Causes and treatment of neonatal respiratory distress syndrome

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Neonatal respiratory distress syndrome is a condition of advancing respiratory distress, commencing at or shortly after birth. The disease follows an acute course, with deterioration within 48 hours followed by stabilisation and improvement. Treatment is to support respiratory function and maintain good oxygenation.

In the alveoli. The result is a vicious cycle (Fig 1), as there is inadequate gaseous exchange, hypoxaemia will result, causing acidosis and subsequent pulmonary vasconstriction. This increases pulmonary vascular resistance, leading to hypoperfusion, capillary damage, and necrosis of the alveoli. The result is a vicious cycle (Fig 1), as necrosis further aggravates surfactant deficiency (Hicks, 1995). Perinatal asphyxia, maternal diabetes, and caesarean section are other important factors in the aetiology of surfactant-deficient RDS (Rodriguez et al, 2002).

Surfactant deficiency leads to increased surface tension in the alveoli and reduced lung compliance, leading to increased work of breathing, hypoventilation, leading to respiratory acidosis; increased intrapulmonary shunting and severe hypoxaemia; fall in lung compliance to 25 per cent; and increased dead space.

The signs and symptoms of neonatal RDS are:

- Tachypnoea (respiratory rate >60/minute);
- Nasal flaring (from the use of *alae nasi* as accessory muscles);
- Sternal and intercostal recession (due to compliant chest wall and noncompliant lungs);
- Central cyanosis;
- Apnoea;
- Expiratory grunt (caused by the infant exhaling against a closed glottis, which maintains a high residual air volume in the lungs preventing alveolar collapse).

Diagnosis is confirmed by history, blood gases showing impaired respiratory function, and an X-ray demonstrating the classic reticulogranular or ‘ground glass’ appearance and air bronchograms (radiolucent air-filled airways).

**Prevention**

The vast majority of babies who develop RDS do so because they are premature. Attempts to prevent early delivery are therefore a major consideration. A number of strategies can be used.

- Late or lack of antenatal care, smoking, alcohol consumption, illegal drug use, domestic violence, lack of social support, high levels of stress, and long working hours with lengthy periods of standing can all increase the risk of premature birth (March of Dimes, 2004; Johnston et al, 2003a). Health education for pregnant women and their families can play an important role in preventing premature birth.

**Cervical cerclage**

Women who have had several second-trimester miscarriages and/or preterm deliveries may benefit from prophylactic cerclage of the cervix in early pregnancy (Bachmann et al, 2003). This is a purse-string suture placed round the cervix.

**Antibiotics, tocolytics, and steroids**

Bacterial infection in the mother has been shown to be a risk factor for preterm delivery. Antibiotics are used to prevent preterm delivery or delay it long enough to allow the baby’s lungs to develop (Thorp et al, 2002).

Tocolytic drugs such as ritodrine are used in an attempt to inhibit preterm delivery by relaxing the uterine muscle. Their main purpose is to delay delivery for at least 48 hours while maternal steroids are administered (Royal College of Obstetricians and Gynaecologists, 2002).

Many clinical trials have demonstrated that prenatal corticosteroids reduce the risk of RDS. The greatest benefit

**TABLE 1. TUBE SIZE ESTIMATION**

<table>
<thead>
<tr>
<th>Tube size (mm)</th>
<th>Weight (g)</th>
<th>Gestation (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.0</td>
<td>450+</td>
<td>22+</td>
</tr>
<tr>
<td>2.5</td>
<td>&lt;1000</td>
<td>&lt;28</td>
</tr>
<tr>
<td>3.0</td>
<td>1000–2000</td>
<td>28–34</td>
</tr>
<tr>
<td>3.5</td>
<td>2000–3000</td>
<td>34–38</td>
</tr>
<tr>
<td>4.0</td>
<td>&gt;3000</td>
<td>&gt;38</td>
</tr>
</tbody>
</table>

**REFERENCES**


Rennie and Roberton, 1999.

Hicks, 1995.

Thorp et al, 2002.

