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COMPARISON OF EFFICACY OF DOPAMINE AND ADRENALINE FOR TREATMENT OF FLUID REFRACTORY SEPTIC SHOCK IN CHILDREN

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Abstract:-

Introduction: There are currently no set standards for the first vasoactive medication to be given to children who are in fluid-refractory septic shock. Each institution has up until now been allowed to choose the first vasoactive drug in these circumstances. This is because there is a dearth of international research on the relative efficacy of inotropes in this type of clinical situation, particularly in Pakistan. By carrying out a preliminary investigation, this study aims to close the gap in this field.

Materials & Methods: This randomized controlled experiment was conducted in the Department of Pediatrics, Children Hospital, Faisalabad, from May 2025 to August 2025, following ethical review committee permission. Patients with fluid-refractory septic shock were included. The patients ranged in this study. Patients who had undergone cardiopulmonary bypass within the previous five days, those with chronic conditions such as cerebral palsy, congenital heart disease, neuromuscular disorders, metabolic disorders, chronic kidney disease, or those who had previously received peripheral treatment for hypovolemia without a medication history or sequential organ failure at presentation were excluded. A computer-generated random number table was used to randomly split all of the patients into two groups. While Group-B patients got dopamine in incremental dosages of 10–20 µg/kg/minute until the end points of shock resolution were reached, Group A patients received epinephrine (0.1–0.3 µg/k/minute). After 20 minutes of treatment, the resolution of clinical signs and symptoms was evaluated. Both at baseline and six hours later, the SOFA score was noted. The effectiveness of the treatment was evaluated in terms of the resolution of clinical signs and symptoms at 20 minutes and the improvement of 4 points in the SOFA score at 6 hours.

Results: The mean age in this study was 5.73 ± 2.38 years, with a range of 1 month to 12 years. Patients in groups A and B had mean ages of 5.84 ± 2.43 and 5.44 ± 2.29 years, respectively. There was a male to female ratio of 1.1:1, with 47 (52.22%) being male and 43 (47.78%) being female. 39 patients (86.67%) responded better to adrenaline than to dopamine when treating fluid-refractory septic shock in children, compared to 26 patients (57.78%).

Conclusion: In children with fluid-refractory cold septic shock, the current study clearly demonstrates that the use of adrenaline is associated with an earlier resolution of shock when compared to dopamine.

Keywords: septic shock, adrenaline, dopamine.

INTRODUCTION:

Sepsis is characterized as a potentially lethal organ dysfunction resulting from a dysregulated host response to infection. Septic shock, on the other hand, is a specific manifestation of sepsis marked by severe circulatory, cellular, and metabolic abnormalities, which confer an elevated mortality risk compared to sepsis alone.[1] Sepsis and septic shock are still seen as major health issues because of their high rates of morbidity and fatality.[2] Because of its high death rate—more than 40% in the case of septic shock—sepsis, and particularly septic shock, remains a mystery in many ways, and managing it presents difficulties for medical professionals.[3] Septic shock is thought

to be the cause of 40–67% of pediatric intensive care unit (PICU) admissions in Asian countries, compared to 2-3% in affluent nations.[4] The treatment of sepsis has not changed significantly in the last 40 years. Current standards suggest giving intravenous (IV) fluids and antibiotics right away, as well as managing the source and using vasopressors carefully. Fluid resuscitation is a fundamental aspect of sepsis therapy. To determine the function of substantial fluid resuscitation in the initial stages of septic shock, it is essential to comprehend the pathophysiology of sepsis.[1] Fluid refractory shock is when clinical indications of hypoperfusion stay the same after a fluid bolus of 60 ml/kg. Dopamine, dobutamine, or adrenaline (epinephrine) can be used as first-line inotropic support.[5]

Children who have fluid-refractory septic shock are treated with vasoactive drugs to maintain organ perfusion after fluid resuscitation.[6] Dopamine is the first-line vasoactive medication in fluid-refractory septic shock. Dopamine acts as an agonist on adrenergic and dopaminergic receptors in a dose-dependent manner. In septic shock, dopamine infusion can decrease prolactin release, raise oxidative stress, inhibit the synthesis of pro-inflammatory cytokines, and boost the production of anti-inflammatory cytokines. Due to catecholamine depletion or receptor insensitivity to dopamine, the dopamine response in infants and young children suffering from decompensated hypotensive septic shock may be unpredictable.[7]

