09.01.2025

The effect of umbilical vein catheterization on splanchnic oxygenation in preterm infants weighing 1000-2000 g: a prospective cohort study

Non-ACT (Not interventional)

1. METHODS

1.1.Study design

This study is a single-center, prospective, observational cohort study conducted at a university hospital between February 9, 2023, and February 1, 2024. This study was conducted in conformity with the principles and regulations of the Helsinki Declaration and it was approved by the Institutional Ethics Committee with decision number 58, dated 09.02.2023. Informed consent was obtained from the parents prior to inclusion in the study.

1.2. Patient Enrollment and Group Formation

The inclusion criteria were as follows: (1) parents agreed to participate in the study (2) infants born in our hospital, who were followed up in the NICU, with a gestational age of <34 weeks and a birth weight of 1000-2000 grams. Infants who indicated UVC placement, and for whom NIRS measurements were taken both before and after UVC placement were included in the UVC (+) Study Group. Infants who did not have a UVC but matched the Study Group regarding gestational age and birth weight constituted the UVC (-) Control Group.

Infants who died during the first week of life, were transferred to another hospital, had chromosomal anomalies, major congenital anomalies affecting splanchnic bed monitoring (such as congenital heart disease, abdominal wall defects, or congenital diaphragmatic hernia), inherited metabolic disorders, hydrops fetalis, TORCH infections, multiple organ failure, spontaneous intestinal perforation, lesions in the area where the NIRS sensor was placed, or

whose UVC was removed for any reason before 24 hours, as well as those with severe anemia or polycythemia, were excluded from the study. Infants with a birth hemoglobin (Hb) level of 10 g/dl or below were considered severely anemic, and those with a Hb level of 22 g/dl or above were considered polycythemic.

1.3.Nutritional protocol and procedures

Breast milk was the first option, according to our NICU enteral nutrition policy, and preterm infant formula was the second option if there was no or insufficient maternal breast milk. On the first day of life (DOL), minimal enteral nutrition was started at volumes of 10–20 ml/kg/day in infants under 1500 g and 21–40 ml/kg/day in infants over 1500 g. If achievable, the enteral nutrition volume was increased by 10–15 ml/kg/day until it reached 150–180 ml/kg/day. Orogastric feeding tubes were used to provide enteral nutrition. Very low birth weight (VLBW) infants and those for whom enteral feeding was insufficient to achieve an energy supply of 120–150 kcal/kg/day had total parenteral nutrition started on the first day of life in accordance with nursery protocol. All infants were fed in accordance with our institution’s NICU nutritional protocol.

1.4.Umbilical Venous Catheter Placement, Use, and Removal

In our NICU, UVC placement is a sterile bedside procedure carried out by pediatric residents, neonatology fellows, and neonatology specialists, using polyurethane, single-lumen catheters sized according to the infant's weight: 3.5 Fr for those under 1500 g and 5 Fr for those over 1500 g. Catheter placement is performed using the Modified Shukla-Ferrara Formula. The position of the catheters is confirmed with chest and/or abdominal radiographs before they are secured. Fluids and medications administered through the catheter are prepared under sterile conditions, and unfractionated heparin at a concentration of 0.5 IU/ml is added to intravenous

fluids and parenteral nutrition solutions. The recommended maximum duration of catheter use in our unit is 7-10 days for UVC.

During follow-up, any catheter malposition, and the postnatal day on which it occurred, if applicable, were recorded. Malposition was defined as follows: The optimal placement of the UVC is at the junction of the inferior vena cava and the right atrium. This area corresponds to the T9-10 level on an anteroposterior chest film (8). In preterm infants, even a difference of one vertebral level on a direct radiograph can be significant. Therefore, in addition to thoracic vertebral levels, the level of the right hemidiaphragm can also be used as a reference point for the catheter tip on direct radiographs. Catheters positioned further intracardially or at a lower level are considered malpositioned (9).

2.5. Data collection

(a) Demographics and clinical data: Maternal obstetric diseases (hypertension, diabetes, premature membrane rupture, chorioamnionitis), and prenatal steroid administration were all included in the prenatal data. The following natal data were recorded: gestational age (GA), gender, birth weight, presence of small for gestational age (SGA), mode of delivery, 5th minute Apgar score, and need for resuscitation at birth, cord blood gas parameters (pH, HCO3, BE, lactate) and initial hemoglobin value. Gestational age was determined by asking about the last menstrual period and performing an ultrasonographic examination. According to Fenton et al. (7), SGA is defined as a birth weight less than the 10th percentile. Nutritional measurements including the time to first feeding, initial feeding type (breast milk, formula or mixed), time to reach full enteral feeding (FEF:120 ml/kg/day), and the presence of delayed passage of the first meconium (> 48 h) were recorded.

Clinical gastrointestinal and/or radiological findings observed during hospitalization were noted as vomiting, gastric residue (residual gastric volume exceeding 50% of the previous

feeding volume), abdominal distension, prominent bowel loops, occult or overt blood in the stool, bowel dilation, pneumatosis intestinalis, portal venous gas, and the presence of pneumoperitoneumin the abdominal radiography. These findings were evaluated both between the groups and within the UVC (+) group, comparing the periods when the catheter was in place and after its removal.

