

| |
|---------------------|
| DRUG PROFILE |
|---------------------|

USE OF INOTROPES IN PICU

***Jeesson C Unni**
****Akanksha Jain**

Abstract: *Inotropes increase myocardial contractility and have variable effects on peripheral vascular resistance. The first-line inotropic agents used in pediatrics are dopamine and epinephrine. Further, depending on cardiac output and systemic vascular resistance, other vasoactive agents indicated in the treatment of shock in children include vasoconstrictors (e.g. norepinephrine, phenylephrine) or vasodilators (e.g. dobutamine, milrinone). The effective inotrope indicated for the given etiology of shock depends on the end-diastolic volume and cardiac contractility. This article attempts to throw light on appropriate use of these agents.*

Keywords: *Inotrope, Epinephrine, Dopamine, Norepinephrine, Isoprenaline, Vasopressor, Bipyridines*

Points to Remember

- *Inotropes are one of the most commonly used drugs in intensive care setting, which increases myocardial contractility and have variable effects on peripheral vascular resistance.*
- *The various classes of drugs include catecholamines, bipyridines, vasopressors, glycosides, Ca sensitizer, afterload reducing agents and sympathomimetics.*
- *Selection of appropriate drug is based on the hemodynamic state, blood pressure and systemic vascular resistance.*
- *They have multiple effects and should be used carefully.*
- *One must know the adverse effects and be prepared to deal with side effects.*

References

1. Allen HD, Adams FH, Moss AJ. Moss and Adams' heart disease in infants, children and adolescents: including the fetus and young adult. Philadelphia, PA: Lippincott Williams and Wilkins, 2021.
2. Basics of cardiac pharmacology. Learn Pediatrics. <https://learn.pediatrics.ubc.ca/body-systems/cardiology>. Accessed on 21st Nov 2021.
3. Bangash MN, Kong M, Pearse RM. Use of inotropes and vasopressor agents in critically ill patients. *Bri J Pharmacol* 2012; 165(7):2015-2033.
4. Overgaard CB, Dzaviiik V. Inotropes and Vasopressors Review of Physiology and Clinical Use in Cardiovascular Disease. *Circulation* 2008;118(10):1047-1056. <https://doi.org/10.1161/CIRCULATIONAHA.107.728840>.
5. Cotecchia S, Stanasila L, Diviani D. Protein-protein interactions at the adrenergic receptors. *Curr Drug Targets* 2012; 13(1):15-27.
6. Hendriks-Balk MC, Peters SL, Michel MC, Alewijnse AE. Regulation of G protein-coupled receptor signalling: focus on the cardiovascular system and regulator of G protein signalling proteins. *Eur J Pharmacol* 2008; 585(2-3): 278-291.
7. Pitcher JA, Freedman NJ, Lefkowitz RJ. G protein-coupled receptor kinases. *Ann Rev Biochem* 1998; 67:653-692.

* Senior Consultant,
Department of Child and Adolescent Health,
Aster Medcity,
Kochi.
email: jeesson1955@gmail.com

