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INDICATIONS AND ADVERSE EFFECTS OF COLLOIDS AND OUTCOME IN CHILDREN WITH DENGUE FEVER

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Abstract: **The critical phase of dengue fever is characterized by severe plasma leakage leading to severe shock. Colloids are indicated in severe dengue with profound shock. In this study, we retrospectively analyzed the physiological status at admission, indications, and adverse effect of colloid in patients with severe dengue over the period of last 4 years. Of 3039 patients with dengue fever admitted to our hospital, there were a total of 143 patients with severe dengue. The compensated shock was the common presentation (n=117) and 26 children presented with hypotensive shock.All patients with severe dengue required colloid therapy(synthetic in 126, natural in 3, both in 14). Though 92% of patients had coagulopathy, clinical bleeding was observed in 1/5th of them and Disseminated Intravascular Coagulopathy(DIC) in 6% of patients. Refractory shock, DIC, Multiorgan Dysfunction Syndrome, Fulminant Hepatic Failure either alone or in combination were the causes of death in 9 children presenting with shock to the Emergency Department(ED).**

Keywords: **Severe Dengue, Shock, Colloid.**

1. INTRODUCTION

Dengue infection causes a broad spectrum of clinical disease, which can range in severity from febrile illness to serious bleeding and shock. Two major pathophysiological responses are associated with severe dengue infection – plasma leakage leading to hypovolaemic shock and/or abnormal hemostasis leading to hemorrhage and severe organ involvement.[1] Close monitoring, early detection and prompt management are the keys in successful treatment. In a hemodynamically unstable patient, crystalloid is the fluid of choice in initial management. However, if they are not responsive despite adequate resuscitation, a careful search for others causes is mandatory and fluids should be switched from crystalloid to colloid. Colloids have been shown to restore blood pressure and reduce the level of hematocrit faster than crystalloids in dengue patients with intractable shock.

Objective:

To review indications and adverse effects of colloid therapy in children with dengue presenting to a pediatric ED with particular focus on physiological status at admission and immediate outcome.

2. METHODS

Retrospective chart review of patients admitted to the pediatric ED of a referral children's hospital in South India with severe dengue over the period of last 4 years. Medical records of only serologically confirmed patients were analyzed. Demographic parameters, including age, gender, underlying comorbidities if any, physiological status at admission, details regarding the volume of crystalloid and colloid solutions used, indications for Pediatric Intensive Care Unit admission(PICU), the department where colloid was administered(ED or PICU), type of colloid whether synthetic or natural, adverse effects of colloids if any, course of the illness, the requirement of blood products, mechanical ventilation, mortality data of the patients were obtained from medical files. Details regarding confirmatory tests for dengue fever, liver and renal functions, coagulation profile including Prothrombin time (PT), activated Partial Thromboplastin Time (aPTT), International Normalized Ratio (INR) were also collected from medical files.

3. RESULTS

Of 3039 patients with dengue fever admitted to the hospital during the study period, 143 cases with severe forms of disease required Pediatric Intensive Care Unit(PICU) admission, of which 9 patients died. 76 patients were below 5 years

of age. Associated comorbidities included germ cell tumour (n=1), seizure disorder(n=6), previous dengue(n=1), bronchial asthma(n=1), Ehler Danlos syndrome(n=1), bronchiectasis(n=1)(Table 1). Compensated shock was the most common presentation (n=117) and 26 children presented with hypotensive shock. Coagulopathy was observed in 92% of patients(n=132) and 8 of them developed disseminated Intravascular coagulation(DIC). Two-thirds of patients (n=96) received a colloid infusion in ED prior to transfer to PICU. Indication for PICU admission was severe shock in 100% (n=143), severe bleeding(n=22), multi organ dysfunction syndrome (MODS, n=17), fulminant hepatic failure (FHF, n=9), myocardial dysfunction(n=3), Acute Respiratory Distress Syndrome(ARDS, n=2), acute kidney injury (AKI, n=2). All patients had thrombocytopenia with high hematocrit and all were serologically confirmed cases of dengue fever. Polypeptides of degraded gelatin was the synthetic colloid infused in 88% patients(n=126) , 20% albumin in crystalloid refractory shock(n=3), albumin along with synthetic colloids (n=14),(Table 2), and included patients with abdominal compartment syndrome(ACS,n=5). The volume range of colloid was from 10 ml/kg to 40ml/kg. Secondary hemophagocytic lymphohistiocytosis (HLH) was a complication in 9 patients. None of them developed pulmonary edema, hemorrhage, renal dysfunction, or anaphylactoid reactions to colloids. Nine patients with refractory shock died and included 7 with MODS and DIC, 1 with FHF and DIC, and 1 with severe myocardial dysfunction(Figure 1). None of the co morbidities affected the outcome.

