Evaluation of Peripheral Tissue Oxygenation in Preterm Neonates with Normal Transition

Original Article

Hania Abd El Fatah, Asmaa Elmesiry, Doaa El Amrousy and Mostafa Awny

Department of Pediatrics, Faculty of Medicine, Tanta University, Tanta, Egypt

ABSTRACT

Background: Any birth that occurred before the full 37 weeks of pregnancy was considered preterm. Prematurity affected normal transitions which might impact tissue perfusion and oxygenation.

Aim: To evaluate mixed venous oxygen saturation ($ScVO_2$) of inferior vena cava as an indicator of peripheral tissue oxygenation in preterm neonates and to correlate findings with hemodynamics reported by electrical cardiometry in preterm neonates during transition.

Methods: This observational prospective cohort study included 31 preterm neonates less than 34 weeks gestation admitted to a special care unit, neonatal intensive care unit, Tanta University Hospital; only for feeding and growth monitoring. Research investigations on postnatal days 4 and 10 included blood gas obtained from a centrally inserted umbilical venous catheter to measure central venous oxygen saturation from the Inferior Vena Cava ($ScVO_2$). A Bedside Electrical cardiometry study was conducted on the same days.

Results: On day 10, $ScVO_2$ was considerably lower than on day 4 (p=0.002). Day 10 had a considerably increased oxygen delivery (DO_2) than Day 4 (p=0.025). Day 10 had a considerably lower Index of Contractility (ICON) than Day 4 (p=0.014).

Conclusions: Preterm newborns showed improved tissue oxygenation after a successful transition that could predict a good outcome.

Key Words: Inferior vena cava, mixed venous oxygen saturation, peripheral tissue oxygenation, preterm neonates.

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Corresponding Author: Hania Ibrahim Abd El Fatah, Assistant Lecturer at Pediatrics Department, Faculty of Medicine, Tanta University, Tanta, Egypt, **Tel.:** +201093789398, **E-mail**: hanarashed735@gmail.com

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INTRODUCTION

Any birth that occurs before the full 37 weeks of pregnancy is considered preterm. Roughly 11% of births globally are affected [1].

Even though most preterm births happen to women with no known cause, several risk factors could lead to preterm birth, such as maternal diabetes, maternal hypertension, medical procedures like assisted reproduction and provider-initiated delivery, maternal socio-demographics, lifestyle characteristics, and environmental factors [2].

All infants experience respiratory, hemodynamic, and neuroendocrine difficulties as they undergo significant physiological changes as they adjust from fetal to postnatal life. For the preterm newborns, this is harder and harder [3].

Systemic vascular resistance (SVR), blood pressure, regional tissue perfusion and oxygenation, and cardiac output (CO) are significant factors that affect newborn hemodynamic stability [4].

Haemoglobin (Hb) and CO levels should be adequate for proper tissue oxygenation [5]. Tissue oxygen consumption depends on the metabolic activity of tissues. The primary goal is to maintain aerobic cellular respiration and adequate oxygen to meet metabolic demands, so oxygen delivery (DO_2) should be adequate to balance oxygen consumption. The balance between DO_2 and consumption is more important than the absolute value of DO_2.

When tissues' oxygen needs are not satisfied and lactic acid generation rises, an anaerobic process takes over. Cell death and organ failure are the outcomes if this illness continues [4].

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Electrical cardiometry (EC) monitors use four standard electrocardiogram (ECG) leads to calculate stroke volume (SV) based on changes in the electrical resistance of aortic blood flow during the cardiac cycle [6].

EC may evaluate the following parameters: SV, heart rate (HR), CO, cardiac index (CI), SVR, index of contractility (ICON) and its variation (VIC), corrected flow time (FTC), and total thoracic fluid capacity (TFC) [7].

We hypothesized that mixed venous oxygen saturation ($ScVO_2$) of the inferior vena cava was an indicator of peripheral tissue oxygenation and correlated findings with hemodynamics reported by electrical cardiometry (EC) in preterm neonates.

AIM OF THE STUDY

Aim of our study was to evaluate mixed venous oxygen saturation ($ScVO_2$) of the inferior vena cava as an indicator of peripheral tissue oxygenation in preterm neonates and to correlate the findings with hemodynamics parameters detected by EC.