Although adrenaline can raise cardiac output and mean arterial pressure, it can also result in increased serum lactate and compromised gut perfusion in septic shock.[4] The myocardium's beta 1 adrenergic receptors are strongly stimulated by adrenaline, while the peripheral vasculature's beta 2 and alpha 1 adrenergic receptors are moderately affected. It functions as a strong inotropic and chronotropic drug at low doses (0.05–0.2 mcg/kg/min) by acting on beta 1 receptors and as a mild vasodilator by stimulating beta 2 adrenergic receptors, which raises CO and lowers systemic vascular resistance. Because it acts on alpha 1 receptors, it mostly produces vasoconstriction at larger doses, which can lower CO by increasing afterload.[8] Dopamine and adrenaline were effective at 20 minutes and 6 hours, respectively, at 30.6% vs. 70.6% and 23% vs. 52.5%.[4]

There are currently no set standards for the first vasoactive medication to be given to children who are in fluid-refractory septic shock. Each institution has up until now been allowed to choose the first vasoactive drug in these circumstances. This is because there is a dearth of international research on the relative efficacy of inotropes in this type of clinical situation, particularly in Pakistan. By carrying out a preliminary investigation, this study aims to close the gap in this field.

METHODOLOGY:

This randomized controlled experiment was conducted in the Department of Pediatrics, Children Hospital, Faisalabad, from May 2025 to August 2025, following ethical review committee permission. P1 = 52.5%[4], P2 = 23%[4], Power of study = 90%, Level of significance = 5%, and Sample size = 90 (45 in each group) were calculated using the WHO sample size calculator. Patients with fluid-refractory septic shock (reduced peripheral or central pulses (< 40 bpm), prolonged CRT, abnormal heart rate for age, modified mental status (GCS < 12), decreased urine output of < 1 ml/kg/hr, systolic blood pressure < 5th centile for child's age after a maximum 60 ml/kg fluid bolus is administered within 60 minutes of presentation, or baseline SOFA score ≥ 11) were included. The patients ranged in this study. Patients who had undergone cardiopulmonary bypass within the previous five days, those with chronic conditions such as cerebral palsy, congenital heart disease, neuromuscular disorders, metabolic disorders, chronic kidney disease, or those who had previously received peripheral treatment for hypovolemia without a medication history or sequential organ failure at presentation were excluded.

A written informed consent form was given to study participants' parents for their signature. A computer-generated random number table was used to randomly split all of the patients into two groups. Group A patients received 0.1–0.3 µg/k/minute of epinephrine, while Group-B patients received dopamine at incremental dosages of 10–20 µg/kg/minute until the end points of shock resolution were established. After 20 minutes of treatment, the resolution of clinical signs and symptoms was evaluated. Both at baseline and six hours later, the SOFA score was noted. The effectiveness of the treatment was evaluated in terms of the resolution of clinical signs and symptoms at 20 minutes and the improvement of 4 points in the SOFA score at 6 hours and the SOFA score improved by 4 points from baseline at 6 hours. On Performa, every piece of information was documented.

SPSS V-26 was used to analyze all of the data. At baseline, 20 minutes, and 6 hours, the mean ± standard deviation was computed for all quantitative data, including age, weight, and clinical features (pulse, B.P., CRT, urine output, GCS, and SOFA score). For every qualitative measure, including gender and efficacy, frequency and percentages were computed at 20 minutes and 6 hours. The chi square test was used to compare two groups' efficacy.

RESULTS:

The age range in this study was 1 month to 12 years, with a mean of 5.73 ± 2.38 years. Group A patients were 5.84 ± 2.43 years old, while group B patients were 5.44 ± 2.29 years old. The bulk of the 64 patients (71.11%) were between the ages of 6 months and 6 years, as shown in Table I.

Table II displays the patient distribution by weight. As indicated in Table III, of the 90 patients, 47 (52.22%) were male and 43 (47.78%) were female, with a male to female ratio of 1.1:1.

When treating fluid-refractory septic shock in children, adrenaline was more effective in 39 patients

(86.67%) than dopamine in 26 patients (57.78%) (Figure I). Table IV displays the stratification of efficacy according to impact modifiers.

Table-I: Age distribution for both groups (n=90).

