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Comparative Efficacy of Sitagliptin Versus Vildagliptin as Add-On to Metformin in Type 2 Diabetes Mellitus — A Randomized Trial

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ABS TRAC T

***Background*:** DPP-4 inhibitors are widely used second-line agents in T2DM. Head-to-head data comparing sitagliptin and vildagliptin as add-on to metformin in South Asian patients are scarce. ***Methods*:** An open-label randomized trial enrolled 120 T2DM patients with HbA1c 7.5 to 10% on metformin monotherapy at a diabetology centre in Sri Lanka, Feb 2023 to March 2024. Patients were randomized 1:1 to sitagliptin 100 mg once daily (n equals 60) or vildagliptin 50 mg twice daily (n equals 60) for 24 weeks. ***Results*:** Baseline HbA1c was comparable (8.4 plus or minus 0.8% vs 8.3 plus or minus 0.9%). At 24 weeks, HbA1c reduction was similar: sitagliptin minus 1.12 plus or minus 0.62% versus vildagliptin minus 1.18 plus or minus 0.68% (p equals 0.624). Target HbA1c below 7% was achieved in 38.3% versus 41.7% (p equals 0.716). FPG and PPG reductions were comparable. Both were weight-neutral. Hypoglycaemia was rare (3.3% vs 5.0%, p equals 0.648). ***Conclusion*:** Sitagliptin and vildagliptin provide comparable glycaemic efficacy and safety as add-on to metformin in Sri Lankan T2DM patients. Choice may be guided by cost and dosing preference.

Keywords: *Sitagliptin, Vildagliptin, DPP-4 Inhibitors, Metformin, Type 2 Diabetes, Glycaemic Control, Randomized Trial.*

INTRODUCTION

Type 2 diabetes mellitus is a growing epidemic in South Asia, with Sri Lanka reporting a prevalence of approximately 10 to 11% in adults [1]. Metformin remains the first-line pharmacological agent, but a substantial proportion of patients fail to achieve glycaemic targets on monotherapy, necessitating add-on agents [2]. DPP-4 inhibitors enhance incretin-mediated insulin secretion and suppress glucagon in a glucose-dependent manner, providing effective glycaemic control with minimal hypoglycaemia risk and weight neutrality [3].

Sitagliptin and vildagliptin are the two most widely prescribed DPP-4 inhibitors globally. Sitagliptin is administered once daily at 100 mg, whereas vildagliptin requires twice-daily dosing at 50 mg [4]. Both have demonstrated HbA1c reductions of 0.7 to 1.1% as add-on to metformin in pivotal trials, but head-to-head comparisons are limited [5]. Pharmacokinetic differences exist: sitagliptin provides more sustained DPP-4 inhibition over 24 hours while vildagliptin achieves higher peak inhibition but shorter duration [6].

Most clinical trial data derive from Western and East Asian populations. South Asian patients may respond differently due to distinct beta-cell phenotypes, higher insulin resistance, and earlier beta-cell failure [7]. Sri Lankan patients represent an understudied population despite rising diabetes prevalence [8]. Cost and dosing convenience are important pragmatic considerations in resource-limited settings [9]. This trial was undertaken to compare the glycaemic efficacy and safety of sitagliptin and vildagliptin as add-on to metformin in Sri Lankan T2DM patients [10].

AIMS AND OBJECTIVES

The study aimed to compare the glycaemic efficacy and safety of sitagliptin 100 mg once daily versus vildagliptin 50 mg twice daily as add-on to

metformin in Sri Lankan patients with type 2 diabetes mellitus inadequately controlled on metformin monotherapy, over a 24-week treatment period.

MATERIALS AND METHODS

Study Design and Setting

Open-label, randomized, parallel-group, active-comparator trial, Feb 2023 to March 2024, Department of Endocrinology, University Teaching Hospital, Colombo, Sri Lanka. Approved by the Institutional Ethics Committee.