PATIENTS AND METHODS

31 preterm newborns less than 34 weeks of gestation who were admitted to, the Neonatal Intensive Care Unit, Tanta University Hospitals, Tanta, Egypt; were the subjects of this prospective observational cohort research. After receiving clearance from the Ethics Committee (Approval code:36072/11/22) and the date (15/11/2022). The study was conducted from May 2023 to May 2024. The patients' family members gave their signed, informed permission. Inclusion criteria were preterm neonates less than 34 weeks gestation admitted for feeding and growth monitoring.

All included newborns needed neither respiratory nor cardiac support. Preterm newborns with congenital cardiac problems, particularly hemodynamically severe patent ductus arteriosus (PDA), renal failure, congenital infections, and preterm infants with serious congenital abnormalities were excluded.

Complete history taking, physical examination (Downes's scoring[8], anthropometric measurements [9], vital signs, neurological, cardiac, chest, and skin examinations). Routine laboratory tests on day 4 (complete blood count (CBC), C-reactive protein (CRP), liver function tests (LFTs), renal function tests (RFTs), and serum electrolyte level) were all performed for all preterm neonates. To rule out hemodynamically significant patent ductus arteriosus (PDA) and structural congenital heart disorders, echocardiography screening was performed on day 4.

Research investigations in the form of venous blood gases from a centrally inserted umbilical venous catheter were obtained on days 4 and 10 of life to evaluate IVC oxygen saturation ($ScVO_2$). Electrical cardiometry (EC) was performed on days 4 and 10 of life to evaluate hemodynamic status during and after circulatory transition. A pulse oximeter was used to monitor peripheral oxygen saturation (SpO_2).

Mixed venous oxygen saturation

In addition to providing vital information on the equilibrium of oxygen supply and consumption throughout the body, the mixed venous oxygen saturation test shows the oxygen reserve following tissue oxygen extraction. A centrally implanted umbilical venous catheter was used to acquire $ScVO_2$. The proper tip placement is at the intersection of the right atrium (RA) and the IVC. The location of the catheter tip was evaluated using thoraco-abdominal radiography (TAR) and ultrasound [10].

A 2 mL blood sample was taken via the umbilical venous catheter from the IVC and used to acquire $ScVO_2$. The Eschweiler Combiline II Blood Gas Analyzer was used to measure SvO_2 and analyze the VBG sample. 2 ml of blood was withdrawn into a heparinized syringe for blood gases sample after withdrawal of 1-2 ml from the catheter into the dry syringe to clear catheter fluid and blood content, that was reinfused after withdrawal of blood gases sample.

Electrical Cardiometry (ICON®)

The Haemodynamics parameters were measured by Electrical Cardiometry ICON ® Device (ICON Cardiotronics, Inc., La Jolla, CA 92307; Osyka Medical GmbH, Berlin, Germany) on days 4 and 10.

The measured parameters included; systemic vascular resistance (SVR), corrected flow time (FTC), cardiac output (CO), cardiac index (CI), stroke volume (SV), Oxygen delivery (DO_2), arterial Oxygen content (CaO_2) and index of contractility (ICON) [10]. EC itself does not directly measure arterial oxygen (CaO_2) and oxygen delivery (DO_2) it provides cardiac output, which, when combined with haemoglobin levels from a blood test, Arterial oxygen saturation (SaO_2) measured via pulse oximetry or blood gas analysis and PaO_2 from arterial blood gas analysis allows for the calculation of arterial oxygen content and oxygen delivery using these formulas

Arterial oxygen content: $CaO_2 = (Hb \times SaO_2 \times 0.01 \times 1.31) + (PaO_2 \times 0.0225)$[11] and Oxygen delivery=cardiac output× arterial oxygen content ($DO_2 = CO \times CaO_2$) or $DO_2 = CO \times [(1.31 \times Hb \times SaO_2 \times 0.01) + (0.0225 \times PaO_2)]$ [12].

Application of sensors of cardiometry

Continuous measurements were taken continuously for 30 minutes, and the average of the highest and lowest values was recorded while the baby was quiet and supine.

