



CLINICAL BENEFITS AND TOLERABILITY OF DAPAGLIFLOZIN IN PATIENTS WITH REDUCED EJECTION FRACTION

Clinical Research

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ABSTRACT

Background: Dapagliflozin, a sodium-glucose cotransporter-2 inhibitor is an anti-diabetic drug approved by the US Food and Drug Administration to reduce the risk of cardiovascular death and hospitalisation in patients with reduced ejection fraction. **Objectives:** The objective of the study is to identify the clinical benefits of dapagliflozin in the symptomatic treatment of heart failure with reduced ejection fraction, to document the incidence of readmission, effects on blood sugar levels and body weight, and to identify the adverse effects and tolerability. **Methodology:** This was a 14 months ambispective study of 85 patients on dapagliflozin along with standard heart failure treatment (Inclusion minimum sample size 72) **Results:** 85.9% of patients shows a significant improvement in their physical functioning, symptoms and quality of life. There was a reduction in the incidence of readmission and 84.8% of diabetic patients showed a decrease in the blood sugar levels while the non diabetic population maintains a euglycemic effect. 13 patients showed side effects like hyponatremia, hypokalemia, acute kidney injury and hypotension. Tolerability in association with adherence was 74.1% and 34.1% showed a reduction in their body weight. **Conclusion:** Dapagliflozin improves the symptoms of heart failure and reduces the incidence of re-hospitalisation. Additionally, dapagliflozin reduced the elevated blood sugar levels in diabetic patients and body weight. The study concludes that dapagliflozin is well tolerated by the patients and is safe to use.

KEYWORDS

Heart failure, Dapagliflozin, Symptomatic improvement, Blood sugar levels, side effects, tolerability, body weight.

INTRODUCTION

Heart failure is defined as a structural or functional abnormality of the heart that results in elevated intracardiac pressure and inadequate cardiac output (at rest or during exercise)[1]. SGLT2 inhibitor dapagliflozin improves the symptoms of heart failure[2] and reduces the incidence of rehospitalization due to heart failure[3]. Dapagliflozin reduces the elevated blood sugar levels in diabetic patients[4] as well as their body weight[5]. Mild side effects includes hyponatremia, hypokalemia, and volume depletion[6].

MATERIALS AND METHOD

Study Design

An ambispective study of 16 months (January 2022 to April 2023) conducted in the cardiology department of a multi-speciality tertiary care hospital.

Method Of Selection

Inclusion Criteria: patients initiated on dapagliflozin and on standard treatment for heart failure with and without diabetes having a left ventricular ejection fraction < 50.

Exclusion Criteria: patients who had history of type 1 diabetes, patients with malignancy, and special population including pregnant and lactating women were excluded.

SAMPLE SIZE

A total of 85 patients who met the inclusion criteria were selected for the study. (minimum sample size was 72 as suggested by the statistician)

Statistical Analysis

The collected data were analyzed and interpreted using SPSS.

RESULTS AND DISCUSSION

Eighty-five cases of heart failure patients with reduced ejection fraction who were on standard treatment and was initiated on

dapagliflozin were randomly selected and evaluated for the clinical benefits of dapagliflozin, incidence of rehospitalization, blood sugar levels, body weight and adverse effects and tolerability.

1. Clinical Benefits Of Dapagliflozin In Symptomatic Treatment Of Heart Failure With Reduced Ejection Fraction

The study evaluated the clinical benefits of dapagliflozin in the symptomatic treatment of HFrEF. KCCQ 12 is a 12-item, self-administered disease-specific instrument that quantifies symptoms (frequency, severity, and recent change), physical function, quality of life, and social function over the previous 2 weeks. Scores ranges from 0 to 100 with higher scores reflecting better health status.

Table 1.1: Paired t test of Physical limitation scale, symptom frequency scale, quality of life scale and social limitation scale

KCCQ-12 SCALE	PRE-TEST	POST TEST	MEAN CHANGE	P- VALUE
PLS	66.18	79.41	13.23 (20%)	P< 0.001
SFS	47.99	66.25	18.26 (38%)	P< 0.001
QOL	54.76	64.58	9.82 (17.9%)	P< 0.001
SLS	30.05	30.22	10.59 (1.8%)	P< 0.001

Summary Score

The KCCQ12 summary score represents the integration of the physical limitation, symptom frequency, quality of life, and social limitation scales. The score is calculated as the average of the scale scores.

Test	Mean KCCQ	SD	Mean change	n	t	df	p-value
Pre-test	56.85	19.90	13.11	85	8.593	84	p < 0.001
Post-test	69.96	14.42	(23%)				

Of 85 patients, 73 patients showed significant improvement while 12 patients had deterioration in KCCQ total score. i.e., 85.9 % of the patients had a mean of 23% symptom improvement from their baseline score to the follow up and this proves that dapagliflozin has a significant effect on physical function, symptom improvement, and

quality of life in patients with HFrEF.

