

NEONATAL NECROTIZING ENTEROCOLITIS: CLINICAL DATA AND TREATMENT POSSIBILITIES

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ABSTRACT

Objectives. The aim of this paper is to identify the correlations between the clinical evolution of the neonates with necrotizing enterocolitis (NEC) and the stage of disease, associated risk factors and the type of treatment used.

Material and methods. A 6 years retrospective study was performed based on reviewing the casuistry of the Regional Centre of Neonatal Intensive Care Unit (NICU) „Cuza Voda” and 205 cases of necrotizing enterocolitis were identified from a total number of 6183 neonates admitted there.

Patients were divided in to study groups based on the gestational age (GA) and birth weight (BW). The analysis protocol was realized based on a working sheet that included the epidemiological data of the patients, the risk factors, type of nutrition, age at diagnosis, stage of disease according to Bell classification, type of treatment (medical, surgical or combined), complications and the general evolution.

The statistical data processing was performed in SPSS Statistics 20 program.

Results. NEC had a frequency of 3.3% in the study group and was diagnosed in premature newborns in 75.6% of cases. The mean GA for the study group was 33 weeks. The mean BW was 1896 g with 43% of the cases in very low birth weight (VLBW) group and 31.2% in low birth weight (LBW) group. The percentage incidence of the risk factors was as follows: persistence of ductus arteriosus 19.5%, perinatal asphyxia 13.7% and respiratory distress 100% of cases. 75.5% were treated and discharged from NICU, 16.6% were transferred to Pediatric Surgery Department „Sf. Maria” and 3.9% died in NICU. From the 34 cases transferred 19 cases were surgically treated: 8 cases with peritoneal drainage (PD), 8 cases with primary laparotomy (LAP) and 3 cases with PD and LAP. The survival rate in this group was 2.4% and for the medically treated group was 4.9%.

Conclusions. Prematurity is statistically correlated with encountering advanced stages of enterocolitis at the time of diagnosis. The option for surgical treatment (peritoneal drainage or laparotomy) does not influence the results and early enteral feeding with formula is the most important risk factor for NEC followed by age of gestation and very low birth weight.

Keywords: necrotizing enterocolitis, newborn, treatment possibilities

Abbreviations:

NEC: necrotizing enterocolitis

LBW: low birth weight

VLBW: very low birth weight

MSOF: multiple syndrome organ failure

PD: peritoneal drainage

LAP: laparotomy

BW: birth weight

GA: gestational age

TPN: total parenteral nutrition

SNAP: score for neonatal acute physiology

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INTRODUCTION

Necrotizing enterocolitis (NEC) represents the most frequent cause of acute abdomen in premature neonate. In 90% of cases it appears in premature newborns especially in association with low (LBW) and very low birth weight (VLBW) and only 10% of cases are appearing in term newborns in association with congenital anomalies, sepsis or mesenteric hypo-perfusion (1). A particular form of NEC is encountered in cases of congenital megacolon with debut in the neonatal period.

The disease is characterized by different degrees of intestinal necrosis that can progress into syndrome of multiple organ failure (MSOF). Causes and mechanisms of affecting the bowel are represented by early enteral nutrition with adapted milk formulas, prematurity, immunological immaturity of the bowel and abnormal bacterial colonization (1,2). The clinical manifestations of NEC appear typically in week 2-3 of life and are represented by feeding intolerance, stools with blood and/or abdominal distension. Cases with rapid progressive NEC are represented with clinical signs of sepsis or MSOF. The therapeutic possibilities in NEC include medical treatment: antibiotics, cessation of enteral feeding, ventilator and volemic support, analgesics and probiotic administration. Cases in which a failure of the medical treatment is encountered are benefiting from surgical treatment consisting of percutaneous peritoneal drainage (PD) and/or open laparotomy (LAP) with resection of the necrotic bowel (3).

The aim of this paper is to identify the correlations between the clinical evolution of NEC and the stage of disease, associated risk factors and the therapeutic management of neonates diagnosed in the Regional Centre of Neonatal Intensive Care Unit “CuzaVoda”.

MATERIAL AND METHODS

A retrospective 6 years study was performed (01.01.2008-31.12.2013) based on reviewing the casuistry of the Regional Centre of Neonatal Intensive Care Unit (NICU) „Cuza Voda” and 205 cases of necrotizing enterocolitis were identified from a total number of 6183 neonates admitted there.