Statistical analysis

The statistical analysis was conducted utilizing the SPSS v26 software (developed by IBM Inc., based in Chicago, Illinois, USA). Quantitative variables were represented by their mean values and standard deviations and were compared by paired T-test. Quantitative non-parametric data were presented as the median and interquartile range (IQR) and were compared by the Wilcoxon test. Qualitative variables were presented as frequency and percentage (%) and were compared by Chi-square test. A two-tailed *P value* of less than 0.05 indicated statistical significance.

RESULTS

Demographic data, anthropometric measures, Maternal risk factors, mode of delivery, APGAR score, and vital signs were enumerated in (Table 1).

Table 1: Demographic data, anthropometric measures, Maternal risk factors, mode of delivery, APGAR score, and vital signs in the studied group.

		(*n* = 31)
Sex	Male	19(61.3%)
	Female	12(38.7%)
GA (w)		32.65±0.49
BW (kg)		1.8±0.5
Length (cm)		41.77±3.31
BSA (m^2)		0.15±0.02
BMI (kg/m^2)		10.12±1.77
Ponderal index (gm/cm^3)		2.42±0.38
MRF		17(54.2%)
Mode of delivery	NVD	5(16.1%)
	CS	26(83.9%)
APGAR score at 5^{th} min		9.0±0.45
Vital signs	HR (b/min)	145.29±9.44
	SBP (mmHg)	88.48±12.69
	DBP (mmHg)	53.39±11.07
	MBP (mmHg)	64.00±10.49
	RR (cycle/min)	38.52±1.59
	Temperature (C)	36.57±0.64

Data is reported as mean ± SD or frequency (%); GA: Gestational Age; BW: Body Weight BSA: body surface area; BMI (Body Mass Index) Maternal risk factors (MRF); normal vaginal delivery (NVD); CS: Caesarean section; HR: Heart rate; SBP is systolic blood pressure; whereas DBP is diastolic blood pressure; MBP: Mean blood pressure; RR: Respiratory rate.

Laboratory investigations were enumerated in (Table 2).

SpO_2, DO_2, and CO were considerably greater on day 10 than on day 4 ($P<0.05$).

Table 2: Laboratory investigations in the studied group.

		(*n*=31)
CBC	HB (gm/dl)	13.75±0.16
	TLC (10^9/l)	8.27 ± 2.57
	PLTS (10^9/l)	265.58 ± 77.99
ALT (U/L)		18.97±10.11
AST (U/L)		42.10±17.52
Albumin (gm/dl)		3.36±0.28
TSB (mg/dl)		5.41±2.19
ISB (mg/dl)		4.89±2.15
DSB (mg/dl)		0.51±0.14
Urea (mg/dl)		23.74±8.59
Creatinine (mg/dl)		0.50±0.21
Na (mmol/L)		137.90±4.72
K (mmol/L)		4.10±0.31
Total Ca (mmol/L)		8.58±0.57
Ionized Ca (mmol/L)		1.07±0.12
CRP		3(9.7%)
PH		7.36±0.06
PCO_2 (mmHg)		30.87±5.84
HCO_3 (mmol/L)		17.57±3.27

The data is shown as mean ± SD or frequency (%); ALT: Alanine aminotransferase; AST: Aspartate aminotransferase. TSB means total serum bilirubin; DB: direct bilirubin; IB: indirect bilirubin; Na is sodium; K is potassium; Ca is calcium; and t is the student t-test; CBC: complete blood count; Hb: hemoglobin; PLT: Platelet count; TLC: Total leukocyte count; CRP: C-reactive protein; PH: Power of hydrogen; PCO_2: partial pressure of carbon dioxide; HCO_3: bicarbonate.

CaO_2, SV, CI, FTC, and SVR did not alter significantly between days 4 and 10. In the group under study, $ScVO_2$ and ICON were considerably lower on day 10 compared to day 4 (*P*=0.04 and <0.001, respectively). (Table 3 and Figure 1).

Table 3: Tissue oxygenation parameters and EC data on days 4 and 10 in the studied group.

