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NEW ANTIDIABETIC DRUGS AND PERSPECTIVES IN THE MANAGEMENT OF CHRONIC HYPERGLYCEMIA

NEW ANTIDIABETICS AND PERSPECTIVES IN CHRONIC HYPERGLYCEMIA MANAGEMENT

Luiza Higino Cruz– Pontifical Catholic University of Minas Gerais
Bernardo Viegas Coelho– Faculty of Medical Sciences of Minas Gerais
Felipe Menezes Andrade– Pontifical Catholic University of Minas Gerais
Lucas Júnio da Silva – Pontifical Catholic University of Minas Gerais

SUMMARY:

The management of type 2 diabetes mellitus (T2DM) has evolved with the emergence of new oral and subcutaneous antidiabetic agents, which aim not only at glycemic control but also at preventing systemic complications. This study reviews the effects of new classes of hypoglycemic agents, such as SGLT-2 inhibitors, GLP-1 agonists and insulin analogues, in the control of chronic hyperglycemia and in the prevention of complications. An integrative literature review was conducted using the PubMed database, with articles published between 2019 and 2024, selected from the search key: 'novel antidiabetic drugs' OR 'SGLT-2 inhibitors' AND 'chronic hyperglycemia'. Clinical trials and systematic reviews with full text in English were included. SGLT-2 inhibitors have been shown to be effective in reducing cardiovascular and renal events, in addition to presenting a significant improvement in glycemic control. GLP-1 agonists and new combination therapies have also demonstrated reductions in HbA1c levels and improvements in the risk profile for complications such as cardiovascular disease, diabetic nephropathy and retinopathy. The inclusion of new devices, such as smart pens, has also contributed to individualized patient management. The introduction of new antidiabetic agents with innovative mechanisms of action has brought significant advances in the treatment of patients with T2DM, helping to prevent complications and optimize glycemic control. The continued evolution of these therapies promises to bring new perspectives in the management of the disease. **Keywords:**Type 2 Diabetes Mellitus. Hyperglycemia. Hypoglycemic agents. Prevention of

Diseases. Combination Therapy.

ABSTRACT:

The management of type 2 diabetes mellitus (T2DM) has evolved with the emergence of new oral and subcutaneous antidiabetic agents, which aim not only at glycemic control but also at the prevention of systemic complications. This study reviews the effects of new classes of hypoglycemic agents, such as SGLT-2 inhibitors, GLP-1 agonists, and insulin analogs, on chronic hyperglycemia control and complication prevention. An integrative literature review was conducted using the PubMed database, with articles published between 2019 and 2024, selected using the search key: 'novel antidiabetic drugs' OR 'SGLT-2 inhibitors' AND 'chronic hyperglycemia'. Clinical trials and systematic reviews with full text in English were included. SGLT-2 inhibitors were found to be effective in reducing cardiovascular and renal events, along with a significant improvement in glycemic control. GLP-1 agonists and new combination therapies also demonstrated reductions in HbA1c levels and improvements in the

risk profile for complications such as cardiovascular disease, diabetic nephropathy, and retinopathy. The inclusion of new devices, such as smart pens, has also contributed to individualized patient management. The introduction of new antidiabetic agents, with innovative mechanisms of action, has brought a significant advancement in the treatment of T2DM patients, aiding in complication prevention and optimizing glycemic control. The continued evolution of these therapies promises new perspectives in disease management.
Keywords: Combined Modality Therapy. Diabetes Mellitus, Type 2. Disease Prevention. Hyperglycemia. Hypoglycemic Agents.

1. INTRODUCTION

Diabetes mellitus (DM), particularly type 2, has an increasing prevalence worldwide, driven by increasing obesity, physical inactivity, and population aging. Adequate glycemic control is crucial to avoid chronic complications, which include cardiovascular disease, retinopathy, nephropathy, and neuropathy, all of which are associated with poor glycemic control (Khan*et al.*, 2022). In addition to macro- and microvascular complications, poorly controlled hyperglycemia significantly increases the risk of hospitalizations and premature mortality (Hussain*et al.*, 2021).

In recent decades, the development of new classes of hypoglycemic drugs, both oral and subcutaneous, has transformed the approach to the management of DM. Among these new therapies, the most prominent are sodium-glucose cotransporter type 2 (SGLT2) inhibitors, which promote urinary glucose excretion, and GLP-1 receptor agonists, which improve insulin secretion and inhibit glucagon release (Ferrannini*et al.*, 2022). Furthermore, the combination of these agents with insulin, as observed in combination treatments such as iGlarLixi, offers a synergistic approach to optimize glycemic control in patients who do not respond adequately to traditional therapies (Panigrahi; Mohanty, 2023).