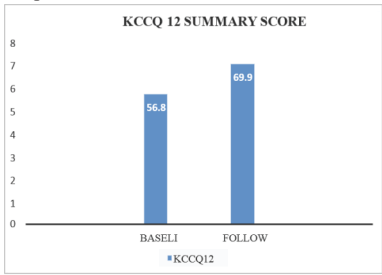


Fig 1.1: KCCQ 12 summary score

2. Incidence Of Readmission

Table 2.1: Incidence of Readmission

Incidence of readmission	n	%
≤1 time	77	90.6 %
More than 1	8	9.4 %

Of 85 participants on dapagliflozin, only 8 (9.4%) patients had two or more readmission while 90.6% of participants had a decreased incidence in their hospitalization.

3. Effect On Blood Sugar Level

Among the 85 participants, 66 (77.65 %) were diabetic patients and during the follow-up 56 patients shows decreased sugar level. 19 (22.35 %) were non-diabetic and there was no change in their blood sugar level. The fasting blood sugar (FBS) of the participants were monitored at first and after two months follow up was taken.

A mean change of 24.2 % between the pretest and post-test mean blood sugar shows $p < 0.001$, indicating a significant difference of blood sugar levels in these patients. This proves that dapagliflozin has a significant effect in reducing blood sugar levels in diabetic patients with reduced ejection fraction along with other antidiabetic drugs.

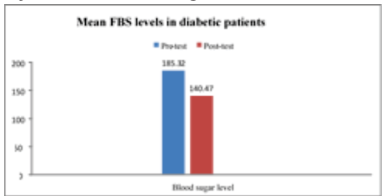


Fig 3.1: Mean baseline and follow up fasting blood sugar levels

4. Adverse Effects And Tolerability Of Dapagliflozin

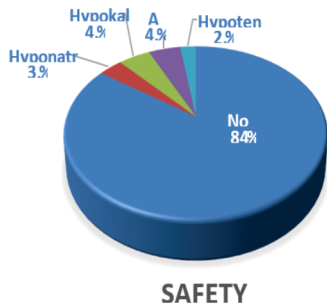


Fig 4.1: observed adverse effects

Table 4.1: Clinicians Rating Scale

CRS SCORE	f	%
Complete refusal	1	1.2 %
Partial refusal	3	3.5 %
Accepts only because compulsory	4	4.7 %
Occasional reluctance	14	16.5 %
Passive acceptance	14	16.5 %
Moderate participation	20	23.5 %
Active participation	29	34.2 %

Table 4.2: Tolerability of patients

TOLERABILITY	n	%
Passive acceptance	63	74.1 %
Partial acceptance	22	25.9 %

The tolerability of the patients in association with adherence was measured by administrating the clinician rating scale to patients during the follow up period. Of 85 patients, 74.1% passively accepted to continue dapagliflozin indicating that the drug is tolerable.

5. Effects On Body Weight

Table 5.1 : effects on body weight

WEIGHT	Frequency	Percentage
No change	48	56.5%
Decreased	29	34.1%
Increased	8	9.4%

Out of 85 patients,48 patients (56.5%) had no change on taking dapagliflozin, 29 patients (34.1%) showed a slight reduction in body weight and 8 patients (9.4%) showed weight gain on taking dapagliflozin.

The mean column displays the mean pre-test and post-test body weight scores among HFrEF patients. SD is the standard deviation of the body weight scores in pre & post respectively. The Mean change, 1.04 is the difference between the pre-test and post-test mean body weight (67.92 is reduced to 66.87). Since the t-value, 3.63 shows $p < 0.001$, there is a significant difference existing between the pre-test & post-test scores of body weight in patients. This proves that dapagliflozin has a significant effect in reducing body weight in patients with reduced ejection fraction.

6. Dapagliflozin On Lv Dysfunction

Table 6.1 :Ejection fraction improvement

Ejection Fraction Improvement	No. of patients
Within 6 months	10
6 month – 1 year	14

During our study period, 39 patients had two Echo scan. Among them, 24 patients (61.5%) showed improvement in their ejection fraction. This indicates dapagliflozin along with standard heart failure treatment improves ejection fraction in patients with HFrEF.

The mean column displays the mean pre-test and post-test ejection fraction scores among the HFrEF patients. SD is the standard deviation of the ejection fraction scores in pre & post respectively. The Mean change, 6.67 is the difference between the pre-test and post-test mean ejection fraction (26.15 increased to 32.82). Since the t-value, 3.33 shows $p < 0.05$ there is a significant difference existing between the pre-test and post-test ejection fraction among patients with HFrEF. This proves that there is a significant improvement in ejection fraction in patients with HF.

CONCLUSION

The study concluded the various clinical benefits of dapagliflozin in heart failure patients with reduced ejection fraction who are on standard treatment for heart failure. The study shows that dapagliflozin along with standard HF therapy significantly improves the symptoms of HF as well as reduces the incidence of hospitalization. The study also concludes that dapagliflozin has a positive effect on blood sugar level, body weight, and ejection fraction. The safety and tolerability of dapagliflozin along with patient adherence were also studied.

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