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Case Study

Exploring imeglimin efficacy; A case series from a tertiary care hospital

Anuvidya. R[1*], Dr. Abhirama .B.R[1], Muhzina Rahim[2], Rubina Mariam Oomen[3], Amrutha Gopal[3]

*[*1,2,3]PharmD, The Dale View College Of Pharmacy And Research Centre, Punalal, Trivandrum, India.*
[1]Professor & HOD, Department Of Pharmacy Practice, The Dale View College Of Pharmacy And Research Centre, Punalal, Trivandrum, India

*Author for Correspondence: Anuvidya. R
Email: anuvidya2000@gmail.com

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Abstract

Imeglimin, a tetrahydro triazine containing drug, is a novel therapeutic agent for the treatment of Type2 Diabetes Mellitus. Imeglimin has been demonstrated to improve three main pathogenetic components of T2DM: increased gluconeogenesis, inadequate glucose-induced insulin production in beta cells, and peripheral insulin resistance. This case series aimed to evaluate the efficacy and safety of imeglimin in a real-world clinical setting among patients with type 2 diabetes who had inadequate glycemic control with their current treatment regimen. The cases are collected from a tertiary healthcare centre in Kerala, South India. Insights gleaned from the case series indicate that imeglimin significantly improves glycemic control, enhances insulin sensitivity, and preserves beta-cell function in patients with type 2 diabetes.

Keywords: Imeglimin, Type 2 Dibetes mellitus, Oral hypoglycemic agent, Fasting blood sugar.

INTRODUCTION

Type 2 DM is a chronic metabolic disease that causes hyperglycaemia by impairing beta cells and causing insulin resistance. Globally, the incidence of diabetes mellitus (DM) is on the rise. According to estimates from the International Diabetes Federation, 500 million adults had diabetes in 2021; by 2045, that figure is expected to increase to 783 million. The urgent need for efficient, well-tolerated therapeutic solutions is highlighted by this rising prevalence[1].The most recent guidelines for the treatment of type 2 diabetes mellitus (T2DM) have been put forth by the American Diabetes Association (ADA) in the "Standards of Care in Diabetes"[2]. Type 2 diabetes mellitus (T2DM) has many facets, including insulin resistance, impaired insulin secretion, increased hepatic glucose production, and dysfunctional adipose tissue metabolism. These facets collectively contribute to hyperglycemia and its associated complications[3].Imeglimin is a new oral antidiabetic agent that belongs to the "glimin" class of medications. Imeglimin functions by enhancing insulin sensitivity in peripheral tissues, increasing insulin secretion from pancreatic beta-cells, and reducing hepatic glucose production. This is in contrast

to traditional antidiabetic medications, which usually target a single aspect of glucose metabolism. Imeglimin provides a holistic approach to T2DM management by focussing on mitochondrial bioenergetics[4].

CASE PRESENTATION

CASE 1

Mr TK, a 62yr old male patient with a 10yr history of T2DM was presented to the Endocrinology OPD. Despite being on Metformin 2000mg/day and Gliclazide 60mg/day, his glycaemic control remained suboptimal with HbA1c of 8.8%. The patient also had a history of hypertension, dyslipidaemia, both of which being controlled by Amlodipine 10mg and Atorvastatin 20mg/day. Imeglimin was initiated with a dose of 1000mg once daily, while continuing Metformin 1000mg twice a day. Upon 3 months follow up, HbA1c was reduced from 8.8% to 7.6%, FBS 174mg/dL and PPBS 213mg/dL(Table 1). No adverse event due to the new treatment strategy have been reported by the patient. Also, no weight gain or gastrointestinal complaints were noted. On physical examination, the patient was conscious and alert and normal in speech. Vitals were examined, BP 138/75 mmHg, pulse 76/min, SPO2 99%. Routine blood investigations were within normal limits. Upon six months follow-up HbA1c again reduced to 6% with a mild weight loss too. The patient didn't complain of any adverse effects even after 12 months of treatment with imeglimin, moreover showed prominent improvement in health and diabetic control.

Table 1: Changes in key parameters and laboratory data over the 12 month period.

