SODIUM-GLUCOSE COSTRANSPORTER-2 INHIBITORS (SGLT2i)

**BACKGROUND**

There are no significant data on the benefit of SGLT2i in pediatric patients with heart failure (HF), although growing literature strongly supports the use of SGLT2i in adults with HF with either reduced or preserved ejection fraction.1,2 The joint ACA/ACC/HFSA guidelines on management of HF includes the use of SGLT2i in adults with HFrEF as a class I recommendation.3 The ESC has a class I recommendation for use of SGLT2i in adults with HFmEF and HFpEF as well.4 The safety of SGLT2i in pediatric patients with HF is not fully established, but early reports demonstrate general safety and tolerability.5

**ACTION REVISED DATE:** 05/23/2024

**OBJECTIVES**

* Provide background and resources regarding use and dosing of SGLT-2 inhibitors (SGLT2i) in children with heart failure
* Provide guidance regarding considerations and precautions for use of SGLT2i in children with heart failure

**PROTOCOL**

For those considering the use of SGLT2i in pediatric patients:

* Timing and indications for SGLT2i initiation are not clear in pediatric heart failure.
* SGLT2i can be considered in the setting of systolic or diastolic HF and in the setting of Fontan circulatory insuffciency. This document provides guidance for usage of SGLT2i but does not address indications for use.
* SGLT2i can be considered in conjunction with other medications used to treat HF or alone. They may be started after other medications have been maximized or may be started sooner due to relatively limited side effect profile and benefit in those with impaired diastolic function.
* Goal Target Dose is based on major guidelines for therapy in adult patients with HF with reduced ejection fraction (HFrEF). See table for recommendations in patients >50kg. Dosing for patients <50kg has not yet been clarified.
* Dosing of pediatric patients with smaller doses of dapagliflozin has been reported with titration upwards if glucosuria is not found on lower doses.

Additional consideration/precautions:

The frequency of urinary tract infections and genital infections is increased in patients receiving an SGLT2i. An individualized discussion of the the risks and benefits based on a patient’s dermatologic and urologic history is encouraged. Concomitant use of immunosuppressive medications should also be taken into consideration.

* Relative dehydration and natriuresis may be possible, and pre-emptive reduction in diuretics can be considered.
* eGFR may initially decline with initiation of SGLT2i due to tubuloglomerular feedback. Among adult patients, SGLT2i use is associated with preservation of kidney function and is now recommended for adults with chronic kidney disease.

SGLT2i associated ketoacidosis and Endocrine Related Considerations

* Euglycemic diabetic ketoacidosis (EuDKA) has been reported in adults on SGLT2i; it should be considered when a patient has an anion gap metabolic acidosis and/or elevated ketones, even when blood glucose < 200, or lactic acidosis of unclear etiology.6 Consider checking ketones regardless of blood glucose levels if EuDKA is suspected.
* The recommendation from the FDA is to consider **holding SGLT2i 3-4 days before scheduled surgery**.7
* During times of fasting, dextrose-containing fluids + insulin can be considered. When DKA is supected, insulin should be started.8
* If a patient is already on insulin or other glucose-lowering medication, consider consultation with an endocrinologist prior to SGLT2i initiation.

Dosing Considerations:

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Medication of Choice | | Initial Dose | Titration Amount | Goal Dose Minimum | Dose Maximum |
| < 50 kg | Dapagliflozin | 0.1 mg/kg/dose daily | 0.1 mg/kg/dose daily | 0.1 mg/kg/dose daily | 0.2 mg/kg/dose daily |
| ≥ 50 kg | Dapagliflozin | 5-10 mg daily | 5 mg daily | 5 mg daily | 10 mg daily |
|  | Empagliflozin | 5-10 mg daily | -- | 10 mg daily | 10 mg daily |

Therapeutic monitoring:

* Baseline renal function and Glucose
  + Check renal panel, HgbA1c, and glucose prior to initiation. Timing based on patient age and clinical status but generally should be within 7 to 14 days of initiation.
  + Repeat assessment should be performed within 2 weeks to 6 weeks or earlier if clinically indicated to assess hydration and renal function.
* Urinalysis for glucosuria
  + For smaller patients on smaller doses of dapagliflozin, repeat urinalysis within 1-3 weeks is reasonable to assess for presence of glucosuria. If glucosuria is not present, it is reasonable to increase to the higher dose if tolerated.

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8. Raiten JM, Morlok A, D’Ambrosia S, Ruggero MA, Flood J. Perioperative Management of Patients Receiving Sodium-Glucose Cotransporter 2 Inhibitors: Development of a Clinical Guideline at a Large Academic Medical Center. *J Cardiothorac Vasc Anesth*. 2024;38(1):57-66. doi:10.1053/j.jvca.2023.10.011

**AUTHORS**

Ryan Butts, Borah Hong, Deip Nandi, Joey Spinner

**CONTRIBUTING CENTERS**

Children’s Health Dallas/UT Southwestern, Seattle Children’s Hospital, Nationwide Children’s Hospital, Texas Children’s Hospital

***Disclaimer:*** *The ACTION network is focused on quality improvement efforts such as harmonizing best practice protocols, disseminating them among institutions, and helping centers to improve care practices at the local level. This protocol was developed as a consensus tool for pediatric VAD programs. The information in the protocols are based on center practices, individual opinions, experiences, and, where available, published literature. Centers may choose to adapt this protocol to include in their center-specific protocols with reference to ACTION with the understanding that these are meant as guidelines and not standard of care. (Revised: 05/23/2024)*