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COMPARISION OF COMPLICATIONS ALONG WITH OUTCOME BETWEEN PATIENTS REQUIRING TOTAL PARENTERAL NUTRITION & ENTERAL NUTRITION IN A PAEDIATRIC INTENSIVE CARE UNIT-A HOSPITAL BASED OBSERVATIONAL STUDY:

Paediatrics

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ABSTRACT

INTRODUCTION*:* The concept of Total Parenteral Nutrition started during the late 1930s when positive nitrogen balance was maintained in children by use of protein hydrosylates. In 1966, an animal model of short bowel syndrome was created at the University of Pennsylvania. Beagle puppies were given PN via a central line and shown to have normal rates of growth PN and had normal rates of growth as compared to the puppies on the right who did not have a central line. Then in 1970, protein hydrosylates were replaced by crystalline amino acid solutions resulting fewer allergic reactions. In 1980 & 81, infant specific & pediatric specific crystalline solutions were introduced. Finally in 1988, the guidelines for TPN were introduced. [1]The recent technological advancements in Paediatric Critical Care has resulted in a more sophisticated care for children and adolescents, making these Intensive care units prepared to treat cases of high complexity. However, the technology available has not been sufficient enough in improving the quality of patient care and higher ability to predict life expectancy becomes an issue that could increase the suffering and prolong death process [2].

Material &Methods: This was a prospective observational study to evaluate the outcome of patients admitted to the paediatric intensive care unit (PICU) of IMS & SUM hospital who required TPN as per ESPHAGN recommendation versus those not requiring the same. *STUDY PERIOD*: 2years.*PLACE OF STUDY:* This study was conducted in the Paediatric Intensive Care Unit of the Department of Paediatrics in the Institute of Medical Sciences and SUM Hospital (IMS & SH) which is a tertiary care centre in Odisha. The total admissions to the PICU was 278 during the study period .After excluding 53 cases, 225 cases were studied in detail .All the patients admitted to the PICU fulfilling the inclusion criteria were the participants. All the paediatric patients between 1 month to14years admitted to PICU, meeting the criteria were included in the study. Out of 225 cases, 59 were given TPN as per ESPHAGN recommendations. All the necessary investigations required as per our PICU protocol were done along with other necessary investigations .New complications that develops before or after TPN were noted and taken care accordingly .All cases were followed till discharge or death. Patients requiring TPN as per guidelines were assessed at regular intervals with different biochemical & other parameters both before & after the initiation of TPN.

Results: Out of total 278 admissions to the PICU during the study period, 53 cases (30 admitted for Post-Operative stabilisation, 12 participants left against medical advice (LAMA) and 11 died within 8 hours of admission) were excluded from the study. The association between various study variables and the outcome was analysed and a p value of < 0.05 was considered as statistically significant. Majority of the study population were within the age group of 5 to 10 years. Males outnumbered the female participants in each sub group. The causes of illness were grouped as per the primary system involved. Respiratory system (n = 89) constituted the major cause of illness at the time admission, followed by CNS (n = 45), Infections (n = 22), GI (4). The others included CVS (n = 7), Haematological (n = 20), Renal (n = 11) and Others (n = 27). The highest mortality rate (28.91%) was observed in the cases that received enteral nutrition (EN) while the cases which received TPN had an excellent recovery rate of 87.3%.TPN had significant association with good outcome (p-value-0.001).Out of the total 225 cases, 59 needed TPN, out of which 51 patients survived.The mortality rate in cases requiring Total Parenteral Nutrition was significantly less as compared to cases which received enteral nutrition(13.96% vs 28.91%).Few Complication among TPN cases were also significantly lower compared to the Enteral cases i.e Hypoglycaemia(3% vs 7%), Hyponatremia(31.7 vs 38.3),Hypokalemia(30.2 vs 40.6),Hypoalbuminemia(13.5 vs 18.1) respectively to name a few.

Conclusion: The present study was done in a tertiary care referral hospital to evaluate the complications & outcome of patients between those requiring TPN against those not requiring it in a paediatric intensive care unit. A total of 225 cases were studied and analyzed. The overall mortality was 19.6%. Our study demonstrated that, nutritional intervention in the form of TPN has many advantages like low mortality, minimal morbidity, better weight gain, lesser metabolic abnormalities & reduced PICU stay.