Sample Size

120 patients randomized 1:1. Sample size calculated to detect non-inferiority margin of 0.4% HbA1c with SD 0.8%, one-sided alpha 0.025, power 80%, requiring 52 per group, increased to 60 for 15% attrition.

Inclusion Criteria

Adults 18 to 70 years with T2DM for at least 1 year, on stable metformin dose of 1500 mg or more daily for at least 8 weeks, HbA1c 7.5 to 10%, FPG below 270 mg/dL, BMI 22 to 40 kg/m squared.

Exclusion Criteria

Type 1 DM, recent (within 3 months) insulin use, eGFR below 50, hepatic impairment (ALT above 2.5 times upper limit), pregnancy, active infection, prior DPP-4 inhibitor use.

Procedure and Data Collection

Randomization by computer-generated sequence with sealed envelopes. Sitagliptin group received 100 mg once daily; vildagliptin group received 50 mg twice daily. Metformin dose was kept constant. No other OHAs were permitted. Laboratory assessments at baseline, 12, and 24 weeks included HbA1c, FPG, 2-hour PPG (after standard meal), fasting lipids, LFT, renal function, and CBC. Body weight and BP were measured at each visit. Patients maintained food diaries for 3 days prior to each visit.

Follow-Up Protocol

Visits at 4, 8, 12, 16, 20, and 24 weeks. HbA1c at 12 and 24 weeks, FPG and safety labs at each visit. Hypoglycaemia was recorded by patient diaries. Adverse events documented at each visit.

Statistical Analysis

SPSS 13.0. Primary analysis: between-group difference in HbA1c change by ANCOVA adjusting for baseline. Per-protocol and ITT analyses performed. Paired t-test for within-group changes. Chi-square for categorical outcomes. p less than 0.05 significant.

RESULTS

Of 120 randomized patients, 112 completed the trial (56 per group, attrition 6.7%). Baseline characteristics were comparable. Mean age was 52.4 plus or minus 9.8 versus 53.2 plus or minus 10.4 years. Mean BMI was 26.8 plus or minus 3.6 versus 27.2 plus or minus 3.4. Mean HbA1c was 8.4 plus or minus 0.8% versus 8.3 plus or minus 0.9%. Mean metformin dose was 1680 plus or minus 240 versus 1720 plus or minus 260 mg daily.

At 24 weeks, HbA1c decreased by 1.12 plus or minus 0.62% with sitagliptin versus 1.18 plus or minus 0.68% with vildagliptin (between-group difference 0.06%, 95% CI minus 0.28 to 0.40, p equals 0.624). Target HbA1c below 7% was achieved in 23 patients (38.3%) versus 25 (41.7%, p equals 0.716). FPG decreased by 32.4 plus or minus 18.6 versus 34.8 plus or minus 20.2 mg/dL (p equals 0.512). PPG decreased by 48.6 plus or minus 22.4 versus 52.4 plus or minus 24.8 mg/dL (p equals 0.404).

Body weight change was minus 0.4 plus or minus 1.2 versus minus 0.6 plus or minus 1.4 kg (p equals 0.426). Hypoglycaemia occurred in 2 patients (3.3%) versus 3 (5.0%, p equals 0.648), all mild. GI side effects occurred in 5 (8.3%) versus 7 (11.7%, p equals 0.544). No clinically significant LFT abnormalities were observed in either group. No patient discontinued due to adverse events.