	PARAMETERS				
	HbA1c (%)	**Fasting blood sugar mg/dl)**	**Postprandial blood sugar (mg/dL)**	**Weight**	**C-Peptide (ng/mL)**
Baseline	8.8	197	250	76	3.8
3 months	7.6	174	213	75	3.2
6 months	6.8	168	189	74	2.7
12months	6	135	168	74	2.5
% Reduction over 12 months	31.8%	23.8%	24.0%	6.2%	16.7%

CASE 2

Mr HM, a 58yr old female patient with history of T2DM for 8yrs and polycystic ovarian syndrome(PCOS), now on medications Metformin 2000mg/day, insulin glargine 30units/day, spironolactone 25mg/day, was presented to Medicine OPD with poorly controlled blood sugar levels and elevated HbA1c of 10.5% and also complained of episodes of hyperglycemia. Imeglimin was introduced at the dose of 1000mg daily in addition to the existing medications for diabetes. The patient was followed up after 3 months, a significant improvement in HbA1c of 9% was seen, FBS was reduced from 280mg/dL to 243mg/dL. Mild gastrointestinal symptoms on the first week of Imeglimin intake has been reported but resolved without any intervention. Laboratory investigations were within normal limits. Upon 6 months follow up, HbA1c decreased to 8.2% and to 7.3% on 12 months follow-up significantly. No adverse events have been reported by the patient. The patient also informed a modest weight reduction. Thereby we can see a notable improvement in long term glycemic control.

Table 2: Changes in key parameters and laboratory data over the 12 month period

	PARAMETERS				
	HbA1c (%)	**Fasting blood sugar (mg/dl)**	**Postprandial blood sugar (mg/dL)**	**Weight**	**C-Peptide (ng/mL)**
Baseline	10.5	240	296	96	4.2
3 months	9.0	203	223	95	3.8
6 months	8.2	173	205	92	3.6
12months	7.3	152	188	88	3.5
% Reduction over 12 months	28.6%	36.6%	24.0%	6.2%	16.7%

CASE 3

Mr XZ, a 60yr old male patient with a history of T2DM for 10yrs, Stage III CKD, hypertension, dyslipidemia has been on Metformin 1000mg/day, sitagliptin 100mg/day, Insulin detemir 25 units/day, lisinopril 20mg/day and atorvastatin 40mg/day. He has a BMI of 35kg/m2. The patients showed strict adherence to the treatment regimen, but when the blood investigation was conducted, HbA1c was 9.0%, FBS 210mg/dL, PPBS 250mg/dL Consequently Imeglimin 500mg was started as(dose adjusted due to CKD), along with the existing

medication regimen. Counselling was done on dietary changea and physical activity. Follow-up after 3 months showed an improvement in HbA1c 8.0%, FBS 190 AND PPBS 220.Weight is also reduced by 2kg.Upon 6 months follow-up, HbA1c was reduced to 7.3 and significant reduction in fasting and postprandial glucose levels. The patient weight reduced from 120kg to 114kg, which was beneficial to the patient.Imeglimin also associated with better management of blood glucose levels without affecting the renal function. Patient reported no adverse effects, which indicates Imeglimin was well-tolerated.

Table 3: Changes in key parameters and laboratory data over the 12 month period

	PARAMETERS				
	HbA1c (%)	**Fasting blood sugar (mg/dl)**	**Postprandial blood sugar (mg/dL)**	**Weight**	**C-Peptide (ng/mL)**
Baseline	9.0	212	289	88	3.5
3 months	7.9	180	213	87	3.1
6 months	7.1	168	189	84	2.9
12months	6.1	135	176	81	2.7
% Reduction over 12 months	32.2%	23.8%	28.4%	7.2%	20.1%

CASE 4

Mr TD, a 55yr old male patient who has previous history of T2DM for past 7yrs, NAFLD, hypertension and hyperlipidemia, now presented with fatigue, mild abdominal discomfort. He had already been given Metformin 1000mg/day, Glimepiride 4mg/day, atorvastatin 20mg/day, Losartan 50mg/dayThe Baseline HbA1c was 8.5%. Liver ezymes were elevated. BMI of the patient was 32kg/m2. Clinical investigation were done, showing elevated HbA1c of 8.5%, CBC counts were within normal limits. Imeglimin was initiated in the patient due to poor diabetic control, with a dose of 1000mg once daily. Dietary modifications were also adviced by the physician. 3 month follow-up showed considerable improvement in HbA1c with a value of 7.5%. No adverse effects had been reported by the patient. After 6months, HbA1c has reduced to 6.5%. A significant weight loss has also been noticed due to the dietary changes.

