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Original Research Article

A Comparative Study of Dextran-40 versus Crystalloid Infusion in Nonhemorrhagic, Nonhypovolemic Shock in Emergency Medicine

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ABSTRACT

Background: Shock is a condition of inadequate tissue perfusion due to an imbalance between oxygen demand and supply, classified into hypovolemic, cardiogenic, obstructive, and distributive types, each with distinct causes and treatment approaches. Crystalloids are the preferred intravenous fluids for resuscitation, while the safety and efficacy of synthetic colloids like dextran-40, as an alternative to albumin in non-hemorrhagic, non-hypovolemic shock, remain under investigation. This study explores the potential of dextran-40 in critical patients, aiming to provide clarity on its role compared to crystalloids.

Objectives: The study aims to evaluate the efficacy of dextran in achieving early hemodynamic stability, compare dextran infusion with crystalloid fluids in managing shock during the initial hours, and assess their outcomes in terms of multi-organ failure.

Methods: This prospective randomized controlled study evaluated the effects of Dextran-40 versus crystalloids in patients with non-hemorrhagic, non-hypovolemic shock presenting to the emergency department. Patients were assessed using qSOFA criteria, and initial resuscitation was performed with normal saline, followed by group-specific interventions. Outcomes were monitored through vital signs, ABG parameters, lactate clearance, and mental status, with statistical analysis performed using SPSS and R software.

Conclusion: The study found no significant advantage of dextran-40 over crystalloids for resuscitation in distributive shock, highlighting the need for larger, multicenter, randomized trials to validate its efficacy and safety. While promising early practices like goal-directed resuscitation and conservative fluid management show potential, further research is essential to establish dextran-40 as a reliable alternative to albumin in sepsis management.

Keywords: Dextran-40, Crystalloid Infusion, Hypovolemic Shock.

INTRODUCTION

Shock refers to inadequate perfusion of tissues because of the imbalance between oxygen demand of tissues and the body's capability to supply the same. Normally, thereare 4 types of shock namely hypovolemic, cardiogenic, obstructive and distributive shock.[1] More than one category can occur simultaneously eg ; hypovolemic and septic shock.

Hypovolemic shock is due to insufficient organ perfusion caused by intravascular volume loss, usually acute. This results in cardiac preload drop to a critical level and reduced macro- and microcirculation, with negative consequences for tissuemetabolism and the triggering of an inflammatory reaction. Cardiogenic shock is mainly a cardiac function disorder in the form of a critical reduction of the heart's pumping capacity due to systolic or diastolic dysfunction causing a reduced Ejection Fraction (EF) or impaired ventricular filling. Obstructive shock is due to the obstruction of the great vessels or the heart itself. Although the symptoms would be similar to those of cardiogenic shock, obstructive shock needs to be clearly differentiated from the cardiogenic shock

because it has to be treated in a different way. Distributive shock[2,3] is a state of relative hypovolemia because of pathological redistribution of the absolute intravascular volume and is the most commonly occurring form of shock. The cause is either a loss of regulation of vascular tone, with volume being shifted within the vascular system, and/or disordered permeability of the vascular system with shifting of intravascular volume into the interstitium. The 3 subtypes of distributive shock are septic, anaphylactic and neurogenic shock.[4]

According to the current Sepsis-3 criteria, sepsis is defined as a dysregulated responseby the body to an infection resulting in life-threatening organ dysfunctions. Patients aged >65 years with immunosuppression or underlying malignant disease are excessively affected. In few of the patients, the inflammatory response is small or nonexistent.[4]

Anaphylactic shock is featured with huge histamine-mediated vasodilation and maldistribution with a shift of fluid from the intravascular to the extravascular space. Anaphylaxis is an acute systemic reaction generally mediated by IgE-dependent hypersensitivity reactions. Mast cells and the histamine they release play a central role in this.[4]

Neurogenic shock is a state of imbalance between sympathetic and parasympathetic regulation of cardiac action and vascular smooth muscle. The dominant signs are intense vasodilation with relative hypovolemia while blood volume remains unchanged, at least at the beginning. Spinal cord injuries are the most common cause of neurogenic shock, at 15% to 20%, followed by surgical intervention in the lumbar region. Neurogenic shock can happen because of cerebral ischemia, subarachnoid hemorrhage, meningitis, during or after epileptic seizures, rapid onset of Guillain–Barre syndrome, pandysautonomia or cerebral herniation. Seldom, stress or severe pain or even after a karate kick can trigger neurogenic shock. Neurogenic shock is characterized by the sudden drop of Systolic Arterial Pressure (SAP) to <100 mmHg and heart rate to <60/min with obtunded consciousness and loss of spinal reflexes in patients with high spinal cord injury. The capacity of the splanchnic venous system and skeletal musculature rises while Systemic Venous Pressure (SVP) drops remarkably. Mortality is approximately 20%.[4]

Crystalloid fluids are a subset of Intravenous (IV) solutions that are frequently used in a clinical setting. Crystalloid fluids are the first line of choice for resuscitation with fluid in the presence of hypovolemia, hemorrhage, sepsis and dehydration. A crystalloid fluid is an aqueous solution of mineral salts and other small water-soluble molecules. Most commercially available crystalloid solutions are isotonic to human plasma. These fluids approximate concentrations of various solutes found in the plasma and do not exert an osmotic effect in vivo.[5,6]

Crystalloid fluids function to expand intravascular volume without disturbing ion concentration or causing large fluid shifts between intracellular, intravascular and interstitial spaces. Hypertonic solutions, e.g., 3% saline solutions, contain higher concentrations of solutes than those found in human serum. Because of this difference in concentration, these fluids are osmotically active and thus will cause fluid shifts. They are primarily used for emergent replacement of serum solutes, e.g., in hyponatremia with neurologic symptoms. Buffered solutions contain molecules that metabolize in vivo to bicarbonate; these solutions were designed to maintain a normalphysiologic plasma pH. The 3 commonly used molecules are lactate, acetate and gluconate; lactate and gluconate are hepatically metabolized to bicarbonate, while acetate is predominantly metabolized peripherally by skeletal muscle.[2]

IV fluids are commonly administered during resuscitation. Mostly, IV fluids can fall into 2 separate categories, crystalloids and colloids. In most of the clinical settings, crystalloids are the choice of fluid for many indications for fluid resuscitation, maintenance or as a solvent for medication delivery.[5,7] Topical studies have reinforced the view that there is little evidence in selecting starches as the fluid of choice in resuscitation,[6,8] especially in emergency medicine.

