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OXFORD

Factors Affecting the Target Oxygen Saturation in the First Minutes of Life in Preterm Infants

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ABSTRACT

Background: The aim of this study was to describe the effect of factors on time to reach a pulse oxygen saturation (SpO_2) level of 90% in preterm infants in the delivery room.
Methods: Preterm (<35 gestational age) infants who did not require supplemental oxygen were included in the study. Continuous recordings were taken by pulse oximetry during the first 15 min of life.
Results: Of 151 preterm infants, 79 (52.3%) were female and 126 (83.5%) were delivered by cesarean section. Target saturation level (≥90%) was achieved faster in preductal measurements. Mean times taken to have a preductal and postductal SpO_2 level of 90% were significantly lower in preterm babies born by vaginal delivery, with umbilical arterial pH ≥ 7.20 and whose mothers were non-smokers during pregnancy.
Conclusions: Differences in achievement of target saturation level were influenced by multiple factors (birth way, probe location, maternal smoking and umbilical blood gas pH) in the delivery room during resuscitation of preterm babies.

KEYWORDS: preterm infants, oxygen saturation, delivery room

BACKGROUND

Approximately 10% of newborns, even higher rates of premature infants, require some form of resuscitation at birth [1]. A number of large studies have demonstrated that standardized resuscitation practices significantly reduce neonatal mortality and improve outcomes [2, 3]. Worldwide, one of the most common causes of neonatal death is preterm birth and related complications [4]. Not only mortality but also morbidity of preterm infants is related to oxygen exposure in the delivery room [5, 6]. Published neonatal resuscitation algorithms have suggested that a pulse oximeter should be used during resuscitation of preterm infants to avoid potentially harmful effects of oxygen [7, 8].

European Consensus Guidelines stated that in preterm babies receiving oxygen, the saturation target should be between 90 and 94% beyond delivery room handling [9]. Now we know very well that newborn infants achieve these levels about 10 min after delivery. The Neonatal Resuscitation Program (NRP) recommends targeted pulse oxygen saturation (SpO_2) levels for only term neonates [7]. However, data on changes in SpO_2 in preterm infants are very limited and are not included in the NRP. Furthermore, preterm infants need significantly more time to reach target saturation [10].

The purposes of this study were to determine the factors that have an impact on oxygen saturation levels and to obtain reliable time for functional pulse oximeter signal and time to reach 90% SpO_2 level in preterm infants with no interventions in the delivery room.

MATERIALS AND METHODS

Preterm infants (<35 weeks' gestation) born between 1 November 2013 and 1 May 2015 who did not require oxygen supplementation in the delivery room were included in this prospective study. Verbal consent and written informed consent were obtained from parents before the infants' birth. The study protocol was approved by the ethical committee.

Patient selection

Inclusion criterion was healthy preterm (<35 gestational age) infants. Exclusion criteria included preterms requiring oxygen, ventilation, medications and interventions (including continuous positive airway pressure [CPAP]) at birth and those with congenital abnormalities, poor biophysical profiles and insufficient records.

Study procedures

All premature infants were assessed at birth. A pediatrician and two neonatal nurses attended each delivery. Resuscitation protocols were performed according to the NRP guidelines by different clinicians, if necessary [11]. The time of birth was determined at the time of cord clamping, which occurred immediately after birth. The chronometer was started at clamping of the cord. The sensors were placed at the right wrist for the preductal SpO_2 measurements and the dorsum of the foot for the postductal SpO_2 measurements immediately after cord clamping. The time to apply the sensor and the time to first reliable reading of SpO_2 level were noted. Oxygen saturation levels and heart rate were recorded and downloaded automatically to a computer every 2 s. The averages of SpO_2 levels 30 s before and after each minute were accepted as 1-min result of that interval. The measurements were recorded during the first 15 min of life.

