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ORIGINAL ARTICLE

Early Clinical Experience with Dapagliflozin in Children with Heart Failure

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Abstract

Pediatric heart failure (HF) is associated with significant morbidity and mortality. Medical treatment for pediatric HF is largely derived from adult studies. Previously, there has been no described use of dapagliflozin in pediatric HF patients. We describe our single-center experience using dapagliflozin in addition to standard HF medical therapy in 38 pediatric HF patients since January 2020. Median age was 12.2 years (interquartile range 6.2–17.5). Majority of patients had dilated cardiomyopathy (68.4%) and reduced left ventricular ejection fraction (LVEF) of 40% or less (65.8%). HF regimens commonly included sacubitril/valsartan, beta-blocker, mineralocorticoid receptor antagonist, and loop diuretic. Median follow-up from dapagliflozin initiation for the whole cohort was 130 days (IQR 76–332). Median B-type natriuretic peptide decreased significantly from 222 to 166 pg/mL at latest clinical follow-up ($P = .04$). Estimated glomerular filtration rate trended lower at latest follow-up but was not significant from baseline. There were no clinically significant changes in blood chemistries or vital signs after initiation of dapagliflozin. No patients experienced symptomatic hypoglycemia or hypovolemia. Six patients (15.8%) experienced a symptomatic urinary tract infection necessitating antibiotic treatment. In a separate analysis of 16 patients with dilated cardiomyopathy who received dapagliflozin for a median of 313 days (IQR 191–414), median LVEF increased significantly from 32 to 37.2% ($P = .006$). Dapagliflozin, when added to a background of guideline-directed medical therapy, appears well tolerated in children with HF. Larger studies are needed to evaluate safety and efficacy of dapagliflozin in this population.

Keywords SGLT2 inhibitors · Dapagliflozin · Pediatric heart failure · Dilated cardiomyopathy

Introduction

Pediatric heart failure (HF) is associated with significant morbidity and mortality in childhood, with in-hospital mortality rates of 7–26%, and high frequency of 30-day HF-related readmissions [1–3]. Clinical guidelines for management of pediatric HF are largely based on expert consensus and extrapolation from adult guidelines due to lower prevalence of HF in children and lack of clinical trials performed in this population [1, 2].

Dapagliflozin, an oral sodium–glucose cotransporter 2 (SGLT2) inhibitor, is recommended as a component of guideline-directed medical therapy in adults with HF with reduced ejection fraction (HFrEF) to reduce cardiovascular death and hospitalization for HF [4]. This is the first description of dapagliflozin use in children treated for HF.

Methods

Study Population

We identified pediatric patients (< 21 years of age) with a diagnosis of HF who were initiated on dapagliflozin starting in January 2020. HF was defined by reduced ventricular systolic function (left ventricular ejection fraction < 55%

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by echocardiography) or impaired ventricular filling (pulmonary capillary wedge pressure > 18 mmHg measured directly and/or E/e' > 14 by echocardiography) with clinical features of congestion and/or low cardiac output. We administered dapagliflozin enterally at a target dose of 0.1–0.2 mg/kg once daily (maximum 10 mg) to patients already receiving standard HF medical therapy. Table 1 summarizes our center's dapagliflozin protocol for monitoring parameters. We included all patients who received dapagliflozin for a minimum of 30 days in this analysis. Patients were followed until latest clinical follow-up through December 2021. Glomerular filtration rate (eGFR) was estimated using Bedside Schwartz equation for children ≤ 18 years, CKD-EPI Creatinine Equation for persons ≥ 19 years, and CKD-EPI Cystatin C equation for persons with Duchenne muscular dystrophy. Acute kidney injury (AKI) was defined according to KDIGO AKI guidelines. Patients with cardiac diagnoses other than dilated cardiomyopathy, those supported by a ventricular assist device at any point during follow-up, and those receiving dapagliflozin for < 90 days were excluded from left ventricular ejection fraction (LVEF) analysis. This study was approved by our center's Institutional Review Board.

Statistical Analysis

Categorical variables were reported as frequencies and percentages and compared using the Chi-square test. Fisher's exact test was used in lieu of the Chi-square test when the expected cell count was < 5. Continuous characteristics and outcomes were assessed for normality using histograms and reported as mean (± standard deviation) or median (interquartile range) values. Continuous variables were compared using a paired *t*-test or the Wilcoxon signed rank exact test. Significance testing was done at the $\alpha = .05$ level. RStudio Team (2020) was used for all analyses.