What is more unclear is whether colloids as a whole are beneficial compared to crystalloids with conflicting evidence in the literature.[9,10]

This study attempt to further investigation safety of synthetic colloid like dextran 40as an alternative to albumin in non-hemorragic, non-hypovolemic shock in critical patients.

MATERIALS & METHODSS

The present study was a prospective observational study conducted between November 2018 to September 2020 in

Department of General Medicine, KIMS Hospital, Bangalore. After obtaining approval from the Institutional Ethics Committee, written informed consent was taken from the patients. 50 patients fulfilling the inclusion criteria were included in the study i.e Patients diagnosed with CKD and initiated on maintenance Hemodialysis were enrolled into the study. NKF KDOQI (National Kidney Foundation Kidney Disease Outcomes Quality Initiative) Guidelines was used to define CKD. Patients with age less than 18 years, CKD patients who are not on Maintenance HD were excluded from the study. Each patient presenting to ED was evaluated at the time of presentation and detailed history along with clinical examination was performed and later subjected to necessary investigations which include GRBS, ECG, Arterial blood gas analysis, Serum Electrolytes, Renal function tests, Chest X ray, 2D Echo (if required) and emergency required treatment was given to the patient.

Information including socio-demographic characteristics, diagnosis at presentation to the ED previous history of similar presentations and duration of MHD were retrieved from the study participants.

Each patient was followed up for their duration of their stay in the hospital and outcomes were documented like Improved, Died and Status Quo for those discharged against medical advice.

Interventions to address life threatening complications of CKD were instituted to patients:

- Intravenous glucose/insulin infusion and intravenous calcium gluconate for patients with elevated serum potassium concentration.
- Oral or Intravenous sodium bicarbonate therapy for patients with low serum bicarbonate concentrations.
- Intranasal oxygen therapy and high dose intravenous loop diuretics for patients with pulmonary edema.
- In patients with respiratory distress, noninvasive positive pressure ventilation (NIPPV) using CPAP and then, if needed, intubation and ventilatory support was provided.

Statistical Analysis

Statistical analysis was done using SPSS software 22.0 Released 2013. Armonk, NY:IBM Corp. SD data obtained was tabulated in the excel sheet and was analysed, Descriptive analysis of all the explanatory and outcome parameters was done using frequency and proportions for categorical variables, whereas in Mean & SD for continuous variables. ChiSquare Test was used to compare the distribution of categorical outcome and explanatory variables based on the outcomes of the study patients. Mann Whitney U test was used to compare the mean values of Continuous variables based on the outcomes of the study patients. The level of significance was set at $P<0.05$.

METHODOLOGY

A prospective study titled "Comparative study of effect of dextrans-40 vs crystalloid infusion in non-haemorrhagic, non-hypovolemic shock in emergency department" was conducted at KIMS Hospital, Bangalore, after receiving approval from the Ethics Committee. The study spanned 1.8 years, from January 2018 to June 2020, and included 40 patients from the Emergency Department (ED) who met the inclusion criteria, with conditions defined according to the Third International Consensus Definitions Task Force.

Each patient presenting to the ED underwent evaluation at admission, including a detailed history and physical examination. Data collected comprised demographic profiles, comorbidities, and quick SOFA (qSOFA) scores. Blood and urine samples were sent for routine investigations, including liver and renal functions, glycemic parameters, coagulation profiles, ABG, and ECG, while blood and urine cultures were sent as required. Bedside investigations like 2D Echo and radiological imaging, such as chest X-ray, abdominal X-ray, and ultrasound, were performed when indicated, and ventilator support was considered if needed. After six hours of resuscitation, patients were followed up to assess outcomes. The inclusion criteria were all patients over 18 years of age with an initial systolic BP ≤100 mmHg and a qSOFA[11] score defined by BP ≤100 mmHg, respiratory rate ≥22 cpm, or altered mental status. Exclusion criteria included patients with hemorrhagic or hypovolemic shock, cardiogenic shock, anaphylactic shock, known renal diseases, hemorrhagic tendencies, prior resuscitation at other hospitals, allergic reactions to dextran, or refusal to participate.

The study followed a prospective randomized controlled design with purposive sampling. Patients were assessed using qSOFA[12] at presentation, and ABG was performed to

evaluate baseline parameters. The study group received an initial 500 ml bolus of 0.9% normal saline; if there was no or marginal improvement, patients were divided into a dextran group (treated with dextran-40 at 20 ml/kg) and a crystalloid group. Patients were monitored for vital signs, qSOFA scores, urine output, ABG parameters, and blood pressure. Responders were defined as those achieving a MAP ≥65 mmHg after one hour, while non-responders continued treatment with crystalloids and vasopressors. The control group received crystalloids and vasopressors, with resuscitation endpoints assessed through parameters such as MAP, pH, bicarbonate, lactate clearance, urine output, and mental status improvement.

