

BAB VI

KESIMPULAN DAN SARAN

6.1 Kesimpulan

Pada penelitian ini dapat ditarik kesimpulan sebagai berikut:

1. Kadar rata – rata reseptor adrenergic α_1 , reseptor vasopressin V_{1A}, norepinefrin, dan copeptin pada pasien syok sepsis akan meningkat pada pasien yang dapat disapih dari vasopressor.
2. Kadar rata – rata reseptor adrenergik α_1 , reseptor vasopressin V_{1A}, norepinefrin, dan copeptin pada pasien syok sepsis akan menurun pada pasien yang syok kembali setelah lepas dari vasopressor.
3. Kadar rata – rata reseptor adrenergik α_1 , reseptor vasopressin V_{1A}, norepinefrin, dan copeptin sebelum terpadang vasopressor pada pasien syok sepsis yang meninggal lebih tinggi dibandingkan dengan pasien yang hidup.

Adapun kesimpulan klinis dari penelitian ini adalah:

Pasien syok sepsis dengan status hemodinamik yang membaik bisa saja masih masih memiliki kadar copeptin yang rendah di plasma yang mengakibatkan resiko terjadinya syok berulang. Sehingga hal ini dapat dijadikan pertimbangan untuk mempertahankan vasopressin sebagai obat yang disapih setelah golongan katekolamin dihentikan.

6.2 Saran

1. Dalam melakukan penyapihan vasopressor, pada pasien syok sepsis di masa pemulihan, vasopressin sebaiknya dipertahankan sebagai vasopressor yang terakhir dihentikan.

2. Sebagai bagian dari upaya pengembangan keilmuan dan aplikasinya dalam bidang klinis, maka penelitian ini dapat dikembangkan dengan menggunakan sampel yang lebih besar, parameter yang lebih banyak, serta desain penelitian yang lebih spesifik sehingga dapat menambah wawasan dan inovasi mengenai syok sepsis dan vasopressor.

DAFTAR PUSTAKA

1. Basodan N, Almehmedi AE, Almehmedi AE, Aldawood SM, Hawsawi A, Fatini F, et al. Septic shock: management and outcomes. *Cureus*. 2022; 14(12): e32158. <http://doi.org/10.7759/cureus.32158>
2. Singer M, Deutchman CS, Seymour CW, Shankar-hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *Jama*. 2016; 315(8): 801 – 10. <http://doi.org/10.1001/jama.2016.0287>
3. Parillo JE, Dellinger RP. Critical care medicine: principles of diagnosis and management in adult. 5th ed. Amsterdam: Elsevier; 2019
4. Egi M, Ogura H, Yatabe T, Atagi K, Inoue S, Iba T, et al. The japanese clinical practice guidelines for management of sepsis and septic shock 2020 (J-SSCG 2020). *J Intensive Care*. 2021;9(53):. <https://doi.org/10.1186/s40560-021-00555-7>
5. Lat I, Coopersmith CM, Backer DD. The surviving sepsis campaign: fluid resuscitation and vasopressor therapy research priorities in adult patients. *Crit Care Med.* 2021;49(4):623 - 35. <http://doi.org/10.1097/CCM.0000000000004864>
6. Sedhai YR, Shrestha DB, Budhathoki P, Memon W, Acharya R, Guire S, et al. Vasopressin versus norepinephrine as the first-line vasopressor in septic shock: a systematic review and meta-analysis. *Crit Care Med.* 2022; 8(3): 185-99. <http://dx.doi.org/10.18053/jctres.08.202203.005>
7. Scheeren TWL, Bakker J, Backer DD, Annane D, Asfar P, Boerma EC, et al. Current use of vasopressors in septic shock. *Ann Intensive Care*. 2019; 9:20. <https://doi.org/10.1186/s13613-019-0498-7>
8. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CG, French C, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. *Crit Care Med.* 2021;49(11):e1063-143 <https://doi.org/10.1097/CCM.0000000000005337>
9. Lat I, Coopersmith CM, Backer DD. The surviving sepsis campaign: fluid resuscitation and vasopressor therapy research priorities in adult patients. *Crit Care Med.* 2021;49(4):623 - 35. <http://doi.org/10.1097/CCM.0000000000004864>
10. DiPiro JT. Pharmacotherapy: A pathophysiologic approach. McGraw-Hill Education. 2022
11. Permpikul C, Tongyoo S, Viarasilpa T, Trainarongsakul T, Chakorn T, Udompanturak S. Early use of norepinephrine in septic shock resuscitation (CENSER) a randomized trial. *Am J Respir Crit Care Med.* 2019; 199(9): 1097 - 105. <http://doi.org/10.1164/rccm.201806-1034OC>
12. Vincent JL, editor. Annual update in intensive care and emergency medicine 2023. Switzerland: Springer; 2023
13. Wieruszewski PM, Khanna AK. Vasopressor choice and timing in vasodilatory shock. *Crit care*. 2022; 26(1): 76 <http://doi.org/10.1186/s13054-022-03911-7>