	Group A (n=45)		Group B (n=45)		Total (n=90)	
Age (years)	No. of patients	%age	No. of patients	%age	No. of patients	%age
1 mon – 6 yrs	31	68.89	33	73.33	64	71.11
7-12 yrs	14	31.11	12	26.67	26	28.89
Mean ± SD	**5.84 ± 2.43**		**5.44 ± 2.29**		**5.73 ± 2.38**	

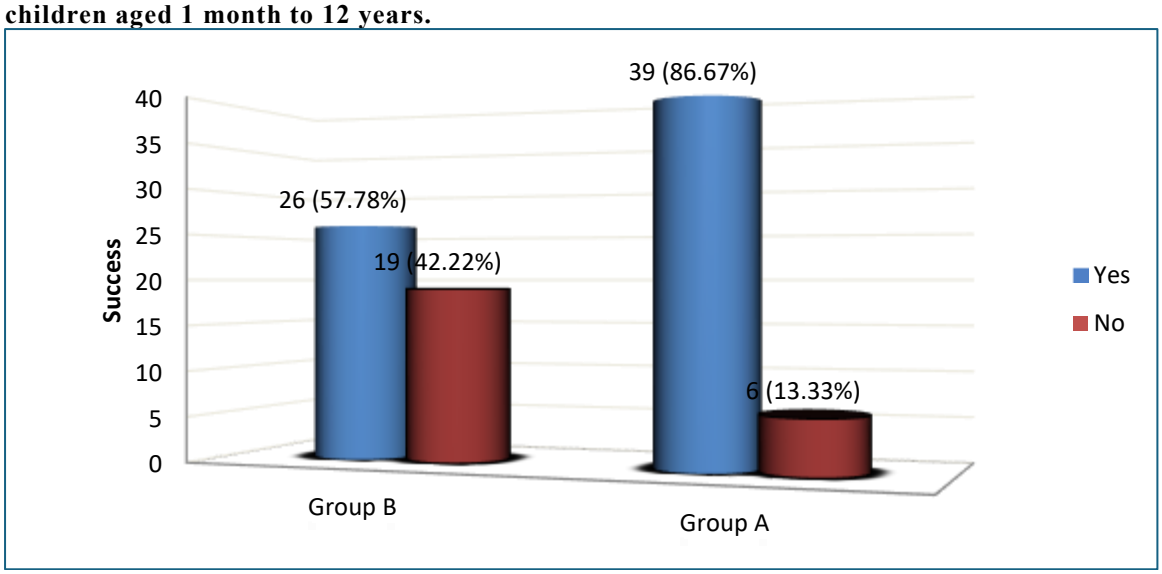
Table-II: Distribution of patients according to weight (n=90).

	Group A (n=45)		Group B (n=45)		Total (n=90)	
Weight (kg)	No. of patients	%age	No. of patients	%age	No. of patients	%age
≤15	19	42.22	16	38.10	35	38.89
>15	26	57.78	29	61.90	55	61.11
Mean ± SD	**23.33 ± 10.13**		**25.82 ± 11.49**		**24.56 ± 10.76**	

Table-III: Distribution of patients according to gender (n=90).

	Group A (n=45)		Group B (n=45)		Total (n=90)	
Gender	No. of patients	%age	No. of patients	%age	No. of patients	%age
Male	25	55.56	22	48.89	47	52.22
Female	20	44.44	23	51.11	43	47.78

Figure I: Efficacy of dopamine with adrenaline for treatment of fluid refractory septic shock in children aged 1 month to 12 years.



- **P-value = 0.002 which is statistically significant**

Table IV: Stratification of efficacy with respect to effect modifiers.

		Group B (n=45)		Group A (n=45)		P-value
		Efficacy		Efficacy		
		Yes	No	Yes	No	
Age (years)	**1 mo-6 yrs**	15 (48.39%)	16 (51.61%)	27 (81.82%)	06 (18.18%)	**0.005**
	7-12	11 (78.57%)	03 (21.43%)	12 (100.0%)	00 (0.0%)	**0.088**
Gender	**Male**	12 (48.0%)	13 (52.0%)	20 (90.91%)	02 (9.09%)	**0.002**
	Female	14 (70.0%)	06 (30.0%)	19 (82.61%)	04 (17.39%)	**0.329**
Weight (kg)	**≤15**	10	09	12 (75.0%)	04	**0.173**

		(52.63%)	(47.37%)		(25.0%)	
	>15	16 (61.54%)	10 (38.46%)	27 (93.10%)	02 (6.90%)	**0.005**

DISCUSSION:

Both dopamine and adrenaline have the ability to have inotropic and vasopressor effects. Vasopressors are vasoactive medications used as the first line of treatment for neonatal septic shock brought on by a decrease in systemic vascular resistance (SVR).[9,10] According to the 2012 "Surviving Sepsis Campaign" guidelines, dopamine should be used as the initial vasoactive drug in fluid-refractory septic shock. It functions as a dose-dependent agonist on adrenergic and dopaminergic receptors.[11] Although epinephrine can raise cardiac output and mean arterial pressure, it can also result in increased serum lactate and compromised gut perfusion in septic shock.[12]

Our research revealed that 86.67% of the epinephrine and 57.67% of the dopamine groups experienced efficacy (p=0.0001). Ramaswamy KN et al.[13] assessed the resolution of shock and discovered that children administered epinephrine exhibited a greater proportion (41%) compared to those receiving dopamine (13%) within the initial hour post-resuscitation (p=0.019), and a comparable trend (48.3% versus 29%; p = 0.184) after 6 hours. The epinephrine group had a lower SOFA score on day three (8 versus 12; p=0.05). It was discovered that children in both research groups had comparatively greater rates of death (58% versus 48%; p=0.605) and unfavorable consequences (16% versus 14%; p=0.80).[13]

In their randomized control experiment (RCT), Ventura et al. divided the 118 patients into two groups: 58.5% were assigned to the dopamine group and 41.5% to the epinephrine group. The median hospital stay for patients receiving epinephrine was 11 days, whereas the median stay for patients receiving dopamine was 13 days (p = 0.554). In contrast, both groups reported an ICU stay of 4 days (0-81 days) (p = 0.748). The dopamine and adrenaline groups had corresponding mortality rates of 9% and 5%.[14]

In a double blind randomized controlled experiment, Baske et al. discovered that dopamine and adrenaline were just as safe and efficacious as first-line vasoactive medications in treating neonatal septic shock. However, epinephrine was linked to better outcomes among newborns < 306/7 weeks on stratified analysis in a small group.[15] For fluid-refractory sepsis, Cruz et al.'s recent publication on "updates of pediatric sepsis" suggests using noradrenaline or adrenaline as first-line vasopressors rather than dopamine.[16] An ongoing pilot multicenter randomized controlled trial is comparing the efficacy of standard administration of adrenaline (after 40–60 ml/kg of fluid resuscitation) to early delivery (after 20 ml/kg of fluid resuscitation), which suggests the need for additional research in this area.[17]

Our results support the use of epinephrine as the first line vasoactive treatment to reduce morbidity and death in children arriving to the PICU with fluid-refractory septic shock. According to certain researchers, dopamine administration in septic shock is clearly linked to an increase in mortality and adverse effects.[18,19] According to a study, children who received dopamine for pediatric septic shock had a significantly higher death rate than those who received epinephrine.[20]

Organ severe dysfunction ratings and biochemical markers were excluded. The children in the study were not followed up with after the study ended, and secondary outcomes such as death, morbidities, including adverse drug effects, and length of PICU stay were not evaluated. We did not register our study with CTRI since it was primarily an institutional project to create a first-line pharmacological regimen for our institution and the medications utilized were based on accepted standard protocols and standards. To guarantee that ethical and methodological requirements were fulfilled, the study was carried out under the supervision of the institutional ethical committee.

CONCLUSION:

In children with fluid-refractory cold septic shock, the current study clearly demonstrates that the use of adrenaline is associated with an earlier resolution of shock when compared to dopamine. Additionally, it has been discovered that while there is a dose-dependent response to adrenaline, shock is not alleviated by higher dopamine dosages. Therefore, in order to treat fluid-refractory cold septic shock in children, we advise using adrenaline as the first-line inotrope. To create standard recommendations, more research that overcomes the constraints of the current study and is conducted on a bigger scale with a larger population and longer follow-up period is required.

REFERENCES:

1. Moschopoulos CD, Dimopoulou D, Dimopoulou A, Dimopoulou K, Protopapas K, Zavras N, et al. New insights into the fluid management in aptients with septic shock. Medicina (Kaunas). 2023;59(6):1047.

2. Zhou H, Yang C, Wang H, Teng Y, He H. Should we initiate vasopressors earlier in aptients with septic shock: a mini systemic review. World J Crit Care Med. 2023;12(4):204-16.