March of Dimes, 2004

is seen when the interval between the start of treatment and delivery is more than 48 hours and less than seven days (RCOG, 1999). Steroids accelerate maturation of foetal lungs by stimulating type II pneumocytes to produce the phospholipids necessary for surfactant production.

**Delivery and resuscitation**

There is usually warning of impending preterm delivery, allowing time for in utero transfer to a centre with a neonatal ICU bed. Although there may be risks it is easier and generally safer for the infant to be moved in utero. Delivery by caesarean section is associated with a higher risk of RDS than vaginal delivery (Morrison et al, 1995). This is presumably because the infant is delivered before the onset of labour and the associated adrenergic surfactant release and reduction of foetal lung fluid.

All preterm and ‘at-risk’ deliveries should be attended by health professionals who are skilled at intubation and resuscitation. The team leader should be aware of the gestation, and maternal and obstetric history, and appropriate facilities should be available.

Healthy newborn babies take their first breath within 60 seconds of the cord being clamped, as clamping causes asphyxia and stimulates respiration. Sick preterm infants should be placed on their backs under a radiant warmer on the neonatal resuscitator immediately after birth. The ABC (D and E) of resuscitation should be commenced – Airway, Breathing, Circulation, Drugs, Evaluation (Boxwell, 2000). The newborn life-support algorithm (Resuscitation Council (UK), 2000) should then be followed (Fig 2, p44). Parents should be kept informed of how resuscitation is progressing.

**Treatment**

**Surfactant**

Administration of intratracheal surfactant has been shown to improve oxygenation and decrease ventilatory requirements (Rodriguez, 2003), and has become universally accepted as the treatment for preterm infants likely to develop RDS. Many neonatologists routinely intubate all infants of less than 29 weeks gestation at birth to administer surfactant. Several preparations (either synthetic or animal-derived) are available for administration directly into the bronchi.

Two therapeutic approaches have been evaluated – ‘prophylactic’ surfactant – immediately the baby is born, and ‘rescue’ – once RDS has been established. Prophylactic doses offer the theoretical advantage of replacing surfactant before severe RDS develops. Rescue treatment is indicated for infants with a clinical and radiographic diagnosis of RDS, and can be administered once the patient has been stabilised. However, the delay of surfactant replacement can decrease its efficacy and allow the progression of lung injury (Rodriguez, 2003).

Surfactant is administered slowly from a syringe via the endotracheal tube during active ventilation. The endotracheal tube should be positioned just beyond the vocal cords to allow for equal distribution to both lungs. Careful observation of the baby is essential, and changes in ventilatory settings may be necessary, although surprisingly little distress is caused to the infant (Johnston et al, 2003b). Endotracheal suction is not recommended for several hours after administration. If the infant appears to be self-ventilating with good gases, the endotracheal tube can be removed and the infant reassessed to receive continuous positive airway pressure (CPAP) or ambient oxygen.

**Ventilation**

Once resuscitated and given surfactant (if appropriate), infants should be assessed. Depending on maturity and severity of the RDS, their care needs could range from basic nursing care in an incubator with or without humidified oxygen, through oxygen therapy via a nasal cannula, to intensive care with mechanical ventilation.

The goals of ventilatory management during the early stages of RDS are to maintain adequate oxygenation and ventilation, while minimising ventilator-induced lung injury (Rodriguez, 2003). Ventilation should be instigated sooner rather than later following repeated apnoeic episodes, poor blood gases, failure of CPAP, and increasing respiratory effort. In the last two decades technological advancement has provided several options in ventilation. However, most neonatal ICUs use positive pressure ventilators.

