



Original Research Article

Improvement in glycemic level with saxagliptin in patients of type 2 diabetes mellitus who were previously on metformin monotherapy with uncontrolled diabetes

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ABSTRACT

Introduction: Type 2 diabetes affects millions of people worldwide and significantly contributes to morbidity and mortality of those affected by it. Current guidelines recommend individualized treatment regimens following first line metformin therapy. Saxagliptin, a dipeptidyl-peptidase 4 inhibitor, provides a secondary mechanism of action to decrease hyperglycemia when used in combination with metformin. In this study we have tried to assess the efficacy of saxagliptin in patients of type 2 DM.

Materials and Methods: A total of 35 patients were enrolled who were on metformin monotherapy and with uncontrolled diabetes. Patients were given saxagliptin 2.5 mg once a day. Patients were followed up at 1st, 3rd and 6th month and HbA1c, FPG and 2h-PG estimation was done during the follow up period.

Results: The mean age \pm SD in male and female patients was 61.42 yrs \pm 6.99 and 55.93 yrs \pm 5.74 respectively. The mean change in value from baseline at 24 weeks was 10.7%, 16.48% and 21.63% for HbA1c, FPG and 2h-PG respectively and 20% of patient had achieved HbA1c $<$ 7%. A highly significant difference has been seen at 0 v/s 1, 0 v/s 3 and 0 v/s 6 months in HbA1c, FPG and 2h-PG values.

Conclusion: Saxagliptin has shown an improvement in glycemic index (HbA1c, FPG, 2h-PG) during 6 months of treatment in patients of type 2 DM.

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1. Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia. It may be due to impaired insulin secretion, resistance to peripheral actions of insulin, or both.¹

In early type 2 DM, symptoms may be more subtle and consist of fatigue, poor wound healing, and paresthesias. The lack of symptoms is the main reason for the delayed diagnosis of type 2 DM. Many pts are diagnosed based on screening or during blood tests taken for other reasons.² This delay in diagnosing the disease results in a high prevalence of chronic complications at the

time of actual diagnosis, thus when Type 2 diabetes is diagnosed, cardiovascular disease and neuropathy are found in approximately 10% of cases, and retinopathy and nephropathy in 15-20%.³

The prevalence of type 2 diabetes has been increasing steadily all over the world. As a result of this trend, it is fast becoming an epidemic in some countries of the world with the number of people affected expected to double in the next decade due to increase in ageing population, thereby adding to the already existing burden for healthcare providers, especially in poorly developed countries.⁴ The greatest increase in the prevalence of diabetes mellitus is reported from low and middle-income countries.^{5,6} Asia, being the epicenter for the epidemics of diabetes, is responsible for more than 60% of the

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global burden of diabetes mellitus.^{7,8} Preliminary results from a large community study conducted by the Indian Council of Medical research (ICMR) revealed that a lower proportion of the population is affected in northern states of India (Chandigarh 0.12 million, Jharkhand 0.96 million) as compared to Maharashtra (9.2 million) and Tamil Nadu (4.8 million). The National Urban Survey conducted across the metropolitan cities of India reported similar trend: 11.7 per cent in Kolkata, 11.6 per cent in New Delhi, and 9.3 per cent in Mumbai compared with 13.5 per cent in Chennai, 16.6 per cent in Hyderabad, and 12.4 per cent in Bengaluru.⁹

Currently, six classes of oral antidiabetic drugs (OADs) are available: biguanides (e.g., metformin), sulfonylureas (e.g., glimepiride), meglitinides (e.g., repaglinide), thiazolidinediones (e.g., pioglitazone), dipeptidyl peptidase IV inhibitors (e.g., sitagliptin), and α -glucosidase inhibitors (e.g., acarbose). Utilization of antidiabetic drugs should be based on the individual patient's characteristics and preferences and balance the need to optimize the benefits of glycaemic control with the need to limit the risk of adverse effects. Saxagliptin is a DPP4 inhibitor, acts by increasing postprandial concentrations of glucagon-like peptide-1 (GLP-1) and glucose-dependent insulinotropic peptide (GIP). GLP-1 and GIP stimulate insulin secretion in a glucose-dependent manner, suppressing glucagon secretion and slowing gastric emptying.¹⁰

2. Materials and Methods

The study was conducted in the department of pharmacology and department of medicine in Dr Rajendra Prasad Government medical college and hospital after getting approval from Protocol review committee letter no. 39/2015 and Institutional Ethics Committee letter no. HFW-H-DRPGMC/Ethics/2015 dated 27/6/2015.