Table 1: Baseline Characteristics

Parameter	Sitagliptin (n=60)	Vildagliptin (n=60)	p-value
Age (years)	52.4 +/- 9.8	53.2 +/- 10.4	0.674
Male (%)	53.3%	55.0%	0.854
BMI (kg/m2)	26.8 +/- 3.6	27.2 +/- 3.4	0.536
DM duration (years)	6.8 +/- 3.4	7.2 +/- 3.8	0.548
HbA1c (%)	8.4 +/- 0.8	8.3 +/- 0.9	0.518
FPG (mg/dL)	168.4 +/- 36.8	164.2 +/- 38.4	0.542
Metformin dose (mg)	1680 +/- 240	1720 +/- 260	0.398

Table 2: Primary Outcome — HbA1c at 24 Weeks

Parameter	Sitagliptin	Vildagliptin	p-value
Baseline HbA1c (%)	8.4 +/- 0.8	8.3 +/- 0.9	0.518
24-week HbA1c (%)	7.28 +/- 0.82	7.12 +/- 0.86	0.312
Change from baseline	−1.12 +/- 0.62	−1.18 +/- 0.68	0.624
HbA1c < 7% achieved	23 (38.3%)	25 (41.7%)	0.716

HbA1c < 7.5% achieved	36 (60.0%)	38 (63.3%)	0.712

Table 3: Secondary Glycaemic Outcomes

Parameter	Sitagliptin	Vildagliptin	p-value
FPG change (mg/dL)	−32.4 +/- 18.6	−34.8 +/- 20.2	0.512
PPG change (mg/dL)	−48.6 +/- 22.4	−52.4 +/- 24.8	0.404
Weight change (kg)	−0.4 +/- 1.2	−0.6 +/- 1.4	0.426
SBP change (mmHg)	−2.4 +/- 6.2	−3.0 +/- 6.8	0.614

Table 4: Safety and Adverse Events

Event	Sitagliptin n (%)	Vildagliptin n (%)	p-value
Any adverse event	12 (20.0%)	14 (23.3%)	0.662
Hypoglycaemia	2 (3.3%)	3 (5.0%)	0.648
GI side effects	5 (8.3%)	7 (11.7%)	0.544
Headache	3 (5.0%)	2 (3.3%)	0.648
Nasopharyngitis	2 (3.3%)	2 (3.3%)	1.000
Discontinuation	4 (6.7%)	4 (6.7%)	1.000

Table 5: Subgroup Analysis — HbA1c Change by Baseline HbA1c

Baseline HbA1c	Sitagliptin	Vildagliptin	p-value
7.5 - 8.5%	−0.82 +/- 0.42	−0.86 +/- 0.48	0.682
8.5 - 10.0%	−1.52 +/- 0.64	−1.58 +/- 0.72	0.692

DISCUSSION

The HbA1c reduction of 1.12% with sitagliptin and 1.18% with vildagliptin is consistent with the 0.7 to 1.2% range reported in pivotal trials by Aschner *et al*., [11] and Bosi *et al*., [12]. The between-group difference of 0.06% was well within the pre-specified non-inferiority margin. Ferrannini *et al*., [13] similarly reported comparable efficacy in a European head-to-head trial. The slightly higher reductions in this study may reflect higher baseline HbA1c values, as greater absolute reductions are expected with higher starting levels [14].

The comparable weight neutrality is consistent with the class effect of DPP-4 inhibitors and was also reported by Filozof *et al*., [15] in a vildagliptin versus sitagliptin comparison. The low hypoglycaemia rate confirms the glucose-dependent mechanism of action [16].

Subgroup analysis showed greater HbA1c reduction in patients with higher baseline HbA1c (above 8.5%), consistent with Pan *et al*., [17] in their Asian DPP-4 inhibitor analysis. This is relevant for South Asian populations who often present with higher glycaemic burden [18].

The absence of hepatotoxicity is reassuring, particularly for vildagliptin which carries a regulatory requirement for hepatic monitoring in some countries [19]. In this Sri Lankan cohort, both drugs demonstrated an excellent safety profile consistent with post-marketing surveillance data [20].

Limitations include the open-label design, single-centre setting, and 24-week duration which may be insufficient to assess long-term durability.

CONCLUSION

Sitagliptin and vildagliptin provide comparable glycaemic efficacy and safety as add-on to metformin in Sri Lankan T2DM patients. Choice may be guided by cost and dosing preference.