The qSOFA score, introduced in 2016, is a tool to identify patients at greater risk for poor outcomes from sepsis outside the ICU. It includes three criteria-altered mental status, systolic BP ≤100 mmHg, and respiratory rate ≥22/min-with scores of ≥2 associated with higher mortality or ICU stays. For arterial blood gas analysis, an ABL80 FLEX analyzer was used, requiring 2 ml of blood from the radial or femoral artery. The system aspirated approximately 65 µL of blood per measurement, displaying results after analysis.

Ethical considerations included informed consent from patients or legal guardians after explaining the study, its procedures, and potential risks. The study involved no additional investigations, significant risks, or financial burdens, and was approved by the institutional ethics committee.

Clinical outcomes were categorized as improved, status quo, or mortality. "Improved" referred to subjective and objective improvement, while "status quo" described patients discharged against medical advice without fitting the other two categories. Results were analyzed statistically using descriptive and inferential methods,[13-17] including Student's t-test, Levene's test, Chi-square/Fisher Exact test, and non-parametric methods for categorical data. Statistical analysis was conducted using SPSS 22.0 and R software (ver. 3.2.2), with Microsoft Word and Excel used for generating graphs and tables.

RESULTS

The study was carried out during a period of 1.8 years (Jan 2018 to June 2020) and 40 patients presented to the Emergency Medicine Department who fulfilled inclusion criteria were included in the study. 40 subjects were included in this study. Two groupswere made dextran-40 group (cases) and crystalloid group (control).

Age in years	Dextran-40 group	Crystalloid group	Total
21-30	3(15%)	6(30%)	9(22.5%)
31-40	4(20%)	0(0%)	4(10%)
41-50	1(5%)	3(15%)	4(10%)
51-60	6(30%)	3(15%)	9(22.5%)
61-70	4(20%)	4(20%)	8(20%)
>70	2(10%)	4(20%)	6(15%)
Total	20(100%)	20(100%)	40(100%)
Mean ± SD	51.30±17.08	53.00±20.13	52.15±18.45
Table 1: Age distribution of patients studied			
Samples are age matched with P=0.775, student t test			

In our study out of 40 patient, In Dextran 40 group 30% patients were lie between 51-60 year age group and ranges from 34-68 years and in crystalloid group 30% lie between 21-30 years age group and ranges from 33-73 years. The mean deviation of 40 patient lies in 52.15±18.45 (Table 1).

Gender	Dexrtan - 40 Group	Crystalloid Group	Total
Female	11(55%)	11(55%)	22(55%)
Male	9(45%)	9(45%)	18(45%)
Total	20(100%)	20(100%)	40(100%)
Table 2: Gender distribution of patients studied			
Samples are gender matched with P=1.000, Chi-Square test			

As can be seen from Table 2 out of 40 patients 22 were female (55%) and 18 (45%) were males. 11 patients were female in each groups and 9 were male in each groups.

Patients with HTN	Dextran-40 group	Crystalloid group
Number of Patients	35% (n=7)	25% (n=5)
Table 3: Distribution of patient with hypertension		

As can be seen from Table 3 out of 40 patients, 35% (7) patients were in Dextran-40 group and 25% (5) patients were in crystalloid group. However incidence of hypertension as a comorbid was more in Dextran-40 group.

Patient with DM	Dextran-40 group	Crystalloid group
Number of patients	11(55%)	12(60%)
Table 4: Distribution of patients with Diabetes		

As can be seen from Table 4 in our study, diabetes were present in both groups almost equally.

Comorbidity

In our study population, 26 patients did not have any diabetes or hypertension. Among them 13 patients had hypertension and 11 patients had diabetes.

qSOFA	Admission	2hrs	6th Hours	% difference
Dextran-40 group (n=20)				
0	0(0%)	0(0%)	0(0%)	0.0%
1	0(0%)	1(5%)	7(35%)	35.0%
2	4(20%)	11(55%)	7(35%)	15.0%
3	16(80%)	8(40%)	6(30%)	-50.0%
Crystalloid group (n=20)				
0	0(0%)	1(5%)	3(15%)	15.0%
1	0(0%)	1(5%)	6(30%)	30.0%
2	8(40%)	11(55%)	11(55%)	15.0%
3	12(60%)	7(35%)	0(0%)	-60.0%
P value	0.301	1.000	0.014*	-
Table 5: qSOFA- Distribution in two groups of patients studied				
Chi-Square/Fisher Exact Test				

qSOFA; quick SOFA (sequential organ failure) score consists of only threecomponents, each allocated one point.

1) GCS<15

2) Respiratory rate >22cpm 3) SBP ≤ 100 mmHg

In the study population, 16 patients had score of 3 and 4 patients had score of 2 indextran-40 group and in crystalloid group 12,8 patients fall in 3 and 2 score respectively at admission.

After 2 hours of the study, 8, 11 and 1 patient fall in score of 3, 2 and 1 respectively in case group and 7,11,1 and 1 patients fall in score of 3, 2, 1 and 0 respectively.

