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Original article

Near-infrared spectroscopy in neonatal intensive care unit: do we make our life more difficult?

Paolo Giliberti, Chiara De Leonibus, Giovanni Chello, Daniela Magri, Lucia Giordano, Paolo Montaldo, Massimiliano De Vivo

Neonatal Intensive Care Unit, "V. Monaldi" Hospital (A.O. dei Colli), Naples, Italy

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Learned lessons, changing practice and cutting-edge research

Abstract

The question has been the following: can the regional oxygenation monitoring change our clinical practices in neonatal intensive care?

Fifty newborns of gestational age ≤ 32 weeks were recruited for regional oxygenation continuous monitoring immediately after their admission. Of these newborns 44 showed a patent ductus arteriosus (PDA) with a left to right shunt. In these subjects, a progressive decrease of the renal oxygenation (rSO_2) up to values of 59.6 ± 3.6% and an increase of the renal oxygen extraction fraction (rFTOE) to 50.9 ± 3 were observed during the first hours of monitoring. The cerebral oxygenation (cSO_2) instead, remained relatively constant at 64.5(± 4.2%)-69.7(± 5.6%) with a cerebral oxygen extraction fraction (cFTOE) between 28.6 ± 4.7 and 24.6 ± 6.5.

Renal oxygenation improved in almost all the subjects, except that in three, up to values of rSO_2 of 75(± 1.0%)-82.2(± 4.9) with a rFTOE of 20.1(± 14.8)-13.4(± 3.5) after a three-six hours treatment with dopamine at 5-7.5 μg/kg/min.

These data, together with echodoppler findings, have allowed us to modify our approach to the newborn with PDA and the left-right shunt. It now consists in using dopamine as soon as ductal shunt has been left to right and waiting until the hemodynamic stability persists or until the end of the first week of life prior to consider the closure of the duct by cyclooxygenase inhibitors.

Besides, 42 newborns with a post-natal age ≥ 2 weeks were selected and submitted to a regional oxygenation monitoring once hematocrit had been less than 30%. Sixteen out of 42 newborns showed a decline of rSO_2 to 50 ± 5% and a rFTOE of 45 ± 3, with a cSO_2 of 69 ± 3% and a cFTOE of 23 ± 4. Of the 26 newborns with normal values of regional saturation, 10 showed a decrease of rSO_2 to 50 ± 3 with a rFTOE of 45 ± 3 when the hematocrit fell to 20-22%.

After a packed red cell transfusion, a progressive rise of the rSO_2 to 83.8 ± 9.4 and a decline of the rFTOE to 8.1 ± 3.4 were observed. These changes started at the end of the transfusion and became stable in the following 12-24 hours.

An increase of the cSO_2 to 82.2 ± 2.9 and a decrease of the cFTOE to 12.2 ± 2.90 were observed after the transfusion and after the progressive normalization of the renal oxygenation as well.

On the basis of these results, in our Unit only the newborns with a hematocrit ≤ 30 and clear sinking renal saturation values are transfused.

In the light of the reported observations, we recognize to the regional oxygenation monitoring a precise role in the process of personalization of the newborn cares in intensive contexts.

Despite the requirement for wider observations, the information drawn by the variations of the regional oxygenation in different pathophysiologic processes can substantially help in the prevention of the organ damage, particularly the brain, that upsets still today the results of the neonatal intensive cares.

Keywords

Cerebral and renal hemoglobin saturation, cerebral and renal oxygen extraction fraction, patent ductus arteriosus with left to right shunt, effects of dopamine, "late" anemia, effects of packed red cell transfusion.

Corresponding author

Paolo Giliberti, Neonatal Intensive Care Unit, "V. Monaldi" Hospital (A.O. dei Colli), Naples, Italy, tel.: 0039817064377 Hospital, 00393393593598 mobile; email: paologiliberti45@gmail.com.

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Introduction

The near-infrared spectroscopy (NIRS) to monitor tissue perfusion and oxygenation was introduced for human tissue by Jobsis and colleagues in 1977 [1] and applied to the newborn since 1985. This technology relies on the transparence of human tissue to light in the near-infrared region, on the absorption of the light travelling the tissue by pigmented compounds (chromophores) and on the different light-absorption of compounds, such hemoglobin, pending on its oxygenation status [2]. Despite the different technical approaches of the now available NIRS devices, they all express an absolute value reflecting the mixed oxygen saturation in the arteries (± 25%), capillaries (± 5%) and veins (± 70%). Measuring a mixed value of saturation, the parameter to be considered is the time-trend of the measure itself.

We can, therefore, have important information about the regional oxygenation and its variations in different clinical conditions. What really we have been waiting for, aiming at a tool that allowed us to appraise the hemodynamic variations of an organism in continuous dynamic adaptation, as the newborn is.

Since January 2012 we have been measuring the cerebral and renal oxygenation by NIRS in all newborns admitted to our NICU during the first 72 hours and for longer time, if necessary. We are, therefore, able to bring out our observations under very different conditions and to report on the impact of the method in our clinical practice.

