DOI: https://doi.org/10.53350/pjmhs221610459

ORIGINAL ARTICLE

A Comparison of the Efficacy of Dapagliflozin Metformin Versus Sitagliptin Metformin: in Newly Diagnosed Type 2 Diabetes

AFRA ISHTIAQUE[1], SHAHREEN MEHMOOD KHAN[2], SALMAN AZHAR[3], MEHREEN MEHMOOD[4], SAIRA SHAHNAWAZ[5]
[1]*Women Medical Officer, Govt ID Hospital Faisalabad*
[2]*House Officer, Mayo Hospital, Lahore*
[3]*Associate professor of medicine, Madinah teaching hospital, Faisalabad*
[4]*Woman Medical Officer, DHQ Hospital, Sheikhupura*
[5]*Senior demonstrator in Niazi Medical and Dental College, Sargodha*
Corresponding author: Salman Azhar, Email: salman_azhar2010@yahoo.com

ABSTRACT

Objective: To comparison of the efficacy of dapagliflozin+metformin versus sitagliptin+metformin: in newly diagnosed type 2 diabetes

Methodology: In this Randomized Control Trial, we enrolled a total of 180 cases; 90 cases newly diagnosed type 2 diabetes mellitus (HbA1c>6.5) in two equal groups A&B on the basis of computer-generated randomization table. Group A was allotted to the cases 100mg q.d sitagliptin plus 850 mg in addition to 500mg metformin 2 times a day. Patients of Group B were advised for 10mg qd dapagliflozin+500mg metformin 2 times a day for six months. Patients were followed up on monthly basis for any inconvenience. The final follow-up was done on 6th month of treatment. All the patients with poor/non-compliance were excluded from the study. All cases with HbA1c <6.0 were considered as effectively treated patients.

Results: Comparison of Efficacy in both groups shows 44(48.9%) in Group A and 31(34.4%) in Group B, the overall efficacy was 41.7%, p-value=0.0.35 showing a significant difference.

Conclusion: Dapagliflozin+metformin is significantly higher than sitagliptin+metformin for newly diagnosed type 2 diabetes

Keywords: Newly type 2 diabetes, treatment, Dapagliflozin & Metformin Vs Sitagliptin & Metformin

INTRODUCTION

Diabetes mellitus type 2, often known as T2DM, is a worldwide health problem that affects over 425 million people,[1] and it is the sixth biggest cause of mortality all over the world.[2] It is anticipated that the disease burden would expand at a faster pace in low- to middle-income countries in Asia, the Middle East, and Africa,[3] which has major consequences for the use of healthcare resources, the quality of life, and the mortality associated with type 2 diabetes. There are now 8.3% of individuals in Pakistan who are affected by type 2 diabetes, which amounts to 7.5 million people according to the International Diabetes Federation (IDF). This gives Pakistan a national age-standardized prevalence of 8.3%.[1] Other studies that were carried out in Pakistan between the years 1995 and 2014 showed that the prevalence of type 2 diabetes was between 8% and 14% of the population. This range was determined by geographical differences, urban vs rural sampling, and the diagnostic criteria that were used.[4–13] Type 2 diabetes mellitus is a gradual but progressing condition, and patients often have a period of time during which they are symptom-free prior to their diagnosis. According to recent estimates, about half of individuals who have diabetes have not yet been diagnosed with the condition, and the percentage in Pakistan (61.5% of the total) is significant. It has also been stated that by the time a diagnosis of type 2 diabetes is made, the condition has already been present for four to seven years.[14]

In the last several decades, a number of innovative anti-diabetic drugs have been created and used for the treatment of diabetic patients in clinical settings. The sodium-glucose cotransporter-2 (SGLT-2) inhibitor and the dipeptidyl peptidase-4 (DPP-4) inhibitor are the ones that are now being used most often among these innovative anti-diabetic drugs.[15-19] In comparison to earlier anti-diabetic drugs (such as sulfonylurea), these treatments not only efficiently decrease the level of glucose in the blood, but they are also linked with a reduced risk of hypoglycemia and have been found to provide superior clinical results.[20-21] It is probable that many factors are responsible for the processes that bring about these advantages. Previous research[22-25] has shown that inhibitors of both SGLT-2 and DPP-4 may be effective in lowering insulin resistance, both in animal diabetic models and in people who already have the condition. However, the majority of these human studies were carried out on populations of Caucasians, and it is not known whether or not these advantages are also present in communities of Chinese people.