CPAP delivers a predetermined continuous pressure (10–15cm) and humidified supplemental oxygen to a spontaneously breathing infant, improving oxygenation by recruiting the collapsed alveoli and increasing the surface area available for gas exchange (Cameron and Haines, 2000). It is usually delivered via short nasal prongs inserted into the nasal openings. Correct fixation is essential to avoid erosion of the nasal septum. CPAP is the first choice treatment after surfactant replacement as there are clear benefits over mechanical ventilation – it is not invasive, requires less inspired oxygen to increase saturation levels, and is good for weaning babies from ventilation. However, CPAP is inadequate in severe RDS, large babies...
Intermittent positive pressure ventilation is time-cycled and pressure-limited, and a constant flow of gas is delivered. During inspiration, the gas distends the lung to a preset peak inflation pressure. An increase in peak inflation pressure decreases the PaCO₂ and improves oxygenation, and should be determined by the compliance of the respiratory system, rather than by size or weight. Infants with low surfactant levels are said to have ‘stiff lungs’, as the collapsed alveoli need a high inspiratory pressure to reinflate them. Observing chest movement is the best guide to inflation pressure. However, inappropriately high peak inflation pressure can cause overstension of the lung and increase the risk of barotrauma. During expiration the flow delivers the positive end-expiratory pressure. Adequate positive end-expiratory pressure prevents alveolar collapse and improves oxygenation. The rate of the ventilator aims to synchronise with the baby’s breathing rate but this will depend to an extent on whether the baby is sedated. Fast rates blow off CO₂. The expiratory time should exceed the inspiratory time to prevent overstension of the alveoli, and inspiratory times are usually limited to a maximum of 0.5 seconds. Blood gas analysis and constant monitoring of oxygen saturation determine requirements.

Patient trigger ventilation can be used to avoid asynchronous breaths. The device-delivered breath is initiated in response to a signal derived from the infant’s own respiratory effort – a pressure level is preset and each time the infant’s breath exceeds this level, the machine delivers a breath. A preset rate is also determined so that the ventilator will deliver that rate even if the infant does not initiate a spontaneous breath. Patient trigger ventilation is not suitable for very immature infants or those with poor respiratory effort (Cameron and Haines, 2000).

Synchronised intermittent mandatory ventilation can also be used to deal with asynchrony associated with conventional ventilation. The rate is determined by the clinician and will be delivered in synchrony with the infant’s own respiratory effort. The ventilator will not support any breaths that the infant takes above this rate. Conversely, if the baby becomes apnoeic, synchronised intermittent mandatory ventilation will deliver breaths at the predetermined rate.

High frequency oscillation delivers a high-pressure flow of gas, which is oscillated by a piston to deliver humidified oxygen at frequencies of about 1,000/minute. It is becoming common practice to use high frequency oscillation as a first-line treatment or as rescue treatment in infants with severe lung disease (Cameron and Haines, 2000). However, due to the rapid, uncountable respiratory rate, and the necessity for frequent X-rays to check the lungs are not becoming overdistended, infants on high frequency oscillation are a challenge to nurse. Also, the sight of a chest that appears to be ‘fibrillating’ can be frightening for the parents.

Other less common ventilatorial modalities are continuous negative end pressure, extracorporeal membrane oxygenation, and liquid ventilation.

Nitric oxide
Inhaled nitric oxide via the ventilatory system may be used in some specialist centres for preterm infants who are critically ill with severe RDS. This influences pulmonary vasodilation, significantly improving oxygenation (Inhaled Nitric Oxide Study Group, 2000).

Blood gas monitoring
Blood gases must be monitored (Table 2) as a guide to ventilatory management and to minimise the risk of retinopathy of prematurity from inappropriate use of high levels of oxygen (McGurk, 2003). Frequent monitoring is essential in the acute stages of RDS. The usual and most reliable method of achieving this is through umbilical artery catheterisation or indwelling arterial cannula. Non-invasive methods such as pulse oximetry and carbon dioxide tension monitors are useful trend detectors but should not be used in isolation. After the acute stage and when lines have been removed, capillary blood gas via a heel-stab will suffice.