		Day 4	Day 10	*P*
Tissue oxygenation parameters	SpO_2 (%)	95.42±1.63	96.26±2.02	0.043*
	$ScVO_2$	80.42±2.98	78.87±3.11	0.04*
EC data	SV (ml)	2.95±0.59	2.97±0.62	0.704
	CO (l/min)	0.44±0.12	0.46±0.12	<0.001*
	CI (l/min/m²)	6.05±9.12	3.05±0.37	0.07
	ICON	114 (108 – 125)	111(102 - 113)	<0.001*
	FTC (ms)	253.06±25.81	252.94±22.92	0.937
	SVR (dyns/cm⁵)	8328.71±2862.25	8917.68±2981.87	0.108
	CaO2 (ml/dl)	16.66±1.07	17.24±1.74	0.112
	DO2 (ml/min)	70.18±11.71	76.96±10.26	<0.001*

Data is presented as mean ± SD or median (IQR); * Significant *P value* < 0.05; SpO_2: Oxygen saturation; CaO_2: Arterial oxygen content; DO_2: Oxygen delivery; SVO_2: Mixed venous oxygen; SV: Stroke volume; CO: Cardiac output; CI: Cardiac index; ICON: Index of contractility; SVR: Systemic vascular resistance; FTC: Corrected flow time; EC: Electrical cardiometry.