3. Ramasco F, Nieves-Alonso J, Garcia-Villabona E, Vallejo C, Kattan E, Mendez R. Challenges in septic shock: from new hemodynamics to blood purification therapies. J Pers Med. 2024;14(2):176.

4. Ahmad S, Khurshid A, Maqsood I, Arshad MS. Comparison of efficacy of dopamine versus epinephrine infusion in fluid refractory septic shock in a tertiary care pediatric ICU. Professional Med J. 2023;30(11):1456-60.

5. Siva P, Ponnusamy V, Srinivasan A. The efficacy of dopamine vs adrenaline in pediatric fluid refractory cold septic shock in a tertiary care hospital. Int J Acad Med Pharm. 2024;6(1):1752-7.

6. Banothu KK, Sankar J, Kumar UV, Gupta P, Pathak M, Jat KR, et al. A randomized controlled trial of norepinephrine plus dobutamine versus epinephrine as first-line vasoactive agents in children with fluid refractory cold septic shock. Crit Care Explor. 2023;5(1):e0815.

7. Wen L, Xu L. The efficacy of dopamine versus epinephrine for pediatric or neonatal septic shock: a meta-analysis of randomized controlled studies. Ital J Pediatr. 2020;46:6.

8. Mehak B, Praveen K. First line vasoactive therapy after fluid resuscitation in pediatric septic shock – dopamine, adrenaline or noradrenaline? J Pediatr Crit Care. 2019;6(2):22-8.

9. Pollard S, Edwin SB, Alaniz C. Vasopressor and inotropic management of patients with septic shock. Pharmacy Therapeut. 2015; 40(7):438-450.

10. Jha A, Zilahi G, Rhodes A. Vasoactive therapy in shock. BJA Educ. 2021; 21(7):270-277. doi:10.1016/j.bjae.2021.03.002

11. Crunelle CL, van den Brink W, Moggi F, Konstenius M, Franck J, Levin FR, et al. International consensus statement on screening, diagnosis and treatment of substance use disorder patients with comorbid attention deficit/hyperactivity disorder. Eur Addict Res. 2018; 24(1):43-51. doi:10.1159/000487767

12. Sasidharan R, Gupta N, Chawla D. Dopamine versus epinephrine for fluid-refractory septic shock in neonates. Eur J Pediatr. 2019; 178(1):113-4.

13. Ramaswamy KN, Singhi S, Jayashree M, Bansal A, Nallasamy K. Double-blind randomized clinical trial comparing dopamine and epinephrine in pediatric f luid-refractory hypotensive septic shock. Pediatr Crit Care Med. 2016; 17:e502-ee12.

14. Ventura AMC, Shieh HH, Bousso A, Góes PF, Fernandes IDCFO, De Souza DC, et al. Double-blind prospective randomized controlled trial of dopamine versus epinephrine as first-line vasoactive drugs in pediatric septic shock. Crit Care Med. 2015; 43(11):2292-302.

15. Baske K, Saini ss, Dutta S, Sundaram V. Epinephrine versus dopamine in neonatal septic shock: a double-blind randomized controlled trial. Eur J Pediatr. 2018;177(9): 1335-1342.

16. Cruz AT, Lane RD, Balamuth F, Aronson PL, Ashby DW, Neuman MI, et al. Updates on pediatric sepsis. J Am Coll Emerg Physicians Open. 2020;1(5): 981–993.

17. Harley A, George S, King M, Phillips N, Keigzers G, Long D et al. Early Resuscitation in Paediatric Sepsis using Inotropes – A Randomised Controlled Pilot Study in the Emergency Department (RESPOND ED): Study Protocol and Analysis Plan. Front. Pediatr. 2021;https://doi.org/10.3389/fped.2021.663028 september 2023].

18. Xu B, Peter O. Dopamine versus noradrenaline in septic shock. Australas Med J. 2011; 4(10):571-574. doi:10.4066/AMJ.2011.761

19. Suzuki R, Uchino S, Sasabuchi Y, Kawarai Lefor A, Sanui M. Dopamine use and its consequences in the intensive care unit: A cohort study utilizing the Japanese Intensive care Patient Database. Crit Care. 2022; 26(1):90. doi:10.1186/s13054-022-03960-y.

20. Wen L, Xu L. The efficacy of dopamine versus epinephrine for pediatric or neonatal septic shock: A meta-analysis of randomized controlled studies. Ital J Pediatr. 2020; 46(1):1-7.