International Journal of Science and Research (IJSR)
ISSN: 2319-7064
SJIF (2022): 7.942

Role of SGLT2 Inhibitors in Heart Failure Patients

Tejaswi Mekala[1], Veganti Sai Harsha[2], Vanukuri Madhupriya Reddy[3], Vardhineni Bhargavi[4], Mandava Mahima Swaroopa[5]

[1]Pursuing Pharm D (Intern) VI/VI Pharm D
Email ID: *tejaswimekala20[at]gmail.com*
[2]Pursuing Pharm D (Intern) VI/VI Pharm D
[3]Pursuing Pharm D (Intern) VI/VI Pharm D
[4]Pursuing Pharm D (Intern) VI/VI Pharm D
[5]Assistant Professor, Department of Pharmacy Practice

Abstract: ***Objective: This study aims to assess the role of SGLT2 inhibitors in patients with heart failure. Methodology: This is a cross - sectional study performed at Pinnamaneni Siddhartha for 6 months to fill out the data collection forms of 120 patients with heart failure. The data was analyzed using the statistical software SPSS. Results: The study's results indicate that SGLT2 inhibitors played a vital role in reducing unfavorable outcomes. Conclusion: Our study compared risk factors with outcomes and concluded that risk factors have been a root cause of unfavorable outcomes. Depending on the study results, SGLT2 inhibitors effectively reduce unfavorable outcomes. Recommendations: Awareness programs to quit the use of tobacco and alcohol in society may help reduce the risk factors to some extent.***

Keywords: Heart failure, SGLT2 inhibitors, Cardiovascular outcomes, Treatment decision making

1. Introduction

Until recent times, there were no therapies for heart failure targeting glucose metabolism. While there is still a need to establish additional therapies for patients with diabetes mellitus, SGLT2 inhibitors have fulfilled this need. [1, 2] SGLT2 is a major transport pathway responsible for the reabsorption of glucose in the kidneys. SGLT2 inhibitors have shown benefits over a placebo in a cardiovascular outcome trial. [3, 4, 5, 6] In patients with HF and HFrEF, a new therapy with SGLT2 inhibitors has emerged. Significant cardiovascular and renal benefits have been observed across various subgroups during large - scale randomized controlled trials of SGLT2 inhibitors. [7] There are only a few Randomized Controlled Trials that evaluated the effectiveness of SGLT2 inhibitors in the HF population. The DAPA - HF (Dapagliflozin and prevention of adverse outcomes in heart failure) trial and the EMPEROR - Reduced (Empagliflozin outcome trial in patients with chronic heart failure with reduced ejection fraction) trial were conducted in patients with HFrEF to assess the effects of Dapagliflozin and Empagliflozin. [8, 9] Cardiovascular outcome trials in patients with T2DM found a reduction in cardiovascular death and HF hospitalizations, prompting further investigation into the drug's potential role in the management of HF. The first study to evaluate the efficacy of an SGLT2 inhibitor in patients with HFrEF is The Dapagliflozin and Prevention of Adverse Outcomes in Heart Failure (DAPA - HF). [10] The trial enrolled 4, 744 patients with stable, chronic HF and LVEF <40%, who were followed over an 18 - month period. Dapagliflozin was found to significantly reduce the primary composite outcome of cardiovascular death, HF hospitalizations, and emergency HF visits compared to placebo. Moreover, Dapagliflozin therapy significantly reduced all the components of the primary composite outcome. [11] In a previous trial named DAPA - HF (Dapagliflozin and Prevention of Adverse Outcomes in HF), Dapagliflozin has shown a beneficial effect in reducing the risk of worsening HF or cardiovascular death among patients with HF and an LVEF of 40% or less. [12] The Dapagliflozin Evaluation to Improve the Patients quality of life with Preserved Ejection Fraction in Heart Failure (DELIVER) trial. [13] The results of the DELIVER trial extend beyond those of the DAPA - HF trial to patients with HF and an LVEF > 40% and are consistent with the overall results of the EMPEROR - Preserved trial (EMPA) in patients with an LVEF of > 40% to assess the effects of Empagliflozin. [14]

2. Methodology

This is a cross - sectional study being performed at Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation (Dr. PSIMS & RF) in Gannavaram, Krishna District, Andhra Pradesh, India.

The study included 120 patients after meeting the inclusion criteria. Based on the inclusion criteria, individuals aged were 18 to 70. Patients with a history of prior cardiovascular events, such as heart failure, were included in the study. Patients below the age of 18 and above 70 were excluded from the study. Immunocompromised and renally compromised patients were also excluded from the study.