Of all newborns followed by NIRS, we select for this presentation two distinct populations:

A. the newborns of gestational age (GA) ≤ 32 weeks with a PDA;
B. the newborns with a post-natal age ≥ 2 weeks, with a hematocrit ≤ 30%.

Methods

For the measure of the regional saturation, we utilize the Somanetics 5100 Invos device (Covidien), using the CNN/SNN sensors applied over the forehead for cSO_2 and over the right or left posterior lateral flank for rSO_2. Between the sensor and the skin we are used to put a layer of hydrokolloid (ConvaTec. Duoderm extrathin), in order to protect the skin during the long-term monitoring, after a comparative study, that has not shown any interference on the founded values with and without this protection. During the monitoring the oxygen extraction fraction (FTOE) was calculated using the formula SaO_2 - tissue SO_2/SaO_2 at 30-60 minutes intervals. The reference values of the regional saturation of the various organic districts have been established through the comparison of serial measurements in normal newborns with the reported data of the literature

[3-5]. Statistical analysis was performed using IBM SPSS Statistics 20 (IBM Corporation). The mean values of cSO_2, rSO_2, cFTOE, rFTOE and their variations were assessed using the non parametric tests (Wilcoxon signed rank test and ANOVA test) for two related samples. Linear regression analysis was performed to assess the relationship between regional SO_2 and FTOE values after dopamine and blood transfusion. Results are presented as mean ± SD, with significance taken at the $p < 0.05$ level. The values > 0.05 and < 0.001 were not reported.

Results

Population A (the newborns of GA ≤ 32 weeks with a PDA)

Between January 2012 and July 2013, 50 newborns of GA ≤ 32 weeks were admitted to our intensive care unit. The mean gestational age was 29 3/7 weeks (25 3/7 - 32 0/7 w.), the mean birth weight 1,305 g (500-2,200 g) and the mean age at admission 7 hours (1-12 h).

Upon admission, 36/50 (72%) newborns were in assisted ventilation and 14/50 (28%) under a continuous positive pressure (CPAP). In all these subjects the cerebral and renal oxygenation were continuously measured by NIRS and all underwent an ultrasound examination of heart and brain every 6 hours, starting immediately after the admission.

In 44/50 (88%) newborns a PDA was detected at the first heart-ultrasound examination, 32/36 (88%) in the group under mechanical ventilation and 12/14 (86%) in the group under continuous positive pressure.

Of all newborns with PDA, 31/44 (70%) showed a diameter of ductus ≥ 1.6 mm at the first echocardiographic examination (26 in the group of ventilated newborns and 5 in the group in CPAP). 36/44 showed a left to right shunt (82%) and 8/44 (18%) a bidirectional shunt. No infant showed a right to left shunt. All these newborns with a bidirectional shunt showed a left to right shunt at the second ultrasound examination 6 hours later. The values of regional oxygenation (cSO_2, rSO_2, cFTOE, rFTOE) in the group with PDA and left to right shunt from the first observation (**Fig. 1**) and in the group with PDA and initial bidirectional shunt (**Fig. 2**), are reported.

In the group of 36 newborns with PDA and left to right shunt from the first examination, the mean value of the cSO_2 was 64.5 ± 4.2% during the first hour and 69.7 ± 5.6% during the second ($p > 0.05$), with a cFTOE of 28.6 ± 4.7 and 24.6 ± 6.5 respectively ($p > 0.05$).

In two newborns of this group the cSO_2 was 50 ± 2% with a cFTOE reaching 45 ± 5. A diastolic steal phenomena in the anterior cerebral artery was found at the cerebral echodoppler examination in these two subjects.

The rSO_2 was 59.6 ± 3.6% with an rFTOE 35.7 ± 4.5 during the first hour and 44.6 ± 2.9 ($p < 0.001$)