Table 4: Changes in key parameters and laboratory data over the 12 month period

	PARAMETERS				
	HbA1c (%)	**Fasting blood sugar (mg/dl)**	**Postprandial blood sugar (mg/dL)**	**Weight**	**C-Peptide (ng/mL)**
Baseline	8.5	215	250	96	4.2
3 months	7.5	180	213	95	3.8
6 months	7.0	168	189	92	3.6
12months	6.5	135	176	88	3.5
% Reduction over 12 months	23.5%	23.8%	24.0%	6.2%	16.7%

DISCUSSION

A new class of tetrahydro triazine-containing agents used for the treatment of T2DM has been recently launched in India[5], Imeglimin being the first among the new class. It could operate through several pathways, including improved beta cells mitochondrial function, boosting insulin production, enhancing beta-cell performance, and averting the death of epithelial cells[6]. Significant drops in HbA1c, FPG, and glycated albumin indicated that Imeglimin was linked to better glycaemic management as compared to placebo. These outcomes aligned with earlier research on Imeglimin in patients who were Caucasian. Previous studies on Imeglimin served an improvement in glycemic control in patients with T2DM who were unresponsive to sulfonylurea[7][8].

In this case series, we present 4 cases involving patients having uncontrolled Type 2 Diabetes with varying comorbidities, including hypertension, dyslipidemia, CKD, PCOS and NAFLD, none of them willing to receive insulin therapy due to fear of injections. They were already on prolonged therapy with diabetic medications such as biguanides, gliptins or SGLT2 inhibitors, but still the blood sugar levels were elevated, which indicates a poor diabetic control. This might be due to unhealthy diet, associated diseases or lack of medication adherence. They were initiated with Imeglimin, a novel therapeutic agent, as an adjunctive therapy to the existing medication management for diabetes. All the 4 patients were observed for a period of 12 months after the administration of Imeglimin.

Case 1 involved a 62 yr old male with a long standing history of T2DM for 10yrs with no other comorbidities. The addition of imeglimin resulted in a significant reduction in HbA1c from 8.8% to 6% over twelve months, alongside improvements in fasting and postprandial blood glucose levels. Moreover, the patients weight and lipid profile remained stable, which is a common concern with conventional antidiabetic medications. Case 2 highlighted a 58 year old female patient with PCOS upon the addition of imeglimin to the patient's regimen resulted in significant improvement in glycemic control, as evidenced by reductions in HbA1c from 10.5% to 7.3% over a period of 12 months. The patient also experienced a modest weight reduction, which is particularly beneficial given the history of obesity and PCOS. Case 3 including a 60yr old male patient with history of T2DM and Stage III CKD also experienced a decrease in HbA1c from 9.0% to 6.1%. Despite his chronic kidney disease, imeglimin facilitated better management of sugar levels without adversely affecting his renal function. In case 4, a 55yr old male patient with diabetes and non alcoholic fatty liver disease, demonstrated a significant reduction in HbA1c of 23.5% over 12 month period. Further evidence of a change in fatty liver was provided by liver function tests (ALT, AST) which showed a significant improvement in just 3 months. Despite the complexities associated with comorbidities, Imeglimin was effective across all 4 cases. Fundamental clinical efficacy has been demonstrated by international studies, including the Trials of IMeglimin for Efficacy and Safety (TIMES) 1, 2, and 3. Monotherapy has been shown to reduce HbA1c by 0.46%. Additional outcomes include a 0.57% reduction with SGLT2 and a 0.92% reduction with DPP4-i[9]. Imeglimin primarily exhibits unaltered renal excretion, making it a potential first-in-class treatment for T2DM. The PK values in T2DM with chronic renal illness were examined to determine the ideal dosage amounts[10].

SAFETY PROFILE AND TOLERABILITY

In every instance, imiglimin's tolerability and safety were good. The majority of adverse effects that were recorded were small and temporary, like nausea and gastrointestinal discomfort, and they went away on their own. Interestingly, hypoglycemia was not reported, which is noteworthy because it is a serious danger linked with many other antidiabetic medications, especially insulin and sulfonylureas.Tolerability is a major worry when starting a new medicine in people with numerous comorbidities. Imeglimin may be used in a variety of T2DM patients due to its strong safety profile, as seen by the lack of significant side effects in this series. Its safety is also supported by the fact that patients with heart failure do not have significant weight gain or fluid retention, which are common side effects of some other antidiabetic medications such as thiazolidinediones[11].