A total of 120 patients who met the inclusion criteria were included in the study. All data, including patients' demographics such as age, sex, body mass index, medical and medication history records, and laboratory records (HbA1c, LVEF, RBS, and creatinine), were collected from the case files and safely documented in suitable forms for the study.

The case files were carefully analyzed for the drug therapies prescribed for heart failure, and the patients were categorized into two groups: 1. Heart failure patients under the treatment of standard therapy for heart failure (N=60).2. Heart failure patients under the treatment of SGLT2 inhibitors as an add - on to standard therapy (N=60).

3. Results

Table 1

	SGLT2	Other drugs	Hazards ratio	95% CI	P Value	Adjusted co - variants
LVEF >60%	2events /4patients =0.5%	0event/ 2patients =0%	0.1353	0.0026 - 6.821	0.317	3.645
LVEF40 - 49%	2event /18patients =0.11%	2events/ 20patients =0.1%	0	- 1.000 - 1.000	0.317	5.578
LVEF 50 - 59%	2events /8patients =0.25%	8events/ 14patients =0.571%	0.65	- 0.50 - - 0.85	>0.05	3.189
LVEF <40%	12events/ 30patients =0.4%	10 events/ 24patients =0.41%	0.1353	0.0026 - 6.821	0.317	5.545

Patients with an ejection fraction >60% under SGLT2 therapy: 4 patients with 2 observed events, under standard therapy: 2 patients with no observed events. Patients with an ejection fraction of 40 - 49% under SGLT2 therapy: 18 patients with 2 observed events, under standard therapy: 20 patients with 2 observed events. Patients with an ejection fraction of 50 - 59% under SGLT2 therapy: 8 patients with 2 observed events, under standard therapy: 14 patients with 8 observed events. Patients with an ejection fraction of <40% under SGLT2 therapy: 30 patients with 12 observed events, under standard therapy: 24 patients with 10 observed events. In the context of heart failure, the study found that dapagliflozin significantly reduced cardiovascular events, including heart failure hospitalizations, a decrease in the percentage of LVEF, and major adverse cardiovascular events by 35% (HR: 0.65, 95% CI: 0.5 - 0.85, p > 0.05)

Table 2

Sex	Smoker	R value	Alcoholic	R valve	obese	R value	Diabetic	R value	Hypertensive	R value	Age>55	R valve
M	55	0.52	36	0.31	30	0.64	75	0.34	40	0.12	30	0.34
F	0	0	0	0	10	0.56	32	0.21	29	0.23	45	0.38

To the best of our knowledge, our study was the first to compare risk factors with outcomes. Irrespective of the drug therapies prescribed risk factors contribute a major role in developing Non favourable outcomes.

Kaneko H,. et al stated that DM is a major risk factor for developing cardiovascular outcomes in our study majority of the population (N=107) is Diabetic. so our study tends to have more non – favourable outcomes [(15)]

Nagasu H, et al concluded that other Non cardiovascular events are also decreased in patients using SGLT2 inhibitors. In our study, we have observed a very few number of other non - cardiovascular events in patients using SGLT2 inhibitors

In our study, we have observed a lower number of non favourable outcomes in the Female population under SGLT2 Therapy while considering risk factors [(16)]

4. Conclusion

We conducted a crosssectional study to thorough assessment of the hazardous risk ratio for the two heart failure drug therapies: standard therapy and SGLT2 therapy as an adjunct. We observed a trend where unfavorable outcomes in females undergoing SGLT2therapy were mitigated, primarily due to their extended mean duration of SGLT2 therapy. Additionally, SGLT2 inhibitors played a role in reducing these adverse outcomes. Combining these findings with evidence from other studies differentiating between individual compounds is advisable. Furthermore, the choice of treatment is a complex decision influenced by various factors, including cost, efficacy, other potential side effects, drug delivery mechanisms, and patient preferences, all of which warrant careful consideration.