KEYWORDS

TPN,PICU, Sepsis, Enteral Nutrition

INTRODUCTION

The recent technological advancements in Paediatric Critical Care has resulted in a more sophisticated care for children and adolescents, making these Intensive care units prepared to treat cases of high complexity. However, the technology available has not been sufficient enough in improving the quality of patient care and higher ability to predict life expectancy becomes an issue that could increase the suffering and prolong death process [1].

The Global Scenario:

Leading causes of severe illness in PICU is mainly due to Sepsis and ARDS, which are also significant causes of morbidity and mortality worldwide. The mortality rate of sepsis among children from PICU in developing countries is higher than 50% [2].As per World Health Organisation (WHO) 80% of deaths in children < 4 years can be classified as sepsis-related deaths. WHO also estimated that every year 10 million children die of which 99% occurs in developing countries. [3] As per the recent survey by WHO, Pneumonia is the major reason behind under 5 mortality in children [4].

Indian scenario:

The intensive care for Paediatric and Neonatal diseases has improved dramatically over the last decade in India. With increase in demand for specialised intensive care unit services in rural India, many tertiary care hospitals have been established with excellent infrastructure and dedicated manpower. The outcome of intensive care has not been widely reported yet but the need for sophisticated equipment and aggressive treatment is still under developing stage.

The practice of paediatric critical care is dynamic and evolving. Paediatric population is a vulnerable group necessitating standard care for medically ill children. Recently, the Pediatric Early vs Late Parenteral Nutrition in Intensive Care Unit (PEPaNIC) randomized clinical trial (RCT), including 1440 critically ill children, showed that withholding PN for 1 week (late PN) resulted in fewer new infections and reduced the duration of PICU stay as compared with initiating PN at day 1 (early PN).[16]These clinical benefits were more in children who were at high risk of developing undernutrition, as reflected by a high score on the Screening Tool for Risk on Nutritional Status and Growth (STRONGkids).[17] However, withholding PN for 1 week in undernourished critically ill children unable to advance past low volumes of enteral nutrition (EN) raised concerns among experts.[15]. Recently updated guidelines advise to start supplemental PN earlier in undernourished children than in well-nourished children if EN intake is insufficient.[15,20].

MATERIALS AND METHODS:

This was a prospective observational study to evaluate the outcome of patients admitted to the paediatric intensive care unit (PICU) of IMS & SUM hospital who required TPN as per ESPHAGN recommendation versus those not requiring the same. *STUDY PERIOD*: 2years.*PLACE OF STUDY:* This study was conducted in the Paediatric Intensive Care Unit of the Department of Paediatrics in the Institute of Medical Sciences and SUM Hospital (IMS & SH) which is a tertiary care centre in Odisha. The total admissions to the PICU was 278 during the study period .After excluding 53 cases, 225 cases were studied in detail .All the patients admitted to the PICU fulfilling the inclusion criteria were the participants. All the paediatric patients between 1 month to14years admitted to PICU, meeting the criteria were included in the study. Out of 225 cases, 59 were given TPN as per NASPGHAN recommendations[14,17]. All the necessary investigations required as per our PICU protocol ie.ABG analysis (for pH, PCo2, PaO2, Total Co2,blood Glucose, serum Potassium) , Complete Blood Count (for TWBC and TPC), PT/INR study, RFT (for BUN and Creatinine) along with other investigations as required were done .New complications that develops before or after TPN were noted and taken care accordingly .All cases were followed till discharge or death. Patients requiring TPN as per guidelines were assessed at regular intervals with different biochemical & other parameters both before & after the initiation of TPN. The main aim was to compare the mortality & morbidity modalities amongst TPN & non-TPN cases.

RESULTS:

Out of total 278 admissions to the PICU during the study period, 53 cases (30 admitted for Post-Operative stabilisation, 12 participants left against medical advice (LAMA) and 11 died within 8 hours of admission) were excluded from the study.

