



Use of isosorbide dinitrate/hydralazine combination in pediatric patients with heart failure

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Introduction

Background

- Children admitted for heart failure have an increased risk of morbidity, mortality, and cost as previously reported.
- Angiotensin converting enzyme inhibitor (ACEI) is the mainstay of medical management. However, in the admitted patient, adverse effects such as hypotension, hyperkalemia, uremia, and worsening renal function can limit its use.
- The combination of isosorbide dinitrate/hydralazine (ISDN/HYD) is approved for use in heart failure in African Americans adults, but it has also been shown to be effective in the general adult heart failure population. It is attractive in that it does not possess the laboratory side effect profile of ACEI.
- Given the lack of published reports of its use in children, we report our preliminary experience with ISDN/HYD in children hospitalized with significant cardiovascular disorders.

Methods

- Design:** single-center, retrospective review
- Period:** 2007-Current
- Inclusion:** age <21 years with a diagnosis of cardiovascular disorder
- Exclusion:** All patients who where admitted on ISDN/HYD or its use for less than 7 days.
- Indications:** Hypertension, systolic dysfunction, renal dysfunction, or side effects from ACEI or as add on therapy to ACEI.
- Dosage:** The combination dose ratio is 1:2 mg and the intended starting dose was0.5 ~ 1mg/kg/day ISDN : 1-2 mg/kg/day HYD divided TID with an up-titration as needed to maximum dose of 5mg:10mg/kg/day or 120mg:240mg/day

Clinical Characteristics

Table 1. Clinical characteristics of study population

	Frequency (Percent or Median Interquartile range IQR)
Sex	
Female	26 (40.6)
Male	38 (59.4)
Race	
Caucasian Non Hispanic	31 (48.4)
African American	8 (12.5)
All others	25 (39.1)
Diagnosis	
Cardiomyopathy	30 (46.9)
Single ventricle CHD	23 (35.9)
Two ventricle CHD	11 (17.2)
Location	
Floor	16 (25)
ICU	47 (75)
Inotropes	
No	18 (28.1)
Yes	46 (71.9)
Weight (kg)	10.7 (IQR 5.8-36.7)
BSA (M ²)	0.41 (0.25-0.95)
Age (Years)	2.7 (0.4-11.4)

Table 2. Descriptive data on the use of ISDN/HYD

	Frequency(Percent or Median Interquartile range IQR)
Indications for ISDN/HYD	
Adjunct therapy for Systolic Dysfunction	27 (42.2)
Hypertension	10 (15.6)
Systolic dysfunction with Renal Dysfunction	20 (31.3)
Systolic dysfunction with Renal dysfunction from ACEI	7 (10.9)
Treatment Course	
Duration on ISDN/HYD(Days)	32.5 (14.3-79.0)
Starting dose(HYD mg/kg/day	1.4 (0.78-2.19)
Final dose (HYD mg/kg/day	3.3 (1.49-6.90)

Table 3. Clinical outcome

Clinical Outcome	Number
Still admitted	1
Discharged	43
Mechanical Circulatory Support	0
Transplantation	14
Death	5

Outcomes with ISDN/HYD

- Starting dose mg/kg (all statistically significant)
 - Inversely correlated with age
 - Correlates with the final dose
 - Inversely correlates with the creatinine at the start and at the end
- Final dose mg/kg (all statistically significant)
 - Inversely correlated with the age
 - Correlated with duration on ISDN/HYD
 - Inversely correlated with creatinine

Conclusion and Limitations

- Conclusions:
- In this retrospective study, use of ISDN/HYD to replace ACEI or to add to therapy was well tolerated.
 - No adverse effects leading to discontinuation of the drug were found
 - Further study is needed to find the optimal dose and assess its efficacy in a larger cohort.
 - Patients in the ICU tolerated ISDN/HYD without significant side effects

- Limitations:
- Retrospective design
 - Small sample size

References

- 1.Terano C, Ishikura K, Miura M, et al. Incidence of and risk factors for severe acute kidney injury in children with heart failure treated with ACEI. Eur J Pediatr (2016) 175:631-637
2. Golwala HB, Thadani U, LiangL, et al. Use of hydralazine-isosorbide dinitrate combination in African American and other race/ethnic group patients with heart failure and reduce left ventricular ejection. J Am Heart Assoc. (2013) Aug 21;2(4)

Abbreviations:
CHD - congenital heart disease
ISDN/HYD –Isosorbide dinitrate – hydralazine
ACEI- Angiotensin converting enzyme inhibitor
TID- three times a day
mg- milligrams
Kg -kilograms