In addition, there is a lack of research that directly compares the effects of SGLT-2 inhibitors and DPP-inhibitors on insulin resistance and the distribution of fat throughout the body in diabetes individuals. Because improved diabetes care is connected with both a decreased risk of complications related to diabetes and improved cost-effectiveness, there is a need for more explanation in this area.

Since metformin remains the standard treatment for diabetes at the moment, we enrolled newly diagnosed type 2 DM patients who were only taking metformin in the current trial and divided them into two groups: those receiving treatment with SGLT-2 inhibitors or DDP-4 inhibitors.

METHODOLOGY

In this Randomized Control Trial, we enrolled a total of 180 cases; 90 cases newly diagnosed type 2 diabetes mellitus (HbA1c>6.5) in two equal groups A&B on the basis of computer-generated randomization table. Duration of data collection was 12 months from October 2021 to September, 2022. After taking routine history and physical examination, baseline labs were done. Group A was allotted to the cases 100mg q.d sitagliptin plus 850 mg in addition to 500mg metformin 2 times a day. Patients of Group B were advised for 10mg qd dapagliflozin+500mg metformin 2 times a day for six months. All the cases were counseled to avoid of taking any type of sweet products and to add 20 minutes brisk walk on daily basis in their routine of life. Patients were followed up on monthly basis for any inconvenience. The final follow-up was done on 6th month of treatment. All the patients with poor/non-compliance were excluded from the study. All cases with HbA1c <6.0 were considered as effectively treated patients. We used chi square test to compare efficacy in both groups with p value<0.05 as significant.

RESULTS

The results of our study reveals that mean age in Group A was 47.27+6.24 and in Group B 47.14+6.38 years, p-value=0.897, BMI in Group A was 29.48+2.93 and in Group 29.33+2.91, p-value=0.740, HbA1c at baseline was 7.65+0.52 and in Group B 7.62+0.51, p-value=0.840 and after treatment it reduced to 6.42+0.60 and in Group B 6.59+0.54, p-value=0.043.

Gender distribution shows that 45(50%) in Group A and 46(51.1%) in Group B were male whereas 45(50%) in Group A and 44(48.9%) in Group-B were females, p-value=0.500. Comparison

of Efficacy in both groups shows 44(48.9%) in Group A and 31(34.4%) in Group B, the overall efficacy was 41.7%, p-value=0.0.35 showing a significant difference.

Table 1:

	Group A (n=90)		Group A (n=90)		P value
	Mean	SD	Mean	SD	
Age(years)	47.27	6.24	47.14	6.38	0.897
BMI	29.48	2.93	29.33	2.91	0.740
HbA1c at baseline	7.65	0.52	7.62	0.51	0.840
HbA1c after treatment	6.42	0.60	6.59	0.54	0.043

Table 2:

Gender	Group A (n=90)		Group A (n=90)		P value
	No. of patients	%	No. of patients	%	
Male	45	50	46	51.1	0.500
Female	45	50	44	48.9	

Table 3: Comparison of Efficacy in both groups

		Group		
		A	B	Total
Efficacy	Yes	44	31	75
		48.9%	34.4%	41.7%
	No	46	59	105
		51.1%	65.6%	58.3%
Total		90	90	180
		100.0%	100.0%	100.0%