Innovations in the treatment of DM also include the incorporation of new technologies, such as smart insulin pens, which help patients better manage their daily insulin doses, resulting in more precise glycemic control and fewer episodes of hypoglycemia (Galindo*et al.*, 2023). Thus, the increasing integration of new classes of drugs and technologies has the potential to transform the management

clinical outcome of DM, improving both clinical outcomes and patients' quality of life (Fukunaga*et al.*, 2023).

In this context, this study aims to explore the impact of new oral and subcutaneous hypoglycemic agents on the control of diabetes mellitus. The specific objectives include comparing the different classes of antidiabetic agents available and discussing future perspectives in the management of the disease, focusing on preventing complications and improving the quality of life of patients.

2. MATERIAL AND METHOD

This study consists of an integrative literature review, conducted by searching for scientific articles in the PubMed and ScienceDirect databases. The research was carried out using the search key: *"('novel antidiabetic drugs' OR 'new antidiabetic agents' OR 'SGLT-2 inhibitors' OR 'GLP-1 agonists' OR 'dual GIP/GLP-1 receptor agonists' OR 'insulin therapy') AND ('chronic hyperglycemia' OR 'type 2 diabetes management')"* in both databases. Studies published in the last 5 years (2019-2024) were selected, including the following study types: clinical trial, meta-analysis, controlled trial and randomized trial. Articles with full text available in Portuguese and English that addressed the impact of new antidiabetics on the control of type 2 diabetes mellitus and the management of chronic hyperglycemia were included.

A total of 14,586 articles were found in the initial search. After applying filters for year, type of study and language, 183 articles were selected. After removing duplicates, 183 articles were eligible for screening by title and abstract. Of these, 26 articles were selected for full reading, resulting in 8 articles that comprised the integrative review (Table 1). Exclusion criteria included studies that did not address direct comparisons between new antidiabetic drugs or that were not related to the management of hyperglycemia in type 2 diabetes mellitus.

Table 1. Works included.

Base	**Title**	**Authors**	**Periodical (vol, no, page, year)**	**Considerations / Theme**

PubMed	Fixed-ratio combination of insulin glargine plus lixisenatide (iGlarLixi) improves ß-cell function in people with type 2 diabetes.	FERRANNINI, He*et al*.	**Diabetes, Obesity and Metabolism**, v. 24, n. 6, p. 1159-1165, 2022.	Evaluate as agonists of GLP-1 improve the function of the β cells and the control glycemic in type 2 diabetes, offering a alternative effective the insulin.
PubMed	A pilot study on the efficacy of a diabetic diet containing the rare sugar d-allulose in patients with type 2 diabetes mellitus: the prospective, randomized, single-blind, crossover study.	FUKUNAGA, Kensaku*et al*.	**Nutrients**, v. 15, n. 12, p. 2802, 2023.	Examine the impact positive of the pens of insulin advanced in the accession to the treatment and in the control glycemic of patients.
PubMed	Efficacy of a smart insulin pen cap for the management of patients with uncontrolled type 2 diabetes:	GALINDO, Rodolfo J.*et al*.	**Journal of diabetes science and technology**, v. 17, n. 1, p. 201-207, 2023.	Investiga to the pens of insulin intelligent, highlighting your

	the randomized cross-over trial.			effectiveness node control glycemic and in the administration of insulin.
PubMed	Comparison Of Efficacy And Safety Profile Of Empagliflozin Versus Dapagliflozin As Add On Therapy In Type 2 Diabetic Patients.	HUSSAIN, Mazhar *et al*.	**Journal of Ayub Medical College Abbottabad-Pakistan**, v. 33, n. 4, 2021.	Compare empagliflozin and dapagliflozin in type diabetes 2, showing that both they are effective, but with differences in effects collaterals and clinical efficacy.
PubMed	Comparison of empagliflozin and vildagliptin for efficacy and safety in type 2 diabetes mellitus in the Pakistani population.	Khan, Asima *et al*.	**Frontiers in Endocrinology**, v. 13, p. 926633, 2022.	It presents the growing prevalence global from the type 2 diabetes and need of best strategies of prevention.
PubMed	Efficacy and safety of Omija (Schisandra chinensis) extract mixture on the	KIM, Da-Som *et al*.	**Nutrients**, v. 14, n. 15, p. 3159, 2022.	Explore the impact of extract of *Schisandra*

