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SHORT REVIEW

Is treatment with liraglutide efficient?☆

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Abstract In the current context of limited economic and health resources, efficiency of drug treatments is of paramount importance, and their clinical effects and related direct costs should therefore be analyzed. Liraglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist approved for the treatment of type 2 diabetes mellitus (T2DM) which, in addition to its normoglycemic effects, induces a significant improvement in body weight and several cardiovascular risk factors. The aim of this narrative review is to summarize the available evidence about the effects of liraglutide upon cardiovascular risk factors and how these improve its cost-effectiveness profile. Despite the relatively higher cost of liraglutide as compared to other alternative therapies, liraglutide has been shown to be cost-effective when clinical indicators and total costs associated to T2DM management are analyzed.

PALABRAS CLAVE
Diabetes mellitus tipo 2;
Liraglutida;
Coste-efectividad;
National Institute for Health and Clinical Excellence

¿Es eficiente el tratamiento con liraglutida?

Resumen En el contexto actual de recursos económicos y sanitarios limitados tiene una gran importancia la eficiencia de los tratamientos farmacológicos, analizando sus efectos clínicos y sus costes directos asociados. La liraglutida es un agonista del receptor del péptido de tipo 1 similar al glucagón (GLP-1) aprobada para el tratamiento de la diabetes mellitus tipo 2 (DM2), que además de su acción normoglucemiante induce mejorías significativas en el peso corporal y sobre diversos factores de riesgo cardiovascular. El objetivo de esta revisión breve es resumir la evidencia disponible acerca de los efectos de la liraglutida sobre los factores de riesgo cardiovascular y cómo estos mejoran su perfil de coste-efectividad. A pesar de su coste farmacológico, relativamente superior al de otras alternativas terapéuticas, la liraglutida ha demostrado ser coste-efectiva cuando se analizan los indicadores clínicos y los costes totales asociados al abordaje de la DM2.

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Introduction

The recently published di@betes study showed a high prevalence of diabetes in Spain, affecting 13.8% of the population.[1] This increase as compared to prior estimates is associated with increased morbidity and mortality rates which represent a significant financial burden for health systems due to the increase in associated direct medical costs. On the other hand, in the current context of limited financial and healthcare resources, it has become even more important not only to prevent complications of diabetes because of their attendant financial burden, but also to assess the efficiency of drug treatments by analyzing both their direct and indirect medical costs. In addition, 50% of the total cost incurred by diabetes is associated with cardiovascular complications,[2] and some reflection is therefore needed regarding the suitability of current antidiabetic treatments, not only with regard to blood glucose control, but also in terms of joint assessment of the effects on other factors that determine their cost, such as effects on body weight, systolic blood pressure (SBP), lipids, and the attendant risk of hypoglycemia.

Liraglutide is a recombinant glucagon-like peptide-1 (GLP-1) receptor agonist which, in addition to its hypoglycemic effect, has a positive impact on body weight and different cardiovascular risk factors such as blood pressure and lipid parameters.[3] Liraglutide has an antidiabetic potency similar to basal insulin,[4] and its additional advantages include its virtually nil risk of hypoglycemia and its ability to induce weight loss.[3] The most common adverse reactions of liraglutide include gastrointestinal complications, mainly nausea, which usually occur in the first weeks after the start of treatment and are generally mild and transient in nature.[5] The main factor limiting the potential benefits of liraglutide in particular, and the class of GLP-1 receptor agonists in general include their higher cost as compared to other treatment options. There are however consistent data, and the results of evaluations by international bodies, which show that drugs in this therapeutic class may decrease the final cost of treatment of type 2 diabetes mellitus (T2DM) as compared to other drugs.[6,7]

Effects on cost of treatment

Drug costs versus total cost of treatment

According to the Cost of Diabetes in a Europe study (CODE-2), the mean direct cost of diabetes in 1999 was €1305 per patient and year, of which 42% was due to pharmacy expenses, 32% to hospitalization expenses, and 26% to outpatient costs.[8] Regarding pharmacy expenses, 4.6% represented expenditure on oral hypoglycemic agents, 4.7% on insulins, 14% on drugs for cardiovascular conditions, and 0.6% on glucose test strips. According to this study, most costs associated with patients with diabetes were expenses derived from hospitalization and the treatment of comorbidities, while the costs of antidiabetic treatment (oral drugs and insulins) accounted for less than 10%. Recent data on the cost of diabetes in Spain are available. In a study conducted in Catalonia in 2011, the mean estimated annual cost per diabetic patient was €3362.8, as compared to €2156.5 per non-diabetic patient (an absolute difference of €1206.3, a 59.9% relative increase).[9] Absolute differences of €340.2 (a 38.4% increase) for the mean annual cost of hospitalizations and of €435.8 (an 89% increase) for pharmaceutical costs were reported.[9] Recently, data reported in two national[8,10] and two regional studies[11,12] were used to estimate the annual costs associated with T2DM in Spain in 2009: the direct annual cost per patient was €1660, the annual cost of productivity losses was €916, and the annual direct cost of microvascular and macrovascular complications was €2930, of which 40.2% was due to hospitalization, 38.5% to drug treatment, and 21.3% to outpatient monitoring, respectively.[13]

Effects on healthcare costs associated with hypoglycemia

The general metabolic control goal defined by current recommendations for T2DM is a glycosylated hemoglobin (HbA_{1c}) value of 7% or less.[14] The control goal may be more ambitious ($HbA_{1c} < 6.5\%$) in young patients with a short duration of diabetes and no microvascular or macrovascular complications, and provided the goal is achieved with no increase in hypoglycemic episodes.[14] By contrast, higher HbA_{1c} values (7.5–8%) are considered adequate in elderly patients, with cardiovascular disease or chronic complications of already established diabetes.[14] However, and despite the wide dissemination of these recommendations, a high proportion of patients do not achieve these control goals. Thus, it is estimated that 45% of Spanish patients with T2DM on non-insulin treatment have an HbA_{1c} level higher than 7%.[15] Low adherence to hygienic and dietary measures[16] and an increased risk of hypoglycemia when treatment for diabetes is intensified[17] represent the main limiting factors to the achievement of optimum control. The therapeutic inertia of healthcare professionals, which may delay the start of treatment intensification, also contributes to this situation.[18]

In this context, the availability of treatments with a potent hypoglycemic effect but a low risk of hypoglycemia may help in achieving adequate metabolic control in a greater number of patients, with a positive impact on the future risk of microvascular complications and, possibly, macrovascular complications also.[19] In the clinical trial program Liraglutide Effect and Action in Diabetes (LEAD), liraglutide, in different treatment combinations, induced a change in HbA_{1c} ranging from 0.2% to 1.3%, with a low hypoglycemia rate (0.03–1.9 episodes per patient and year).[3]

In addition to promoting adequate metabolic control, the use of drugs involving less risk of hypoglycemia may also decrease the direct costs derived from this complication. As regards the direct costs of hypoglycemia, the greatest expense is associated with severe hypoglycemic episodes, according to data published in 2004 (€3597).[20] Mild hypoglycemic episodes have a lower economic impact, but because of their greater frequency they also have a significant impact resulting from changes of medication, the increased use of glucose test strips, increased nurse visits, greater need for health education, and increased work absenteeism. The mean estimated cost of mild hypoglycemia ranges from €30 to €35.[20] Increased attention to