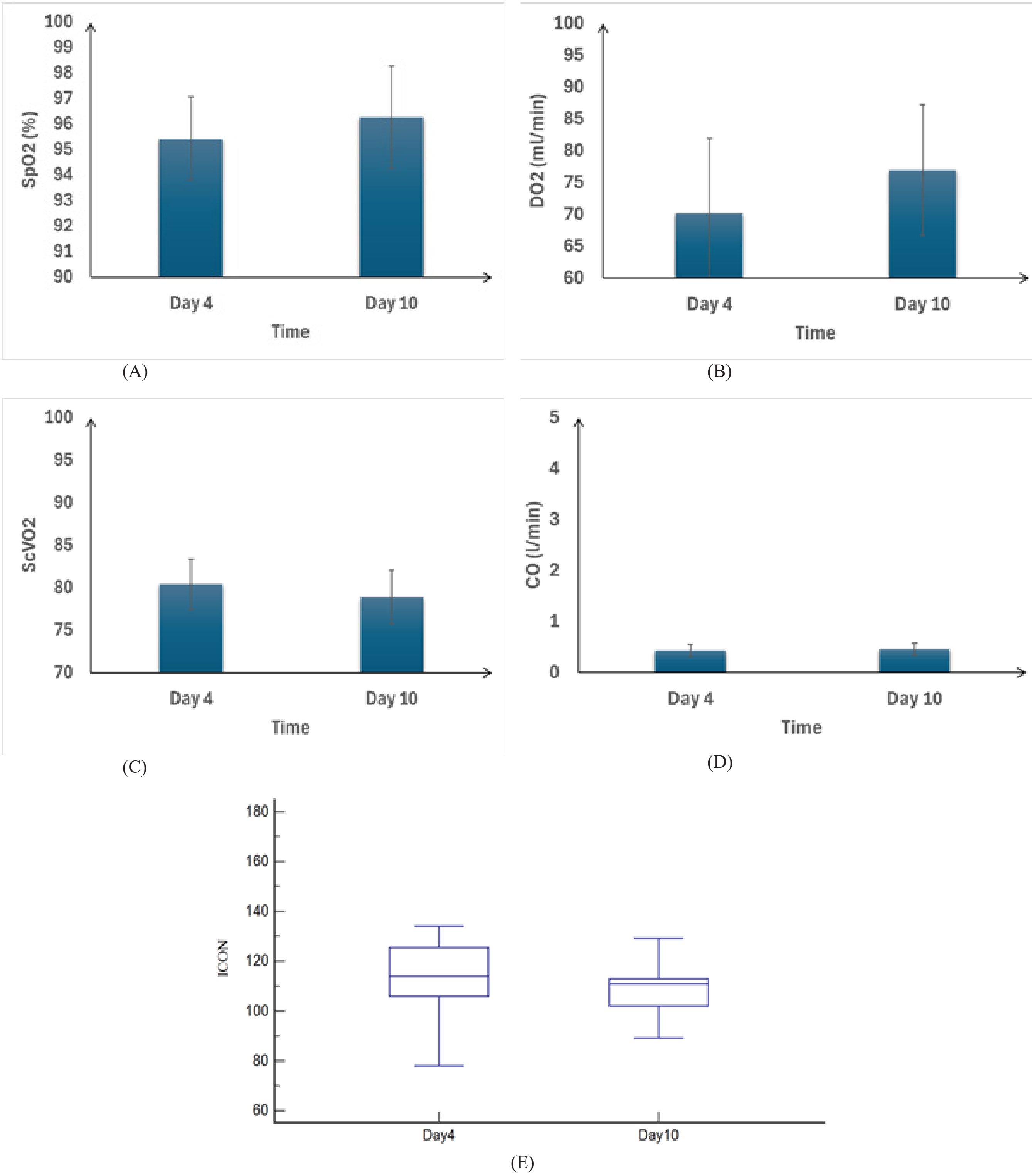

Fig. 1: (A) SpO_2, (B) DO_2, (C) $ScVO_2$, (D) CO, and (E) ICON of the studied patients on day 4 and day 10.

DISCUSSION

The pulmonary cellular structure, thoracic structure and muscle strength mature in the last trimester, and metabolic substances that are important for effective breathing, such as pulmonary surfactant and antioxidant enzymes, are highly reserved in the last trimester [13].

This study aimed to evaluate mixed venous oxygen saturation of the inferior vena cava as an indication of peripheral tissue oxygenation together with hemodynamic status reported by electrical cardiometry.

In the examined group, on day 10, $ScVO_2$ and ICON values were substantially lower than on day 4 (P=0.002 and

P=0.014, respectively), whereas DO_2 was notably higher on day 10 compared to day 4 (P=0.025).

Supporting our results, improvement in DO_2 from Day 4 to Day 10 in Preterm Neonates was due to improvement in cardiovascular function (better cardiac output and tissue perfusion and lower oxygen demands due to more efficient organ systems. ***Saleemi et al*** [13] research was conducted in the newborn intensive care unit at the Rotunda Hospital in Dublin, Ireland, on stable preterm infants following the first 36 hours of life, between the gestational ages of 24 and 35 weeks. Infants with varying gestations who received less than 30 percent oxygen without inotropic support showed improvement in their cardiac systolic and diastolic functions over the first four weeks of life, as measured by TDI.

A decline in systemic vascular resistance (SVR) leads to a reduction in afterload and an enhancement in cardiac output. As a consequence of the increase in cardiac output, a greater amount of DO_2 is delivered to the peripheral tissues, which supports the elevated oxygen consumption and basal metabolic rate [14].

Since SvO_2 was a measure of sufficient DO_2, a change in SvO_2 corresponds to a change in cardiac output, provided that other DO_2 determinants remained constant [13]. Premature and ineffective contractile tissue causes systolic dysfunction in the premature heart's myocardium, whereas a prevalence of stiff fibers and a lack of elastic, compliant tissue cause diastolic dysfunction. Because preterm infants have a faster heart rate, the percentage of time spent in diastole (LV filling) is significantly shorter [13].

In the present study, the examined groups $ScVO_2$ and ICON were considerably lower on day 10 compared to day 4 (P=0.002 and 0.014, respectively). The increase in oxygen extraction was thought to be caused by capillary recruitment, which increased the surface area available for passive oxygen diffusion. In this manner, when oxygen delivery was restricted, the oxygen extraction might be increased from ±30% under normal conditions to 50–60%. In newborns, these compensating systems were crucial. The neonate's growing metabolic needs were the cause of this. It might indicate adaptability as the neonate's organs and cardiovascular system developed throughout the shift from fetal to extrauterine life.

ICON was significantly lower on day 10 compared to day 4 (P = 0.014). ICON was calculated from the maximal rate of change in thoracic electrical impedance. As cardiac contractility increased, the impedance decreased faster, resulting in a larger ICON value. The value of ICON varied between individuals and showed a minor negative association with gestational age (GA), weight, and body surface area (BSA). It had no association with cardiac output (CO) as supported by ***Sumbel et al.*** [15] although it was moderately correlated with cardiac index (CI) [16].

Limitations of the study included that the sample size was relatively small. The study was in a single center. It lacked a healthy control group. It needed multiple operators and Instruments.