14. Song X, Liu X, Evans KD, Frank RD, Barreto EF, Dong Y, et al. The order of vasopressor discontinuation and incidence of hypotension: a retrospective cohort analysis. *Sci Rep.* 2021; 11: 11680. <https://doi.org/10.1038/s41598-021-96322-7>
15. Buckley CT, Turner B, Walsh D, Garrett MJ, Ooka VN. Analysis of vasopressor discontinuation and the incidence of rebound hypotension in patients with septic shock. *Hosp. Pharm.* 2019; 56(1):1-7. <http://doi.org/10.1177/0018578719867646>
16. Bauer SR, Aloj JJ, Ahrens CL, Yeh JY, Culver DA, Reddy AJ. Discontinuation of vasopressin before norepinephrine increases the incidence of hypotension in patients recovering from septic shock: A retrospective cohort study. *J Crit. Care.* 2010; 25: 362.e7-11. <http://doi.org/10.1016/j.jcrc.2009.10.005>
17. Hammond DA, Sacha GL, Bissell BD, Musallam N, Altshuler D, Flannery AH, et al. Effects of norepinephrine and vasopressin discontinuation order in the recovery phase of septic shock: A systematic review and individual patient data meta-analysis. *Pharmacotherapy.* 2019;39(5): 544 – 52. <http://doi.org/10.1002/phar.2265>
18. Musallam N, Altshuler D, Merchan C, Zakhary B, Aberle C, Papadopoulos J. Evaluating vasopressor discontinuation strategies in patients with septic shock on concomitant norepinephrine and vasopressin infusions. *Ann Pharmacother.* 2018; 52(8): 733 – 9. <http://doi.org/10.1177/1060028018765187>
19. Bissell BD, Magee C, Moran P, Bastin MLT, Flannery AH. Hemodynamic instability secondary to vasopressin withdrawal in septic shock. *J Intensive Care Med.* 2017; 34(9):761 – 5. <http://doi.org/10.1177/0885066617716396>
20. Duclos G, Baumstarck K, Dunser M, Zieleskiewicz L, Leone M. Effects of the discontinuation sequence of norepinephrine and vasopressin on hypotension incidence in patients with septic shock: A meta-analysis. *Heart & lung.* 2019; 48(6). 560 – 5. <https://doi.org/10.1016/j.hrtlng.2019.05.007>
21. Sacha G, Lam SW, Dugal A, Torbic H, Reddy AJ, Bauer S. Hypotension risk based on vasoactive agent discontinuation order in patients in the recovery phase of septic shock. *Pharmacotherapy.* 2018; 38(3): 319 – 26. <http://doi.org/10.1002/phar.2082>
22. McDaniel CM, Moyer A, Brown JE, Baram M. Impact of vasopressor initiation and discontinuation sequence on mortality in septic shock: A retrospective review. *Surg case reports.* 2020; 3(2): 1 – 7. <http://doi.org/10.31487/j.SCR.2020.02.05>
23. Jeon K, Song JU, Chung CR, Yang JH, Suh GY. Incidence of hypotension according to the discontinuation order of vasopressors in the management of septic shock: A prospective randomized trial (DOVSS). *Crit Care.* 2018; 22:131. <https://doi.org/10.1186/s13054-018-2034-9>
24. Burgdorff AM, Bucher M, Schumann J. Vasoplegia in patients with sepsis and septic shock: pathways and mechanisms. *J int med res.* 2018; 46(4): 1303 – 10. <http://doi.org/10.1177/0300060517743836>
25. Hahn PY, Wang P, Tait SM, Ba ZF, Reich SS, Chaudry IH. Sustained elevation in circulating catecholamine levels during polymicrobial sepsis. *Shock.* 1995; 4(4): 269 –73. <http://doi.org/10.1097/00024382-199510000-00007>