Postnatal morbidities such as respiratory distress syndrome (RDS), hemodynamic significant patent ductus arteriosus (HsPDA), grade 2-3 intraventricular hemorrhage (IVH), FI, NEC, and sepsis were noted. Gastric residual volume of more than 50% of the previous feeding volume, emesis, abdominal distention, or both, and a reduction, delay, or cessation of enteral feedings were the criteria used to define feeding intolerance (8). According to the modified Bell's criteria (9), stage II/III NEC was used as an outcome parameter. Echocardiography was used to determine the presence of HsPDA. Positive blood culture was used to define proven sepsis. The Papile classification system was used to classify IVH (10). Furthermore, the need for inotropic support during the first week of life, parenteral nutrition durations, invasive/non-invasive mechanical ventilation support, total respiratory support, oxygen support, hospitalization, and mortality were recorded.

(b) **Splanchnic near-infrared spectroscopy (NIRS) monitoring**: As soon as the infants were admitted to the NICU on the first day of life (DOL), a self-adhesive transducer (cerebral/somatic-neonatal NIRSensor) with a light-emitting diode and two remote sensors was applied to the infra-umbilical abdominal region to continuously record regional splanchnic saturation (rSO_2S). Continuous rSO_2S monitoring was carried out for 1 week using NIRS (INVOS 5100; Covidien Somanetics, Troy, MI), simultaneously together with continuous preductal oxygen arterial saturation (SaO_2) monitoring using a pulse oximetry device (Nellcor, Covidien-Medtronic, Minneapolis, MN) with a target band of 90–95% and alarm settings of 89 and 96% in the case of oxygen therapy. Based on the simultaneous measurements of rSO_2S and

SaO_2, the infants' fractional tissue oxygen extractions (FOE= SaO_2− rSO_2S/ SaO_2), which represent the balance between oxygen delivery and oxygen consumption, were assessed. After removing artifacts that may indicate sensor misplacement, SaO_2 and NIRS parameters (rSO_2S, FOE) were calculated as means on each day of the first week of life (WOL).

Infants with an UVC were included in the UVC (+) Study Group, while those without a catheter were included in the UVC (-) Control Group. Continuous measurements taken during the first WOL were compared both between the groups and within each group on a day-to-day basis. Splanchnic NIRS monitoring was terminated 24 hours after the removal of the UVC. In the UVC (+) Group, the day and time of catheter placement and removal were recorded. Splanchnic oxygenation measurements were compared at the following time intervals: one hour before UVC placement, one hour after UVC placement, 24 hours before UVC removal, and 24 hours after UVC removal. Additionally, the daily means in the UVC (+) Group during the period when the UVC was in place were compared with the daily means in the UVC (-) Group. Clinical parameters and splanchnic NIRS data were compared between the UVC (+) and UVC (-) Groups. The birth hemoglobin (Hb) value of the UVC (+) Group, as well as the Hb value on the day the UVC was removed, were recorded, and a repeated measures analysis was performed.

The primary outcomes included comparing continuously recorded rSO_2S and FOE values during the first WOL between the UVC (+) and UVC (-) groups, assessing rSO_2S and FOE measurements within the UVC (+) Group before and after UVC placement and removal, and determining the impact of UVC on splanchnic oxygenation. The secondary outcomes involve evaluating the relationship between UVC presence and the incidence of feeding intolerance and necrotizing enterocolitis.

1.5. Data analysis

1.5.1. Sample size

A power analysis was performed prior to the study using the summary values from our previous study, 'The Effect of Drip Versus Intermittent Feeding On Splanchnic Oxygenation In Preterm Infants With Intrauterine Growth Restriction: A Prospective Randomized Trial' (6). A sample size of at least 21 infants per group (UVC (+) versus UVC (-) group) was estimated to obtain statistically significant results with a Type-1 error rate of 0.05 (95% confidence level), an effect size of 0.8 (high), and 80% power.

1.5.2. Statistical analysis

The statistical data were analyzed using IBM SPSS 21.0 software (IBM Corp. Released 2012. IBM SPSS Statisticsfor Windows, Version 21.0. Armonk, NY: IBM Corp.). The normality of variable distribution was assessed by Shapiro–Wilk test. The data were presented as a mean±standard deviation (SD), median (Q1–Q3), frequency, and percentage. For comparing normally distributed groups with two groups, the independent samples t-test was used. For comparing non-normally distributed groups with two groups, the Mann-Whitney U test was used. For comparing values at different time points, the Wilcoxon test was used when there were two groups, and the Friedman test was used when there were three or more groups. For repeated measurements, the two-way repeated measures ANOVA (One Factor Repetition) test was used. To determine the direction and magnitude of the relationship (correlation) between variables, Pearson correlation coefficients were calculated for normally distributed variables, and Spearman correlation coefficients were calculated for non-normally distributed variables. For the analysis of cross-tabulations, Pearson Chi-Square, Yates' Chi-Square, and Pearson Exact Chi-Square tests were used. The McNemar-Bowker test was used for comparing categorical clinical findings at two different time points. Covariance analysis was used to assess the importance of the model that had been installed with the confounding factors. A p-value of <0.05 was considered the criterion for statistical significance.