Finally 225 cases were participants of the study out of which, 181(80.4%) patients recovered and 44(19.6%) died. The association between various study variables and the outcome was analysed and a p value of < 0.05 was considered as statistically significant. Majority of the study population were within the age group of 5 to 10 years. Males outnumbered the female participants in each sub group.(Table 1)

Table 1: Age and gender of the study population

AGE GROUP	MALEn(%)	FEMALEn(%)	Total n (%)
<12 months	33(55.9%)	26(44.1%)	59(100%)
13-60 months	33(73.3%)	12(26.7%)	45 (100%)
61-120 months	59(69.4%)	26(30.6%)	85 (100%)
>120 months	22(61.1%)	14(38.9%)	36(100%)
GRAND TOTAL	147(65.3%)	78(34.6%)	225 (100%)

Male children were the majority 147 (65%) with a survival rate of 76.87%. whereas female patients were 78 (35%) with a survival rate of 87.17%. Though the survival rate was more in female participants there was no statistically significant association between the gender and the outcome (p = 0.064).(Table 2)

Table 2: Association of Demographic Profile with Outcome

Demographic profile		Total n (%) number	Recovery n (%)	Death n(%)	P value
Sex	Males	147(100%)	113(76.87%)	34(23.12%)	0.064
Age	<12 months	59	51	8	0.287
	13-60months	45	34	11	
	61-120months months	85	70	15	
	>120 months	36	26	10	

(Std.Error-3.407, df=3, x^2-3.776)

TABLE 3: ASSOCIATION OF SOCIOECONOMIC STATUS WITH MORTALITY

Out of total 44 deaths, 29(32.2%) belonged to the group with lower socio-economic status and the association between socio-economic status and PRISM score was statistically significant (p value-0.001)(Table 3).

SOCIOECONOMIC STATUS	TOTAL n (%)	RECOVERY n (%)	DEATH n (%)	P-Value
Upper	25(100%)	24(96%)	1(4%)	0.001
Middle	110(100%)	96 (87.2%)	14(12.7%)	
Lower	90(100%)	61(67.8%)	29(32.2%)	
Grand Total	225(100%)	181(80.4%)	44(19.8%)	

(X^2= 16.285, df=2)

The causes of illness were grouped as per the primary system involved. Respiratory system (n = 89) constituted the major cause of illness at the time admission, followed by CNS (n = 45), Infections (n = 22), GI (4). The others included CVS (n = 7), Haematological (n = 20), Renal (n = 11) and others (n = 27). The survival rate of patients with major causes of illness like Respiratory disorders was 92.13%, CNS 84.44%, CVS was 100%, and Infectious diseases were 90.90%. Higher mortality was seen in diseases involving GI, Renal and Haematological system i.e. 75 %, 72.7% and 60% respectively. The cause of illness showed significant correlation with the outcome (p = 0.001).(Table 4)

Table-4: Association of Cause of Illness with Outcome

CAUSE OF ILLNESS	TOTAL NUMBER n (%)	RECOVERY n (%)	DEATH n (%)	P-Value
RESPIRATORY	89(100%)	82(92.13%)	7(7.86)	0.001
CNS	45(100%)	38(84.44%)	7(15.5%)	
INFECTIOUS	22(100%)	20(90.90%)	2(10.10%)	
GI	4(100%)	1(25%)	3(75%)	
HEMATOGICAL	20(100%)	8(40%)	12(60%)	
CVS	7(100%)	7(100%)	0	
RENAL	11(100%)	3(27.27%)	8(72.72%)	
OTHERS	27(100%)	22(81.48%)	5(18.51%)	
TOTAL	225(100%)	181(80.45%)	44(19.55%)	

(X^2=59.823, df=7)

There was 50% recovery and 50% death in the cases who received mechanical ventilation and the cases which didn't need mechanical ventilation had a good recovery rate of 98%.The association was statistically significant (p value-0.001).(Table 5)

TABLE 5: ASSOCIATION OF MECHANICAL VENTILATION WITH OUTCOME:

MECHANICAL VENTILATION	TOTAL n (%)	RECOVERY n n(%)	DEATH n(%)	P-Value
Needed	82(100%)	41(50%)	41(50%)	0.001
Not Needed	143(100%)	140(98%)	3 (2%)	
Grand Total	225(100%)	181(80.4%)	44(19.5)	

(X^2= 76.017, df=1)

The table -6 shows that highest mortality rate (38.9%) was observed in the cases that received total parenteral nutrition (TPN) while the cases which did not receive TPN had an excellent recovery rate of 87.3%.TPN had significant association with mortality (p-value-0.001)

TABLE 6: ASSOCIATION OF TPN WITH MORTALITY

TPN	TOTAL n (%)	RECOVERY	DEATH	P- Value
Given	59 (100%)	51 (86.44%)	8(13.56%)	0.001
Not Given	166 (100%)	118 (71.08%)	48(28.91%)	
Grand Total	225(100%)	169(75.11%)	56(24.89%)	