** Consultant Pediatric Intensivist,
Aster Medcity,
Kochi.

8. Robertson GL, Shelton RL, Athar S. The osmoregulation of vasopressin. *Kidney Int* 1976; 10(1):25-37.
9. Demiselle J, Fage N, Radermacher P, Asfar P. Vasopressin and its analogues in shock states: a review. *Ann Intensive Care* 2020; 10: 9. doi: 10.1186/s13613-020-0628-2.
10. Omori K, Kotera J. Overview of PDEs and Their Regulation. *Circul Res* 2007; 100:309-327.
11. Zimmerman JJ, Rotta AT. Pharmacology of the Cardiovascular system. Fuhrman and Zimmerman's Pediatric Critical Care, 6th Edition. Philadelphia: Elsevier; 2021.
12. Turner MA, Baines P. Which inotrope and when in neonatal and pediatric intensive care? *Arch Dis Child Educ Pract Ed* 2011; 96(6):216-222. doi:10.1136/adc.2008.143925.
13. Sasada M, Smith S (2003). *Drugs in Anaesthesia and Intensive Care*. Oxford University Press: Oxford.
14. Van den Berghe G, de Zegher F. Anterior pituitary function during critical illness and dopamine treatment. *Crit Care Med* 1996; 24:1580-1590.
15. Aviado DM Jr, Schmidt CF. Effects of sympathomimetic drugs on pulmonary circulation: with special reference to a new pulmonary vasodilator. *J Pharmacol Exp Ther* 1957; 120:512-527.
16. Bearn AG, Billing B, Sherlock S. The effect of adrenaline and noradrenaline on hepatic blood flow and splanchnic carbohydrate metabolism in man. *J Physiol* 1951; 115: 430-441.
17. Clutter WE, Bier DM, Shah SD, Cryer PE. Epinephrine plasma metabolic clearance rates and physiologic thresholds for metabolic and hemodynamic actions in man. *J Clin Invest* 1980; 66:94-101.
18. Galster AD, Clutter WE, Cryer PE, Collins JA, Bier DM. Epinephrine plasma thresholds for lipolytic effects in man: measurements of fatty acid transport with [1-13C]palmitic acid. *J Clin Invest* 1981; 67:1729-1738.
19. Alexander SPH, Mathie A, Peters JA. *Guide to Receptors and Channels (GRAC)*, 5th Edn. *Br J Pharmacol* 2011; 164 (Suppl.1): S1-S324.
20. Levick J. *An Introduction to Cardiovascular Physiology*. Hodder Arnold: London, 2003.
21. Barrett LK, Singer M, Clapp LH. Vasopressin: mechanisms of action on the vasculature in health and in septic shock. *Crit Care Med* 2007; 35:33-40.
22. Rehberg S, Ertmer C, Vincent JL, Morelli A, Schneider M, Lange M, Aken HV, Traber DL, Westphal M. Role of selective V1a receptor agonism in ovine septic shock. *Crit Care Med* 2011; 39:119-125.
23. Ruffolo RR Jr. The pharmacology of dobutamine. *Am J Med Sci* 1987; 294:244-248.
24. Mousdale S, Clyburn PA, Mackie AM, Groves ND, Rosen M. Comparison of the effects of dopamine, dobutamine, and dopexamine upon renal blood flow: a study in normal healthy volunteers. *Br J Clin Pharmacol* 1988; 25:555-560.
25. Olsen NV, Lund J, Jensen PF, Espersen K, Kanstrup IL, Plum I, Leyssac PP. Dopamine, dobutamine and dopexamine. A comparison of renal effects in unanesthetized human volunteers. *Anesthesiology* 1993; 79(4):685-694.
26. Prielipp RC, MacGregor DA, Butterworth JF, Meredith JW, Levy JH, Wood KE, Coursin DB. Pharmacodynamics and pharmacokinetics of milrinone administration to increase oxygen delivery in critically ill patients. *Chest* 1999; 115:1291-1301.
27. Petersen JW, Felker GM. Inotropes in the management of acute heart failure. *Crit Care Med* 2008; 36:S106-S111.
28. Greeley W, Steven J, Nicolson S, Kern F. Anesthesia for pediatric cardiac surgery. In: Miller R (ed.). *Anesthesia*. Churchill Livingstone: New York, 2000; pp1805-1847.
29. Colucci WS. Cardiovascular effects of milrinone. *Am Heart J* 1991; 121:1945-1947.
30. Toller WG, Stranz C. Levosimendan, a new inotropic and vasodilator agent. *Anesthesiology* 2006; 104:556-569.
31. Tavares M, Rezlan E, Vostroknoutova I, Khoudja H, Mebazaa A. New pharmacologic therapies for acute heart failure. *Crit Care Med* 2008; 36:S112-S120.
32. Isoproterenol C11H17NO3 - PubChem. <https://pubchem.ncbi.nlm.nih.gov/compound/Isoproterenol>. Accessed on 7/12/21.
33. Ehle M, Patel C, Giugliano RP. Digoxin: Clinical Highlights: a review of digoxin and its use in contemporary medicine, *Crit Pathw Cardiol* 2011; 10:93-98.
34. Weiss SL, Pomerantz WJ. Septic shock in children: Rapid recognition and initial resuscitation (first hour). <https://www.uptodate.com/contents/septic-shock-in-children-rapid-recognition-and-initial-resuscitation-first-hour>. Accessed on 8/12/21.
35. Ventura AM, Shieh HH, Bousso A, Góes PF, Fernandes ICFO, Souza DC, Paulo RLP, Chagas F, Gilio AE. Double-Blind Prospective Randomized Controlled Trial of Dopamine Versus Epinephrine as First-Line Vasoactive Drugs in Pediatric Septic Shock. *Crit Care Med* 2015; 43: 2292-2302.
36. Ramaswamy KN, Singhi S, Jayashree M, Bansal A, Nallasamy K. Double-Blind Randomized Clinical Trial Comparing Dopamine and Epinephrine in Pediatric Fluid-Refractory Hypotensive Septic Shock. *Pediatr Crit Care Med* 2016; 17:e502-e512. doi: 10.1097/PCC.0000000000000954.

37. Martin K, Weiss SL. Initial resuscitation and management of pediatric septic shock. *Minerva Pediatr* 2015; 67(2): 141-158.
38. Donnino MW, Andersen LW, Berg KM, Chase M, Sherwin R, Smithline H, et al. Corticosteroid therapy in refractory shock following cardiac arrest: a randomized, double-blinded, placebo-controlled, trial. *Crit Care* 2016; 20:82.
39. Venkatesh B, Finfer S, Cohen J, Rajbhandari D, Arabi Y, Bellomo R, et al. Adjunctive glucocorticoid therapy in patients with septic shock. *N Eng J Med* 2018; 378:797-808.
40. Brissaud O, Botte A, Cambonie G, Dager S, de Saint Blanquat L, Durand P, Gournay V, Guillet E, Laux D, Leclerc F, Mauriat P, Boulain T, Kuteifan K. Experts' recommendations for the management of cardiogenic shock in children. *Ann Intensive Care* 2016; 6:14. doi: 10.1186/s13613-016-0111-2
41. Ferré F, Martin C, Bosch L, Kurrek M, Lairez O, Minville V. Control of Spinal Anesthesia-Induced Hypotension in Adults. *Local Reg Anesth* 2020; 13: 39-46.