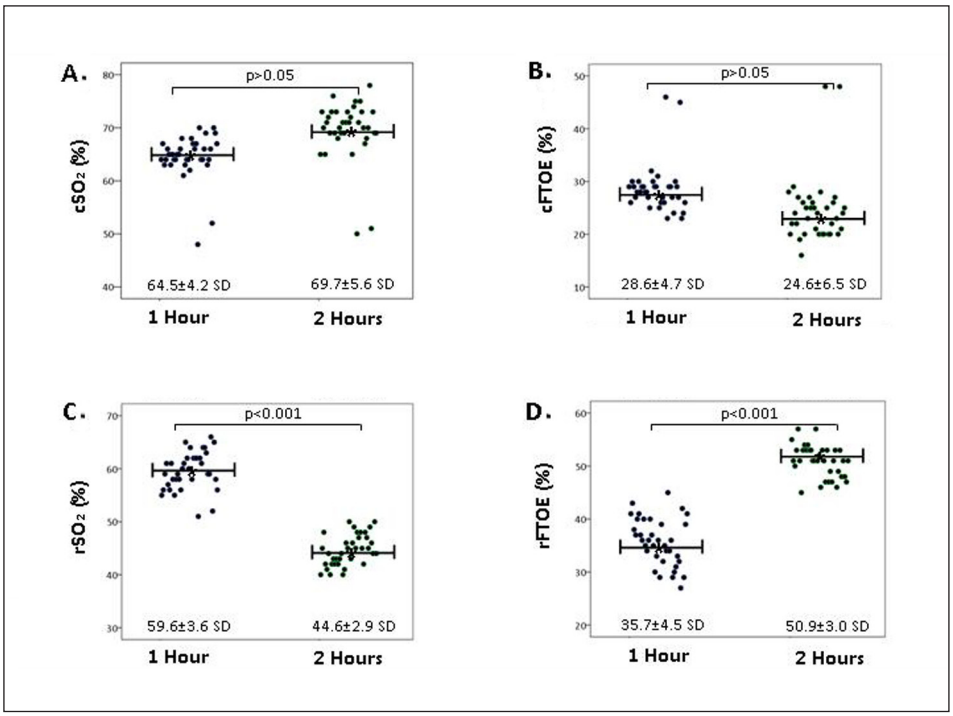

Figure 1. Regional oxygenation (**A.** cSO_2, **B.** cFTOE, **C.** rSO_2, **D.** rFTOE) in the first hours of observation in 36 newborns of GA ≤ 32 w. with PDA and left to right shunt. The data show a statistical significant variation of the rSO_2 and rFTOE ($p < 0.01$) in the time range, while the cSO_2 and cFTOE remain relatively stable. These results are interpreted as signs of a precocious hemodynamic destabilization caused by the left to right shunt through the open ductus.

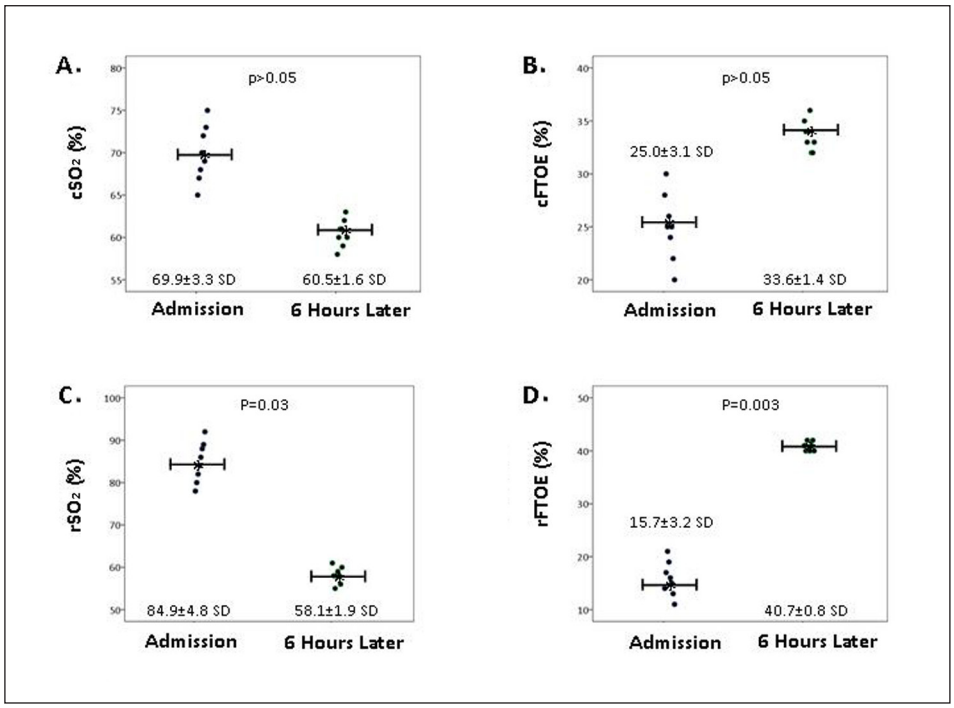

Figure 2. Regional oxygenation (**A.** cSO_2, **B.** cFTOE, **C.** rSO_2, **D.** rFTOE) in the first hours of observation in 8 newborns of GA ≤ 32 w. with PDA and initial bidirectional shunt, that changed in left to right in 6 hours. The appearance of left to right shunt causes a statistical significant fall of the rSO_2 ($p = 0.03$) with increased extraction ($p = 0.003$). Also the values of cSO_2 and cFTOE show a worsening of the cerebral oxygenation that is not statistical significant ($p > 0.05$). This last result scales down, due to the small number of the observed subjects.

with rFTOE of 50.9 ± 3.0 ($p < 0.001$) during the second.

In the group of 8 newborns with PDA and bidirectional shunt the values of cSO_2 and rSO_2 were 69.9 ± 3.3% and 84.9 ± 4.8% with a cFTOE of 25.0 ± 3.1 and rFTOE of 15.7 ± 3.2 respectively. Thereafter they declined when the shunt changed from bidirectional to left to right, reaching the values observed in the first group with initial left to right shunt: cSO_2 60.5 ± 1. 6 ($p > 0.05$) with a cFTOE of 33.6 ± 1.4 ($p > 0.05$) and a rSO_2 58.1 ± 1.9 ($p = 0.03$) with a rFTOE of 40.7 ± 0.8 ($p = 0.003$).