Results

Dapagliflozin was initiated in 42 non-diabetic children with a diagnosis of HF as outlined in our methods. Of these 42 patients, four were excluded as three received dapagliflozin for < 14 days before undergoing heart transplant and one received dapagliflozin for > 30 days but was excluded due to lack of follow-up. Median age was 12.2 years (IQR 6.2–17.5 years) and 50% were female (Table 2). Nine of the 38 patients (23.7%) included in our analysis were newly diagnosed with HF at the time of dapagliflozin initiation. Most had at least one hospitalization for HF in the preceding

Table 1 Dapagliflozin monitoring protocol for pediatric heart failure

Parameter	Baseline	Weekly for First Month (inpatient only)	Every 4–12 Weeks	Annually
Blood glucose	X	X	X	X
Hemoglobin A1C	X			X
Renal function[a]	X	X	X	X
Liver function[b]	X			X
Vitals and volume status[c]	X	X	X	X
Complete blood count[d]	X	X	X	X
Urinalysis[e]	X	X	X	X
Serum electrolytes[f]	X	X	X	X
Fasting lipid panel	X			X
Adverse effects[g]	X	X	X	X

Avoid initiating dapagliflozin in patients with concurrent urinary tract infection (UTI). Start dapagliflozin at 0.1–0.2 mg/kg rounded to nearest ¼ tablet (maximum 10 mg) once daily in the morning

[a]Includes serum creatinine, BUN, height, and if applicable, Cystatin C

[b]Includes AST, ALT, conjugated bilirubin, unconjugated bilirubin, INR and albumin

[c]Includes weight, blood pressure, heart rate, and hematocrit

[d]Includes white blood cell count, hemoglobin, and hematocrit

[e]Assess for glucosuria no sooner than one week after starting dapagliflozin with target of 1 + to 3 +. If negative or trace glucosuria, increase dose by no less than ¼ tablet (either 5 mg or 10 mg tablet) to maintain target 0.1–0.2 mg/kg/day (maximum 10 mg once daily)

[f]Included in basic metabolic panel

[g]Monitor for signs and symptoms of UTI, hypotension, volume depletion, hypersensitivity reactions, and/or hypoglycemia

Table 2 Baseline clinical characteristics of children receiving dapagliflozin for treatment of heart failure

Characteristic	$N=38$
Age, median years	12.2 (IQR 6.2–17.5) [range 0.27–20.2]
3–12 months, *n* (%)	2 (5.3)
> 1 year and < 5 years, *n* (%)	7 (18.4)
5–11 years, *n* (%)	10 (26.3)
12–17 years, *n* (%)	13 (34.2)
18–21 years, *n* (%)	6 (15.8)
Female sex, *n* (%)	19 (50)
Cardiac diagnosis, n (%)	
Dilated cardiomyopathy	26 (68.4)
Restrictive cardiomyopathy	1 (2.6)
Diastolic heart failure	4 (10.5)
Single ventricle physiology	7 (18.5)
New diagnosis of heart failure, *n* (%)	9 (23.7)
Left ventricular assist device (LVAD) support, n (%)	2 (5.2)
Berlin Heart EXCOR	1 (2.6)
HeartMate 3	1 (2.6)
Left ventricular ejection fraction ≤ 40%, *n* (%)	25 (65.8)
Previous cardiac transplant, *n* (%)	3 (7.9)
Heart failure hospitalization in preceding year, *n* (%)	29 (76.3)
Dapagliflozin started during inpatient admission, *n* (%)	24 (63.2)

year (76.3%) and 63.2% were initiated on dapagliflozin during an inpatient admission. Majority of patients had dilated cardiomyopathy (68.4%) and reduced LVEF ≤ 40% (65.8%). Four patients had diastolic HF (three heart transplant patients and one with repaired truncus arteriosus). Of the seven single ventricle patients, four had hypoplastic left heart syndrome, one had pulmonary atresia with intact ventricular septum, one patient had double outlet right ventricle, large ventricular septal defect, and pulmonary stenosis, and one patient had tricuspid atresia. The seven single ventricle patients were at various stages of single ventricle palliation including three status post Fontan palliations, two status post Glenn palliations, one status post stage hybrid procedure, and one status post pulmonary artery band.

