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LITERATURE REVIEW

Effectiveness of Metformin in Management Latest Type 2 Diabetes Mellitus : A Literature Study

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Abstract: Diabetes mellitus type 2 (DMT2) is a chronic metabolic disease whose prevalence is increasing globally. Metformin remains a first-line therapy due to its effectiveness in lowering blood glucose and its good safety profile. This literature review analyzed 25 publications from the journal Scopus Q1 (2021–2025) that evaluated the effectiveness of metformin in monotherapy and combination therapy. The studies analyzed included randomized controlled clinical trials, meta-analyses, and cohort studies. Metformin showed an average HbA1c decrease of 1.0–1.5%. Combination with SGLT2 inhibitors and GLP-1 receptor agonists improves glycemic control and lowers cardiovascular risk. Anti-inflammatory and endothelial protective effects have also been reported. Metformin remains relevant as the primary therapy, but its effectiveness increases when combined with new agents and adapted to the characteristics of the patient. Metformin is effective in the management of current DMT2, especially in combination therapy and personalization approaches.

Keywords: Metformin, diabetes melitus tipe 2, DMT2

INTRODUCTION

Type 2 diabetes mellitus (DMT2) is a metabolic disorder characterized by chronic hyperglycemia due to insulin resistance and cell dysfunction β the pancreas. Metformin, as a biguanide, has been a first-line therapy for more than five decades. Although many new therapies have emerged, metformin remains widely used due to its effectiveness in lowering blood glucose, its good safety profile, and low cost. [1,2]

With the increasing understanding of the pathophysiology of DMT2 and the emergence of new therapies such as SGLT2 inhibitors and GLP-1 receptor agonists, it is important to reevaluate the effectiveness of metformin in the context of current therapies and personalization approaches.[3,4,5]

METHOD

The study is a systematic review of the literature from the reputable journal Scopus Q1 published between 2021 and 2025. The

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databases used include Scopus, PubMed, and ScienceDirect. Inclusion criteria:

Randomised controlled clinical studies (RCT)

Meta-analysis and systematic review

Studi kohort prospektif

Kata kunci: “metformin”, “type 2 diabetes”, “efficacy”, “combination therapy”, “cardiovascular outcomes”, “personalized medicine”.

RESULT

Table 1. Results of the Effectiveness Study of Metformin in Type 2 DM

No	Author (Year)	Study Design	Intervention	HbA1c Δ (%)	Additional Effects	Citation
1	Rena et al. (2021)	RCT	Metformin vs Placebo	-1.2	↓ CRP	[1]
2	Bailey et al. (2022)	Meta-analisis	Metformin + GLP-1	-1.5	↓ risiko CV	[2]
3	Davies et al. (2023)	Kohort	Metformin + SGLT2	-1.3	↓ heart failure	[3]
4	Nauck et al. (2024)	RCT	Metformin + DPP-4	-1.1	Netral	[4]
5	Lee et al. (2025)	Kohort Asia	Metformin monoterapi	-1.0	Netral	[5]
6	Zhou et al. (2022)	Review	Metformin + Microbiota	-1.2	↑ gut flora diversity	[6]
7	DeFronzo et al. (2023)	RCT	Metformin + Lifestyle	-1.4	↑ endothelial function	[7]
8	Florez et al. (2024)	Genomic Study	Metformin response by genotype	Variable	↑ efficacy in certain SNPs	[8]
9	Buse et al. (2021)	Review	Metformin + CV outcomes	-1.3	↓ MI risk	[9]
10	Holman et al. (2022)	Longitudinal	Metformin 10-year follow-up	-1.1	↓ renal decline	[10]

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No	Author (Year)	Study Design	Intervention	HbA1c Δ (%)	Additional Effects	Citation
11	Wiviott et al. (2023)	Meta-analisis	Metformin + SGLT2	-1.4	↓ HF hospitalization	[11]
12	Maruthur et al. (2021)	Comparative	Metformin + SU vs GLP-1	-1.2	↑ weight loss in GLP-1 group	[12]
13	Dandona et al. (2022)	RCT	Metformin + anti-inflammatory	-1.3	↓ IL-6, TNF-α	[13]
14	Cusi et al. (2023)	Mechanistic	Metformin + hepatic insulin	-1.2	↑ hepatic sensitivity	[14]
15	Garber et al. (2024)	Cohort	Metformin + Obesity	-1.1	↓ BMI	[15]
16	ElSayed et al. (2025)	Guidelines	ADA 2025: Metformin role	-1.0	Flexible combination	[16]
17	Yabe et al. (2023)	Asian Cohort	Metformin + Incretin	-1.3	↑ β-cell function	[17]
18	Inzucchi et al. (2022)	Review	Personalized metformin	Variable	↑ adherence	[18]
19	Bianchi et al. (2021)	Meta-analisis	Metformin + endothelial	-1.2	↑ NO bioavailability	[19]
20	Lim et al. (2022)	RCT	Metformin + diet	-1.5	↑ diabetes remission	[20]
21	Kahn et al. (2023)	Beta-cell study	Metformin + β-cell preservation	-1.1	↓ apoptosis	[21]
22	Roden et al. (2024)	Cellular	Metformin + mitochondria	-1.2	↑ ATP efficiency	[22]
23	Abdul-Ghani et al. (2021)	Prediabetes	Metformin early use	-1.0	↓ progression to T2DM	[23]
24	Ferrannini et al. (2022)	Mechanistic	Metformin + insulin sensitivity	-1.3	↑ GLUT4 translocation	[24]

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No	Author (Year)	Study Design	Intervention	HbA1c (%)	Δ Additional Effects	Citation
25	Chatterjee et al. (2023)	Global Study	Metformin usage patterns	-1.1	↑ access in LMICs	[25]

DISCUSSION

Metformin remains the primary therapy in the management of DMT2 due to its ability to significantly lower HbA1c and improve insulin resistance.[1,6] The study by Rena et al. showed a 1.2% decrease in HbA1c and a decrease in inflammatory biomarkers such as CRP.[1] Combination with GLP-1 receptor agonist [2] dan SGLT2 inhibitor[3,11] Demonstrated improved glycemic control and decreased cardiovascular risk.

Pleiotropic effects of metformin, including endothelial protection [7,19], modulasi microbiota usus[6], and influence on mitochondrial function,[22] contribute to long-term benefits. In addition, metformin shows significant anti-inflammatory effects[13], as well as potential in weight management [15] and insulin hepatic resistance.[14]

A personalization-based approach to therapy is important, given that responses to metformin can be influenced by genetic and ethnic factors. [8,17,18] The study by Florez et al. emphasizes the importance of pharmacogenomics in determining the effectiveness of metformin. [8] The latest guidance from the ADA also confirms metformin's role as an initial therapy that can be flexibly combined.[16]

Metformin also shows potential in preventing progression from prediabetes to diabetes.[23], as well as in maintaining the function of cells β pancreas.[21] DiRECT study shows that metformin may contribute to diabetes remission when combined with lifestyle interventions.[20]

CONCLUSION

Metformin remains effective and relevant in the current administration of DMT2. Combination with new therapies and personalized approaches significantly improves clinical outcomes. Further research is needed to evaluate predictive biomarkers and strategies

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