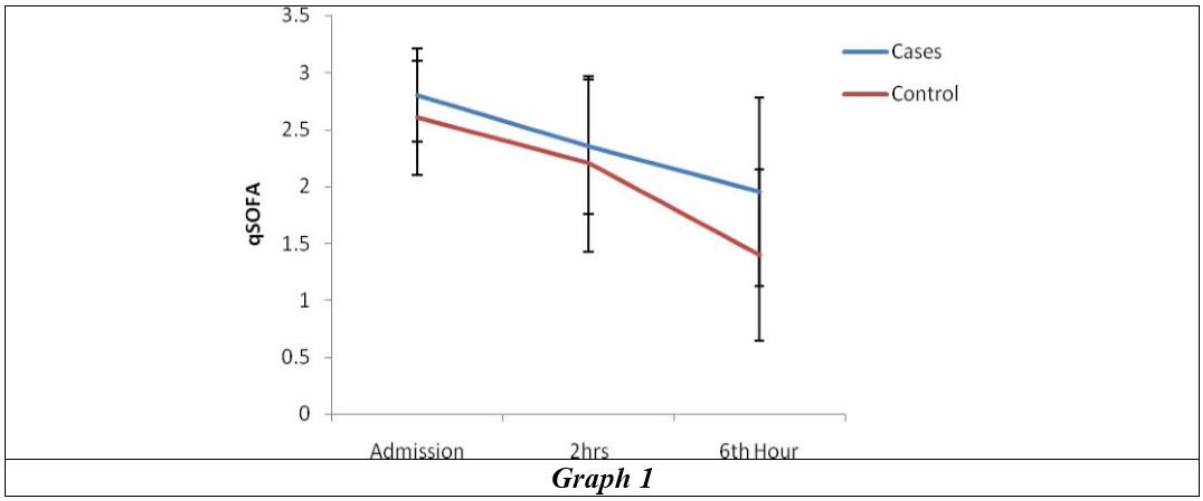
After 6 th hour 6, 7 and 7 patients fall in 3, 2 and 1 respectively in dextran-40 group and 0, 11, 6 and 3 patients fall in 3, 2,1 and 0 in crystalloid group.

Comparing between two groups cases with score of 2.80±0.41 and 2.60±0.46 in dextran-40 and crystalloid group respectively at admission and after 2 hour 2.35±0.59 and 2.20±0.77, after 6th hour score improved to 1.94±0.83 and 1.40±0.75 in dextran-40 and crystalloid groups respectively. In dextran -40 group 80% with qsofa score of 3 showed improvement after dextran- 40 at admission. Score at 2nd hour showed improvement in 50% of patients and at 6th hour 30% of patients were improved. In crystalloid group 60% with qsofa score of 3 at admission showed improvement with crystalloid, 35% showed improvement in 2nd hour, no improvement even after6th hour of crystalloid infusion as evident from Table 5.

qSOFA	Dextran-40 Group	Crystalloid Group	Total	P value

Admission	2.80±0.41	2.60±0.50	2.70±0.46	0.176
2hrs	2.35±0.59	2.20±0.77	2.28±0.68	0.492
6th Hour	1.95±0.83	1.40±0.75	1.68±0.83	0.034*
Table 6: qSOFA- A comparison in two groups of patients studied				

At 6th hour after admission dextran-40 group showed significant improvement with mean of 1.95±0.83 compared with crystalloid group (1.40±0.75) was statistically significant with p value = 0.034 (Table 6).



Graph 1

Heart Rate (bpm)	Dextran-40 Group	Crystalloid Group	Total	P value
Admission	122.20±22.58	108.40±22.86	115.30±23.49	0.062+
15 min	120.10±20.19	109.60±20.63	114.85±20.84	0.112
30min	116.80±18.65	110.75±20.88	113.78±19.78	0.340
1hr	116.55±18.57	110.25±22.53	113.40±20.63	0.341
2hr	117.45±16.22	109.20±22.64	113.33±19.88	0.193
3hr	114.90±15.13	109.20±19.85	112.05±17.66	0.314
4hr	113.00±17.32	109.15±20.00	111.08±18.57	0.519
5hr	113.05±18.63	107.05±18.72	110.05±18.68	0.316
6hr	109.25±17.71	104.80±18.28	107.03±17.91	0.439
Table 7: Heart Rate (bpm) - A Comparison in two groups of patients studied				

Heart Rate Comparison; in a study population the HR initially there was tachycardia of 115.3±23.49 bpm, among that dextran-40 group was 122.20±22.58 andcrystalloid groups were 115±23.49.

Tachycardia gradually improved from 0 to 6th hour to 107±17.91, among dextran-40 group HR improve to 109.25±17.71 and crystalloid group HR improves to 104±18.28 significant difference was not observed between two groups (Table 7).

SBP (mm Hg)	Dextran-40 Group	Crystalloid Group	Total	P value
Admission	76.25±9.16	77.50±8.56	77.08±8.59	0.745
15 min	76.25±9.16	77.50±6.83	77.08±7.51	0.710
Table 8: SBP (mm Hg) - A Comparison in two groups of patients studied				

SBP (mm Hg)	Dextran-40 Group	Crystalloid Group	Total	P value
Admission	76.25±9.16	77.50±8.56	77.08±8.59	0.745
15 min	76.25±9.16	77.50±6.83	77.08±7.51	0.710
30min	79.00±7.38	80.63±6.80	80.00±6.93	0.571
1hr	86.15±8.70	83.33±5.94	84.52±7.23	0.291
2hr	89.29±9.17	88.42±6.88	88.79±7.81	0.759

3hr	89.41±12.98	90.53±7.05	90.00±10.14	0.747
4hr	98.13±10.47	97.50±9.67	97.78±9.89	0.854
5hr	104.00±10.56	105.50±6.86	104.86±8.53	0.614
6hr	110.13±10.01	107.50±7.86	108.63±8.81	0.389
Table 8: SBP (mm Hg) - A Comparison in two groups of patients studied				

SBP Comparison; in a study population, the DBP initially was 77.08±8.59 and gradually improved to 108.63±7.07 at 6th hour. And 76.25±9.16, 77.08±8.59 at admission in dextran-40 and crystalloid group respectively. It improved to 110.13±10.01, 107.50±7.86 in dextran-40 and crystalloid respectively. However, the outcome was not statistically significant between the 2 groups (Table 8).