Oxygen saturation (%) level measurements were performed using two new-generation pulse oximeters (Masimo Radical, Masimo Corporation, Irvine, CA, USA) secured with a Coban wrap (3M Health Care, St. Paul, MN, USA). Prior to the measurement, the precision was set to maximum sensitivity and the alarm was muted. Sensors were placed at the right wrist (preductal) and right dorsum of the foot (postductal) after cord clamping. Next, the probes were connected to the pulse oximeters.

Temperatures of newborn preterm infants were continuously monitored with a skin probe, with servocontrol to keep skin temperature at 36.5 °C. The body temperatures were measured at 1-min intervals during the first 15 min of life.

Gestational age assessment was defined as follows: it was calculated from the first day of the mother's last menstrual period, if it was not known according to sonographic evidence of early pregnancy or the criteria of the New Ballard Score [12]. Mothers who reported smoking any cigarettes per day or week throughout pregnancy were considered smokers. Groups that may affect the oxygen saturation were determined: gender, delivery route, umbilical arterial [UA] $pH < 7.20$ vs. ≥ 7.20 and maternal smoking. The SpO_2 levels and mean time to reach 90% level during the first 15 min of life were compared between groups.

Statistical methods

Statistical analyses were performed by using the MedCalc Statistical Software (Turkey). All results are expressed as means ± standard deviations, median and interquartile range (IQR). MedCalc Statistical software program was used for the calculation of continuous variable nomogram. Comparisons between two independent groups for numerical variables were made by Student *t*-test if samples were normally distributed and Mann–Whitney *U* test if samples were not normally distributed. Paired-sample *t*-test was used if numerical variables were normally distributed, and Wilcoxon test was used if variables were not normally distributed, for comparison of dependent groups. A $p < 0.05$ was considered to indicate significant difference.

RESULTS

During the study period, 319 preterm babies were born at <35 weeks' gestation. Of these, 106 required oxygen and/or resuscitation and/or any intervention (CPAP), 7 had anomalies and 55 were excluded for other reasons (insufficient records, lack of sufficient medical staff, simultaneous delivery, etc.).

After enrollment, 151 preterm newborns were analyzed. Seventy-nine of the infants (52.3%) were female and 126 (83.5%) were delivered by cesarean section. Mean gestational age was 32.9 ± 1.04 weeks (there were 14 infants with <32 weeks' gestation and the lowest gestational age was 30), and birthweight was 1888.8 ± 344.5 g. Thirteen of the preterm infants' mother (8.6%) had used cigarettes during pregnancy. There were 30 (19.9%) infants whose UA pH values were <7.20.

The mean time to apply the sensor was 19.5 ± 3.8 s (median time 19 s, IQR: 16–22 s), and the mean times to first SpO_2 reading measurements were 48.1 ± 9.3 s for preductal (median time 48 s, IQR:42–53 s) and 50.9 ± 9.0 s (median time 51 s, IQR: 44–53 s) for postductal location.

At all time segments, preductal SpO_2 levels were found to be higher than the postductal SpO_2 levels (Table 1). During the 15 min after birth, preductal SpO_2 levels were significantly higher than postductal SpO_2 levels (Fig. 1).

Preductal SpO_2 levels were lower in preterm babies born by cesarean delivery (Fig. 2). There were no significant differences in SpO_2 values between male and female infants (Fig. 3). Preterm infants with UA pH <7.20 and whose mother was a smoker had lower SpO_2 values (Figs. 4 and 5) in all time segments.

Target saturation level (≥90%) was achieved faster in preductal measurements (preductal, 9.2 ± 6.4 min; postductal, 11.0 ± 7.2 min). The mean times taken to have a preductal and postductal SpO_2 level of 90% were significantly lower in preterm babies born by vaginal delivery, with UA pH ≥ 7.20 and whose mother was a non-smoker during pregnancy. No evidence was found for gender differences. The mean times to reach a preductal and postductal SpO_2 level of 90% with respect gender, route of delivery, UA blood pH value and maternal smoking are shown in Table 2. There were no differences between groups of infants according to body temperatures.

