Retrospective analysis of patient outcomes of angiotensin II (Giapreza®) use at a level 1 trauma center

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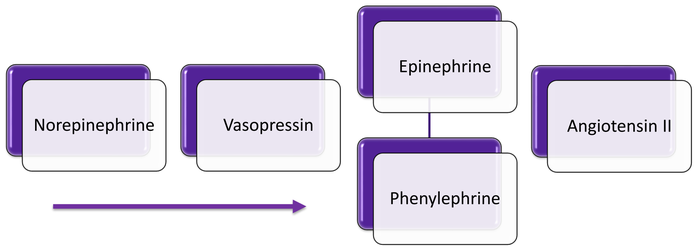
ABSTRACT

Angiotensin II (ATII) is a synthetic hormone that causes vasoconstriction through ACE-2 stimulation and release of aldosterone.

ATII is used as an adjunctive vasopressor for patients who are unable to meet MAP or BP goals with typical vasopressors and hydrocortisone in the setting of fluid-resuscitated vasodilatory shock. The proposed place in therapy can be see in the chart below.

The ATHOS-III trial found that patients given ATII vs placebo were more likely to achieve a MAP of ≥75 mmHg or MAP increase of ≥10 mmHg (70% vs 23%, P < 0.001), but no change in SOFA scores, 7-day (29% vs 35%, P=0.22), or 28-day mortality (46% vs 54%, P = 0.12).



OBJECTIVES

Evaluate the efficacy and clinical benefit in patient outcomes with the addition of ATII to a background vasopressor regimen in fluid-resuscitated vasodilatory shock

Provide retrospective chart review of patients receiving ATII since publication of ATHOS-III trial

PATIENT POPULATION

Inclusion Criteria

- Patients age 18 – 90 years old
- Patients with vasodilatory (septic) shock
- Presence of documented initiation of ATII infusion on patient's MAR
- Currently on 1 or more vasopressors for 6-48 hours to maintain MAP/BP goals defined in EPIC orders

Exclusion Criteria

- Burn > 20% of total BSA
- Pregnancy

PLANNED OUTCOMES

Primary Outcome: ability to wean off of other vasopressors at any point while on ATII defined as:

- Ability to reduce background vasopressors (defined as a decrease in 0.1 mcg/kg/min of norepinephrine or equivalents) at any time during the infusion of ATII

Vasopressor Equivalents of 0.1µg/kg/min Norepinephrine	
Drug	Dose
Vasopressin	0.04 units/min
Epinephrine	0.1 µg/kg/min
Phenylephrine	1.0 µg/kg/min
Dopamine	15 µg/kg/min

Secondary Outcomes:

- Response to ATII within 3 hours of initiation
- Ability to discontinue background vasopressors while on ATII
- Length of stay in ICU and hospital
- Mortality while on drug, at 7 days, at 28 days
- Survival to hospital discharge
- Adverse events while on therapy: new thrombosis, new infection

Exploratory Outcomes:

- Ordering service
- Average cost per patient
- Total cost
- Total drug infused
- Duration of use

PREVIEW N=25

- Diagnosis: septic 16/25, cardiogenic 2/25, COVID-19 septic 2/25, hemorrhagic, distributive, and hypovolemic shock
- Average MAP at ATII initiation: **58.4 mmHg**
- Average MAP after 3 hrs of ATII: **76.6 mmHg**

N= 16	Yes	No
Primary: able to wean background vasopressors while on ATII	12 (75%)	4 (25%)
Able to DC all vasopressors after ATII initiation	6 (37.5%)	10 (62.5%)
Able to discontinue one background vasopressor	10 (62.5%)	6 (37.5%)
Survived to hospital discharge	5	11
Deceased on drug	5	11
Deceased at 7 days	8	8
Deceased at 28 days	10	6
MAP Increased by ≥10 mmHg in 3 hours	13 (81.25%)	3 (18.75%)
MAP Goal met	14 (87.5%)	2 (12.5%)