DBP (mm Hg)	Dextran-40 Group	Crystalloid Group	Total	P value
0hr	53.33±5.77	45.00±10.00	48.57±9.00	0.259
15 min	52.50±5.00	55.45±6.88	54.67±6.40	0.450
30min	48.75±6.41	58.00±4.14	54.78±6.65	<0.001**
1hr	54.55±8.20	59.38±4.43	57.41±6.56	0.058+
2hr	59.23±10.38	61.67±3.83	60.65±7.27	0.366
3hr	63.08±8.55	63.68±4.96	63.44±6.53	0.801
4hr	65.33±7.43	65.79±5.07	65.59±6.13	0.833
5hr	68.00±7.75	67.00±4.70	67.43±6.11	0.639
6hr	70.67±9.61	69.00±4.47	69.71±7.07	0.498
Table 9: DBP (mm Hg) - A Comparison in two groups of patients studied				

DBP Comparison; in a study population, the DBP initially was 48.57±9.00 and gradually increases to 69±7.07 at 6th hour. And 53.33±5.77, 45±10.00 at admission in dextran-40 group and crystalloid group respectively. It improves to 70.67±9.67,69.71±7.07 in dextran-40 group and crystalloid group respectively. However no significant difference in improvement of DBP was seen in both the groups even after 6th hours of resuscitation (Table 9).

Variables	Dextran- 40 Group	Crystalloid Group	Total	P value
pH				
• before dextran-40	7.22±0.26	7.30±0.13	7.26±0.21	0.241
• after 6 hours	7.31±0.18	7.34±0.14	7.32±0.16	0.607
LACTATE				
• before dextran-40	5.60±4.10	4.44±2.94	5.02±3.57	0.309
• after dextran-40	4.30±3.73	3.28±1.27	3.79±2.80	0.257
Creatinine Clearance				
• at admission	1.90±1.00	1.82±1.74	1.86±1.40	0.853
• at 6th hour	1.97±0.99	1.78±1.74	1.87±1.40	0.682
HCO3				
• before dextran-40	13.06±3.36	16.61±3.77	14.84±3.96	0.003**
• After dextran-40	14.94±3.18	17.35±3.41	16.14±3.48	0.026*
Table 10: Comparison of pH/Lactate/Creatinine Clearance and HCO3 in two groups of patients studied				

In our study population, the mean pH of population is 7.26±0.21 at admission and after 6th hour pH is 7.32±0.16 among them 7.22±0.26 and 7.30±0.13 pH was Dextran – 40 group and Crystalloid group respectively at admission and after 6th hour pH improved to 7.31±0.18 and 7.34±0.14 for Dextran – 40 group and Crystalloid group respectively. However, the patient improvement between 2 groups were not statistically significant. In our study population, the mean lactate of population was 5.02±3.57 at admission and after 6th hour lactate is 3.79±2.80. among them lactate of Dextran – 40 group and Crystalloid group was 5.60±4.10 and 4.44±2.94 respectively at admission and after

6th hour lactate was 4.30±3.73 and 3.28±1.27 for case and control respectively.Improvement in lactate levels were noted in both the groups, but was not was statistically significant.

In our study population, the mean creatinine clearance of population is 1.86±1.40 at admission and after 6th hour creatinine clearance is 1.87±1.40. Amongst them, creatinine clearance of Dextran – 40 group and Crystalloid group was 1.90±1.0 and 1.97±0.99 respectively at admission and after 6th hour creatinine clearance was 1.82±1.74 and 1.78±1.74 for Dextran – 40 group and Crystalloid group.

Marginal decline in creatinine clearance was noted in Dextran – 40 group patients and improvement in crystalloid group. However it was not statistically significant.

In our study population, the mean HCO3 of population is 14.84±3.96 at admission and after 6th hour lactate is 16.14±3.48. Amongst them HCO3 of dextran-40 group and crystalloid group was 13.06±3.36 and 16.61±3.77 respectively at admission and after 6th hour HCO3 was 14.94±3.18 and 17.38±3.41 for both groups respectively. HCO3 improvement was statistically significant in dextran group with p value of 0.026.

Urine Output	Dextran-40 group (n=20)	Crystalloid group (n=20)	Total (n=40)	P value
0hr				
• Nil	20(100%)	18(90%)	38(95%)	0.487
• 1-50	0(0%)	2(10%)	2(5%)	
• 51-100	0(0%)	0(0%)	0(0%)	
• 101-150	0(0%)	0(0%)	0(0%)	
• 151-200	0(0%)	0(0%)	0(0%)	
• >200	0(0%)	0(0%)	0(0%)	
1hr				
• Nil	10(50%)	12(60%)	22(55%)	0.802
• 1-50	7(35%)	8(40%)	15(37.5%)	
• 51-100	1(5%)	0(0%)	1(2.5%)	
• 101-150	1(5%)	0(0%)	1(2.5%)	
• 151-200	0(0%)	0(0%)	0(0%)	
• >200	1(5%)	0(0%)	1(2.5%)	
2hr				
• Nil	6(30%)	6(30%)	12(30%)	0.198
• 1-50	10(50%)	14(70%)	24(60%)	
• 51-100	3(15%)	0(0%)	3(7.5%)	
• 101-150	0(0%)	0(0%)	0(0%)	
• 151-200	0(0%)	0(0%)	0(0%)	
• >200	1(5%)	0(0%)	1(2.5%)	
3hr				
• Nil	6(30%)	2(10%)	8(20%)	0.002**
• 1-50	7(35%)	18(90%)	25(62.5%)	
• 51-100	5(25%)	0(0%)	5(12.5%)	
• 101-150	1(5%)	0(0%)	1(2.5%)	
• 151-200	0(0%)	0(0%)	0(0%)	
• >200	1(5%)	0(0%)	1(2.5%)	
4hr				
• Nil	5(25%)	1(5%)	6(15%)	0.018*
• 1-50	9(45%)	18(90%)	27(67.5%)	
• 51-100	3(15%)	1(5%)	4(10%)	
• 101-150	3(15%)	0(0%)	3(7.5%)	
• 151-200	0(0%)	0(0%)	0(0%)	
• >200	0(0%)	0(0%)	0(0%)	