Patients were divided in to study groups based on the gestational age (GA) and birth weight (BW). The analysis protocol was realized based on a working sheet that included the epidemiological data of the patients (sex, place and type of birth) the risk factors (maternal and/or newborns factors), type of nutrition at the onset of symptoms, age at diagnosis and stage of disease according to Bell classification, type of treatment (medical, surgical or combined), complications related to surgical treatment and the general evolution.

The statistical data processing was performed in SPSS Statistics 20 program.

RESULTS

A number of 155 cases of NEC were identified in premature newborns (75.6%) respectively 50 cases (24.4%) in term newborns. The general incidence of NEC was 3.3% – 205 cases from a total number of 6183 neonates admitted in Regional Neonatal Centre “CuzaVoda”. The GA ranged between 24-41 weeks with a mean GA of 33 weeks. The mean BW in the study group was 1896g (limits between 550 to 4600g). For the premature groups of newborns the distribution was as follows: VLBW 43% of cases, LBW 31.2% of cases and the rest encountered in newborns with BW > 2500 g. The incidence of risk factors encountered was: persistence of ductus arteriosus in 40 cases (19.5%), perinatal asphyxia in 28 cases (13.7%) and respiratory distress of different degrees that was encountered in all cases of NEC (100%).

Distribution in the study group according to Bell classification was: 70.7% of newborns diagnosed in Bell stage I, 23.9% in Bell stage II and only 5% in stage III (Table 1).

TABLE 1. Distribution of NEC

Total cases of NEC	Stage I BELL	Stage II BELL	Stage III BELL
205	70.7%	23.9%	5.0%

A negative correlation between the GA and advanced stages of disease was identified, prematurity being correlated statistically with stage II and III Bell ($F=17.89$, $p<<0.01$, 95% CI) – Fig. 1.

Age of patients at diagnosis ranged between 1 day and 54 days with a mean age of 8.2 days for stage I, 11.1 days for stage II and 14.3 days for stage III. The type of nutrition of the premature patients was as follows: 39.4% total parenteral nutrition (TPN) at the time of symptoms onset, 31% parenteral nutrition in association with formula

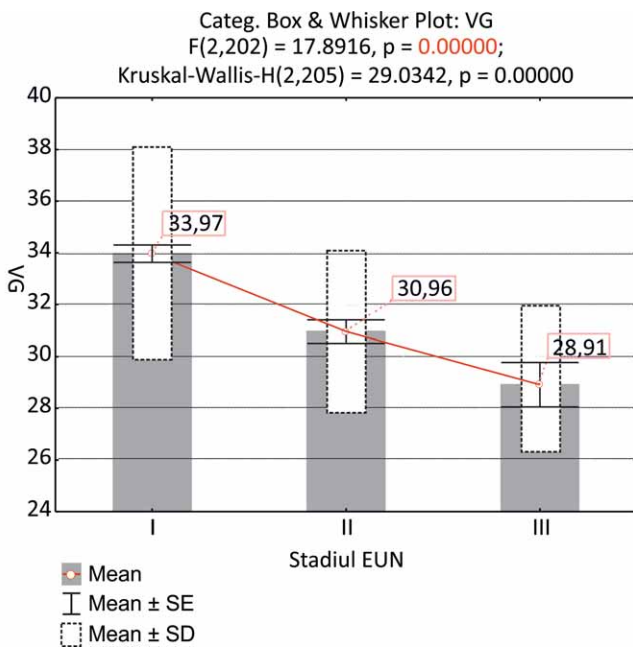


FIGURE 1. Mean GA vs. Stages of NEC

milk enteral feeding, 8.4% enteral feeding with formula, 18.7% parenteral nutrition in association with enteral feeding with human milk and only 2.5% were exclusively on enteral feeding with human milk. In correlation with type of nutrition there is a statistically significant correlation between TPN and the onset of advanced stages of NEC and nutrition with human milk is a protective factor with no cases of stage III, Fig. 2.

The evolution in the study group was as follows: 75.5% were successfully treated and discharged from NICU “Cuza Voda”, 16.6% were transferred to Pediatric Surgery Department “Sf Maria” and 3.9% deceased in NICU “Cuza Voda”. From the pediatric surgery transferred group of 34 cases only in 19 cases a surgical intervention was performed. There were 8 cases treated by peritoneal drainage (PD), 8 cases of laparotomy (LAP) with resection

of the necrotic bowel and creating an enterostomy and 3 cases of PD followed by LAP. In the surgically treated group of patients the survival rate was 2.4% (5 cases) with a mortality rate of 6.8% (14 cases). In the pediatric surgery transferred group of patients 15 (7.3%) were medically treated. The survival rate was 4.9% in this group (10 cases) and the mortality rate was 2.4% (5 cases).