Dapagliflozin was added to a HF regimen that frequently included sacubitril/valsartan (73.7%), beta-blocker (71%), mineralocorticoid receptor antagonist (63.2%), and loop diuretic (71%) (Table 3). Median target dapagliflozin dose received was 7.5 mg (IQR 2.5–10 mg) or 0.16 mg/kg/day (IQR 0.12–0.19 mg/kg/day). Median follow-up for all 38 patients was 130 days (IQR 76–332 days). Mean serum sodium increased significantly from 135.8 to 137.5 mEq/L ($P=.01$), mean magnesium from 2 to 2.12 mg/dL ($P=.02$), median hemoglobin from 11.5 to 13.3 mg/dL ($P=.004$), median hematocrit from 35.5 to 39.6% ($P=.002$) while median BNP decreased significantly from 222 to 166 pg/mL ($P=.04$) at latest clinical follow-up (Table 3). Urinalysis was negative for glucose before dapagliflozin initiation and 1 + to 3 + glucosuria was measured for most patients ≥ 1 week after starting dapagliflozin, confirming its pharmacodynamic effect. New York Heart Association (NYHA) Functional Classification improved in 5/38 (13.2%), worsened in 5/38 (13.2%), and remained unchanged in 28/38 (73.6%). Median eGFR decreased from 118 to 100 mL/min/1.73 m^2 though this did not reach statistical significance ($P=.09$). From a hemodynamic standpoint, there were no significant changes to heart rate or blood pressure from baseline to latest follow-up (Table 3).

Safety

A summary for each patient, including individual duration of follow-up and events experienced while receiving dapagliflozin, is detailed in Table 4. Five patients (13.1%) with history of hospitalization for HF in the preceding year experienced HF rehospitalization after starting dapagliflozin. Of seven patients already actively listed for heart transplant, two were transplanted by latest follow-up. One patient with dilated cardiomyopathy underwent HeartMate 3 left ventricular assist device (LVAD) placement at 24 days after starting dapagliflozin due to acute decompensated HF. One patient with failed Fontan physiology and known history of ventricular tachycardia and in-home

Table 3 Clinical characteristics compared from baseline to latest clinical follow-up

Characteristic	Baseline	Latest follow-up	*P* value
NYHA Class I, *n* (%)	0 (0)	3 (7.9)	.24
NYHA Class II, *n* (%)	24 (63.2)	21 (55.3)	.64
NYHA Class III, *n* (%)	9 (23.7)	6 (15.8)	.56
NYHA Class IV, *n* (%)	5 (13.1)	8 (21)	.54
Weight, median kg	37 (17.7–76.3)	41.4 (17.9–78.2)	.09
Height, median cm	142.5 (103–166)	145.7 (104–168.8)	< .001
Body Mass Index, median kg/m^2	18.55 (15.7–26.3)	18.58 (15.4–25.2)	> .99
LVEF, median %[a]	32 (25.75–36.12)	37.2 (31.75–49.55)	.006
LVEF > 40%, *n* (%)[a]	1 (6.3)	7 (43.8)	.04
BNP, median pg/mL	222 (124–748)	166 (49–419)	.04
eGFR, median mL/min/1.73 m^2	118 (79–138)	100 (74–127)	.09
Systolic blood pressure, median mmHg	95 (87–107)	96 (86–106)	.98
Diastolic blood pressure, median mmHg	54 (48–60)	54 (45–62)	.52
Heart rate, median beats per minute	91 (73–106)	88 (76–101)	.56
Sodium, mean mEq/L	135.8 (3.5)	137.5 (3.9)	.01
Chloride, mean mEq/L	102.3 (3.9)	102 (3.5)	.58
Potassium, mean mEq/L	4.29 (0.48)	4.27 (0.53)	.83
Blood glucose, mean mg/dL	95.3 (15.2)	92.3 (12.6)	.36
BUN, median mg/dL	18 (12–28)	19 (13–28)	.29
Magnesium, mean mg/dL	2 (0.19)	2.12 (0.23)	.02
Hemoglobin, median g/dL	11.5 (10–14.2)	13.3 (11.2–14.8)	.004
Hematocrit, median %	35.5 (31.2–43.7)	39.6 (35–43.5)	.002
HbA_{1c}, mean %[b]	5.28 (0.62)	5.24 (0.5)	.83
Heart failure pharmacotherapy			
Loop diuretic, *n* (%)	27 (71)	25 (65.8)	.81
Thiazide diuretic, *n* (%)	9 (23.7)	10 (26.3)	> .99
Sacubitril/valsartan, *n* (%)	28 (73.7)	27 (71)	> .99
ACE inhibitor, *n* (%)	6 (15.8)	4 (10.5)	.74
Angiotensin II receptor blocker, *n* (%)	1 (2.6)	1 (2.6)	> .99
Beta-blocker, *n* (%)	27 (71)	30 (78.9)	.74
Ivabradine, *n* (%)	0 (0)	2 (5.3)	.49
Mineralocorticoid antagonist, *n* (%)	24 (63.2)	25 (65.8)	> .99
Isosorbide dinitrate/hydralazine, *n* (%)	5 (13.2)	5 (13.2)	> .99
Digoxin, *n* (%)	19 (50)	15 (39.5)	.65
Milrinone, *n* (%)	13 (34.2)	9 (23.7)	.45