26. Hwang TL, Lau YT, Huang SF, Chen MF, Liu MS. Changes of α 1-adrenergic receptors in human liver during intraabdominal sepsis. *Hepatology*. 1994; 20(3): 638 – 42.
27. Treschan TA, Peters J. The vasopressin system: physiology and clinical strategies. *Anesthesiology*. 2006; 105(3): 599–612. <http://doi.org/10.1097/00000542-200609000-00026>
28. Bucher M, Hobbhahn J, Taeger K, Kurtz A. Cytokine-mediated downregulation of vasopressin V1A receptors during acute endotoxemia in rats. *Am j physiol regulatory integrative comp physiol*. 2002; 282(4): R979 – 84. <http://doi.org/10.1152/ajpregu.00520.2001>
29. Wu LL, Tang C, Liu MS. Hyper and hypocoardiodynamic states are associated with externalization and internalization, respectively, of alpha adrenergic receptors in rat heart during sepsis. *Shock*. 1997; 7(5): 318 – 23. <https://doi.org/10.1097/00024382-199705000-00002>
30. Landry DW, Levin HR, Gallant EM, Ashton Jr RC, Seo S, D'Allesandro D, et al. Vasopressin deficiency contributes to the vasodilation of septic shock. *Circulation*. 1997; 95(5): 1122 – 5. <http://doi.org/10.1161/01.cir.95.5.1122>
31. Lambden S, Creagh-brown BC, Hunt J, Summers C, Forni LG. Definitions and pathophysiology of vasoplegic shock. *Crit care*. 2018; 22(1). <http://doi.org/10.1186/s13054-018-2102-1>
32. Chawla LS, Ostermann M, Forni L, Tidmarsh G. Broad spectrum vasopressors: A new approach to the initial management of septic shock?. *Crit care*. 2019; 23(1): 124. <http://doi.org/10.1186/s13054-019-2420-y>
33. Norman, A. W., Dean, M. C. & Henry, H. L. *Hormones*. Elsevier; 2015
34. Smith, M. D. & Maani, C. V. *Norepinephrine*. StatPearls. Internet; 2023
35. Sharman A, Low J. Vasopressin and its role in critical care. *Contin educ anaesthesia, Crit care pain*. 2008; 8(4): 134 – 7.
36. Bankir L, Bichet DG, Morgenthaler NG. Vasopressin: physiology, assessment and osmosensation. *J of int med*. 2017; 282(4). 284 – 97. <http://doi.org/10.1111/joim.12645>
37. Fink MP, Homer LD, Fletcher JR. Diminished pressor response to exogenous norepinephrine and angiotensin II in septic, unanesthetized rats: evidence for a prostaglandin-mediated effects. *J of surg research*. 1985; 38(4): 335 – 42. [https://doi.org/10.1016/0022-4804\(85\)90046-0](https://doi.org/10.1016/0022-4804(85)90046-0)
38. Innamorati G, Sadeghi H, Birnbaumer M. Transient Phosphorylation of the V1a Vasopressin Receptor. *J biol chem*. 1998; 273(12): 7155 – 61. <http://doi.org/10.1074/jbc.273.12.7155>
39. Barrett LK, Singer M, Clapp LH. Vasopressin: Mechanisms of action on the vasculature in health and in septic shock. *Crit care med*. 2007; 35(1): 33 – 40. <http://doi.org/10.1097/01.CCM.0000251127.45385.CD>
40. Hammond DA, Sacha GL, Bissell BD, Musallam N, Altshuler D, Flannery AH, et al. Effects of norepinephrine and vasopressin discontinuation order in the recovery phase of septic shock: A systematic review and individual patient data meta-analysis. *Pharmacotherapy*. 2019;39(5): 544 – 52. <http://doi.org/10.1002/phar.2265>

41. Musallam N, Altshuler D, Merchan C, Zakhary B, Aberle C, Papadopoulos J. Evaluating vasopressor discontinuation strategies in patients with septic shock on concomitant norepinephrine and vasopressin infusions. *Ann Pharmacother.* 2018; 52(8): 733 – 9. <http://doi.org/10.1177/1060028018765187>
42. Jeon K, Song JU, Chung CR, Yang JH, Suh GY. Incidence of hypotension according to the discontinuation order of vasopressors in the management of septic shock: A prospective randomized trial (DOVSS). *Crit Care.* 2018; 22:131. <https://doi.org/10.1186/s13054-018-2034-9>
43. Carrara M, Ferrario M, Pinto BB, Herpain A. The autonomic nervous system in septic shock and its role as a future therapeutic target: a narrative review. *Ann intensive care.* 2021; 11(1): 80. <http://doi.org/10.1186/s13613-021-00869-7>.
44. Álvarez RG, Salazar AR. Vasopressin in sepsis and other shock states: state of the art. *J Pers Med.* 2023; 13:1548. <https://doi.org/10.3390/jpm13111548>
45. Jochberger S, Dorler J, Luckner G, Mayr VD, Wenzel V, Ulmer H, et al. The vasopressin and copeptin response to infection, severe sepsis, and septic shock. *Crit Care Med.* 2009; 37(2): 476 –82. <http://doi.org/10.1097/CCM.0b013e3181957532>