In correlation with Bell staging criteria from the total number of stage III Bell cases, 9.1% were treated and discharged from NICU and 27.3% deceased. For the stage II Bell, the total number of NICU discharged cases was 67.4% and 10.2% deceased.

From the pediatric surgery transferred group with Bell III stage of disease 27.3% were successfully treated and discharged and 36.4% deceased. For the stage II Bell patients 8.2% were discharged from pediatric surgery department and 14.3% deceased, Fig. 3.

In the surgically treated group we noted an equal number of patients (8 cases) with PD and with LAP and a mortality of 6, respectively 7 cases. 3 patients required more than 1 surgical intervention, PD followed by LAP. From these 3, 2 survived and 1 died. The complications encountered in patients treated in the pediatric surgery department include surgical complications such as postoperative evisceration (1 case), short bowel syndrome (1 case), ileal stenosis (2 cases) and general complications related to NEC progression or prematurity.

The mean age of patients at the time of surgical intervention for the survival group was 23.2 days, respectively 35.4 days for the surgically treated patients that have died.

Statistical analysis of the data in the study group indicates that the most important risk factor for NEC is enteral nutrition with formula followed by prematurity and VLBW.

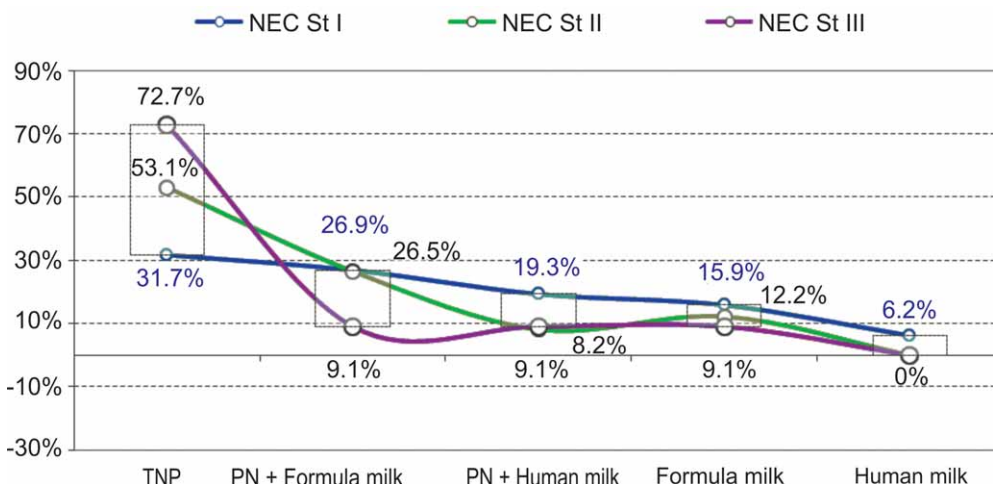


FIGURE 2. Type of feeding vs. Stage of NEC

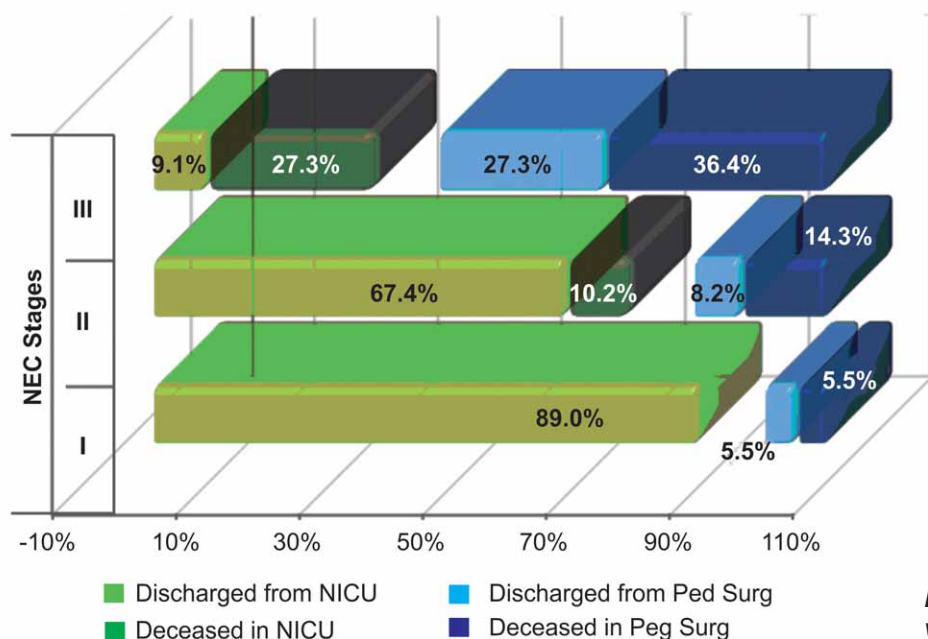


FIGURE 3. Evolution of newborns vs. Stages of NEC

DISCUSSION

The surgical management for NEC patients was individualized in correlation with patient weight at the time of diagnosis.

For the neonates weighting 1.500 g the surgical approach was LAP with resection of the necrotic bowel. The aim was to remove the necrotic tissue and/or the contaminated intraperitoneal fluid and to preserve the viable bowel with stoma formation avoiding extensive resections in order to prevent the short bowel syndrome (4,5). There were no cases with intestinal resection followed by primary anastomosis and for cases with multiple areas of necrosis multiple enterostomy were not used. The surgical options mentioned in literature of “patch, drain and wait” or “clip and drop back” have not been used in this study group (5,6,7).

The surgical options recommended for the neonates weighting 1.500 g are: percutaneous PD for the clinically instable patients and ”salvage” LAP after a period of maximal support therapy (4,6,7). The peritoneal drainage was used in 8 cases as a singular method of treatment in unstable patients and 6 patients has died. In 3 cases PD was used as a temporary stabilization method and it was followed by LAP. For this small group of patients in 2 cases the outcome was favorable and 1 patient died. The initial PD has reduced the intra-abdominal pressure with the drainage of the bowel perforation and permitted the stabilization of the neonate. The results obtained in the study group confirm the fact that there are no statistically significant differences