[a]Includes $n = 16$ of 26 patients with dilated cardiomyopathy who received dapagliflozin for a median of 313 days (IQR 191–414)

[b]Follow-up HbA1c data available for $n = 12$ patients

NYHA Class New York Heart Association Functional Classification, *LVEF* left ventricular ejection fraction, *BNP* B-type Natriuretic Peptide, *eGFR* estimated glomerular filtration rate, *HbA_{1c}*, glycated hemoglobin,; *NA* not applicable, *ACE* Angiotensin Converting Enzyme

cardiac arrest died at home from sudden cardiac arrest after 190 days without prior known complications from dapagliflozin.

No patients experienced symptomatic hypovolemia requiring fluid resuscitation or hypoglycemia requiring glucose treatment. Four patients experienced an AKI event. Of these, two occurred during a HF hospitalization, one during routine ambulatory clinical follow-up, and one after aggressive diuresis in the setting of bilateral pleural effusions. Only one patient had dapagliflozin temporarily held surrounding the AKI event.

Dapagliflozin was discontinued in six patients for various indications: patient 1 with underlying progressive mitochondrial disease after 119 days when all oral medications were discontinued during HF hospitalization, patient 2 was a heart transplant recipient with diastolic dysfunction and stage IIIB chronic kidney disease declined for second heart transplant listing after 120 days when hospitalized for

Table 4 Summary of patients ($n=38$) included in clinical case series who received dapagliflozin for heart failure

Case	Age (yrs)	DX	Prior HHF	F/U (days)	[a]HF regimen at latest clinical follow-up	Prior NYHA Class	F/U NYHA Class	F/U UA	D/C	Events experienced (days to event)
1	17.9	DCM	Y	491	3, 6, 7	II	I	2+	N	None
2	11.2	DCM	Y	627	1, 2, 3, 6, 9	III	II	3+	N	HHF (233 d) AKI (370 d)
3	17.7	DCM	Y	549	1, 3, 6, 7, 9	II	II	NA	N	None
4	11.0	DCM	Y	119	1, 2, 4, 6, 7, 9, 10	IV	IV	3+	Y	HHF (119 d)
5	14.3	SVP	Y	478	3, 6, 7	II	II	3+	N	None
6	19.4	DCM	Y	420	1, 3, 6, 7, 9, 11	II	II	3+	N	UTI (121 d)
7	9.1	DHF	Y	427	1, 2, 6, 7	II	II	3+	N	AKI (178 d)
8	15.2	DCM	N	343	3, 6, 7	II	II	NA	N	None
9	14.2	SVP	Y	190	1, 3, 6	II	II	3+	N	Death (190 d)
10	18.0	DCM	Y	397	1, 3, 6, 7, 9	II	II	NA	N	None
11	18.5	DHF	Y	335	1, 2, 3, 7	II	II	3+	N	None
12	19.6	DCM	N	301	3, 6, 7, 9	II	II	3+	N	UTI (245 d)
13	7.6	DCM	Y	225	3, 7	II	I	1+	Y	Txt complete (225 d)
14	13.1	DHF	Y	120	1, 2, 6, 10	III	IV	NA	Y	Hospice (120 d)
15	10.9	DCM	Y	324	1, 2, 3, 6, 7, 9, 10	IV	IV	3+	N	UTI (13 d) HHF/AKI (310 d)
16	17.0	DCM	N	339	3, 6, 7	II	II	3+	N	None
17	17.8	DCM	Y	287	3, 7	II	I	3+	N	UTI (10 d)
18	20.2	DCM	Y	195	1, 3, 6, 8	II	II	3+	N	HHF (63 d)
19	16.7	SVP	Y	276	4, 6	II	II	NA	N	None
20	17.8	DCM	Y	141	3, 6, 7	II	II	NA	N	None
21	15.8	DCM	Y	75	1, 3, 6, 9	III	III	2+	N	None
22	6.8	DCM	N	141	1, 3, 6, 7, 8, 9	II	II	2+	N	None
23	1.9	SVP	Y	97	1, 2, 6, 7, 8, 9, 10	III	III	2+	N	None
24	1.1	DCM	Y	119	1, 2, 6, 7, 8, 10	III	IV	2+	N	AKI (75 d) HHF (73 d)
25	18.4	SVP	N	93	1, 5	II	III	NA	N	None
26	3.4	DCM	Y	83	1, 3, 7, 9	II	III	3+	N	None
27	1.0	DCM	Y	47	1, 3, 6, 7	II	II	NA	N	None
28	1.1	[b]DCM	Y	81	4, 6	IV	IV	3+	N	None
29	2.8	RCM	N	41	1, 4	II	II	3+	N	None
30	6.4	DCM	N	30	3, 7, 9	II	II	NA	N	None
31	16.7	DCM	Y	30	1, 3, 6, 7, 10	III	III	3+	N	None
32	0.3	DCM	Y	38	1, 3, 6	III	II	3+	N	None
33	14.1	[b]DCM	Y	30	3, 6, 7, 10	IV	IV	3+	Y	TXP (30 d)
34	0.6	SVP	Y	43	1, 2, 6, 7, 9, 10	IV	IV	1+	N	None
35	6.2	DCM	N	79	1, 3, 6, 8, 9	II	II	3+	N	None
36	2.1	SVP	Y	72	1, 2, 3, 6, 7, 9, 10	III	III	2+	Y	TXP (72 d)
37	9.8	DHF	N	77	3, 6	II	II	3+	N	UTI (45 d)
38	9.8	[b]DCM	Y	32	1, 10, 11	III	IV	3+	Y	UTI (32 d)