Table 1. Preductal and postductal measurements during the first 15 min of life

Time (s)	SpO_2 (mean ± SD)		p
	Preductal	Postductal	
1	61.92 ± 6.76	58.07 ± 6.38	<0.001
2	67.40 ± 6.97	63.74 ± 6.43	<0.001
3	71.61 ± 7.19	67.78 ± 6.64	<0.001
4	75.83 ± 7.31	71.93 ± 6.72	<0.001
5	79.30 ± 7.14	76.46 ± 6.67	<0.001
6	82.54 ± 6.74	79.35 ± 6.02	<0.001
7	85.32 ± 6.17	82.43 ± 6.08	<0.001
8	87.44 ± 4.98	84.58 ± 5.51	<0.001
9	89.01 ± 4.26	86.43 ± 4.98	<0.001
10	89.77 ± 3.82	87.99 ± 4.08	<0.001
11	91.95 ± 2.65	89.74 ± 3.72	<0.001
12	93.18 ± 2.30	91.53 ± 2.93	<0.001
13	94.26 ± 2.36	92.91 ± 2.50	<0.001
14	95.15 ± 2.61	93.93 ± 2.44	<0.001
15	95.81 ± 2.90	94.97 ± 2.60	<0.001

CONCLUSIONS

It is the basic paradox of life that oxygen is necessary for survival, but, on the other hand, it can be damaging in variable amounts, especially for preterms. This contradiction was defined as 'the albatross of neonatal medicine' or as a 'double edge sword' [13, 14]. Otherwise, increasing the production of free oxygen radicals is an independent risk factor for mortality owing to low intracellular antioxidant activity at birth in premature infants [15]. Furthermore, several studies have shown evidence of oxygen toxicity in the delivery room that influenced the pathogenesis of many diseases of the infants [16, 17]. Pulse oximetry has provided an objective follow-up measurement of oxygen saturation that allows administrating a medical approach especially for preterm infants in the delivery room [18].

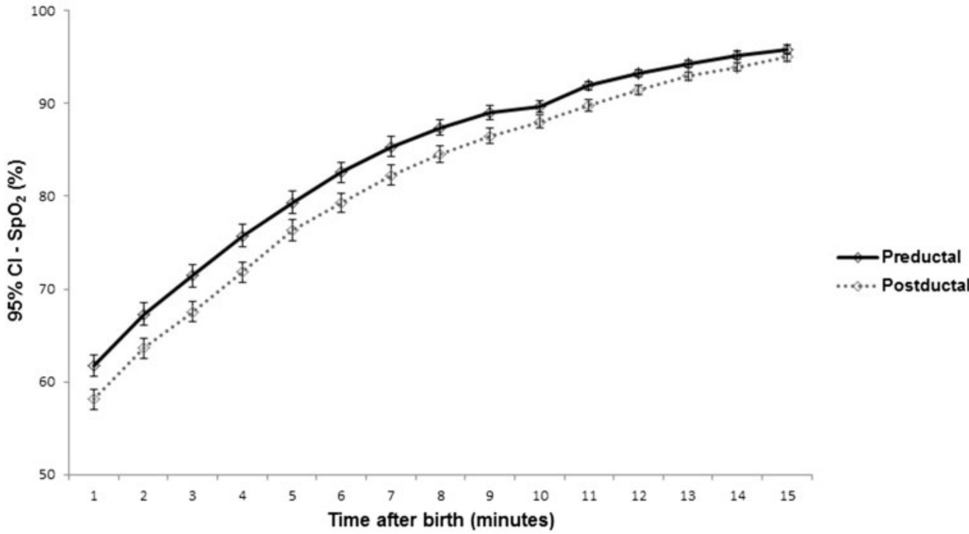

Fig. 1. Preductal and postductal SpO_2 levels during the first 15 min after birth (means; 95% confidence interval for mean). Postductal levels were lower than preductal levels during the first 15 min ($p < 0.05$).