5hr				
• Nil	5(25%)	1(5%)	6(15%)	0.020*
• 1-50	8(40%)	17(85%)	25(62.5%)	
• 51-100	3(15%)	2(10%)	5(12.5%)	
• 101-150	3(15%)	0(0%)	3(7.5%)	
• 151-200	0(0%)	0(0%)	0(0%)	
• >200	1(5%)	0(0%)	1(2.5%)	
6hr				
• Nil	3(15%)	0(0%)	3(7.5%)	0.002**
• 1-50	9(45%)	16(80%)	25(62.5%)	
• 51-100	5(25%)	4(20%)	9(22.5%)	
• 101-150	1(5%)	0(0%)	1(2.5%)	
• 151-200	2(10%)	0(0%)	2(5%)	
• >200	0(0%)	0(0%)	0(0%)	
Table 11: Urine output distribution in two groups of patients studied				
Chi-Square/Fisher Exact Test				

In our study population, urine output at 0 hr in majority of the patients (95%) had nil urine output. After the 3rd hour of the study urine output of Dextran-40 group were improved compared to Cryatalloid group with statistical significance of 0.002, 0.018, 0.020 and 0.002 at 3rd, 4th, 5th and 6th hour (Table 11).

Improved	65%(13)	60%(12)
SQ	20%(4)	20%(4)
Mortality	15%(3)	20%(4)
Table 12: outcome of two groups were studied		

In our study the mortality in Crystalloid group is 20% (n-4) and Dextran – 40 groupis 15% (n-3).Though not statistically significant, multiple co morbid factors have contributed to the mortality in Crystalloid group (Table 12).

	Dextran-40Group (n=20)	**Crystalloid Group (n=20)**	**Total (n=20)**	**P value**
HTN	7(35%)	5(25%)	12(30%)	0.490
DM	11(55%)	12(60%)	23(57.5%)	0.749
Mortality	20(100%)	20(100%)	40(100%)	1.000
Table 13: Comparison of Comorbid and mortality in cases and controls studied				
Chi-Square/Fisher Exact Test				

In our study population, majority of patients had diabetes (57%). Amongst them, majority of them (60%) were in the Crystalloid group, followed by hypertension in30% of the patients which was statistically insignificant (Table 13).

	Non Responders to Dextran-40	**Responders to Dextran-40**	**Total**	**P value**
Age in years	61.60±8.20	47.87±18.06	51.30±17.08	0.122
qSOFA admission	3.00±0.00	2.73±0.46	2.80±0.41	0.217
qSOFA 2hrs	2.80±0.45	2.20±0.56	2.35±0.59	0.044*
qSOFA 6th hour	3.00±0.0	1.60±0.63	1.95±0.83	<0.001**
Table 14: A Comparison of clinical variables responders and non-responders to Dextran-40				

Gender	**Non Responders to Dextran-40**	**Responders to Dextran-40**	**Total**
Female	4(80%)	7(46.7%)	11(55%)
Male	1(20%)	8(53.3%)	9(45%)
Total	5(100%)	15(100%)	20(100%)

Table 15: Gender distribution of patients study
P=0.319, Not Significant, Fisher Exact Test

In our study group, 20 patients received Dextran-40 (1500ml) for resuscitation. Out of these 20 patients, 5 patients did not show improvement even after resuscitation. (qsofa after 6th hour was 3.00 ± 0 since admission of 0 hrs.) Probable reason would be susceptible age group of 61.60 ±8.20 years with female gender predominance (46.7%) (Table 14 & 15)

	Non Responders to Dextran-40	**Responders to Dextran-40**	**Total**	**P value**
Ph before dextran-40	6.95±0.29	7.31±0.18	7.22±0.26	0.004**
Ph after 6 hours	7.19±0.24	7.35±0.15	7.31±0.18	0.085+
Lactate before dextran-40	8.07±3.41	4.78±4.07	5.60±4.10	0.123
Lactate after dextran-40	7.25±4.71	3.31±2.90	4.30±3.73	0.037*
Creatinine clearance at admission	1.64±0.36	1.99±1.14	1.90±1.00	0.519
Creatinine clearance at 6th hour	2.24±0.83	1.87±1.05	1.97±0.99	0.490
HCO3 before dextran-40	9.66±2.16	14.19±2.91	13.06±3.36	0.005**
HCO3 After dextran-40	12.88±4.12	15.62±2.62	14.94±3.18	0.096+
Table 16: Comparison of study variables in responders andnon responders				

In our study group, non-responders compared with responders of study group in pH was 6.95±0.29, 7.31±0.18 for non-responders and responders respectively. Those patients having low pH had not responded to dextran 40 compared to rest of patients. After 6th hour the pH of non-responders and responders were 7.19±0.24 and 7.35±0.15 respectively, they did not improve over responders. This is statistically significance withp=0.004.

In our study group, non-responders compared with responders of study group in lactatewas 8.07±3.41, 4.78±4.07 for non-responders and responders. Those patients having high lactate have not responded to dextran 40 compared to responders of patients. After 6th hour the lactate of non-responders and responders were 7.25±4.71 and 3.31±2.90 respectively and it was statistically significance with p value of= 0.037.

In our study group, non-responders compared with responders of study group in creatinine was 1.64±0.36, 1.99±1.14 for non-responders and responders. After 6th hourthe creatinine of non-responders and responders were 2.24±0.83 and 1.87±1.05 respectively. However, this shows rapid deterioration of RFTs in non-responders though not statistically significant.

In our study group, non-responders compared with responders of study group in HCO3was 9.66±2.16, 14.19±2.91 for non-responders and responders respectively. Those patients having low HCO3 have not responded to dextran 40 compared to rest of patients. After 6th hour the HCO3 of non-responders and responders were 12.88±4.12and 15.62±2.62 respectively and it was statistically significant (Table 16).