DISCUSSION

With an estimated incidence of 26.3%, Pakistan currently holds the fourth-highest percentage of people with diabetes mellitus in the entire world.[26] Therefore, efficient treatment drugs are required to control diabetes as well as to stop the microvascular and macrovascular problems linked to diabetes.[27] When used alone or in combination with other medications, sodium-glucose cotransporter-2 inhibitors (SGLT2i) are a novel family of medications that are successful in treating type 2 diabetes.[28] Dapagliflozin, a highly powerful and selective SGLT2i, belongs to this class and was initially approved for use in Pakistan in 2017.[29-30] When it comes to managing Type 2 Diabetes Mellitus, the cost of dapagliflozin is lower than that of sitagliptin.[31]

Dapagliflozin has been thoroughly examined and its safety and effectiveness in actual clinical situations have been validated by numerous research. Pakistani people differ from Western populations in terms of genetic traits as well as demographic, cultural, and lifestyle traits.[32-36] However, Metformin is still the first-line therapy for diabetes at the moment; hence, in the present trial, we included newly diagnosed type 2 DM patients who were solely treated with metformin, and we separated these patients into a group that was treated with SGLT-2 inhibitors or DDP-4 inhibitors.

Our findings reveal that comparison of Efficacy in both groups shows 44(48.9%) in Group A and 31(34.4%) in Group B, the overall efficacy was 41.7%, p-value=0.0.35 showing a significant difference. A previous study reveals that in individuals with type 2 diabetes mellitus, the effectiveness of dapagliflozin plus metformin was compared to that of sitagliptin and metformin; the p value for this comparison was 0.10. The effectiveness of Metformin and Dapagliflozin in individuals with Type 2 Diabetes Mellitus was shown to be comparable to that of Metformin and Sitagliptin, however, our findings differ from the above findings. However, the efficacy in sitagliptin is also higher but statistically significantly lower than Dapagliflozin. A previous study reveals that dapagliflozin is superior than sitagliptin in treating Type 2 diabetes.[38] 18% of patients using sitagalptin and 22% of those on dapagliflozin for type 2 diabetes mellitus achieved effectiveness. (p>0.05).[39] Our findings are in agreement regarding higher efficacy of dapagliflozin.

In another trial, Sitagliptin was more effective than dapagliflozin in controlling Type 2 diabetes in 43% of patients (p0.05). In addition, more patients (a higher percentage, in fact) reached their HbA1c target after being treated with sitagalptin for 24 weeks than with dapagliflozin.[10] These results contradict the aforementioned research.

Finally, we believe that more large-scale multicenter trials are necessary to verify our findings.

REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas – 8th Edition. 2017 [Internet]. . Available from: http://www.diabetesatlas.org/across-the-globe.html
2. WHO. Top 10 causes of death, 2015. [Internet]. Geneva, Switzerland: WHO, 2017. Available from: http://www.who.int/gho/mortality_burden_disease/causes_death/top_10/en/
3. WHO. Global Report on Diabetes, 2016 [Internet]. Geneva, Switzerland: WHO, 2016.. Available from: http://apps.who.int/iris/bitstream/10665/204871/1/9789241565257_eng.pdf?ua=1&utm_source=blog&utm_campaign=rc_blogpost
4. Shera AS, Rafique G, Khwaja IA, Ara J, Baqai S, King H. Pakistan national diabetes survey: prevalence of glucose intolerance and associated factors in Shikarpur, Sindh Province. Diabet Med 1995;12(12):1116–21.
5. Shera AS, Rafique G, Khawaja IA, Baqai S, Khan IA, King H. Pakistan National Diabetes Survey: prevalence of glucose intolerance and associated factors in Baluchistan province. Diabetes Res Clin Pract1999;44(1):49–58.
6. Shera AS, Rafique G, Khwaja IA, Baqai S, Khan IA, King H. Pakistan National Diabetes Survey prevalence of glucose intolerance and associated factors in North West at Frontier Province (NWFP) of Pakistan. J Pak Med Assoc 1999;49(9):206–11.
7. Basit A, Hydrie MZ, Ahmed K, Hakeem R. Prevalence of diabetes, impaired fasting glucose and associated risk factors in a rural area of Baluchistan province according to new ADA criteria. J Pak Med Assoc 2002;52(8):357–60.
8. Jafar TH, Levey AS, White FM, Gul A, Jessani S, Khan AQ, et al. Ethnic differences and determinants of diabetes and central obesity among South Asians of Pakistan. Diabet Med2004;21(7):716–23.
9. Shera AS, Jawad F, Maqsood A. Prevalence of diabetes in Pakistan. Diabetes Res ClinPract 2007;76(2):219–22.
10. Shera AS, Basit A, Fawwad A, Hakeem R, Ahmedani MY, Hydrie MZ, et al. Pakistan National Diabetes Survey: prevalence of glucose intolerance and associated factors in the Punjab Province of Pakistan. Prim Care Diabetes 2010;4(2):79–83.
11. Mahar PS, Awan MZ, Manzar N, Memon MS. Prevalence of type-II diabetes mellitus and diabetic retinopathy: the Gaddap study. J Coll Physicians Surg Pak 2010;20(8):528–32.
12. Zafar J, Bhatti F, Akhtar N, Rasheed U, Bashir R, Humayun S, et al. Prevalence and risk factors for diabetes mellitus in a selected urban population of a city in Punjab. J Pak Med Assoc2011;61(1):40–7.1
13. Meo SA, Zia I, Bukhari IA, Arain SA. Type 2 diabetes mellitus in Pakistan: current prevalence and future forecast. J Pak Med Assoc 2016;66(12):1637–42.
14. Heydari I, Radi V, Razmjou S, Amiri A. Chronic complications of diabetes mellitus in newly diagnosed patients. Int J Diabetes Mellit 2010;2:61–3.
15. Nassif ME, Windsor SL, Tang F, et al. Dapagliflozin effects on biomarkers, symptoms, and functional status in patients with heart failure with reduced ejection fraction: The DEFINE-HF Trial. Circulation. 2019;140(18):1463–76.
16. Perkovic V, Jardine MJ, Neal B, et al. Canagliflozin and renal outcomes in type 2 diabetes and nephropathy. N Engl J Med. 2019;380(24):2295–306.
17. Packer M. Reconceptualization of the molecular mechanism by which sodium-glucose cotransporter 2 inhibitors reduce the risk of heart failure events. Circulation. 2019;140(6):443–45.
18. Scheen AJ. Cardiovascular effects of new oral glucose-lowering agents: DPP-4 and SGLT-2 inhibitors. Circ Res. 2018;122(10):1439–59.
19. Aroor AR, Manrique-Acevedo C, DeMarco VG. The role of dipeptidylpeptidase-4 inhibitors in management of cardiovascular disease in diabetes; focus on linagliptin. Cardiovasc Diabetol. 2018;17(1):59.
20. Kerru N, Singh-Pillay A, Awolade P, Singh P. Current anti-diabetic agents and their molecular targets: A review. Eur J Med Chem. 2018;152:436–88.
21. Abdelaziz TS, Ali AY, Fatthy M. Efficacy and safety of dipeptidyl peptidase-4 inhibitors in kidney transplant recipients with post-