Table 7 shows that cases that received ionotropic support had significant mortality rate of 40.77% (n=42) while the patients who did not require ionotropic support had a mortality of 1.63% which was statistically significant (p value=0.001)

TABLE 7: ASSOCIATION OF IONOTROPIC SUPPORT WITH MORTALITY

IONOTROPIC SUPPORT	TOTAL n(%)	RECOVERY n(%)	DEATH n(%)	P-Value
Given	103 (100%)	61(59.2%)	42(40.77%)	0.001
Not Given	122 (100%)	120(98.3%)	2(1.63%)	
Grand Total	225(100%)	181(80.4%)	44(19.6%)	

The mean duration of PICU stay was 5.74 ± 0.198 days .The association between the duration of PICU stay with the mortality showed that as the duration of stay increased, there was significant increase in mortality. Patients with length of stay >10 days had a death rate of 64.2% whereas those with duration <5 days had only 2.4% mortality and a recovery rate of 97.6. and the association was statistically significant p-value (0.001).

TABLE 8: ASSOCIATION OF DURATION OF PICU STAY WITH MORTALITY

DURATION OF PICU STAY	TOTAL n (%)	RECOVERY n(%)	DEATH n(%)	P-Value
<5 DAYS	128 (100%)	125(97.6%)	3(2.4%)	0.001
6-10DAYS	83(100%)	51(61.44%)	32(38.55%)	
>10 DAYS	14 (100%)	5(35.71%)	9(64.2%)	
Grand Total	225(100%)	181(80.45%)	44(19.55%)	

Complications arising from both TPN & enteral nutrition were analysed & it was found that the percentage rate of complications like hypoglycaemia (3 vs 7), hyponatremia(31.7 vs 38.3), hypokalemia(30.2 vs 40.6) and hyperphosphatemia (3.7 vs 0.9) was significantly lesser in case of TPN compared to enteral nutrition.Significant number of patients developed sepsis following TPN is a matter of concern for this group(Table9).

Table 9: Complications of Parenteral & Enteral Nutrition.

COMPLICATIONS	PARENTERAL NUTRITION{%}	ENTERAL NUTRITION{%}
Hypoglycaemia	3	7
Hypokalemia	30.2	40.6
Hyperkalemia	23	8
Hyponatremia	31.7	38.3
Hypocalcemia	24	2
Hypertriglyceridemia	32.3	14.2
Hypoalbuminemia	13.5	18.1
Cholestasis	16.8	1
Hyperglycemia	23.6	9
Thrombocytopenia	28.5	2
Hypermagnesemia	7.8	0.2
Hypophosphatemia	6.9	0.7
Hyperphosphetemia	3.7	0.9
Hypercholesterolemia	13.9	4.3
Sepsis	10.3	

No significant difference was noted in few variables like duration of PICU stay,weight gain,Neutrophil count,Lymphocyte count & serum albumin level in both the study groups as depicted in table no 10.

Table 10: Comparison of some variables in Parenteral & Enteral Nutrition.

VARIABLE	TPN	ENTERAL NUTRITION	P-VALUE
Duration of PICU stay	9±5.5 days	12±7.5 days	0.47
Weight (entry& exit)	p=0.75	p=0.82	0.53
Neutrophil (entry& exit)	p=0.45	P=0.58	0.2
Lymphocyte(entry& exit)	p=0.41	p=0.33	0.34
Hypoalbuminaemia	64 % vs 35%	77% vs 62%	0.46

DISCUSSION:

The benefits of EN include: reduction of gut atrophy. Improvement of gut motility, reduction in infections (enhanced gut immune function and avoidance of translocation), cost effectiveness and the fact that it is less likely to overfeed the patient. The limitations of PN include that it is more likely to underfeed the patient.