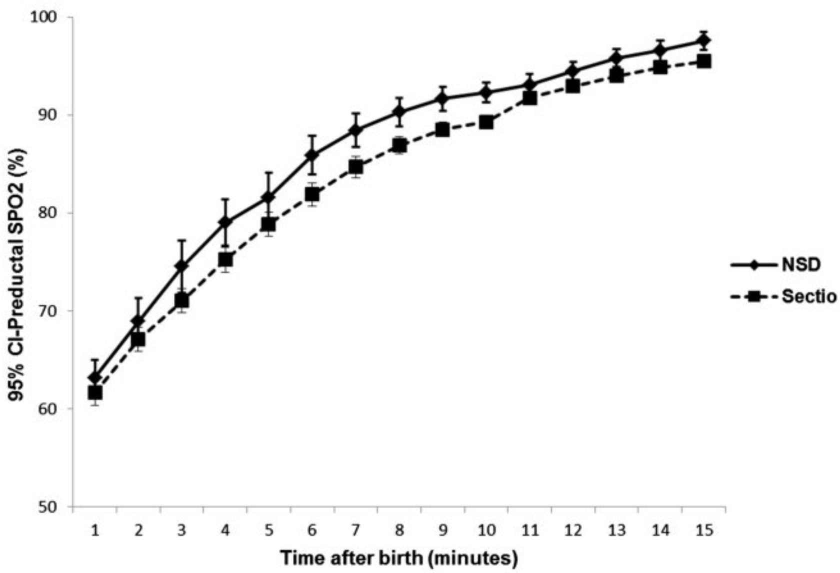

Fig. 2. Preductal SpO_2 levels of premature infants delivered by vaginal and cesarean route during the first 15 min after birth (means; 95% confidence interval for mean).

Many studies have stated that preductal SpO_2 levels are significantly higher than postductal SpO_2 levels immediately after birth, similar to our study [19, 20]. Previous studies did not demonstrate the need to require longer time to reach SpO_2 of >90% in postductal measurements for newborn preterm infants. It was described as owing to high pulmonary artery pressure and right-to-left shunt through the ductus arteriosus for term neonates in many previous trials, but a similar explanation may also apply in premature infants.

Vento *et al.* stated that preterm female newborns achieved targeted SpO_2 significantly earlier than

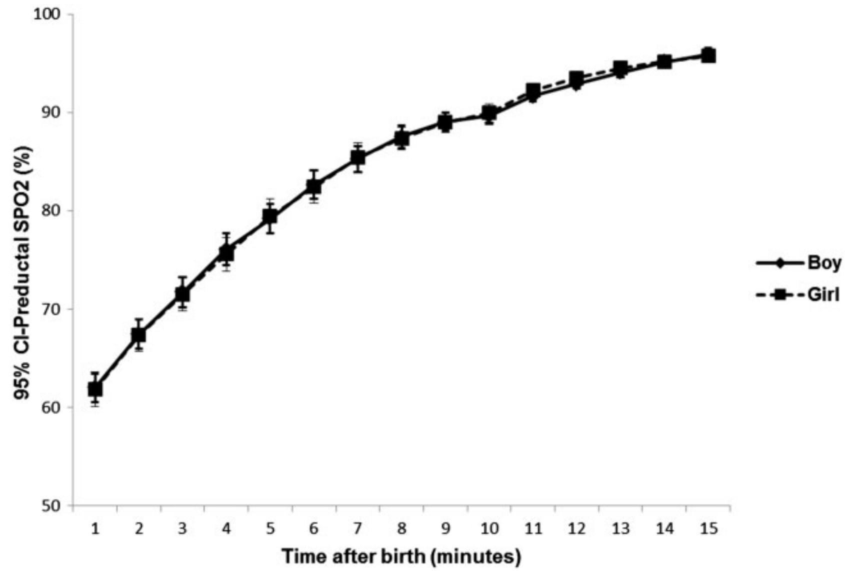

Fig. 3. Preductal SpO_2 levels of male and female premature infants during the first 15 min after birth (means; 95% confidence interval for mean).