[a]HF regimen at latest clinical follow-up: 1 = loop diuretic, 2 = thiazide diuretic, 3 = sacubitril/valsartan, 4 = ACE inhibitor, 5 = angiotensin II receptor blocker, 6 = beta-blocker, 7 = mineralocorticoid antagonist, 8 = hydralazine/isosorbide dinitrate, 9 = digoxin, 10 = milrinone, 11 = ivabradine

[b]DCM = supported by left ventricular assist device at latest follow-up. DX = cardiac diagnosis; HHF = hospitalization for heart failure; F/U = duration of follow-up; HF = heart failure; NYHA = New York Heart Association; F/U UA = degree of glucosuria closest to latest follow-up: 1 + equates to 250 mg/dL, 2 + equates to 500 mg/dL, and 3 + equates to ≥ 1000 mg/dL; D/C = dapagliflozin discontinued

DCM dilated cardiomyopathy, *SVP* single ventricle physiology, *DHF* diastolic heart failure, *RCM* restrictive cardiomyopathy, *NA* not available, *Y* yes, *N* no, *AKI* acute kidney injury, *UTI* urinary tract infection, Txt complete HF medications weaned off, *TXP* underwent heart transplant

central line-associated sepsis and multi-organ failure, patient 3 had dapagliflozin discontinued at 32 days due to new urinary tract infection (UTI) while supported by HeartMate 3 LVAD, patients 4 and 5 at 30 and 72 days, respectively, at time of heart transplant, and patient 6 after 225 days given significant improvement in left ventricular function leading to weaning of HF pharmacotherapy.

Urinary Tract Infections

Six patients experienced a symptomatic UTI requiring antibiotic treatment at 10, 13, 32, 45, 121 and 245 days, respectively, after starting dapagliflozin. All six patients had 3 + glucosuria closest to UTI diagnosis. Four of the six patients had microbiologically confirmed UTIs while the remaining two patients did not have urine cultures assessed but presented with acute cystitis, hematuria, and urinalysis consistent with UTI diagnosis. Three of the six patients were females aged 9.8, 10.9, and 17.8 years with a recent history of UTI prior to dapagliflozin initiation. The other three patients had more complicated histories that predisposed them to UTI: a 19.4 year-old male with Duchenne muscular dystrophy and new radiographic evidence of renal infarction at time of UTI diagnosis; a 9.8 year-old male with LMNA muscular dystrophy supported by HeartMate 3 LVAD and had recent Foley catheter in place; and a 19.6 year-old female with history of mixed incontinence and radiographic evidence of medical renal disease prior to starting dapagliflozin. No patients required hospital admission or prolongation of hospitalization due to UTI while receiving dapagliflozin.