between the 2 method of surgical treatment (PD and LAP) in premature neonates with LBW. In the group of patients in which PD was used as a temporary method before open LAP the results were better even this patients had more surgical interventions. The results in the study group are similar with results published in the literature regarding the comparison between postoperative results following PD or LAP in children with LBW (6,7,8).

The discussion is about the right timing of a LAP after a PD and establishing some criteria for quantification of deterioration of the clinical status of these patients (9).

In the study group the appreciation of this deterioration was done based on calculation of modified SNAP score in correlation with: increasing of inotrope requirements, aggravation of ventilator support parameters, decreasing of urine output, appearance or aggravation of pneumoperitoneum, increased abdominal distension and the presence of a palpable abdominal mass (10).

The absolute indications for surgical treatment in the study group were: deterioration of clinical status despite maximal medical treatment and pneumoperitoneum. The relative indications for surgical intervention were: presence of a fixe bowel loop on x-ray, abdominal palpable mass, abdominal wall erythema and thrombocytopenia. The results showed in the study group certify the fact that necrotizing enterocolitis is a disease that is characteristic for the premature newborns with a significant morbidity and mortality especially in the presence of associated risk factors. For the treatment of this

disease none of the surgical methods available (peritoneal drainage, laparotomy with enterostomy) has proven its superiority. For patients in the first stages of disease developing of new early methods of diagnosis with identification of biochemical markers to measure in dynamics could lead these patients out of the indication for surgical treatment with a significant improvement of survival. On the other hand, using strategies of prevention such as enteral feeding with human milk could represent a major improvement from the actual results to a more efficient management of NEC.

CONCLUSIONS

The correct management of NEC involves a prompt diagnosis with collaboration between neo-

natology and pediatric surgeon especially in the presence of risk factors such as prematurity, LBW and VLBW, TPN or respiratory distress.

Regardless of the therapeutic possibilities, the variables that are influencing the postoperative results are: BW, stage of disease at the time of diagnosis and age at surgical intervention. The type of surgical intervention (LAP or PD) does not affect the postoperative result and in this condition the surgical option remain controversial. We conclude that PD can be chosen only for the unstable patients as a short temporary method until a definitive procedure of LAP can be performed (9,11).

Early enteral feeding with human milk can be a strategy of prevention for “at risk” neonate.

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