International Journal of Contemporary Pediatrics
Chaurasiya D et al. Int J Contemp Pediatr. 2024 Sep;11(9):1218-1222
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20242332

Original Research Article

The efficacy and safety of dopamine versus norepinephrine in management of paediatric septic shock

Dharmendra Chaurasiya, Kawalpreet Chhabra, Anuj S. Sethi, Omshankar Chaurasiya*

Department of Paediatrics, Maharani Laxmibai Medical College, Jhansi, Uttar Pradesh, India

Received: 24 June 2024
Revised: 15 July 2024
Accepted: 01 August 2024

***Correspondence:**
Dr. Omshankar Chaurasiya,
E-mail: chaurasiyaom@gmail.com

ABSTRACT

Background: Septic shock is one of most common cause of death in pediatric patients. The optimum septic shock vasopressor support strategy is currently debated. This study was performed to evaluate the efficacy and safety of norepinephrine (NE) and dopamine (DA) as the initial vasopressor in pediatric septic shock patients.
Methods: A prospective, randomized, clinical trial was carried out between January 2022 to January 2023 in a pediatric intensive care unit comparing DA with NE as the initial vasopressor in fluid-resuscitated 100 pediatric patients with septic shock. Normalization of blood pressure was taken as end point. If the maximum dose of the initial vasopressor was unable to attain the hemodynamic goal, then another vasopressor agent was added. Patients were monitored for response and side effect.
Results: DA had a mortality of 50% as compared to 40% in NE. Arrhythmias occurred in 27.5% cases in DA group and 8.33% cases in NE group. There was a significantly greater incidence of sinus tachycardia with DA (12.5%) than NE (5%).
Conclusions: NE showed better efficacy than DA in pediatric patients with septic shock with lesser event of arrhythmias.

Keywords: Dopamine, Norepinephrine, Septic shock, Vasopressor therapy, Arrhythmia, Safety profile

INTRODUCTION

Septic shock, a decompensated form of sepsis characterized by abnormalities at the circulatory, cellular and metabolic level, continues to be one of the main causes of pediatric mortality worldwide. Studies have reported 10–50% of mortality in developed countries and up to 80% of mortality in developing countries. Important in the management of septic shock is hypovolemia correction and use of vasoactive agents to sustain perfusion pressure.

Vasoactive therapy is initiated in children with septic shock whose clinical picture has not improved following initial fluid resuscitation with 40-60 ml/kg of isotonic crystalloid, wherein the first-line is epinephrine or dopamine for cold shock and nor-epinephrine for warm shock.[1]

Recently, several studies have investigated the efficacy of dopamine versus norepinephrine for pediatric or neonatal septic shock, but the results are conflicting. Our study was designed to evaluate whether the choice of norepinephrine over dopamine as the first-line vasopressor agent in pediatric septic shock was safe and effective.

METHODS

A randomized comparative study was carried out in the pediatric intensive care unit from January 2022 to January 2023 in pediatric department MLBMC Jhansi after approval from the ethics committee. Patients of age 6 month-18 years with septic shock who fulfilled inclusion criteria were selected for the study.

One hundred patients, diagnosed as pediatric septic shock were included for the study. These patients were randomly assigned to two groups. Group A received dopamine and group B received noradrenaline.

The inclusion criteria were age 6 months to <18 years of patients with septic shock. Pediatric septic shock was defined as the subset with cardiovascular dysfunction, which included at least one of the following: hypotension, reliance on vasoactive drug administration to maintain a normal blood pressure and two or more of the following signs of inadequate tissue perfusion that is prolonged capillary refill, oliguria, metabolic acidosis and altered mental status.

Patients with congenital malformations, chromosomal anomalies and who received vasopressor drugs prior to enrolment were excluded.

Patients who fulfilled inclusion criteria were randomly assigned to receive either dopamine (5-20 µg/kg/min) or norepinephrine (0.1-1 µg/kg/min) through a parenteral line. The demographic information along with presenting symptoms and signs were entered in predesigned proforma. Patients assigned to group A received inj. dopamine in the dose of 5-20 µg/kg/min and the patients assigned to group B received injection norepinephrine. The vitals of the patients were noted at the start of therapy. The patients were monitored and response noted. Antibiotics and supportive therapy was continued according to protocol.

Statistical analysis

The responses obtained were entered in Microsoft Office excel. Data analysis was done by statistical package for the social sciences (SPSS) software ® version 24.0. Descriptive statistical analysis, which included frequency and percentages, was used to characterize the data. Chi-square test and unpaired student t-test was used for association between factors and $p<0.05$ was considered statistically significant.

RESULTS

A total of 100 paediatric septic shock patients were enrolled in this study during a 1-year period (Figure 1).