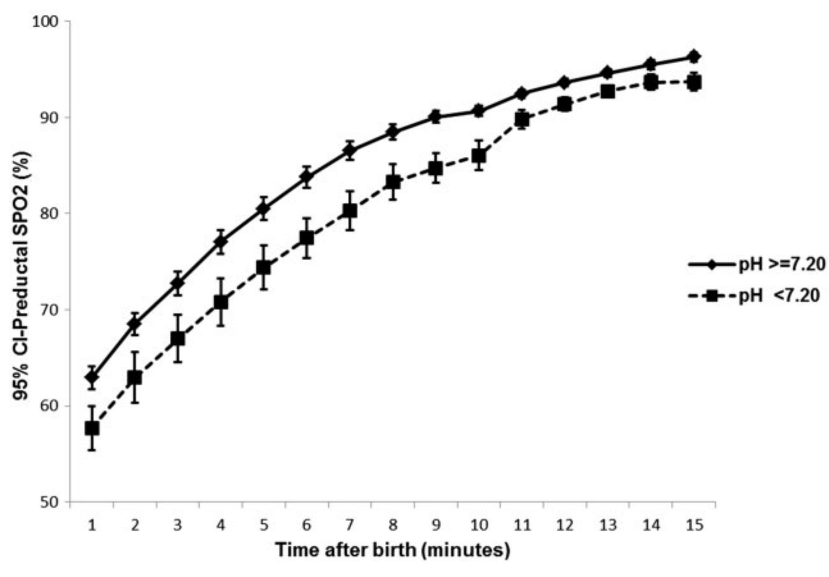

Fig. 4. Preductal SpO_2 levels of premature infants at two different levels of cord blood gas pH group ($pH < 7.20$ vs. $pH \geq 7.20$) during the first 15 min after birth (means; 95% confidence interval for mean).

male babies [21]. On the other hand, no evidence was found for gender differences to time to reach SpO_2 level of 90% in our study and similarly in several previous trials [19, 22, 23]. All of these studies consisted of term or near-term infants and there was no explanatory information on this subject. In Vento's study, small-for-gestational-age infant ratio was significantly higher among male babies and lesser (<32) gestational weeks than our study.

In the present study, preterm infants born by vaginal delivery had higher SpO_2 levels and took a shorter time to reach SpO_2 level of 90% compared with those

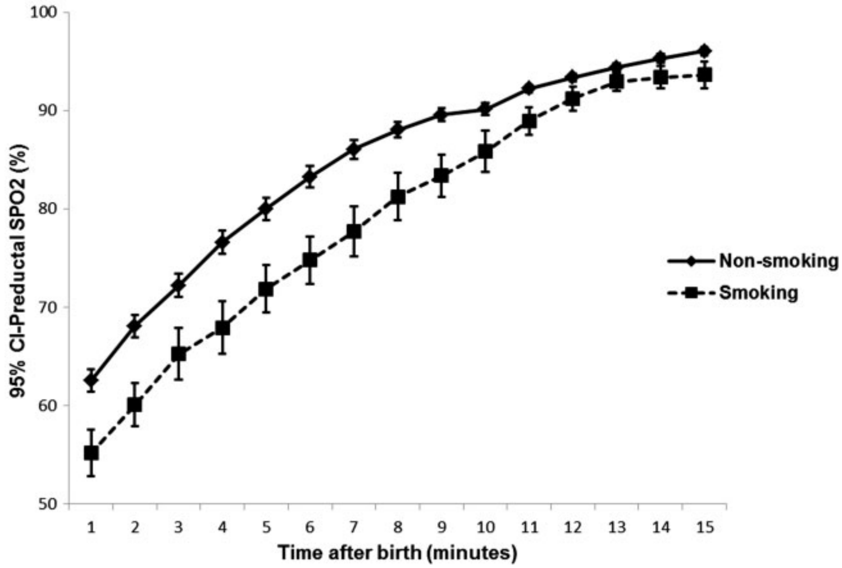

Fig. 5. A comparison of the preductal SpO_2 levels of premature infants according to maternal smoking status during the first 15 min after birth (means; 95% confidence interval for mean).