Table 1: ASSOCIATED CO MORBIDITIES AND NUMBER OF CHILDREN

Co morbidities	Number(n)
Germ cell tumour	1
Seizure disorder	6
Previous dengue	1
Bronchial asthma	1
Ehler Danlos syndrome	1
Bronchiectasis	1

Table 2: TYPES OF COLLOID USED

Types of Colloid used	Number(n)
Synthetic colloid(Gelatin polypeptide)	126
20% Albumin	3
Synthetic colloid and 20% albumin	14

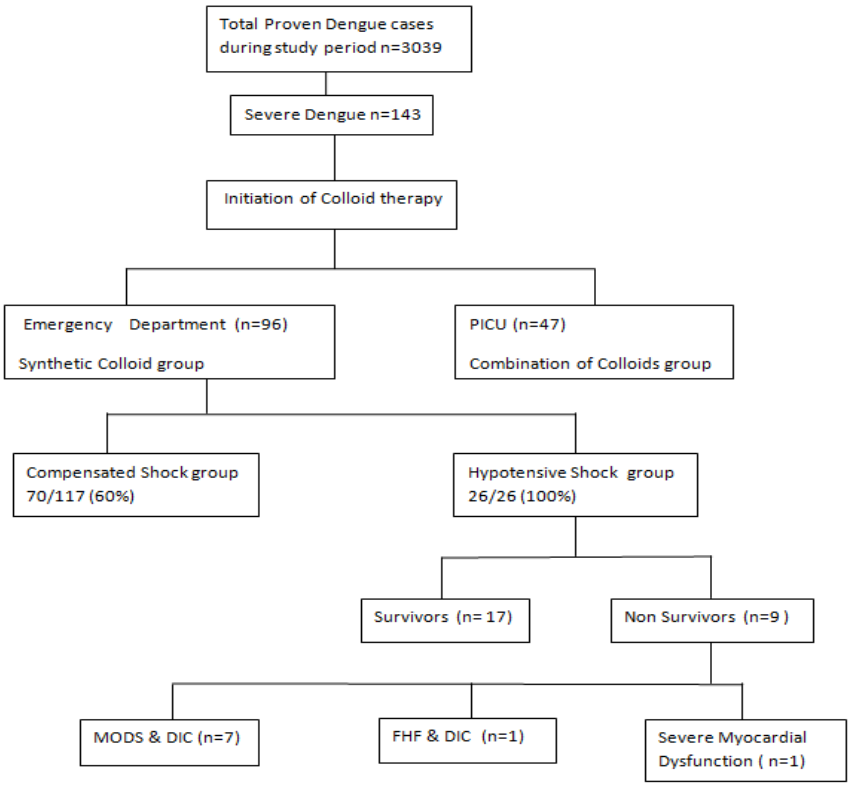

Figure 1

4. DISCUSSION

Severe dengue is a potentially fatal complication, due to plasma leaking, fluid accumulation, respiratory distress, severe bleeding, or organ impairment. 5% of our study population had severe dengue though the incidence as high as 18.6% have been reported.[2] Replacement of plasma lost because of increased vascular permeability is a mainstay of severe dengue management, particularly during the critical stage. Two main types of volume expanders are used to replace lost fluid in the management of dengue fever: crystalloids and colloids. Crystalloids are aqueous solutions of mineral salts or other water-soluble molecules, whereas colloids contain larger insoluble molecules. A colloid is defined as a high molecular weight substance that largely remains in the intravascular compartment, thereby generating an oncotic pressure. Colloids are considered to have a greater intravascular persistence when compared to crystalloids. This property is lost, however, when capillary membranes are altered in a diseased state. Colloids are of two types: natural, i.e., human albumin, and artificial(synthetic), i.e., gelatin and dextran, hydroxyethyl starches (HES).[3]In our setup, early gelatin-based colloid was commonly used in crystalloid refractory shock and was the fluid of choice in the patients with hypotensive shock at admission. One of the greatest concerns regarding colloid use has been the impact on coagulation. Dextrans theoretically bind to Von Willebrand Factor/Factor VIII complex and impair coagulation.[4]They can potentially cause osmotic renal injury in hypovolaemic patients. [5]