All the newborns (44) with suboptimal value of renal oxygenation ($rSO_2 \leq 50\%$ and/or rFTOE ≥ 40) received a treatment with dopamine starting at 5 µg/kg/min, but the two newborns with severely reduced cSO_2 at the first observation were also treated with ibuprofen.

In **Fig. 3** the trend of cSO_2 and rSO_2 after dopamine were reported. In 32/44 subjects the rSO_2 progressively increased during the first three hours up to 75.1 ± 14.3% with a rFTOE of 20.1 ± 14.8 ($p < 0.001$, calculated on the difference between variables at time 0 and at 3 hours), while the cSO_2 remained around 69.0 ± 6.2%, with cFTOE of 26.2 ± 6.8%. In the figure only the cSO_2 and cFTOE at time 0 and at 1 hour are reported.

In the case of no response after 3 hours (12/44), the dopamine was increased at 7.5 µg/kg/min. In **Fig. 4** only the changes of rSO_2 and rFTOE in this subgroup are reported. In 9/12 subjects rSO_2 increased after dopamine up to 82.2 ± 4.9 with a rFTOE 13.4 ± 3.5 during the next three hours of treatment ($p = 0.005$ and $p = 0.007$ respectively [significance calculated on the difference between variables at time 0 and at 6 hours]). The 3/12 non-responder newborns, who also showed increasing dimensions of ductal diameter and decrease or absence of the diastolic flow in anterior cerebral artery at echodoppler examinations, were treated with ibuprofen, with ductal closure in 2 days.

Population B (the newborns with a post-natal age ≥ 2 weeks, with a hematocrit under 30%)

Between September 2012 and July 2013, we followed the brain and the renal oxygenation by NIRS in 42 newborns who reached a hematocrit ≤ 30% after the second week of life. 38/42 were born preterm at GA of 33 ± 3 weeks and 4/42 were term newborns with ABO incompatibility.

In **Fig. 5** the values of cSO_2 and rSO_2 and of cFTOE and rFTOE, during the six hours preceding a decision for a blood transfusion, were reported. In 26/42 (62%) the cSO_2 was 69 ± 3% with a cFTOE of 23 ± 3 and the rSO_2 82 ± 5 with a rFTOE of 10 ± 5; in 16/42 (38%) the cSO_2 and the cFTOE resulted in the same range, but the rSO_2 was decreased to 50 ± 3% with an rFTOE 45 ± 3 ($p < 0.001$). There was no difference of the hematocrit values between the two groups. On 10 out 26 newborns with normal values of regional saturation, rSO_2 decreased to 50

± 3 with a rFTOE of 45 ± 3 (p = 0.005) when the hematocrit fell to 20-22%.

Only the newborns with a rSO_2 of 50 ± 5% and a rFTOE ≥ 40 were submitted to a blood transfusion while the others (16/26) were treated conservatively. The blood transfusion consisted in the infusion at a rate ≤ 1 ml/min of packet red cells to reach a hematocrit of 40. In **Fig. 6** the regional saturations and oxygen extraction fractions in the 24 hours following the transfusion were reported. In all the 26 transfused newborns a progressive rise of rSO_2 from 49.7 ± 2.7 at time 0 to 83.8 ± 9.4 at 24 h (p < 0.001) with a rFTOE declining form 45.2 ± 2.8 to 8.1 ± 3.4 (p < 0.001) was observed. starting at the end of transfusion. Also the cSO_2 showed an increase to 82.2 ± 2.9 (p < 0.001) and a decrease of