Table 2. The mean time to reach preductal and postductal SpO_2 level of 90%

Characteristics		Time to reach an SpO_2 of 90% (min)			
	n	Preductal	*p*	Postductal	*p*
Gender					
Male	79	8.7 ± 2.2	0.811	10.5 ± 2.2	0.872
Female	72	8.7 ± 2.0		10.4 ± 2.1	
Delivery route					
Vaginal	25	7.5 ± 2.0	0.001	8.9 ± 2.2	<0.001
Cesarean	126	8.9 ± 2.0		10.8 ± 2.1	
pH value					
pH <7.20	30	10.8 ± 1.3	<0.001	12.7 ± 1.4	<0.001
pH ≥7.20	121	8.2 ± 1.9		9.9 ± 2.0	
Maternal smoking					
Smoker	13	8.5 ± 2.0	<0.001	10.2 ± 2.1	<0.001
Non-smoker	138	11.4 ± 1.0		12.7 ± 1.2	

born by cesarean section. Few studies addressed these issues for preterm infants, and this situation was described as secondary to delayed clearance of lung fluid during cesarean delivery [24, 25].

Maternal smoking during pregnancy is associated with stillbirth [26], lower birth weight [27] and preterm delivery [28]. The present study is the first to reveal the relationship between maternal smoking and SpO_2 values in preterm infants during the first 15 min of life. Schneider *et al.* showed that, compared with infants of non-smoking mothers, oxygen saturation values are adversely affected in maternal smoking-exposed preterm infants during pregnancy [29]. Two possibilities were put forward to explain this situation, tobacco's content exposure effects on neural control of breathing and altered pulmonary development. Nicotine interacts with highly selective endogenous neuronal nicotinic acetylcholine receptors and may affect the development of areas in the central nervous system that are essential for respiratory control. On the other hand, alterations in lung development may also cause suboptimal gas exchange, leading to lower oxygen saturation. However, it is difficult to differentiate the effect of maternal smoking and other confounders.

We concluded that term infants with $pH < 7.20$ had lower SpO_2 levels in the first 11 min of life, and they took longer to reach >90% SpO_2 level compared with infants with $pH \geq 7.20$ in our previous study [22]. We have reached similar results in preterm infants in the present study with base pH values determined from our previous study. Arikan *et al.* stated that low preductal fetal oxygen saturation measured at birth is associated with low fetal pH [30]. Linhartova *et al.* found that in the group of fetuses with fetal oxygen saturation levels >30%, the umbilical blood pH values were ≥7.2 in 82.2%, and in the other group of fetuses with fetal oxygen saturation values <30%, the umbilical blood pH values were <7.2 in 67.7% [31]. Our study also gave evidence about the relationship between low fetal SpO_2 levels in the intrauterine period and low pH values that continued immediately after birth similarly, as investigators highlighted.

The median time for reaching a preductal $SpO_2 > 90\%$ was found to be about 5.8–7.5 min in several studies for term infants [19, 32]. Dawson *et al.* stated that preterm infants needed significantly more time to reach SpO_2 levels of >90% [24]. Kamlin *et al.* determined this time for preterm babies as 6.5 min, and Kopotic *et al.* stated that the mean time to reach SpO_2 of ≥80% was 4.4 min, although the infants have received oxygen therapy [32, 33]. Nuntrarumit *et al.* found the median SpO_2 was 90% at 6 min after birth [25], but 75 preterm babies they dealt with had bigger gestational weeks (median 35) than our study and 68% of the babies born via vaginal delivery. It is noteworthy that achievement of target SpO_2 levels in premature babies is influenced by multiple factors.