METHODS

- Retrospective chart review at Regions Hospital
- Data will be extracted from EPIC database
- Dates of 6/29/2018 to 6/29/2020
- Patients will include: adequately fluid-resuscitated and are on ≥1 vasopressors, not meeting perfusion goals
  - We will presume that patients were given guideline directed fluid resuscitation if they fit the criteria of severe sepsis/septic shock by the time of ATII initiation

CONCLUSIONS

Data collection is underway for this project. We hope this project will help evaluate patient outcomes with the use of ATII. Our study will provide clinical evidence into ATII's use in weaning other vasopressors, length of stay, mortality, and adverse events. This study will also provide guidance and evidence for future use of ATII in this setting, and can potentially elucidate its use in the setting of COVID-19 as well.

Strengths

- Focused on improving healthcare for patients with clinically meaningful endpoints like length of stay and mortality
- Focused on improving our knowledge in an area with minimal published data

Limitations

- Retrospective nature as it is difficult to distinguish causation from correlation
- Number of patients in which data will be collected due to the small number of patients available and the limited time frame of the study

REFERENCES

1. Chawla LS, Russell JA, Bagshaw SM, et al. Angiotensin II for the Treatment of High-Output Shock 3 (ATHOS-3): protocol for a phase III, double-blind, randomised controlled trial. *Crit Care Resusc*. 2017;19(1):43-49.
2. Farina N, Bixby A, Alaniz C. Angiotensin II brings more questions than answers. P & T. 2019; 43 (11): 685- 687
3. Senchenkova EY, Russell J, Almeida-Paula LD, et al. Angiotenin II-mediated microvascular thrombosis. Hypertension. 2010; 56 (6): 1089-1095.
4. Zhang P, Zhu L, Cai J, et al. Association of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers with mortality among patients with hypertension hospitalized with COVID-19. Circ Res. 2020: 126 (12): 1671-1681
5. Tralhao A, Moita LF, Povoa P. Potential benefits of angiotensin II in COVID-19 patients: beyond reasonable doubt? Crit Care. 2020; 243 (324).
6. Zangrillo A, Landoni G, Beretta L, et al. Angiotensin II infusion in COVID-19-associated vasodilatory shock: a case series. Crit Care. 2020; 24: 227
7. Want H, Das S, Wieruszewski PM, et al. Unexpected BP sensitivity to angiotensin II in a patient with coronavirus disease 19, ARDS, and septic shock. CHEST. 2020; 158 (2): e55-58
8. Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R, Kumar A, Sevransky JE, Sprung CL, Nunnally ME, Rochwerg B, Rubenfeld GD, Angus DC, Annane D, Beale RJ, Bellinghan GJ, Bernard GR, Chiche JD, Coopersmith C, De Backer DP, French CJ, Fujishima S, Gerlach H, Hidalgo JL, Hollenberg SM, Jones AE, Karnad DR, Kleinpell RM, Koh Y, Lisboa TC, Machado FR, Marini JJ, Marshall JC, Mazuski JE, McIntyre LA, McLean AS, Mehta S, Moreno RP, Myburgh J, Navalesi P, Nishida O, Osborn TM, Perner A, Plunkett CM, Ranieri M, Schorr CA, Seckel MA, Seymour CW, Shieh L, Shukri KA, Simpson SQ, Singer M, Thompson BT, Townsend SR, Van der Poll T, Vincent JL, Wiersinga WJ, Zimmerman JL, Dellinger RP. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Intensive Care Med. 2017 Mar;43(3):304-377. doi: 10.1007/s00134-017-4683-6. Epub 2017 Jan 18. PMID: 28101605.
9. Busse LW, Wang XS, Chalikonda DM, Finkel KW, Khanna AK, Szerlip HM, Yoo D, Dana SL, Chawla LS. Clinical Experience With IV Angiotensin II Administration: A Systematic Review of Safety. Crit Care Med. 2017 Aug;45(8):1285-1294. doi: 10.1097/CCM.0000000000002441. PMID: 28489648; PMCID: PMC5515638.

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