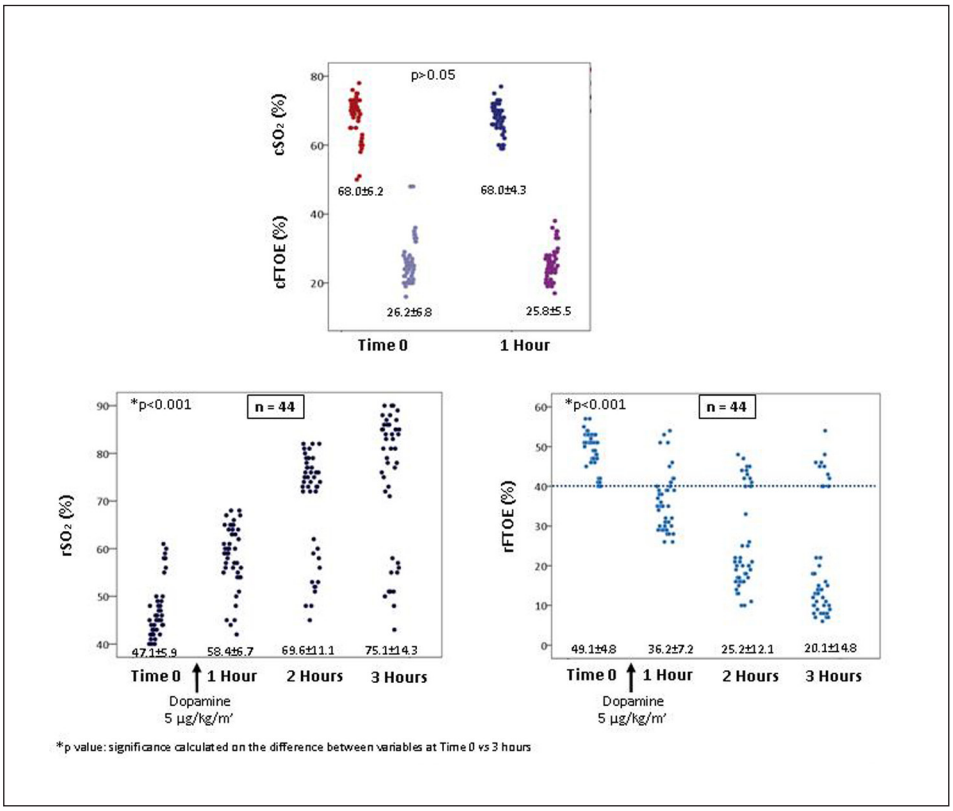

Figure 3. 44 newborns with ductal left to right shunt and suboptimal value of renal oxygenation (rSO_2 ≤ 50% and/or rFTOE ≥ 40) treated with dopamine. In 32/44 subjects, rSO_2 progressively increases during the first three hours of treatment (p < 0.001, calculated on the difference between variables at time 0 and at 3 hours), while the cSO_2 remains stable. In the figure only the cSO_2 and cFTOE at time 0 and at 1 hour are reported. In cases of no response after 3 hours (12/44), the dopamine was increased to 7.5 µg/kg/min.

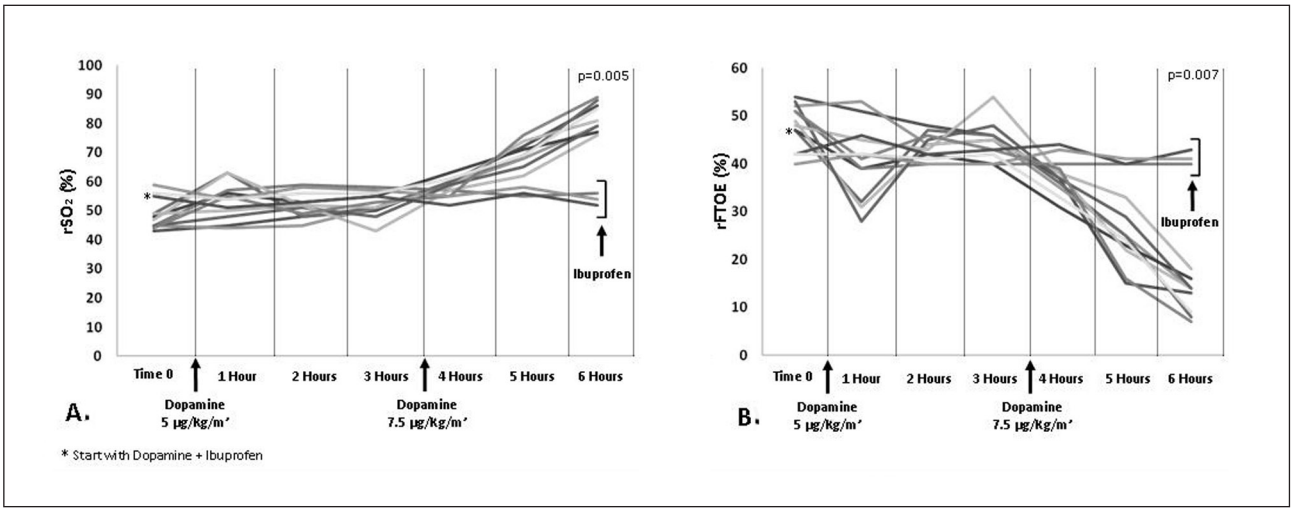

Figure 4. Increase of dopamine in 12/44 subjects non-responder at the initial dose. In 9/12 subjects, rSO_2 significantly increases after dopamine (**A**) with a mirror-like decrease of rFTOE during the next three hours of treatment (p = 0.005 and p = 0.007 respectively). The 3/12 non-responder newborns have been afterwards treated with ibuprofen, with ductal closure in 2 days.