Another gray zone is time to achieve stable pulse oximetry values in premature infants. Gandhi *et al.* stated that mean time to achieve functional pulse oximetry was 79 ± 42 s, median time was 67 s for ≤1500 g preterm babies [34]. In the study by Nuntnarumit *et al.*, basic steps of resuscitation were as long as 60 s for preterm babies, so they found that reliable values were obtained at about 160 s [25]. These results indicate that the SpO_2 monitoring cannot be performed in the first minutes of life. We attribute the earlier detection time to the following factors: methodology difference, greater median gestational age, experienced researchers, application of sensors immediately after birth before basic steps of resuscitation and skin-to-skin contact was not used in the study. On the other hand, the time obtained for premature babies in this study was longer than that for term babies that was obtained in our previous study (median time 43 vs. 48 s for preductal measurement) [22]. In management of premature babies in the delivery room, it will be a more appropriate approach to place the saturation probe from the time of birth with a predetermined procedure, taking into account this long period. Hereby, targeted oxygen saturation levels recommended in the NRP can be used by the first minute of life.

As a result, one should know that, using new generation pulse oximeters, binding time of saturation probe from the moment of birth (including late umblical cord clamping strategy), paying attention to application technique (set to maximum sensitivity, muting the alarm and connection to the oximetry cable before being applied to the newborn) and differences in achievement of target saturation level (90%) influenced by multiple factors (gestational week, birth way, location of probe, maternal smoking and umbilical artery blood gas values) are effective for the delivery room resuscitation of preterm babies.

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CONGRESS PRESENTATION

The manuscript preliminary results were presented at the 1st Congress of Joint European Neonatal Societies, 16–20 September 2015, as an oral presentation.