2.1. Inclusion criteria

Patients of age between 18 to 80 years with non-insulin dependent diabetes mellitus, taking metformin in the doses of 1500mg having HbA1c level between 7% to 10% along with FPG levels ≥ 126 mg/dl and / or 2hPG ≥ 200 mg/dl were included in the study.

2.2. Exclusion criteria

Patients with -

1. Acute complications of diabetes
 - a. Hyperglycemic hyperosmolar state
 - b. Diabetic ketoacidosis
2. Renal or liver disease
3. Congestive heart failure
4. Acute coronary syndrome
5. Pregnancy

2.3. Sample size

Total 35 patients of either sex with type 2 DM attending diabetic clinic in Medicine OPD on Saturday were screened and enrolled in the study.

2.4. Methods

Patients were screened for diabetes status with the help of HbA1C, FPG, and PPPG. Detailed history taking, clinical examination, and lab investigation including Lipid profile, Liver function test and Kidney function test of all the patients was also done. Patients were prescribed metformin 500 mg twice a day + saxagliptin 2.5 mg (onglyza) once a day and were followed up on 1st, 3rd and 6th month. All the investigations that were done during the enrollment were repeated during the follow up of patient. In patients with uncontrolled diabetes saxagliptin up to 5 mg once a day was administered. If a patient was found to have uncontrolled diabetes even with the adjustment in the doses on follow up visits, he / she was considered failure of therapy and was managed appropriately.

2.5. Statistical Analysis

Analysis was done using Microsoft excel version 2013 and Graph pad online software.

3. Results

Total 35 patients were enrolled, out of which 4 patients lost to follow up and 1 patient reported with the side effect of bilateral knee arthralgia so she was shifted to alternative therapy and was managed appropriately. Total 30 (14 males and 16 females) patients completed treatment with saxagliptin as add on therapy to metformin. The mean age \pm SD in male and female patients was 61.42 yrs \pm 6.99 and 55.93 yrs \pm 5.74 respective.



Fig. 1: Mean age \pm SD of male and female patients in yrs.

Mean decrease in HbA1c from baseline at 24 weeks was 10.7%, and 20% of patients have achieved HbA1c value $< 7\%$. When comparison was done between 0 vs 1, 0 vs 3 and 0 vs 6 months the p value was < 0.00001 (** p value < 0.001).

Mean decrease in FPG from baseline at 24 weeks was 16.48%. When comparison was done between 0 vs 1, 0 vs 3

Table 1: Improvement in HbA1C levels over a period of 6 months

Investigation	Duration (Month)	Mean ± SD
HbA1C	0	8.41% ± 0.68
	1	8.2 % ± 0.65**
	3	7.98 %± 0.59**
	6	7.51% ± 0.40**

Unit - mmol/mol, Normal value: <42mmol/mol / <5.6%

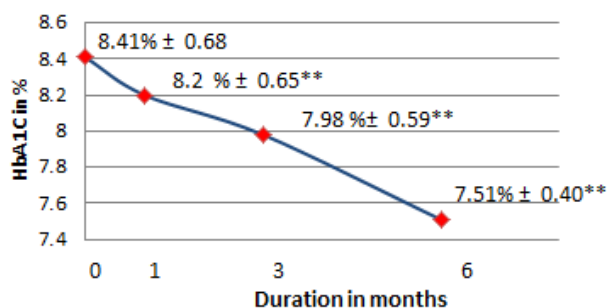


Fig. 2: Improvement in HbA1C over a period of 6 months

Table 2: Improvement in FPG levels over a period of 6months

Investigation	Duration (Month)	Mean ± SD
FPG	0	166.36 ± 9.40
	1	156.83 ± 9.82**
	3	148.63 ± 9.21**
	6	138.96 ± 9.41**

Unit – mg/dl, Normal value: <100 mg/dl

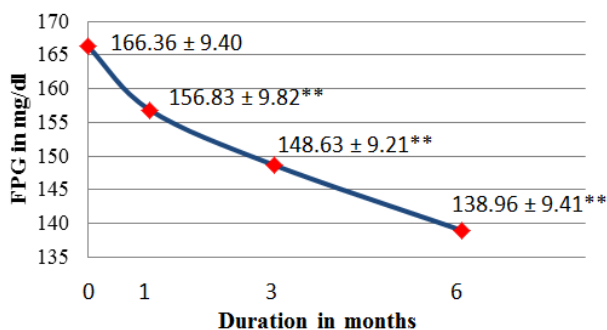


Fig. 3: Improvement in FPG levels over a period of 6 months

and 0 vs 6 months the p value was < 0.00001. (** p value <0.001)