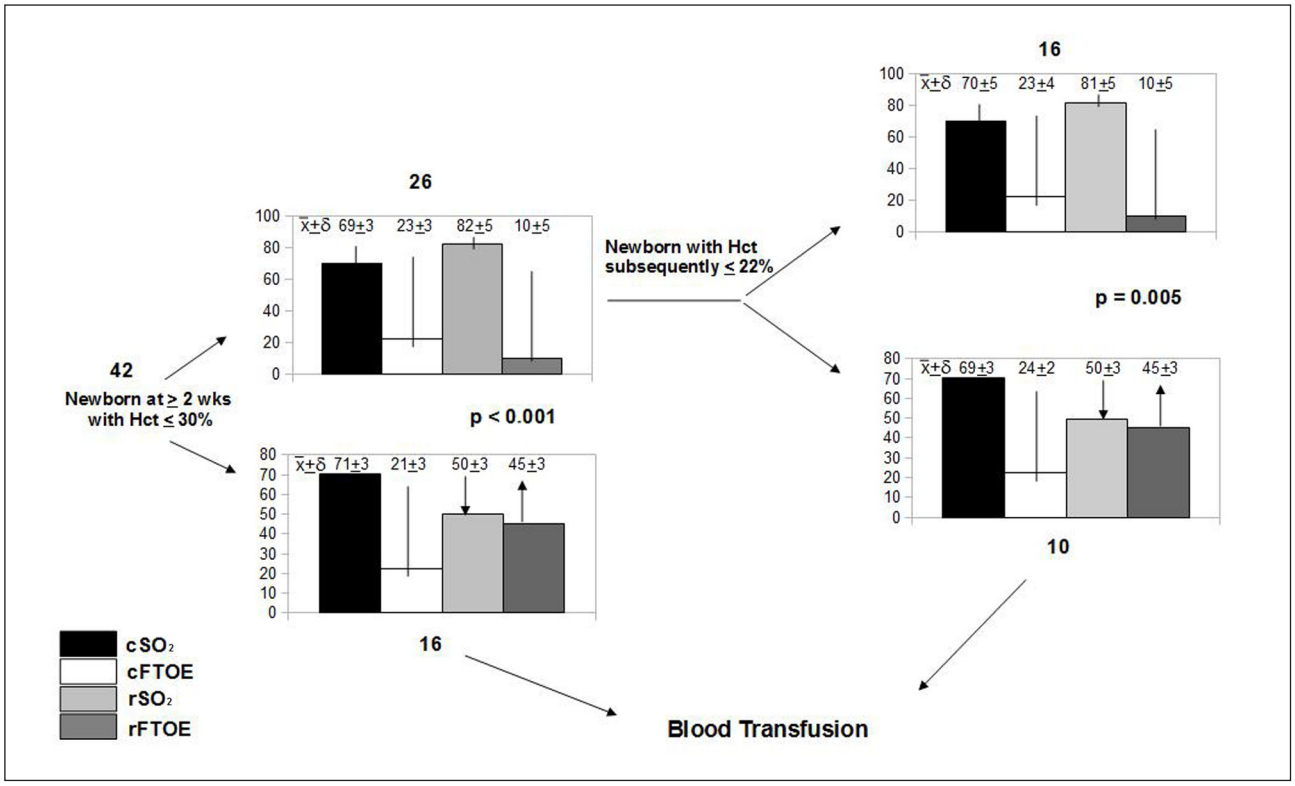

Figure 5. Values of regional oxygenation in 42 newborns with a post-natal age ≥ 2 w. and a hematocrit ≤ 30 during the six hours preceding a decision for a blood transfusion. In 26/42 the values are unaffected, while 16/42 show a decline of rSO_2 with corresponding increase of rFTOE ($p < 0.001$). There was no difference of the hematocrit values between the two groups. Of the 26 newborns with normal values of regional saturation, 10 (38%) showed a decline of rSO2 with increase of rFTOE when the hematocrit fell to 20-22% ($p = 0.005$). Only the 26 newborns with compromised renal oxygenation have been transfused.

the cFTOE to 12.2 ± 2.9 ($p < 0.001$) after transfusion and after the progressive normalization of the renal oxygenation.

Discussion

Population A

PDA is a frequent problem we encounter in very low birthweight infants with the development of left to right shunt appearing very soon after birth [6]. If the left to right shunt through the ductus takes place, the results are a progressively lung overcirculation and a left ventricular volume overload. Both animal and human studies show, in the time range, a compromise of organ blood flow, with the development of systemic hypotension, steal phenomena, organ hypoperfusion and ultimately congestive heart failure [7].

To counteract these effects, our historical therapeutic approach to PDA was mainly a treatment with cyclooxygenase inhibitors (ibuprofen) as soon as the shunt became left-to-right. The unpredictability of the timing of ductal closure after ibuprofen [8] and the consequent time-related risk of brain hypoperfusion led us to change the treatment with the simultaneous use of dopamine [9] and ibuprofen in the presence of a left to right shunt before any signals of cerebral hypoperfusion.

After the first results of the continuous monitoring of cerebral and renal oxygenation, we have subsequently modified our approach, starting with dopamine as soon as the renal oxygenation decreases and its extraction fraction results ≥ 40. The ibuprofen is only used if the ductus still results open at or near the end of the first week or before, if signs of systemic and/or cerebral hypoperfusion appear or persist.