Recommendations of the study included that electric cardiometry was a safe, accurate, bedside, and reproducible technique for hemodynamic measurements in newborns. Accurate and continuous assessment of COP was critical in the assessment of the cardiovascular state of infants. Further prospective multicenter studies with larger sample sizes were needed to evaluate tissue oxygenation in preterm neonates and its relation to hypoxic complications. Trials to correlate our study findings with non-invasive tissue perfusion and oxygenation e.g. NIRS should be established.

CONCLUSIONS

Preterm newborns' peripheral tissue oxygenation and hemodynamics go through change during the transitional period with improvement in cardiac muscle contractility, oxygen delivery, and tissue oxygen consumption indicated by $ScVO_2$.

CONFLICT OF INTEREST

No conflict of interest is declared.

AUTHORS' CONTRIBUTION

All contributing authors played a role in the conception and design of the study. Material preparation, data collection, and analysis were carried out by Hania Ibrahim Abd El Fatah, Asmaa Mahmoud Elmesiry, and Doaa Mohamed El Amrousy. The initial draft of the manuscript was composed by Mostafa Mohamed Awny and all contributing authors reviewed and provided feedback on earlier revisions. All authors have reviewed and agreed to the final version of the manuscript.

LIST OF ABBREVIATIONS

$ScvO_2$: Central-venous oxygen saturation

DO_2: Oxygen delivery

ICON: Index of Contractility

SVR: Systemic vascular resistance

CO: Cardiac output

Hb: Hemoglobin

SV: Stroke volume

ECG: Electrocardiogram

HR: Heart rate

FTC: Corrected flow time

CI: Cardiac index

SPO_2: Oxygen saturation

PDA: Patent ductus arteriosus

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تقييم أكسجة الأنسجة المحيطية عند الولدان الخدج ذوي التحول الطبيعي

هانيا عبد الفتاح، أسماء المسيري، دعاء العمروسي و مصطفى عوني
قسم طب الأطفال، كلية الطب، جامعة طنطا، طنطا، مصر

المقدمة: أي ولادة تحدث قبل اكتمال الأسبوع ٣٧ من الحمل تعتبر ولادة مبكرة. وتتأثر حوالي ١١٪ من الولادات على مستوى العالم.

الهدف: تقييم تشبع الأكسجين الوريدي المختلط ($ScPO_2$) في الوريد الأجوف السفلي كمؤشر على أكسجة الأنسجة المحيطية عند الولدان الخدج وربط النتائج مع ديناميكا الدم التي أبلغ عنها قياس القلب الكهربائي.

الطرق: كان ٣١ من حديثي الولادة المبتسرين الذين تقل أعمارهم عن ٣٤ أسبوعًا من الحمل والذين تم إدخالهم إلى المستشفى للحصول على رعاية خاصة هم موضوع هذا البحث الأتراب الرصدي المحتمل. لم يكن أي من الرضع في هذه المجموعة بحاجة إلى مساعدة في الجهاز التنفسي بعد دخولهم إلى وحدة العناية المركزة لحديثي الولادة بمستشفى طنطا الجامعي. شملت التحقيقات البحثية في اليومين ٤ و ١٠ بعد الولادة غازات الدم التي تم الحصول عليها من قسطرة سرية يتم إدخالها مركزيًا لقياس تشبع الأكسجين الوريدي المختلط المركزي من الوريد الأجوف السفلي ($ScVO_2$). تم إجراء دراسة قياس القلب الكهربائي بجانب السرير في نفس الأيام أيضًا.

النتائج: في اليوم ١٠، كان $ScVO_2$ أقل بكثير مما كان عليه في اليوم ٤ (ع = ٠,٠٠٢). كان اليوم العاشر يحتوي على زيادة كبيرة في توصيل الأكسجين (DO_2) مقارنة باليوم الرابع (ع = ٠,٠٢٥). كان لليوم ١٠ مؤشر انقباض (ICON) أقل بكثير من اليوم ٤ (ع = ٠,٠١٤).

الاستنتاجات: يُظهر الأطفال حديثي الولادة المبتسرين تحسنًا في أكسجة الأنسجة بعد التحول الناجح الذي يمكن أن يتنبأ بنتيجة جيدة.