Baseline characteristics at the time of enrollment in terms of patient demographics, (such as age and gender), baseline vitals (heart rate, respiratory rate, and blood pressure) hemoglobin level, pH values, were comparable with no significant difference between the two groups. In group A, epinephrine was used in 50.0% cases, dobutamine in 52.5% cases, corticosteroid in 25.0% cases and in only 1 (2.5%) case vasopressin was used as second inotropes. In group B, epinephrine was used in 40.0% cases, dobutamine in 40.0% cases, corticosteroid in 11.6% cases and only 1 (2.5%) case vasopressin was used as add on drugs.

The overall mortality from the septic shock was 44% (44/100). The mortality rate in the patients who received DA as the initial vasopressor was 50% (20/40) as compared with 40% (24/60) for NE treatment group ($p=0.323$). Importantly, there was a significant difference in the occurrence of arrhythmias between the two vasopressor treatment arms. The incidence of arrhythmias (Table 1) in the DA-treated group was 27.5% (11/40) versus 8.33% (5/60) in the NE-treated patients ($p=0.01$). Table 2 depicts the arrhythmias that were noted in the two study populations.

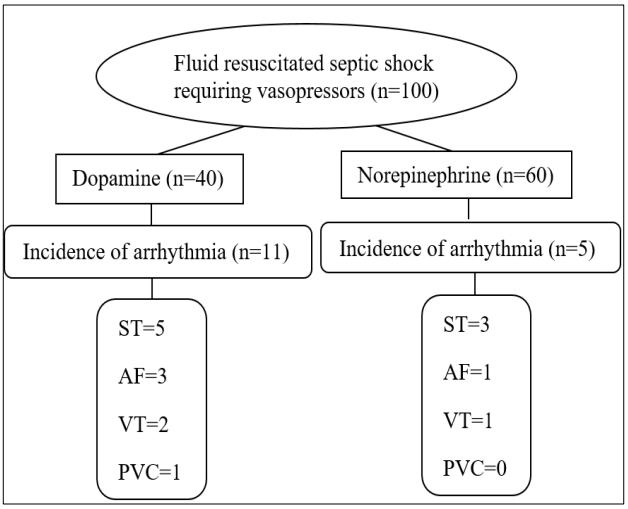

Figure 1: Patients enrollment.

ST=Sinus tachycardia, AF=atrial fibrillation, VT=ventricular tachycardia, PVC=premature ventricular contraction

Table 1: Demographics and baseline characteristics.

Category	DA, n=40	NE, n=60	Significance p value
Male	19	37	
Female	21	23	
HR	123.35±16.33	117.18±16.0	0.0640 (NS)
RR	36.22±9.502	32.8±8.84	0.5267 (NS)
Temperature	100.43±2.27	100.38±2.05	0.9091 (NS)
Mean arterial pressure	50.02±10.239	53.43±8.98	0.0818 (NS)
Urine output	1.30±0.251	1.41±0.34	0.0830 (NS)
Hb	11.17±1.44	11.27±1.69	0.7594 (NS)

Continued.

Category	DA, n=40	NE, n=60	Significance p value
pH	7.31±0.06	7.29±0.08	0.1809 (NS)
Respiratory infection	8	9	
Central nervous system	17	18	
GI Infection	8	14	
Viral infections	7	18	
Parasitic infestation	0	1	
Gram-positive bacteria	17	23	0.4477 (NS)
Gram-negative bacteria	13	15	
Blood culture negative	10	22	

NS: non-significant, S: significant

Table 2: Outcome data.

Outcome	DA (%)	NE (%)	P value
Mortality	50 (20/40)	40 (24/60)	0.3237 (NS)
Incidence of arrhythmia	27.5 (11/40)	8.33 (5/60)	0.0104 (S)

Table 3: Arrhythmia analysis.

Variables	DA (N)	NE (N)	P value
Sinus tachycardia (ST)	5	3	0.11
Atrial fibrillation (AF)	3	1	0.21
Ventricular tachycardia (VT)	2	1	0.12
Premature ventricular contraction (PVC)	1	0	0.00
NO	29	55	0.35

DISCUSSION

This study was designed to evaluate both the efficacy and safety of NE and DA in the treatment of pediatric septic shock. Septic shock continues to be a significant cause of morbidity and mortality despite the use of broad-spectrum antibiotics, modern intensive care unit (ICU) management, and treatment based on specific guidelines.[4-8] Current guidelines stress the importance of early recognition of sepsis, prompt institution of effective antibiotics, and aggressive source control when indicated.[9] Important in the management of septic shock is the use of vasoactive agents to sustain perfusion pressure while hypovolemia is corrected. Initiating vasoactive treatment in septic shock children whose clinical condition has not improved after initial fluid resuscitation with 40–60 ml/kg of isotonic crystalloid, in the first-line form of dopamine or epinephrine for cold shock and nor-epinephrine for warm shock.[1] Dopamine is the precursor for nor-adrenaline in the sympathetic nervous system.[2] At doses of 1–2 µg/kilogram/minute, it mainly acts on vascular dopamine-1 receptors causing selective vasodilatation. At doses between 5 and 10 µg/kilogram/minute, dopamine also acts on beta-1 adrenergic receptors in the heart to increase cardiac output by increasing stroke volume and heart rate; at doses above 10 µg/kilogram/minute, it mainly acts on vascular alpha-1 adrenoceptors to cause vasoconstriction, increasing the systemic vascular resistance.[3] Endogenously, noradrenaline is released from the nerve terminal of post-ganglionic sympathetic neurons. It acts on alpha-1 adrenoceptors to cause vasoconstriction.[2] It also has a weaker action on beta-1 adrenoceptors.[3]