	Non Respondersto Dextran-40 (n=5)	**Responders to Dextran-40 (n=15)**	**Total (n=20)**	**P value**
HTN	3(60%)	4(26.7%)	7(35%)	0.260
DM	5(100%)	6(40%)	11(55%)	0.038*
Mortality	5(100%)	15(100%)	20(100%)	1.000
Table 17: Comorbid conditions				
Chi-Square/Fisher Exact Test				

Comparison of Comorbid and Mortality in Cases and Controls Studied

In our study, in non-responders 3 out of 5 patients outcome is mortality and status quo and associated with more comorbidity.

DISCUSSION

The most common categories of shock are hypovolemic, cardiogenic and high cardiac output with decreased SVR. The optimal fluid therapy for patients with non hemorragic, non-hypovolemic shock is debatable. Topical studies have reinforced the view that there is little evidence in selecting starches as the fluid of

choice in resuscitation, especially in emergency medicine. What is more unclear is whether colloids as a whole are beneficial compared to crystalloids with conflicting evidence in the literature. Goal- directed therapy has been demonstrated as being beneficial although the best method ofassessing the response to fluid remains to be elucidated.as described by Kumar G et al..,study.[18] Albumin may be beneficial in patients with septic shock but availability is limited and cost is high.

The objective of the present study was to investigate the dextran-40 in place of albumin for patient in distributive shock. Hence dextran-40 a colloid was used in our study to know the efficacy of dextran-40 in resuscitation and its outcome in comparison to crystalloids (0.9% NS).

Clinical Profile of the Study Population

A total of 40 patients were included in our study as per patient selection methods, inclusion and exclusion criteria. The age groupof our patients in our study ranged from 37 to 82 years. The number of patients in the age groups ≤30,30-40, 40-50, 50-60, 60-70, ≥70 were 9 (22.5%), 4(10%), 4 (10 %), 9 (22.5%), 8(20%) and 6(15%) respectively. mean age group of our study was 52 ± 18 years compared to Peter Bentzer et al[9] who noted mean age group of 66 years. The difference above findings between the studies may be due to different study settings with different rates of admission.In our study out of 40 patients 22 were female (55%) and 18 (45%) were male included in study.[19] patients were female in each groups and 9 were male in each groups. Compared to peter bentzer et al, 40 % of his population under dextran group were males.

qSOFA; quick SOFA (sequential organ failure) score consists of only three components, each allocated one point.

Altered mental status 2. Respiratory rate >22 cpm 3. SBP ≤ 100 mmHg. In the study population, 16 patients had score of 3 and 4 patients had score of 2 in dextran-40 group and in crystalloid group 12,8 patients fall in 3 and 2 score respectivelyat admission. After 2 hours of the study, 8, 11 and 1 patient fall in score of 3, 2 and 1 respectively in case group and 7,11,1 and 1 patients fall in score of 3, 2, 1 and 0 respectively.

After 6th hour 6, 7 and 7 patients fall in 3, 2 and 1 respectively in dextran-40 group and 0, 11, 6 and 3 patients fall in 3, 2,1 and 0 in crystalloid group.

Comparing between two groups cases with score of 2.80±0.41 and 2.60±0.46 in dextran-40 and crystalloid group respectively at admission and after 2 hour 2.35±0.59 and 2.20±0.77, after 6 th hour score improved to 1.94±0.83 and 1.40±0.75 in dextran-40 and crystalloid groups respectively.

In dextran -40 group 80% with qsofa score of 3 showed improvement after dextran- 40 at admission. Score at 2nd hour showed improvement in 50% of patients and at 6th hour 30% of patients were improved. In crystalloid group 60% with qsofa score of 3 at admission showed improvement withcrystalloid, 35% showed improvement in 2nd hour, no improvement even after 6th hour of crystalloid infusion.

A qSOFA of >2 even though was high among non survivors and predicts mortality butwas not statistically significant. However other studies show, a positive qSOFA had a sensitivity of 61% (57–65) and a specificity of 80% (79–81). The positive likelihood ratio of a positive qSOFA for in-hospital mortality was 3.09 (2.86–3.35).according to study by Emmanuel et al.[20]

In a study population the HR initially there was tachycardia of 115.3±23.49 bpm, among that dextran-40 group was 122.20±22.58 and crystalloid groups were 115±23.49.

Tachycardia gradually settled from 0 to 6th hour to 107±17.91, among dextran-40 group HR improve to 109.25±17.71 and crystalloid group HR improves to 104±18.28. Significant difference was not observed between two groups.

However, our study parameter were similar to Peter Bentzer et al, study hadshowed mean HR was 110 bpm.

Dong Nai et al, study mean HR was 113.9 5± 14.3 with confounding factor of age our studies did not show significance differences with other studies.

In a study population, the SBP initially was 77.08±8.59 and gradually improved to 108.63±7.07 at 6th hour. And 76.25±9.16, 77.08±8.59 at admission in dextran-40 and crystalloid group respectively. It improved to 110.13±10.01, 107.50±7.86 in dextran-40 and crystalloid respectively. However, the outcome was not statisticallysignificant between the 2 groups.

Compare to Peter Bentzer et al, study mean SBP at admission 103 mmHg before resuscitation and after dextran mean SBP was 108 mmHg.

In a study population, the DBP initially was 48.57±9.00 and gradually increases to 69±7.07 at 6th hour. And 53.33±5.77, 45±10.00 at admission in dextran-40 group and crystalloid

group respectively. It improves to 70.67±9.67, 69.71±7.07 in dextran-40 group and crystalloid group respectively. However no significant difference in improvement of DBP was seen in both the groups even after 6th hours of resuscitation.In our study population, the mean pH of population is 7.26±0.21 at admission and after 6th hour pH is 7.32±0.16 among them 7.22±0.26 and 7.30±0.13 pH was Dextran – 40 group and Crystalloid group respectively at admission and after 6th hour pH improved to 7.31±0.18 and 7.34±0.14 for Dextran – 40 group and Crystalloid group respectively. However, the patient improvement between 2 groups were not statistically significant.