Contraindications to enteral feeding include: a nonfunctional gut, anatomical disruption, obstruction, ischemia, peritonitis and severe shock states; frequent interruptions for fasting for diagnostic and other procedures limit efficacy of EN, especially in malnourished patients and the risk of aspiration.[23]If enteral nutrition is not possible within 4-5 days in children,parenteral nutrition must be started.[23] As per the ASPEN Guidelines,the indications of parenteral nutrition are-Inability to tolerate feeds for 4-5 days in children,small bowel obstruction,hemodynamic instability with a high risk of mesenteric ischemia & conditions associated with intestinal failure.[23]

In the present study done over a period of 1year, out of 225 participants 181(80.4%) cases recovered and got discharged and 44 (19.6%) cases died, this is similar to other studies by Singhal.D et al [7]and K.Ali et al [20] where the mortality was 18% and 21.2% respectively. However a study by Ahmed El Nawawy [22]in Egypt showed a high death rate of 50.49% .The outcome of an intensive care unit depends on the patient profile, the available services the lag period in admission to ICU and prompt initiation of treatment.As shown in the table no -1 the gender distribution showed 147(65.3%) were males and 78 (34.6%) were females. Males outnumbered females in each age category .Maximum number of patients belonged to category of 60 months to 120 months. The age of the patients was in the range of 1month to 168 months.As shown in the table no - 2 mean age of the study population was 68.37months (± 6.80m 95%CI) .The mean age of patient who survived 66.20 months (± 7.40m 95% CI) and who died is 77.30months (± 16.20m 95% CI). The age and gender distribution of the study population has no significant association with the outcome. This is in agreement with other Indian study by Mehta J S et al[40], and Singhal D et al.[7] The mean age of the study population is different from that of the original study by Pollack et al[8] where they had a mean age of 33 months. As shown in the table no 3 patients belonging to lower socio-economic status had a significantly higher mortality rate with p value <0.05 which can be explained in terms of poor nutritional condition and delay in initiation of medical help .As depicted in table no-4, majority of patients were admitted for respiratory illness number -89 (39.5%) followed by Central nervous system diseases number 45 (20%) and infectious 22 (9.7%) cases like septicemia .The cause of illness has a significant association with mortality (P = 0.001).Though maximum cases were with respiratory illness but there was good recovery rate in them (92.13%). Patients admitted for Gastro intestinal illness had maximum mortality 3 out of 4 cases died. This may be explained as out of 4 cases with Gastro intestinal diseases, 3 cases were hepatic failure with encephalopathy. Patients with hematological conditions also had high mortality rate of (60%).As shown in table 5, mechanical ventilation has a statistically significant correlation with mortality. As observed by 50% mortality in the group which needed mechanical ventilation (P = <0.001), which is in agreement with the study by Mukhtar et al[10] .This can be explained in terms of complications and nosocomial infections in patients requiring mechanical ventilation. As described in table no 6, the need of TPN also had significant reduced mortality (P = 0.001as compared to enteral group which had significantly higher mortality rate. This is similar to study conducted by Daza et al [20].As described in table no 7,the need of ionotropic support also had significant association with mortality (P = 0.001), this is suggestive of more hemodynamic instability which had significantly higher mortality rate. This is similar to other study by Mukhtar et al[10] As depicted in the table no 8, the duration of PICU stay also had a significant association with mortality, (60.4%) mortality with PICU stay of more than 10 days. This is in agreement with study by Nawawy et al[9] Graziela et al[7] .The appropriate time to start total parenteral supplementation in pediatric critical patients is not clear, it is better not to start early. Nutritional status at admission and severity of the disease are mainly responsible for energy expenditure during PICU stay, so variables need to be accurately analysed in each patient. When malnutrition is detected at admission, early TPN may be reasonable, particularly if it is estimated that the patient cannot achieve 60% of caloric requirement with EN. In the other cases, exclusive EN may be advocated in the first few days, with the possibility of initiating PN at seven days if nutritional requirements cannot be achieved or if patient evolution is not optimal. Enteral and parenteral nutritional intakes should therefore be assessed in each case and the prior nutritional status probably makes all the difference.

CONCLUSION

The present study was done in a tertiary care referral hospital to evaluate the complications & outcome of patients between those requiring TPN against those not requiring it in a pediatric intensive care unit. A total of 225 cases were studied and analyzed. The overall mortality was 19.6%. Our study demonstrated that, nutritional intervention in the form of TPN has many advantages like low mortality, minimal morbidity, better weight gain,lesser metabolic abnormalities & reduced PICU stay. So, early intervention by administration of TPN in recommended cases should be practiced in PICU to prevent morbidity & mortality as mentioned above. Nevertheless, it is also important to have a nutritional support team to counter these issues .However, few TPN related complications like Sepsis should be addressed judiciously.

Conflict of Interest

The authors report no conflicts of interest.

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