Mean decrease in 2h-PG from baseline at 24 weeks was 21.63%. When comparison was done between 0 vs 1, 0 vs 3 and 0 vs 6 months the p value was < 0.00001. (** p value <0.001)

Table 3: Improvement in 2h-PG over a period of 6 months

Investigation	Duration (Month)	Mean ± SD
2h-PG	0	225.53 ± 16.64
	1	211.03 ± 17.03**
	3	190.66 ± 7.97**
	6	176.76 ± 8.21**

Unit – mg/dl, Normal value: <140 mg/dl

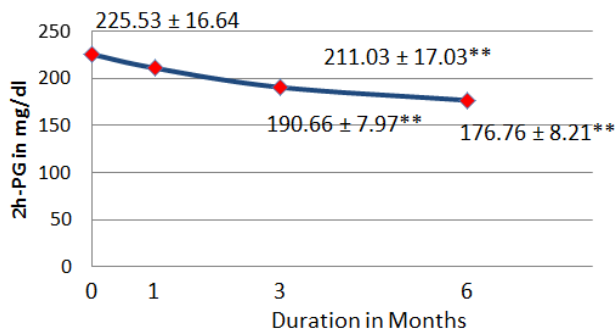


Fig. 4: Improvement in 2 h – PG levels over a period of 6 months

4. Discussion

The current study evaluated the efficacy of adding saxagliptin as add-on therapy to metformin for the duration of 6 months in the patients of type 2 diabetes mellitus who were previously on metformin monotherapy with inadequate glycemic control. We found that Saxagliptin improved glycemic control when added to metformin, a progressive significant improvement has been seen in saxagliptin group in HbA1C, FPG and PPPG levels at 0 vs 1, 0 vs 3 and at 0 vs 6 month (P value ≤ 0.001). Mean decrease in HbA1c, FPG and 2h-PG from baseline at 24 weeks were 10.7%, 16.48% and 2.63% respectively and 20% of patients have achieved HbA1c <7%. In one of the studies conducted by Dhillon S. et al, it has been seen that the DPP4 inhibitor saxagliptin was effective in improving glycemic control, as shown by reductions in HbA1C, FPG, PPPG, and by an increased proportion of patients achieving the glycemic goal of HbA1c < 7.0% with saxagliptin. The additional glycaemic benefit observed in the saxagliptin + metformin combination therapy groups is likely to be a consequence of each component’s different MOA working in concert.

5. Conclusion

The combination of saxagliptin plus metformin for the treatment of type 2 diabetes offers an oral treatment regimen that is effective and well tolerated. This agent provides an attractive combination to utilize metformin, recommended as the first line treatment, with a DPP-4 inhibitor when tailoring patient specific therapies in the treatment of type 2 diabetes.

6. Source of Funding

None.

7. Conflict of Interest

None.

References

1. Goyal R, Jialal I. Diabetes Mellitus Type 2; 2020.
2. Kasper D, Fauci A, Hauser S, Longo D. *Harrisons Manual of Medicine*; 2016.
3. Muggeo M. Accelerated complications in Type 2 diabetes mellitus: the need for greater awareness and earlier detection. *Diabet Med.* 1998;15(S4):S60–2.
4. Olokoba AB, Obateru OA, Olokoba LB. Type 2 Diabetes Mellitus: A Review of Current Trends. *Oman Med J.* 2012;27(4):269–73.
5. Global Report on Diabetes. WHO, http://apps.who.int/iris/bitstream/handle/10665/204871/9789241565257_eng.pdf;jsessionid=1C87D795D989E8C7FD4703DED26C9157?sequence=1;
6. Bhutani J, Bhutani S. Worldwide burden of diabetes. *Indian J Endocrinol Metab.* 2014;18(6):868–70.
7. International Diabetes Federation. *Diabetes Atlas*; 2017. Available from: <http://www.diabetesatlas.org/resources/2017-atlas.html>.
8. Hu FB. Globalization of Diabetes: The role of diet, lifestyle, and genes. *Diab Care.* 2011;34(6):1249–57.
9. Kaveeshwar S. The current state of diabetes mellitus in India. *Aus Med J.* 2014;7(1):45–8.
10. Men P, Li XT, Tang HL, Zhai SD. Efficacy and safety of saxagliptin in patients with type 2 diabetes: A systematic review and meta-analysis. *PLoS One.* 2018;13(5):E197321.

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