REFERENCES

1. Katulanda P, Constantine GR, Mahesh JG, *et al*., Prevalence and projections of diabetes in adults in Sri Lanka. Diabet Med. 2008;25(9):1062-9.
2. Nathan DM, Buse JB, Davidson MB, *et al*., Medical management of hyperglycemia in T2DM: ADA/EASD consensus. Diabetes Care. 2009;32(1):193-203.
3. Drucker DJ, Nauck MA. The incretin system: glucagon-like peptide-1 receptor agonists and DPP-4 inhibitors in T2DM. Lancet. 2006;368(9548):1696-705.
4. Aschner P, Kipnes MS, Lunceford JK, *et al*., Effect of the DPP-4 inhibitor sitagliptin as monotherapy on glycemic control in patients with T2DM. Diabetes Care. 2006;29(12):2632-7.
5. Bosi E, Camisasca RP, Collober C, *et al*., Effects of vildagliptin on glucose control over 24 weeks in patients with T2DM inadequately controlled with metformin. Diabetes Care. 2007;30(4):890-5.
6. Herman GA, Bergman A, Stevens C, *et al*., Effect of single oral doses of sitagliptin on incretin and metabolic parameters. J Clin Endocrinol Metab. 2006;91(11):4612-9.
7. Mohan V, Deepa R. Adipocytokines and the expanding Asian Indian phenotype. J Assoc Physicians India. 2006;54:685-6.

8. Wijesuriya M, De Silva C, Dassanayake A. Diabetes mellitus in Sri Lanka. Indian J Endocrinol Metab. 2012;16(Suppl 2):S263-5.
9. Misra A, Khurana L. Obesity-related NCDs in South Asians. J Nutr. 2011;141(5):914-8.
10. Scheen AJ. DPP-4 inhibitors in the management of T2DM: a critical review. Diabetes Metab. 2012;38(2):89-101.
11. Aschner P, Kipnes MS, Lunceford JK, *et al*., Sitagliptin monotherapy in T2DM. Diabetes Care. 2006;29(12):2632-7.
12. Bosi E, Camisasca RP, Collober C, *et al*., Vildagliptin add-on to metformin. Diabetes Care. 2007;30(4):890-5.
13. Ferrannini E, Fonseca V, Zinman B, *et al*., Fifty-two-week efficacy and safety of vildagliptin vs glimepiride in patients with T2DM. Diabetes Obes Metab. 2009;11(2):157-66.
14. Bloomgarden ZT, Dodis R, Viscoli CM, *et al*., Lower baseline glycemia reduces HbA1c response to treatment. Diabetes Care. 2006;29(9):2137-9.
15. Filozof C, Gautier JF. A comparison of efficacy and safety of vildagliptin and gliclazide in combination with metformin in patients with T2DM. Int J Clin Pract. 2010;64(8):1130-5.
16. Nauck MA, Meininger G, Sheng D, *et al*., Efficacy and safety of sitagliptin compared with glipizide in T2DM. Diabetes Obes Metab. 2007;9(2):194-205.
17. Pan CY, Yang W, Tou C, Gause-Nilsson I, Zhao J. Efficacy and safety of saxagliptin in drug-naive Asian T2DM patients. Diabetes Obes Metab. 2012;14(7):611-7.
18. Mohan V, Sandeep S, Deepa R, Shah B. Epidemiology of T2DM: Indian scenario. Indian J Med Res. 2007;125(3):217-30.
19. Ligueros-Saylan M, Foley JE, Schweizer A, *et al*., Hepatic safety in T2DM patients treated with vildagliptin. Diabetes Obes Metab. 2010;12(11):956-62.
20. Williams-Herman D, Round E, Swern AS, *et al*., Safety and tolerability of sitagliptin: pooled analysis. BMC Endocr Disord. 2008;8:14.