Compare to Peter Bentzer et al, study pH before dextran was 7.32 and post pH was 7.34.

In our study population, the mean lactate of population was 5.02±3.57 at admission and after 6th hour lactate is 3.79±2.80. among them lactate of Dextran – 40 group and Crystalloid group was 5.60±4.10 and 4.44±2.94 respectively at admission and after 6th hour lactate was 4.30±3.73 and 3.28±1.27 for case and control respectively. Improvement in lactate levels were noted in both the groups, but was not was statistically significant. Compare to Peter Bentzer et al, study the lactate before dextran was 2.9 and it increases post dextran was 3.8.

In our study population, the mean creatinine clearance of population is 1.86±1.40 at admission and after 6th hour creatinine clearance is 1.87±1.40. Amongst them, creatinine clearance of Dextran – 40 group and Crystalloid group was 1.90±1.00 and 1.97±0.99 respectively at admission and after 6th hour creatinine clearance was 1.82±1.74 and 1.78±1.74 for Dextran – 40 group and Crystalloid group.

Marginal decline in creatinine clearance was noted in Dextran – 40 group patients and improvement in crystalloid group. However it was not statistically significant.

Compare to Peter Bentzer et al mean, creatinine was 1.968 mg/dl before dextran and after detran was 2.036, in this study Detran shows raise in creatinine value.

In our study population, the mean HCO3 of population is 14.84±3.96 at admission and after 6th hour lactate is 16.14±3.48. Amongst them HCO3 of dextran-40 group and crystalloid group was 13.06±3.36 and 16.61±3.77 respectively at admission and after 6th hour HCO3 was 14.94±3.18 and 17.38±3.41 for both groups respectively. HCO3 improvement was statistically significant in dextran group with p value of 0.026.In our study population, urine output at 0 hr in majority of the patients (95%) had nil urine output. After the 3rd hour of the study urine output of Dextran-40 group were improved compared to Cryatalloid group with statistical significance of 0.002, 0.018, 0.020 and 0.002 at 3rd, 4th, 5th and 6th hour.

In our study the mortality in control group is 20% (n-4) and study group is 15% (n-3), it shows not much significant difference because multiple confounding factors affects tomortality.

In our study out of 40 patients, 35% (7) patients were in Dextran-40 group and 25% (5) patients were in crystalloid group were hypertensive. However incidence of hypertension as a comorbid was more in Dextran-40 group.

In our study population, majority were diabetes (57%), among this in dextran-40 group 55% (n=11) and crystalloid group 60% (n=12). In our study group, 20 patients received Dextran-40 (1500ml) for resuscitation. Out of these 20 patients, 5 patients did not show improvement even after resuscitation. (qsofa after 6th hour was 3.00 ± 0 since admission of 0 hrs.) Probable reason would besusceptible age group of 61.60 ±8.20 years with female gender predominance (46.7%).In our study group, non-responders compared with responders of study group in pH was6.95±0.29, 7.31±0.18 for non-responders and responders respectively. Those patientshaving low pH had not responded to dextran 40 compared to rest of patients. After 6th hour the pH of non-responders and responders were 7.19±0.24 and 7.35±0.15 respectively, they did not improve over responders. This is statistically significance with p=0.004.

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In a study done by Upadhyay M et al, shows. Both normal saline and gelatin polymersolution were equally effective as resuscitation fluid with respect to restoration of plasma volume and hemodynamic stability.[21]

In the study done by Bayer o et al[22] Effects of fluid resuscitation with synthetic colloids alone on shock reversal studied and they considered shock reversal whenserum lactate ≤2.2 mmol/L, hemodynamics goals MAP>70 mmHg, CVP>8mmHg Study shows shock reversal was achieved equally fast with synthetic colloids or crystalloids. Use of colloids resulted in only marginally lower required volumes ofresuscitation fluid.

There is a paucity of high quality data regarding effects of dextran solutions on outcome.

Limitation

The sample size was limited because it was a single-center study.

- Large volume of dextran cannot be given because dosage not exceeding20ml/kg body weight during the first 24 hours.
- Dextran-40 is costly compared to crystalloid.
- Dextran-40 may interfere with blood grouping and typing.
- Limited use because of its adverse effect like AKI, bleeding tendency.
- Sole use of dextran-40 cannot be demonstrated on patients.
- Lack of post hospital follow up data.
- Vulnerability to errors in judgment
- Low level of reliability and high level of bias
- Inability to generalize research findings

CONCLUSION

Recent studies have suggested that early goal-directed resuscitation of patients with distributive shock and conservative fluid management of patients with acute lung injury (ALI) can improve outcomes. Because these may be seen as potentially conflicting practices, we set out to determine the influence of fluid management on the outcomes of patients with septic shock complicated by Ali.

In our study, there was no significant difference between patients who received dextran-40 as a resuscitative fluid and patients with conventional treatment with crystalloids. Dextran -40 did not show any added benefits compared to crystalloids. Need larger group and multicentric studies to prove advantages and adverse effects.

A prospective large trial with low risk of bias is needed to further evaluate effects of dextran-40 before it can be recommended as an alternative to albumin in the resuscitation of sepsis.

Patients the cross-sectional nature would not allow the cause effect relationship to be established, making generalization of the findings difficult.

Larger randomized prospective trials (on the basis of the results provided here) are needed to address these questions and validate the findings of this study.

Recommendation

From our study for patients with distributive shock, choice of resuscitation fluid iscrystalloid solution.

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