References

[1] Bhatt D. L. Verma S. Braunwald E. The DAPA - HF Trial: a Momentous Victory in the War against Heart Failure**.** *CellMetab.*2019; 30: 847 - 849
[2] Verma S. Bhatt D. L. More CREDENCE for SGLT2 Inhibition. *Circulation.*2019; 140: 1448 - 1450
[3] Packer M. Anker S. D. Butler J. et al. Cardiovascular and Renal Outcomes with Empagliflozin in Heart Failure. *NEngl J Med.*2020; 383: 1413 - 1424
[4] Bhatt D. L. Szarek M. Pitt B. et al. Sotagliflozin in Patients with Diabetes and Chronic Kidney Disease. *NEngl J Med.*2020;
[5] Bhatt D. L. Szarek M. Steg P. G. et al. Sotagliflozin in Patients with Diabetes and Recent Worsening Heart Failure. *NEngl J Med.*2020;
[6] Cannon C. P. Pratley R. Dagogo - Jack S. et al. Cardiovascular Outcomes with Ertugliflozin in Type 2 Diabetes. *NEngl J Med.*2020; 383: 1425 - 1435
[7] Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, Silverman MG, Zelniker TA, Kuder JF, Murphy SA, Bhatt DL, Leiter LA, McGuire DK, Wilding JPH, Ruff CT, Gause-Nilsson IAM, Fredriksson M, Johansson PA, Langkilde AM, Sabatine MS. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. *N Engl J Med* 2019; 380: 347–357.
[8] McMurray JJV, Solomon SD, Inzucchi SE, Køber L, Kosiborod MN, Martinez FA, Ponikowski P, Sabatine MS, Anand IS, Bělohlávek J, Böhm M, Chiang CE, Chopra VK, de Boer RA, Desai AS, Diez M, Drozdz J,

Dukát A, Ge J, Howlett JG, Katova T, Kitakaze M, Ljungman CEA, Merkely B, Nicolau JC, O'Meara E, Petrie MC, Vinh PN, SchouM, Tereshchenko S, Verma S, Held C, DeMets DL, Docherty KF, Jhund PS, Bengtsson O, Sjöstrand M, Langkilde AM. Dapagliflozin in patients with heart failure and reduced ejection fraction. *N Engl J Med* 2019; 381: 1995–2008.

[9] Packer M, Anker SD, Butler J, Filippatos G, Pocock SJ, Carson P, Januzzi J, Verma S, Tsutsui H, Brueckmann M, Jamal W, Kimura K, Schnee J, Zeller C, Cotton D, Bocchi E, Böhm M, Choi DJ, Chopra V, Chuquiure E, Giannetti N, Janssens S, Zhang J, Gonzalez Juanatey JR, Kaul S, Brunner-La Rocca HP, Merkely B, Nicholls SJ, Perrone S, Pina I, Ponikowski P, Sattar N, Senni M, Seronde MF, Spinar J, Squire I, Taddei S, Wanner C, Zannad F. Cardiovascular and renal outcomes with empagliflozin in heart failure. *N Engl J Med* 2020; 383: 1413–1424.

[10] McMurray JJ, Solomon SD, Inzucchi SE, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med.2019; 381: 1995–2008.

[11] Packer M, Anker SD, Butler J, et al. Cardiovascular and renal outcomes with empagliflozin in heart failure. N Engl J Med.2020; 383: 1413–1424.

[12] McMurray JJV, Solomon SD, Inzucchi SE, et al. Dapagliflozin in patients with heart failure and reduced ejection fraction. N Engl J Med 2019; 381: 1995 - 2

[13] Solomon SD, McMurray JJ, Claggett B, et al. Dapagliflozin in heart failure with mildly reduced or preserved ejection fraction. N Engl J Med.2022; 387: 1089–1098.

[14] Hicks KA, Mahaffey KW, Mehran R, et al.2017 Cardiovascular and stroke end point definitions for clinical trials. Circulation 2018; 137: 961 - 72

[15] Wiviott SD, Raz I, Bonaca MP, Mosenzon O, Kato ET, Cahn A, et al. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. N Engl J Med.2019; 380 (4): 347–357. https: //doi. org/10.1056/ NEJMoa1812389 PMID: 30415602

[16] Kaneko H,. et al stated that DM is a major risk factor for developing cardiovascular outcomes in our study majority of the population (N=107) are Diabetic. so our study tend to have more non favourable outcomes

Author Profile

Tejaswi Mekala, D/o Nagaraju Mekala, Pharm D Intern (VI/VI Pharm D)
Mail: Tejaswimekala20[at]gmail.com

Veganti. SaiHarsha, S/o Veganti Srinivasa Rao, Pursuing Pharm D Intern (VI/VI Pharm D)
Mail: Saiharsha veganti[at]gmail.com

Vanukuri. Madhupriya Reddy, D/o Vanukuri Venkata Konda Reddy, Pursuing Pharm D internship (VI/VI Pharm D)
Mail: Madhupriyavanukuri373[at]gmail.com

Vardhineni Bhargavi, D/o Vardhineni Baburao, Pursuing Pharm D internship (VI/VI Pharm D)
Mail: Vardinenibhargavi[at]gmail.com

Mandava Mahima, Assistant Professor, Department of Pharmacy Practice
Mail: Mandavamahima[at]gmail.com