In the 44 newborns studied we have not had to resort to ibuprofen, observing in all a spontaneous closure or a flow closing pattern at echocardiodoppler examination in the fifth-seventh day of life, except that in the three newborns who did not improve after dopamine and showed echodoppler findings of progressive hemodynamic deterioration (6.8%) and in the two who showed a depression of cSO_2 since the first observation for which they were immediately treated with dopamine and ibuprofen.

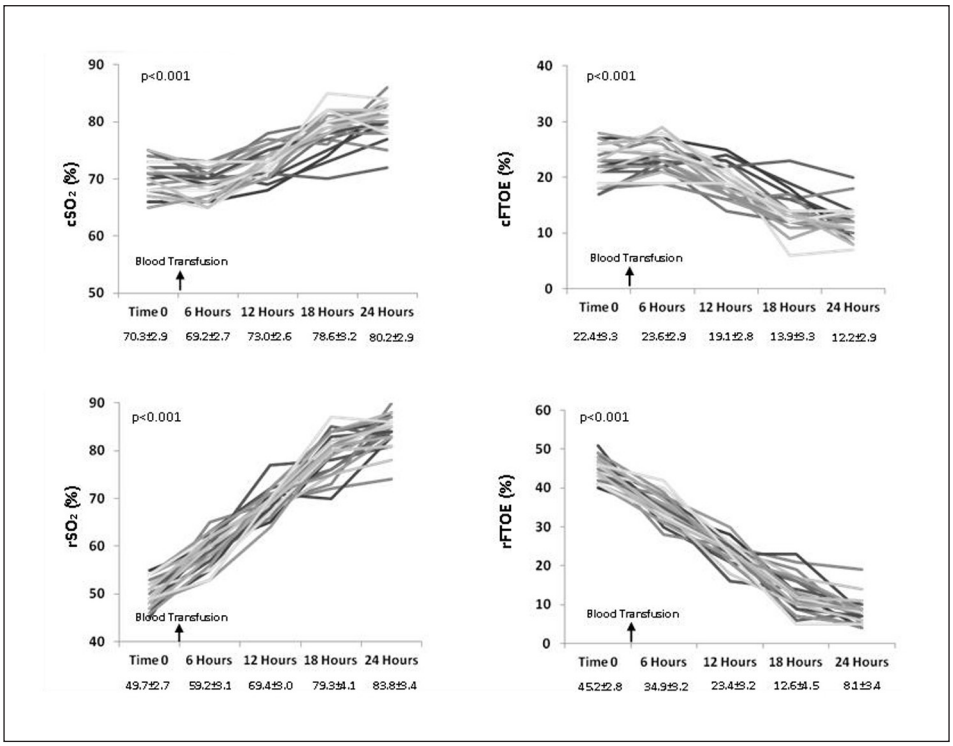

Figure 6. Regional oxygenation (cSO_2, cFTOE, rSO_2, rFTOE) in the 26 transfused newborns during the following 24 hours. A progressive statistical significant rise of rSO_2 and decrease of rFTOE ($p < 0.001$) is evident, starting at the end of transfusion. Also the cSO_2 shows an increase with an expected decrease of the cFTOE ($p < 0.001$) after transfusion and after the progressive normalization of the renal oxygenation.

No infant had shown a persistent patency of ductus during the following weeks, needing a course of ibuprofen or a surgical ligation.

With this conservative approach, we believe to protect the brain perfusion well before the appearance of any hemodynamic trouble of the cerebral circulation, identifying in the fall of the renal saturation the timing of treatment with dopamine, that has shown to be effective in controlling the entity of the left to right shunt and therefore the systemic perfusion [9]. Our progressive disaffection to the use of cyclooxygenase inhibitors derives from the hemodynamic stability, relatively soon reached with dopamine and from the existing perplexities on the use of such therapeutic agents in the newborn [10-14].

We judge these results, although meaningful, as provisional, postponing a definitive evaluation to the results of the follow-up of the so treated newborns and to a more consistent case studies.

Population B

Although the numerous studies about the indications for blood transfusion in the newborn, these issue remains very controversial [15], with significant different practices among neonatal intensive care units [15]. The optimal hemoglobin threshold for blood transfusion is unknown, particularly in the preterm infants [15, 17], with the result to fluctuate between liberal and restrictive guidelines, depending on the newborn clinical conditions [18-20]. In our unit the decision to transfuse a newborn older than 2 weeks with a hematocrit ≤ 30 has been founded on clinical grounds (signs of hemodynamic instability [tachycardia, tachypnea, metabolic acidosis], feeding refusal, stable reduction of the growth under 15 g/die).

In the followed newborns, the cerebral and renal oxygenation monitoring has allowed to distinguish two different populations, despite the same value of hematocrit found: the first that preserves an absolute normality of the cerebral and renal oxygenation and the second that shows a reduction of the renal saturation, that we consider as the first signal of hemodynamic adaptation induced by the anemia. The effect of the transfusion in these group is the progressive normalization of the renal saturation with a drastic reduction of the oxygen extraction fraction, followed in the time by an increase of the cerebral saturation and a decrease of the cerebral oxygen extraction.