On the basis of large-scale pharmacovigilance study results, albumin infusion resulted in a low rate of anaphylactoid reactions and coagulopathy when compared to synthetic colloids.[6]25%Albumin has a greater degree of volume expansion as compared to the rest of colloids. In our cohort of 143 patients, 17 were given 20% albumin infusion either alone or in combination with synthetic colloid. 5% albumin solution has a similar degree of volume expansion as compared to hetastarch but greater than gelatins and dextrans. Albumin is expensive as compared to synthetic colloids. However review article from the departments of Anesthesia and intensive care from North India, found that the third generation HES (tetrastarches) provide a unique combination of safety and efficacy, and best suited for use in the intensive care setting. [7] Acute respiratory distress syndrome (ARDS) is a severe clinical syndrome of acute lung injury. Despite a large number of initiating factors, the pathophysiologic events are similar: pulmonary hypertension, intra-pulmonary shunting with severe hypoxemia, and myocardial dysfunction. Sepsis is the commonest cause of indirect lung injury. Another major predisposing factor reported is dengue shock syndrome.[8]We noted the low incidence of 1.3% in our patients with ARDS requiring ventilator support and did not contribute to mortality. In a similar way to our observation of 5 patients with ACS, a study from South India has reported that 3 patients out of 109 with severe dengue had ACS which if not corrected will lead to fluid refractory shock. [9] Our other PICU aggressive supportive measures such as a high-risk intubation management protocol, intensive monitoring of ACS, etc. were similar to the strategies from a tertiary care PICU referral center with improved outcome.[10,11] A western study has reported 22 cases of dengue-associated HLH among a total of 694 patients over a span of 5 years from 2008.[12]In our study, the major factor that contributed to mortality was MODS. It was observed in 12% of patients as against 2.4% of patients in another study from South India. [13]The study has reported few atypical manifestations like portal hypertension, acalculous cholecystitis, appendicitis, pericardial effusion, paroxysmal supraventricular tachycardia (PSVT), etc. We did not observe any of these atypical manifestations in our study group. To conclude most children with dengue shock syndrome respond well to judicious treatment with isotonic crystalloid solutions. Early intervention with colloid solutions is indicated in hypotensive dengue shock.

5. CONCLUSION

Colloid was administered in all patients with severe dengue presenting with severe plasma leakage. The compensated shock was a common presentation of severe dengue in children. Refractory shock, DIC, MODS, FHF either alone or in combination were causes of death in children presenting with shock to the ED.

REFERENCES

[1] World Health Organization. Geneva, Switzerland: WHO; 2009. Dengue: Guidelines for Diagnosis, Treatment, Prevention and Control. [Google Scholar].

[2] Shastri PS, Gupta P, Kumar R. A prospective 3 year study of clinical spectrum and outcome of dengue fever in ICU from a tertiary care hospital in North India. Indian J Anaesth 2020;64:181-6

[3] Kaye AD, Kucera IJ. Intravascular fluid and electrolyte physiology. In: Miller RD, editor. Miller's Anesthesia. 6th edition. Philadelphia: Churchill Livingstone; 2005. pp. 1763–98.

[4] Linder P, Ickx B. The effects of colloid solutions on hemostasis. Can J Anesth. 2006;53:30–s39

[5] Drumi W, Polzleitner D, Laggner AN, et al. Dextran-40, acute renal failure and elevated plasma oncotic pressure. N Engl J Med. 1988;318:252–54.

[6] Barron ME, Wilkes MM, Navickis RJ. A systematic review of the comparative safety of colloids. Arch Surg. 2004 May;139(5):552-63..

[7] Mitra S, Khandelwal P. Are all colloids same? How to select the right colloid?. *Indian J Anaesth*. 2009;53(5):592-607.

[8] Rakesh Lodha, S.K. Kabra, R.M. Pandey. Acute Respiratory Distress Syndome: Experience at a Tertiary Care hospital. Indian Pediatrics 2001; 38: 1154-1159

[9] Kamath SR, Ranjit S. Clinical features, complications and atypical manifestations of children with severe forms of dengue hemorrhagic fever in South India. Indian J Pediatr. 2006 Oct;73(10):889-95.

[10] Ranjit S, Kissoon N, Jayakumar I. Aggressive management of dengue shock syndrome may decrease mortality rate: a suggested protocol. Pediatr Crit Care Med. 2005 Jul;6(4):412-9.

[11] Ranjit S, Ramanathan G, Ramakrishnan B, Kissoon N. Targeted Interventions in Critically Ill Children with Severe Dengue. Indian J Crit Care Med. 2018 Mar;22(3):154-161.

[12] Ellis EM, Sharp TM, Pérez-Padilla J, González L, Poole-Smith BK, Lebo E, Baker C, et al. Incidence and Risk Factors for Developing Dengue-Associated Hemophagocytic Lymphohistiocytosis in Puerto Rico, 2008 - 2013. PLoS Negl Trop Dis. 2016 Aug 24;10(8):e0004939.

[13] Pothapregada S, Kamalakannan B, Thulasingam M. Clinical Profile of Atypical Manifestations of Dengue Fever. Indian J Pediatr. 2016 Jun;83(6):493-9.