	improvement of hyperglycemia: A randomized, double-blind, and placebo-controlled clinical trial.			*chinensis* node control glycemic, suggesting benefits additional to the treatment conventional.
PubMed	Efficacy and safety of HIMABERB® Berberine on glycemic control in patients with prediabetes: double-blind, placebo-controlled, and randomized pilot trial.	PANIGRAHI, Antarmayee; MOHANTY, Susant.	**BMC Endocrine Disorders**, v. 23, n. 1, p. 190, 2023.	Review the combination of insulin glargine and lixisenatide, showing what improve the control glycemic and and well tolerated by patients.
PubMed	Early time-restricted carbohydrate consumption vs conventional dieting in type 2 diabetes: the randomised controlled trial.	KNITTING, Domenico *et al.*	**Diabetology**, v. 67, n. 2, p. 263-274, 2024.	Discuss you benefits of the inhibitors of SGLT2, in addition to the control glycemic, including risk reduction cardiovascular and

				improvement from the renal function.

Source: own authorship, 2024.

3. RESULTS AND DISCUSSION

Analysis of the selected studies showed that new classes of hypoglycemic agents, mainly SGLT2 inhibitors and GLP-1 agonists, have played a crucial role in glycemic control and in the prevention of complications associated with type 2 DM. In a direct comparison, patients treated with empagliflozin, an SGLT2 inhibitor, presented better glycemic control and weight reduction compared to those who used vildagliptin, a DPP-4 inhibitor, reinforcing the multifactorial benefits of empagliflozin. These findings support the idea that effective glycemic control is not limited to reducing glucose levels, but also includes reducing risk factors associated with metabolic syndrome (Khan *et al.*, 2022).

In the case of combined therapies, such as iGlarLixi, which combines insulin glargine with lixisenatide, studies indicate a significant improvement in the function of pancreatic β cells and greater stability in glycemic levels throughout the day (Ferrannini *et al.*, 2022). This combination has been shown to be effective mainly in patients who are unable to achieve glycemic targets with the use of insulin alone, offering a complementary approach that facilitates the management of DM and reduces the total insulin load required (Hussain *et al.*, 2021).

Another relevant point in recent literature is the use of technologies associated with diabetes management. Smart insulin pens, which allow automatic adjustments in insulin doses based on real-time glucose readings, have shown great effectiveness in improving adherence to treatment and reducing adverse events, such as hypoglycemic episodes. The use of this technology represents a significant advance, as it gives patients greater control over their treatment, especially for those who have difficulty maintaining their blood glucose levels within the recommended range (Galindo *et al.*, 2023).

In addition to pharmacological therapies, experimental studies involving bioactive supplements have also been promising. Supplementation with D-allulose, for example,

has been shown to be effective in reducing postprandial glucose levels in patients with type 2 DM, offering an interesting non-pharmacological alternative for glycemic control (Fukunaga*et al.*, 2023). Similarly, plant extracts such as Schisandra chinensis have shown potential in improving insulin sensitivity and reducing hyperglycemia. Although these studies are still in the early stages, they highlight the importance of continued research into complementary interventions that can be integrated into the management of DM (Kim*et al.*, 2022).

Therefore, the reviewed evidence reinforces that, in addition to promoting glycemic control, the new hypoglycemic agents offer additional benefits, such as reducing cardiovascular risk and supporting weight loss, characteristics that are essential in the management of patients with type 2 DM and metabolic syndrome (Tricò*et al.*, 2024).

FINAL CONSIDERATIONS

New oral and subcutaneous hypoglycemic agents, including SGLT2 inhibitors and GLP-1 agonists, have contributed significantly to advances in the management of type 2 diabetes mellitus. In addition to providing more effective glycemic control, these agents have demonstrated additional benefits, such as body weight reduction and cardiovascular protection, which makes them valuable therapeutic options for patients with multiple risk factors (Ferrannini*et al.*, 2022).

Combination therapies, such as iGlarLixi, are particularly promising for patients who fail to achieve glycemic targets with single therapies, offering an effective alternative that improves β-cell function and stabilizes glycemic levels (Hussain*et al.*, 2021). The introduction of technologies, such as smart insulin pens, is also an important innovation, allowing more precise and efficient management of the disease, with a lower incidence of complications, such as hypoglycemia (Galindo*et al.*, 2023).

Although advances in pharmacological and technological therapies represent a significant milestone in the management of diabetes mellitus, it is crucial that long-term studies be conducted to evaluate the efficacy and safety of these interventions, especially in populations with multiple comorbidities. Diabetes management continues to evolve, and the integration of new agents and technologies into the therapeutic armamentarium offers a promising perspective

optimistic about controlling the disease and improving the quality of life of patients (Tricò*et al.*, 2024).

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