In our study patients were randomly assigned to two groups. There was statistically no significant difference between the two groups with regards to demographic, baseline clinical and biochemical profile.

In dopamine group, 16 (40%) patients were from the age group of 6 months to 5 years of age, 14 (35%) cases were from 5-10 years of age, while in norepinephrine group, 14 (23.33%) cases were from 6months to 5 years of age, 22 (36.67%) cases belonged to 5-10 years of age.

Most common age group to be affected with septic shock was between to 1 month to 1 year (38.6%) in the study conducted by Chowday et al similar to the study El-Nawawy et al and study by Vekaria-Hirani et al.[10-12] While in our study maximum patients belonged to 5-10-year age group.

Our study demonstrated a relatively increased prevalence of gram-positive organism infection as compared to gram negative organism infections in pediatric septic shock cases which is much similar to other studies pointing towards similarity in organism causing sepsis in pediatric age group.

Arrhythmias were observed in 11 (27.5%) cases with dopamine and 5 (8.33%) cases with norepinephrine. Sinus tachycardia was seen in 5 patients with dopamine and 3

patients with norepinephrine. Atrial fibrillation was observed in 3 patients with dopamine only in 1 patient with norepinephrine. Ventricular tachycardia occurred in 2 patients and 1 patient from with dopamine and norepinephrine groups respectively. One patient had premature ventricular contraction who required dopamine. Normal rhythm was observed in 29 patients with dopamine and 55 patients with norepinephrine. It was evident that 91.67% cases with norepinephrine did not have arrhythmias. Statistically significant difference was present between the two groups.

Patel et al also concluded in their study that DA was associated with a significantly increased incidence of arrhythmia that is 19.4% versus 3.4% in the nor-adrenaline group.[13] Sakr et al too inferred in their study that dopamine is associated with increased arrhythmic events compared to nor-adrenaline, and may even be associated with increased mortality.[14]

The Australia New Zealand Critical Care Trials group found that the use of "renal dose" DA was associated with increased arrhythmias.[15] However, it should be noted that Levy et al did not demonstrate an increased risk for cardiac arrhythmias with the use of DA in the trial.[16] The use of NE and epinephrine in the French vasopressor study did not pose an increased risk for the development of cardiac arrhythmias or adverse neurologic or ischemic events.[17] The vasopressin study of Russell et al also reported a low incidence of cardiac arrhythmias.[18] Our finding of arrhythmias in 27.5% of the DA group in contrast to approximately 8.33% of the NE group we think is noteworthy and should prompt a change in vasopressor selection. The 8.33% incidence of arrhythmias in the NE group was similar to those results reported by Annane et al in their study of sustained arrhythmias in critically ill patients.[19]

With dopamine the mean duration of oxygenation required was 20.52±19.39 hours. while with norepinephrine the mean duration of oxygenation was 19.3±19.11 hours. Both the groups had no significant difference in terms of oxygen requirement. 50% with dopamine cases required ventilation, while 41.67% with norepinephrine cases required ventilation. There are not many studies which have compared the mean duration of oxygen requirement and need of mechanical ventilation when using these two drugs.

The mean duration of hospital stay with norepinephrine was 4.21±2.98 while it was 3.125±2.12 days with dopamine. Statistically significant difference was found between dopamine and norepinephrine. Patel et al observed that mean duration of hospital stays in dopamine treated cases was 14.2±16.3 days while in nor-epinephrine treated cases the duration of hospital stay was 13.5±13.3 days. In both the groups maximum expiry occurred in the first 2 days of the treatment.[13]

Among patients in dopamine group 21 (52.5%) patients required another inotrope while it was in 14 (40%) patients with norepinephrine which points towards better efficacy of norepinephrine.

A mortality of 50% was evidenced in dopamine group whereas it was 40% with norepinephrine though notable but not statistically significant (Table 1).

Our study points towards better efficacy of norepinephrine as compared to dopamine as a statistically significant difference was seen in use of another add-on drug with dopamine. Also, statistically significant difference was perceived in occurrence of arrhythmia between the two groups.