On the basis of these results, in our Unit all newborns with progressively falling hematocrit are now submitted to a cerebral and renal oxygenation monitoring and transfused only when the renal saturation shows clear sinking values. Even though we consider these observations deserving further studies, we believe to give in that way a contribution to the problem of transfusions in the newborn.

Conclusions

In the light of the reported observations, we recognize to the regional oxygenation monitoring a precise role in the process of personalization of the newborn cares in intensive contexts.

Despite the requirement for wider observations, the information drawn by the variations of the regional oxygenation in different pathophysiologic processes can substantially help in the prevention of the organ damage, particularly the brain, that upsets still today the results of the neonatal intensive cares.

Declaration of interest

The Authors declare that there is no conflict of interest.

References

1. Jobsis FF. Noninvasive, infrared monitoring of cerebral and myocardial oxygen sufficiency and circulatory parameters. Science. 1977;198(4323):1264-7.
2. Victor S, Weindling M. Near-infrared spectroscopy and its use for the assessment of tissue perfusion in the neonate. In: Kleinman CS, Seri I, Polin RA (Eds.). Hemodynamic and Cardiology: Neonatology questions and controversies. Elsevier Saunders, 2012, pp. 151-72.
3. McNeill S, Gatenby JC, McElroy S, Engelhardt B. Normal cerebral, renal and abdominal regional oxygen saturations using near-infrared spectroscopy in preterm infants. J. Perinatol. 2011;31:51-7.
4. Petrova A, Mehta R. Near-infrared spectroscopy in the detection of regional tissue oxygenation during hypoxic events in preterm infants undergoing critical care. Pediatr Crit Care Med. 2006;7:449-54.
5. Lemmers PMA, Toet M, van Schelven LJ, van Bel F. Cerebral oxygenation and cerebral oxygen extraction in the preterm infant: the impact of respiratory distress syndrome. Exp Brain Res. 2006;173:458-67.
6. Kluckow M, Evans N. Early echocardiografic prediction of symptomatic patent ductus arteriosus in preterm infants undergoing mechanical ventilation. J Pediatr. 1995;127(5):774-9.
7. Giliberti P, De Leonibus C, Giordano L, Giliberti P. The physiopathology of the patent ductus arteriousus. J Matern Fetal Neonatal Med. 2009;22(Suppl 3):6-9.
8. Noori S, Seri I. Treatment of the patent ductus arteriosus: when, how and for how long? J Pediatr. 2009;155(6):774-6.
9. Bouissou A, Thameur R, Klosowski S, Tourneux P, Vanderborght M, Storme L. Hypotension in preterm infants with significant patent ductus arteriosus: Effects of dopamine. J Pediatr. 2008;153(6):790-4.
10. Noori S. Patent ductus arteriosus in the preterm infant: to treat or not to treat? J Perinatol. 2010;30(Suppl):S31-7.
11. Bose CL, Laughon MM. Patent ductus arteriosus: Lack of evidence for common treatments. Arch Dis Child Fetal Neonatal Ed. 2007;92(6):F498-502.
12. Benitz WE. Treatment of persistent patent ductus arteriosus in preterm infants: time to accept the null hypothesis? J Perinatol. 2010;30(4):241-52.
13. Benitz WE. Patent ductus arteriosus: to treat or not to treat? Arch Dis Child Fetal Neonatal Ed. 2012;97(2):F80-82.
14. Brunner B, Hoeck M, Schermer E, Streif W, Kiechl-Kohlendorfer U. Patent ductus arteriosus, low platelets, cyclooxygenase inhibitors and intraventricular hemorrhage in very low birth weight preterm infants. J Pediatr. 2013;163:23-8.
15. Luban NL. Management of the anemia in the newborn. Early Hum Dev. 2008;84(8):493-8.
16. Ringer SA, Richardson DK, Sacher RA, Keszler M, Churchill WH. Variations in transfusion practice in neonatal intensive care. Pediatrics. 1998;101(2):194-200.
17. Strauss RG. How I transfuse red blood cells and platelets with the anemia and thrombocytopenia of prematurity. Transfusion. 2008;48(2):209-17.
18. Slonim AD, Luban NL. Too much, too little, too soon, too late? Transfusion and long term survival in children. Transfusion. 2008;48(5):796-8.
19. Kirpalani H, Whyte RK, Andersen C, Asztalos EV, Heddle N, Blajchman MA, Peliowski A, Rios A, La Corte M, Connelly R, Barrington K, Roberts RS. The Premature Infants in Need of transfusion (PINT) study: a randomized, controlled trial of a restrictive (low) versus liberal (high) transfusion threshold for extremely loiw birth weight infants. J. Pediatr. 2006;149(3): 301-7.
20. Bell EF, Strauss RG, Widness JA, Mahoney LT, Mock DM, Seward VJ, Cress GA, Johnson KJ, Kromer IG, Zimmermann MB. Randomized trial of liberal versus restrictive guidelines for red cell transfusion in preterm infants. Pediatrics. 2005;115(6): 1685-91.