Left Ventricular Ejection Fraction Analysis

Among the 26 patients with dilated cardiomyopathy in our cohort, 16 were included in a separate LVEF sub-analysis (10 excluded for receiving dapagliflozin for < 90 days at latest follow-up; 3 of these 10 patients were supported by a LVAD during follow-up). Over a median of 313 days (IQR 191–414), LVEF increased in 12/16 (75%), decreased in 3/16 (18.8%), and remained unchanged in 1/16 (6.2%). Median LVEF increased significantly from 32 to 37.2% ($P = .006$) and significantly more patients had LVEF > 40% at latest follow-up compared to baseline (43.8 vs 6.3%, $P = .04$).

Discussion

This is the first description of SGLT2 inhibitor use in pediatric HF. Dapagliflozin was well tolerated without clinically significant electrolyte derangements, hypovolemia, or hypoglycemia. Although dapagliflozin induces natriuresis, our results suggest that dapagliflozin may not cause hyponatremia regardless of diuretic use. Additionally, mechanisms other than hemoconcentration, including augmentation of erythropoiesis, may partly explain a sustained increase in hemoglobin and hematocrit [5]. The occurrence of AKI in our study was notable but could not be attributed to dapagliflozin alone as these events occurred months after dapagliflozin initiation and AKI in pediatric cardiac patients is not uncommon [6].

Dapagliflozin is postulated to have favorable effects on myocardial remodeling and improve outcomes in HF via various physiological functions including downregulation of sympathetic activity and reduction of preload and afterload lessening cardiac stress/injury resulting in less hypertrophy [4]. While we did note an improvement in LVEF in patients with dilated cardiomyopathy, we are not positing that it was due to dapagliflozin alone as many of the patients were on guideline-directed therapy including sacubitril/valsartan, beta-blockers, and aldosterone antagonists, which adult studies have shown to improve LVEF [7–11]. National data indicate the frequency of 30-day readmissions for HF in children is approximately 13%; no patients in our cohort experienced a HF-related hospital readmission within the first 30 days of starting dapagliflozin and the frequency of HF readmissions described in our analysis is not higher than the readmission rate reported nationally for children with HF (3).

By inducing glucosuria, dapagliflozin may have increased risk for UTI in those with predisposing risk factors in our cohort, including recent UTI and Foley catheter placement. Consistent with our results, UTIs were reported more frequently in patients receiving the SGLT2 inhibitor empagliflozin for chronic HF [12]. However, trials of dapagliflozin in patients with chronic HF suggest no effect on incidence of UTIs [13].

This single-center analysis is limited by its observational nature and small sample size. Our study included a heterogenous cohort of children with HF due to primary cardiomyopathies or congenital structural heart disease, which further limits broad interpretations. In effort to minimize the impact of this limitation, our LVEF analysis included only those patients with dilated cardiomyopathy. Concomitant HF medications such as sacubitril/valsartan and beta-blockers were actively being titrated in some patients during follow-up and could have certainly contributed to decreased BNP and improved LVEF observed in our analysis. Although a matched case–control study design might better ascertain changes in BNP and LVEF, the timing of sacubitril/valsartan gaining FDA approval for pediatric HF preceded publication of DAPA-HF Trial by only one month; thus most patients in our cohort were already receiving or transitioned to sacubitril/valsartan at baseline when dapagliflozin was started [14, 15]. A control cohort would consist predominantly of patients receiving ACE inhibitors or angiotensin II receptor blockers, not sacubitril/valsartan, which would comprise HF

regimens that are too dissimilar and a major limitation of that type of analysis. Lastly, there are no published data on pharmacokinetics or pharmacodynamics of dapagliflozin in pediatric HF patients, so we were assuming pharmacodynamic effect based on the presence of glucosuria.

Conclusions

This first description of dapagliflozin use in pediatric HF demonstrates a reasonable safety profile and when added to guideline-directed medical therapy, is well tolerated. There may be a possible association of dapagliflozin use with UTIs in at-risk individuals. While there was improvement in LVEF in patients with dilated cardiomyopathy in our small cohort, larger studies in children should be undertaken to determine if dapagliflozin is as beneficial in children with HF as it has been demonstrated in adults with HF.

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Declarations

Conflict of Interest All authors listed in this manuscript have no conflicts of interest to disclose and have approved the final article.

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