Limitations

The study has few limitations. Firstly, the sample size of the study was very limited which cannot have generalized the population so the study lacked the external validity, Secondly the characteristics of the patient population can influence the applicability of the findings to other pediatric populations. Thirdly, lack of blinding (where patients, clinicians, or outcome assessors are aware of the treatment being given) can introduce bias.

CONCLUSION

We concluded that nor epinephrine showed better efficacy than dopamine in pediatric patients with septic shock since nor-epinephrine used as first ionotrope in septic shock precluded use of other additional ionotropes and also had lesser event of arrhythmias.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Brierley J, Carcillo JA, Choong K, Cornell T, DeCaen A, Deymann A, et al. Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine. Crit Care Med. 2009;37(2):666.
2. Rang HP, Dale MM and Ritter JM. Pharmacology. 4th edition. Edinburgh: Churchill Livingstone Harcourt Publishers Limited. 2001.
3. Gooneratne N, Manaker S. Use of vasopressors and inotropes. Uptodate. 2010. Available at: https://www.uptodate.com/contents/use-of-vasopressors-and-inotropes. Accessed on 12 March 2024.
4. Angus DC, Linde-Zwirble WT, Lidicker J, Clermont G, Carcillo J, Pinsky MR. Epidemiology of severe sepsis in the United States: analysis of incidence, outcome, and associated costs of care. Crit Care Med. 2001;29(7):1303-10.

5. Balk RA. Optimum treatment of severe sepsis and septic shock: evidence in support of the recommendations. Disease-a-Month. 2004;50(4):168-213.
6. Dellinger RP, Carlet JM, Masur H, Gerlach H, Calandra T, Cohen J, et al. Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock. Intens Care Med. 2004;30:536-55.
7. Wheeler AP. Recent developments in the diagnosis and management of severe sepsis. Chest. 2007;132(6):1967-76.
8. Russell JA. Management of sepsis. N Engl J Med. 2006;355(16):1699-713.
9. Kumar A, Roberts D, Wood KE, Light B, Parrillo JE, Sharma S, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006;34(6):1589-96.
10. Chowday SS, Chandra TJ. A study on prevalence of shock among the paediatric age group in and around west Godavari district, Andhra Pradesh. Pediatr Rev. 2021;8(5):231-5.
11. El-Nawawy A, El-Kinany H, Hamdy El-Sayed M, Boshra N. Intravenous polyclonal immunoglobulin administration to sepsis syndrome patients: a prospective study in a pediatric intensive care unit. J Trop Pediatr. 2005;51(5):271-8.
12. Vekaria-Hirani V, Kumar R, Musoke RN, Wafula EM, Chipkophe IN. Prevalence and management of septic shock among children admitted at the Kenyatta National Hospital, longitudinal survey. Int J Pediatr. 2019;1502963.
13. Patel GP, Grahe JS, Sperry M, Singla S, Elpern E, Lateef O, Balk RA. Efficacy and safety of dopamine versus norepinephrine in the management of septic shock. Shock. 2010;33:4:375-80.
14. Sakr Y, Reinhart K, Vincent J-L, Sprung CL, Moreno R, Ranieri M, et al. Does dopamine administration in septic shock influence outcome? Results of the Sepsis Occurrence in Acutely Ill Patients (SOAP) Study. Crit Care Med. 2006;34:3:589-97.
15. Bellomo R, Chapman M, Finfer S, Hickling K, Myburgh J. Low-dose Sdopamine in patients with early renal dysfunction: a placebo-controlled randomised trial. Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group. Lancet (London, England). 2000;356(9248):2139-43.
16. Levy B, Dusang B, Annane D, Gibot S, Bollaert PE. College Interregional des Reanimateurs du NE. Cardiovascular response to dopamine and early prediction of outcome in septic shock: a prospective multiple-center study. Crit Care Med. 2005;33(10):2172-7.
17. Annane D, Vignon P, Renault A, Bollaert PE, Charpentier C, Martin C, et al. Norepinephrine plus dobutamine versus epinephrine alone for management of septic shock: a randomised trial. The Lancet. 2007;370(9588):676-84.
18. Russell JA, Walley KR, Singer J, Gordon AC, Hébert PC, Cooper DJ, et al. Vasopressin versus norepinephrine infusion in patients with septic shock. N Engl J Med. 2008;358(9):877-87.
19. Annane D, Sebille V, Duboc D, Le Heuzey JY, Sadoul N, Bouvier E, et al. Incidence and prognosis of sustained arrhythmias in critically ill patients. Am J Respir Crit Care Med. 2008;178:20-5.

Cite this article as: Chaurasiya D, Chhabra K, Sethi AS, Chaurasiya O. The efficacy and safety of dopamine versus norepinephrine in management of paediatric septic shock. Int J Contemp Pediatr 2024;11:1218-22.