Utilization of Angiotensin II for Catecholamine-Resistant Shock in Children: A Single Center Descriptive Case Series

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Introduction

- Catecholamine-resistant shock (CRS) is associated with high rates of morbidity and mortality in children, however, no evidence-based recommendations exist for management
- Angiotensin II (Ang II) is a novel vasoactive agent for CRS that has demonstrated efficacy in adults (Khanna et al, NEJM, 2017), particularly in those with acute kidney injury (Tumlin et al, CCM, 2018) and presumed renin-angiotensin system (RAS) derangement (Bellomo et al, AJRCCM, 2020) **(Figure 1)**

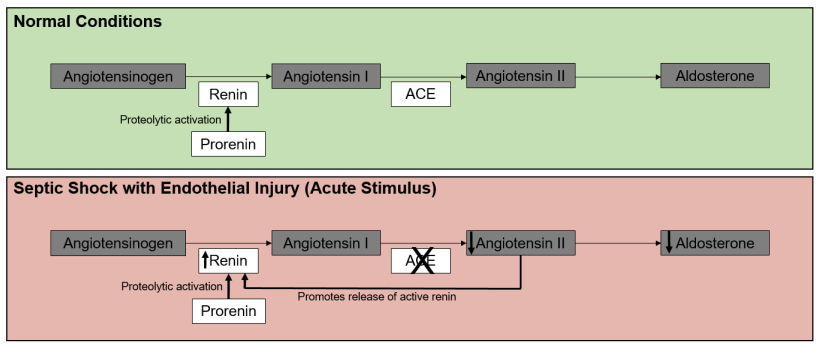


Figure 1

- Preliminary data in children with septic shock suggest evidence of RAS derangement, as they demonstrate very elevated renin+prorenin concentrations (Stanski et al, Pediatr Nephrol, 2023) and reduced angiotensin-converting enzyme (ACE) activity on Day 1. Given these findings, Ang II may be particularly beneficial in this population.
- However, no data regarding the use of Ang II in children has been published . As such, we aimed to describe the clinical characteristics and outcomes of children with CRS receiving Ang II.

Methods and Materials

- Single center retrospective study of all children and young adults (ages 0-25) who received Ang II for CRS (defined as refractory to 2 vasoactives) from January 2018 to November 2022.
- Demographic, clinical (including direct renin concentrations, when available) and outcome data were assessed for each subject. Vasoactive inotropic scores (VIS) were examined pre- and post-initiation of Ang II to assess response to therapy.

VIS= 100 x epinephrine dose (µg/kg/min) + 10 x vasopressin dose (mU/kg/min) + 100 x norepinephrine dose (µg/kg/min) + dopamine dose (µg/kg/min) + dobutamine dose (µg/kg/min) + 10 x milrinone dose (µg/kg/min)

Results

Patient Demographics:

	Cohort Data (n=20)
Age, years	10.2 (1.6-18) (Range: 1 month-23 years)
Sex at birth, female (%)	13 (65)
Immunocompromised, yes (%)	10 (50)
History of previous blood clot, yes (%)	10 (50)
Sepsis at Ang II Initiation, yes (%)	19 (95)

Table 1: Cohort Demographics. Continuous data reported as median (IQR)

Results (Continued)

Clinical Data at Time of Ang II Initiation:

	Cohort Data (n=20)
PELOD-2	9.5 (7.3-11)
Time from Vasoactive Initiation to Ang II, hours	142 (18.1-350)
Serum renin (pg/ml)*	3527 (1697-5571)
Urine NGAL (ng/ml)**	3456 (763-15000)
VIS	64 (38-90)
Severe AKI, yes (%)	18 (90)
Extracorporeal Support, yes (%) ECMO CRRT	15 (75) 2 (10) 15 (75)

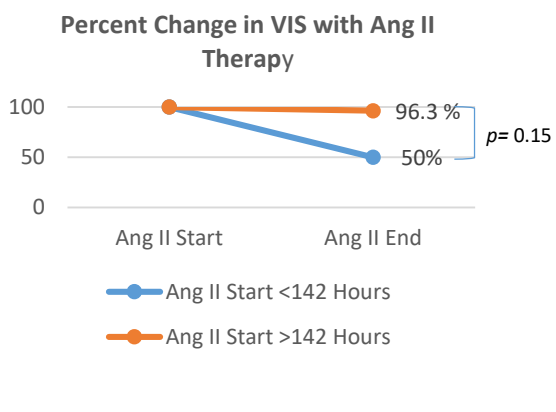
Table 2: Pre-Ang II Data. Continuous data reported as median (IQR). *8 patients with serum renin obtained prior to initiation. **7 patients with urine NGAL obtained prior to initiation.

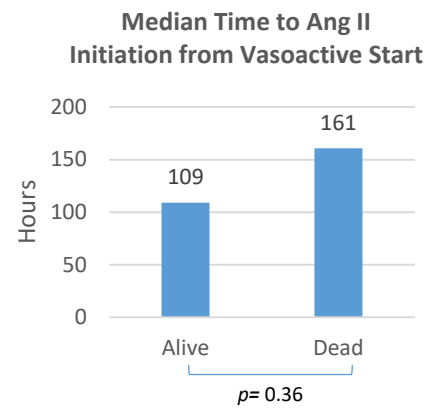
Outcome Data:

	Cohort Data (n=20)
Duration of Ang II Therapy, hours	26.9 (4.0-73.3)
% Change in VIS At 6 hours At Ang II discontinuation	 -24.4% (-45.7,-1.4) -19.6% (-81.6, 14.4)
New Blood Clot on Ang II, yes (%)	1 (5)
ICU Mortality, yes (%)	16 (70)

Table 3: Cohort Outcome Data. Continuous data reported as median (IQR).

Initiation of Ang II Earlier May Improve Outcomes:





Conclusions

- Ang II appears to reduce vasoactive burden in children with CRS, though outcomes for these patients are overall poor.
- In this cohort, Ang II was initiated late in vasoactive course, and commonly in children with severe AKI and evidence of RAS derangement by elevated serum renin.
- Though more data are needed, earlier initiation of Ang II may be beneficial. Further study is needed to determine when and in whom its use is warranted.

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