Improving Survival in People

A recent editorial discussed that glucagon-like peptide 1 (GLP-1) receptor agonists (RAs) may potentially transform health outcomes for individuals with serious mental illnesses (SMIs). The authors emphasized that these agents are most likely to improve outcomes by addressing the cardiometabolic drivers of excess morbidity and mortality rather than replacing established psychiatric treatments.

Study

In 2005, the United States (US) Food and Drug Administration approved the first GLP-1 receptor agonist, exenatide, for the treatment of type 2 diabetes (T2D). Since then, several GLP-1 mono-agonists have been approved, along with tirzepatide, the first dual GLP-1 and glucose insulinotropic polypeptide (GIP) receptor agonist. Additional dual and triple agonists targeting GIP, GLP-1, and glucagon receptors are in late-stage development.

Beyond T2D and weight management in individuals with overweight or obesity, GLP-1 receptor agonists are approved for metabolic dysfunction associated steatohepatitis in people with moderate or advanced fibrosis, obstructive sleep apnea in obese adults, reduction of major adverse cardiovascular events in adults with T2D and cardiovascular disease (CVD), and slowing progression of chronic kidney disease and cardiovascular mortality in adults with both chronic kidney disease and T2D.

Synthetic small-molecule oral GLP-1 receptor agonists are expected to be approved in 2026, while oral semaglutide is already available. These formulations may ease barriers related to manufacturing, supply chains, and access. There is a broad consensus that GLP-1 receptor agonists have transformed the management of T2D, obesity, and related morbidity and have been associated with reduced progression of renal disease, cardiovascular disease, and mortality in people with metabolic disorders.

Schizophrenia, major depressive disorder, bipolar disorder (BD), and other SMIs are severe, prevalent, and lifelong conditions that are major contributors to disability, reduced healthspan, and diminished social and economic participation, particularly in younger populations. Individuals with SMIs experience premature and excess mortality, with years of life lost often estimated between 5 and 25 years, largely due to earlier onset and substantially higher rates of CVD.

Affordable, scalable, and effective interventions are therefore essential to increase healthspan and reduce cardiovascular-related mortality among people with SMIs. Each condition for which GLP-1 receptor agonists are approved contributes differently to cardiometabolic risk and healthspan loss in this population. In addition, several agents are in mid- or late-stage development for chronic diseases such as peripheral artery disease and atherosclerotic heart disease, which disproportionately affect individuals with SMIs.

Findings

Despite the availability and clinical effectiveness of antipsychotics, lithium, antidepressants, and anticonvulsants, reductions in healthspan loss and cardiovascular mortality have been demonstrated only for selected classes and agents, including second-generation long-acting antipsychotics, lithium, and clozapine. Lithium, in particular, remains under-prescribed despite its strong efficacy in BD, limiting its overall public health impact.

GLP-1 receptor agonists are recommended for managing weight gain associated with psychotropic medications when discontinuation of psychiatric treatment is not feasible. Preliminary evidence also suggests a potential protective effect against lithium-induced nephrotoxicity, a condition for which no approved therapy currently exists. Additionally, several GLP-1 receptor agonists are being developed or repurposed for the treatment of alcohol, tobacco, and opioid use disorders.

Preclinical studies, small controlled trials, and observational research further suggest that GLP-1 receptor agonists may have beneficial effects in the prevention and treatment of mood disorders and in psychopathology domains that substantially impair quality of life, including cognitive dysfunction and anhedonia.

Conclusion

Overall, individuals with SMIs account for a disproportionate share of years of life lost and disability-adjusted life years. Despite decades of advances in psychopharmacology, the mortality gap between the general population and people with SMIs has not meaningfully narrowed. Therapeutic strategies that directly reduce mortality and extend healthspan are therefore urgently needed.

In this context, GLP-1 receptor agonists represent one of the most promising pharmacological classes, particularly if challenges related to cost, equitable access, reimbursement policy, and supply constraints are addressed. Prioritizing individuals with SMIs within fair allocation frameworks may help reduce excess and premature mortality in this vulnerable population in the near term.

Source:

https://www.news-medical.net/news/20260125/New-role-for-GLP-1-drugs-Improving-survival-in-people-with-severe-psychiatric-disorders.aspx