transplant diabetes mellitus (PTDM) – a systematic review and meta-analysis. Curr Diabetes Rev. 2019
22. Aschner P, Kipnes MS, Lunceford JK, et al. Effect of the dipeptidyl peptidase-4 inhibitor sitagliptin as monotherapy on glycemic control in patients with type 2 diabetes. Diabetes Care. 2006;29(12):2632–37
23. List JF, Whaley JM. Glucose dynamics and mechanistic implications of SGLT2 inhibitors in animals and humans. Kidney Int Suppl. 2011;(120):S20–27.
24. Utzschneider KM, Tong J, Montgomery B, et al. The dipeptidyl peptidase-4 inhibitor vildagliptin improves beta-cell function and insulin sensitivity in subjects with impaired fasting glucose. Diabetes Care. 2008;31(1):108–13.
25. Ahren B, Foley JE. The islet enhancer vildagliptin: Mechanisms of improved glucose metabolism. Int J Clin Pract Suppl. 2008;(159):8–14.
26. Prevalence of diabetes, pre-diabetes and associated risk factors: second National Diabetes Survey of Pakistan (NDSP), 2016-2017. Basit A, Fawwad A, Qureshi H, Shera AS. BMJ Open. 2018;8:0.
27. Vascular complications of diabetes. Beckman JA, Creager MA. Circ Res. 2016;118:1771–85.
28. Dapagliflozin: a sodium glucose cotransporter 2 inhibitor for the treatment of diabetes mellitus. Davis PN, Ndefo UA, Oliver A. J Pharm Pract. 2016;29:165–171.
29. United States Food and Drug Administration: Highlights of prescribing information for Farxiga (dapagliflozin) tablets. [Dec;2019];https://www.accessdata.fda.gov/ drugsatfda_docs/label/2019/202293s015lbl.pdf 2019
30. Dapagliflozin add-on to metformin in type 2 diabetes inadequately controlled with metformin: a randomized, double-blind, placebo-controlled 102-week trial. Bailey CJ, Gross JL, Hennicken D, Iqbal N, Mansfield TA, List JF. BMC Med. 2013;11:43.
31. Hayward RA, Reaven PD, Wiitala WL, et al. Follow-up of glycemic control and cardiovascular outcomes in type 2 diabetes. N Engl J Med. 2015;372(23):2197–2206.
32. Genetic variation among the major Pakistani populations based on 15 autosomal STR markers. Anwar I, Hussain S, Rehman AU, Hussain M. Int J Legal Med. 2019;133:1037–8.
33. Genome-wide implicated risk variants of TCF7L2 gene contribute to type 2 diabetes susceptibility by modulating serum lipids in Pakistani population. Shahzadi S, Shabana Shabana, Sarwar S, Shahid SU. Int J Diabetes Dev Ctries. 2019;39:302–307
34. National Institute of Population Studies (NIPS), Pakistan and ICF. Pakistan Demographic and Health Survey 2017-18. [Dec;2019];National Institute of Population Studies (NIPS) [Pakistan] and ICF. https://dhsprogram.com/pubs/pdf/FR354/FR354.pdf Pakistan Demographic and Health. 2019
35. Sathar ZA, Royan R, Bongaarts J (Eds) New York: UNPF/Population Council; 2013. Capturing the demographic dividend in Pakistan.
36. Canadian Diabetes Association 2013 Clinical practice guidelines for the prevention and management of diabetes in Canada. Canadian Diabetes Association Clinical Practice Guidelines Expert Committee, Cheng AYY. Can J Diabetes. 2013;37:0. [Google Scholar]
37. Faiq Abdullah, Abdul Sattar, Kamran Shaukat. To Compare the Efficacy of Dapagliflozin & Metformin Vs Sitagliptin & Metformin in Newly Diagnosed Type 2 Diabetic patients. PJMHS 2021;15:85-6.
38. Kang BK, An SH, Kim JY, Gwak HS. Comparisons of efficacy between dapagliflozin and sitagliptin in combination with metformin in type 2 diabetes mellitus patients. Korean J Clin Pharm 2017;27:99-104.
39. Rosenstock J, Hansen L, Zee P, Li Y, Cook W, Hirshberg B, etal. Dual add on therapy in type 2 diabetes poorly controlled with metformin monotherapy: a randomized double-blind trial of saxagliptin plus dapagliflozin addition versus single addition of saxagliptin or dapagliflozin to metformin. Diab Care 2015;38:376-83.
40. Scott RS, Morgan JD, Zimmer Z, Lam RL, O'Neill EA, Kaufman KD, et al. safety and efficacy of Sitagliptin (SITA) Compared with Dapagliflozin (DAPA) in subjects with T2D, Mild Renal Impairment, and inadequate glycemic control on metformin (MET)+a Sulfonylurea (SU). Am Diab Assoc 2018;67:1142-P.