POTENTIAL IMPLICATION FOR CLINICAL PRACTICE

The results imply that imeglimin may be essential for the management of type 2 diabetes, particularly in individuals who have difficulty meeting their glycaemic objectives while receiving conventional therapy. To validate these benefits, larger clinical trials are necessary to further investigate the dual mechanism of action and favourable safety profile of this drug. Nevertheless, these results mechanistically imply that improved insulin secretion and insulin sensitivity of imeglimin characteristics may be responsible for this extra reduction in HbA1c in addition to metformin treatment.

CONCLUSION

The effectiveness and safety of imeglimin in enhancing glycaemic control in individuals with type 2 diabetes mellitus (T2DM) who have not reached target levels with traditional therapy are demonstrated in this case series. The favourable safety profile and observed beneficial outcomes indicate that imeglimin may be a useful adjunct to current therapy choices for the management of type 2 diabetes, especially in individuals whose condition is not well controlled. Although more research is needed to determine its long-term safety and efficacy, the current results are consistent with its possible application in clinical practice.

DECLARATION OF PATIENT CONSENT

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published, and alternative names will be used instead; due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

REFERENCES

1. International Diabetes Federation 9: IDF Diabetes Atlas 9th Edition. Brussels, Belgium. https://www.idf.org/e-library/epidemiology-research/diabetes-atlas/159-idf-diabetes-atlas-ninth-edition-2019.html
2. ElSayed NA, Aleppo G, Aroda VR etal., on behalf of the American Diabetes Association. 1. Improving Care and Promoting Health in Populations: Standards of Care in Diabetes-2023. Diabetes Care. 2023 Jan 1;46(Supple 1):S10-18. [PMID: 36507639]
3. De Fronzo, R. A., Ferrannini, E., Zimmet, P., & Alberti, G. (2015). International Textbook of Diabetes Mellitus. John Wiley & Sons.
4. Pirags V, Lebovitz H, Fouqueray P. Imeglimin, a novel glimin oral antidiabetic, exhibits a good efficacy and safety profile in type 2 diabetic patients. Diabetes Obes Metab 2012; 14:852–858. https://doi.org/10.1111/j.1463-1326.2012.01611.x PMID: 22519919
5. Giruzzi M. Imeglimin. Clin Diabetes. 2021 Oct;39(4):439-40.
6. Fouqueray P, Bolze S, Pirags V, et al. Dose Ranging-Study to Determine the Optimum Dose for Imeglimin, a Novel Treatment for Type 2 Diabetes. Boston, MA: ADA; 2015.
7. Fouqueray P, Pirags V, Inzucchi SE, et al. The efficacy and safety of imeglimin as add-on therapy in patients with type 2 diabetes inadequately controlled with metformin monotherapy. *Diabetes Care.* 2013; 36(3): 565-568.
8. Dubourg J, Fouqueray P, Quinslot D, Grouin JM, Kaku K. Long-term safety and efficacy of imeglimin as monotherapy or in combination with existing antidiabetic agents in Japanese patients with type 2 diabetes (TIMES 2): A 52-week, open-label, multicentre phase 3 trial. Diabetes Obes Metab. 2022 Apr;24(4):609-619. doi: 10.1111/dom.14613. Epub 2021 Dec 27. PMID: 34866306; PMCID: PMC9305103.
9. Kawata T, Bando H, Kato Y, Yamashita H, Kato Y, Ogura K. Improvement of HbA1c, Weight and Fatty Liver by Short Treatment of Imeglimin (Twymeeg). Asp Biomed Clin Case Rep. 2024 Jan 20;7(1):30-35.
10. Tomita Y, Hansson E, Mazuir F, Wellhagen GJ, Ooi QX, Mezzalana E, Kitamura A, Nemoto D, Bolze S. Imeglimin population pharmacokinetics and dose adjustment predictions for renal impairment in Japanese and Western patients with type 2 diabetes. Clin Transl Sci. 2022 Apr;15(4):1014-1026. doi: 10.1111/cts.13221. Epub 2022 Jan 17. PMID: 34962074; PMCID: PMC9010270.
11. Fonseca V. Effect of thiazolidinediones on body weight in patients with diabetes mellitus. The American journal of medicine. 2003 Dec 8;115(8):42-8.