REFERENCES

1. International Liaison Committee on Resuscitation. The International Liaison Committee on Resuscitation [ILCOR] consensus on science with treatment recommendations for pediatric and neonatal patients: neonatal resuscitation. Pediatrics 2006;117:e978–e88.
2. Pammi M, Dempsey EM, Ryan CA, *et al*. Newborn resuscitation training programmes reduce early neonatal mortality. Neonatology 2016;110:210–24.
3. Dempsey E, Pammi M, Ryan AC, *et al*. Standardised formal resuscitation training programmes for reducing mortality and morbidity in newborn infants. Cochrane Database Syst Rev 2015;9:CD009106.
4. Liu L, Oza S, Hogan D, *et al*. Global, regional, and national causes of child mortality in 2000–13, with projections to inform post-2015 priorities: an updated systematic analysis. Lancet 2015;385:430–40.
5. Kapadia VS, Chalak LF, Sparks JE, *et al*. Resuscitation of preterm neonates with limited versus high oxygen strategy. Pediatrics 2013;132:e1488–96.
6. Hartnett ME, Lane RH. Effects of oxygen on the development and severity of retinopathy of prematurity. J AAPOS 2013;17:229–34.
7. Wyckoff MH, Aziz K, Escobedo MB, *et al*. Part 13: neonatal resuscitation: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Circulation 2015;132:S543–60.
8. Vento M, Saugstad OD. Resuscitation of the term and preterm infant. Semin Fetal Neonatal Med 2010;15:216–22.
9. Sweet DG, Carnielli V, Greisen G, *et al*. European consensus guidelines on the management of respiratory distress syndrome—2016 update. Neonatology 2016;111:107–25.
10. Vento M, Aguar M, Brugada M, *et al*. Oxygen saturation targets for preterm infants in the delivery room. J Matern Fetal Neonatal Med 2012;25: 45–6.
11. Richmond S, Wyllie J. European Resuscitation Council Guidelines for Resuscitation 2010 Section 7. Resuscitation of babies at birth. Resuscitation 2010;81:1389–99.
12. Ballard JL, Khoury JC, Wedig K, *et al*. New Ballard Score, expanded to include extremely premature infants. J Pediatr 1991;119:417–23.
13. Silverman WA. A cautionary tale about supplemental oxygen: the albatross of neonatal medicine. Pediatrics 2004;113:394–6.
14. Paul M. Oxygen administration to preterm neonates in the delivery room: minimizing oxidative stress. Adv Neonatal Care 2015;15:94–103.
15. Lee JW, Davis JM. Future applications of antioxidants in premature infants. Curr Opin Pediatr 2011;23:161–6.
16. Tan A, Schulze A, O'Donnell CP, *et al*. Air versus oxygen for resuscitation of infants at birth. Cochrane Database Syst Rev 2005;CD002273.
17. Saugstad OD. Oxidative stress in the newborn–a 30-year perspective. Biol Neonate 2005;88:228–36.
18. Torres-Cuevas I, Cernada M, Nuñez A, *et al*. Oxygen supplementation to stabilize preterm infants in the fetal to neonatal transition: no satisfactory answer. Front Pediatr 2016;4:29.
19. Zubarioglu U, Uslu S, Can E, *et al*. Oxygen saturation levels during the first minutes of life in healthy term neonates. Tohoku J Exp Med 2011;224:273–9.
20. Toth B, Becker A, Seelbach-Gobel B. Oxygen saturation in healthy newborn infants immediately after birth measured by pulse oximetry. Arch Gynecol Obstet 2002;266:105e7.
21. Vento M, Cubells E, Escobar JJ, *et al*. Oxygen saturation after birth in preterm infants treated with continuous positive airway pressure and air: assessment of gender differences and comparison with a published nomogram. Arch Dis Child Fetal Neonatal Ed 2013;98:F228–32.
22. Uslu S, Bulbul A, Can E, *et al*. Relationship between oxygen saturation and umbilical cord pH immediately after birth. Pediatr Neonatol 2012;53:340–5.
23. Levesque BM, Pollack P, Griffin BE, *et al*. Pulse oximetry: what's normal in the newborn nursery? Pediatr Pulmonol 2000;30:406–12.
24. Dawson JA, Kamlin CO, Vento M, *et al*. Defining the reference range for oxygen saturation for infants after birth. Pediatrics 2010;125:e1340–7.
25. Nuntnarumit P, Rojnueangnit K, Tangnoo A. Oxygen saturation trends in preterm infants during the first 15 min after birth. J Perinatol 2010;30:399–402.
26. Flenady V, Koopmans L, Middleton P, *et al*. Major risk factors for stillbirth in high-income countries: a systematic review and meta-analysis. Lancet 2011;377:1331–40.
27. Jaddoe VW, Troe EJ, Hofman A, *et al*. Active and passive maternal smoking during pregnancy and the risks of low birthweight and preterm birth: the Generation R Study. Paediatr Perinat Epidemiol 2008;22:162–71.
28. Shiono PH, Klebanoff MA, Rhoads GG. Smoking and drinking during pregnancy. Their effects on preterm birth. Jama 1986;255:82.
29. Schneider J, Mitchell I, Singhal N, *et al*. Prenatal cigarette smoke exposure attenuates recovery from hypoxemic challenge in preterm infants. Am J Respir Crit Care Med 2008;178:520–6.
30. Arikan GM, Scholz HS, Haeusler MC, *et al*. Low fetal oxygen saturation at birth and acidosis. Obstet Gynecol 2000;95:565–71.
31. Linhartova L, Kurtansky A, Suska P. Correlation between fetal blood oxygen saturation and umbilical blood pH values. Bratisl Lek Listy 2009;110:684–7.
32. Kamlin CO, O'Donnell CP, Davis PG, *et al*. Oxygen saturation in healthy infants immediately after birth. J Pediatr 2006;148:585–9.
33. Kopotic RJ, Lindner W. Assessing high-risk infants in the delivery room with pulse oximetry. Anesth Analg 2002;94:S31–6.
34. Gandhi B, Rich W, Finer N. Time to achieve stable pulse oximetry values in VLBW infants in the delivery room. Resuscitation 2013;84:970–3.