Implications for nursing practice
Nursing the naked infant supine in an incubator will allow unrestricted access for intubation, cannulation, and other procedures, and observation of the endotracheal tube position, chest movement, and arterial and venous lines. The head should ideally be slightly extended to stabilise the tube and prevent laryngeal trauma. However, altering the infant’s position with each set of caring procedures is usually recommended. Side-lying postures tend to lessen hip and shoulder rotation and abduction. In any position the infant should be supported with flexible boundaries of, for example, rolled blankets.

| TABLE 2. NORMAL BLOOD GASES (SaO₂ SHOULD BE MAINTAINED <92–94%) |
|-----------------------------|-----------------|-------------------|
|                          | Term infants    | Preterm infants   |
| pH                         | 7.3–7.4         | 7.3–7.38          |
| PCO₂                       | 4.5–6.0 kPa     | 4.5–6.5 kPa       |
| PO₂                        | 8.0–12 kPa      | 7.5–10 kPa        |
| Bicarbonate                | 18–25 µmol/L    | 18–25 µmol/L      |
| Base excess                | -7 to +3        | -5 to +5          |


be kept to a minimum – known as minimal handling or cluster care – (Turrill, 2002), as sick infants can react to any disturbance by becoming hypoxic. Crying (or silent crying in the case of an unsedated ventilated infant) causes irregular respiration and compromises ventilation, increases pulmonary artery pressure and shunting, lowering oxygen levels (SpaRshott, 1994).

**Thermoregulation**
Neonates have poorly developed mechanisms for thermoregulation and maintenance of a neutral thermal environment is a perpetual challenge. Core temperature should be maintained at 37°C to minimise oxygen consumption and acidosis. Peripheral temperature should be maintained above 36°C – a fall below 34°C is indicative of underperfusion, which may be due to hypovolaemia or infection. To minimise heat loss, it is recommended that sick infants are nursed in an incubator with a controlled temperature, or an open cot with an overhead heater controlled by a temperature probe on the skin.

**Fluid and electrolyte balance**
RDS delays the onset of normal postnatal diuresis, and oedema often appears after 24–48 hours. Mucous attention to fluid and electrolyte balance is crucial to avoid fluid overload, which contributes to complications such as patent ductus arteriosus and chronic lung disease. The ratio of body surface area to volume is about three times greater for an infant than for an adult, which significantly increases water loss through the skin. To an extent, a humidified environment can help but insensible losses should be an essential part of the fluid balance equation.

Fluids should be administered intravenously during the acute stages of RDS either through an umbilical line or a peripheral ‘long line’ if the infant is small and sick. For bigger babies who require only short-term ventilation, a peripheral cannula may suffice. Dextrose 10 per cent is used for the first 24 hours, usually followed by total parenteral nutrition, to which electrolytes can be added according to blood tests. Although full enteral feeding will probably be withheld, ‘gut-priming’ with 1ml or so of breast milk every four hours is usually recommended. This is slowly increased as the baby’s condition improves.

Preterm babies with RDS can become anaemic from blood sampling, and top-up transfusions are often needed.

**Pharmacological support**
As the radiological appearance of RDS is similar to that of congenital pneumonia, all infants should be given prophylactic antibiotics until an infection screen proves negative. First-line antibiotics should be administered until a positive culture dictates specific medication.

Sedation with or without medical paralysis is usually recommended for ventilated infants to avoid discomfort. The use of paralysing agents can cause tissue oedema and necessitate fluid restriction. Sedation given by continuous infusion will also aid synchronous ventilation, and should therefore be avoided in babies on CPAP and synchronised intermittent mandatory ventilation.

Hypotension is common in sick infants with RDS who may require volume expansion or inotropic support to improve cardiac function, and thus organ perfusion. Calculations of medications must be carefully individualised. The infant’s weight must be taken into account in association with consideration of the immature renal and hepatic systems’ incapacity to metabolise and excrete drugs. Serum levels of drugs should be closely monitored to avoid toxicity.

**Intensive care monitoring**
Successful treatment of RDS requires careful monitoring and attention to the details of the intensive care needed by preterm babies. This includes frequent blood gases, urea, electrolytes, full blood count, and glucose estimation. Continuous monitoring of heart rate, respiration, temperature, and blood pressure are the minimum requirements for a ventilated baby. Visual observation should be recorded hourly. The chest should be auscultated regularly to check for bilateral breath sounds and endotracheal tube positioning. All intravenous and arterial lines should be checked at least hourly for patency.

**Endotracheal suction**
Endotracheal suctioning to maintain airway patency is a necessary component of care for the intubated baby. It removes secretions, while preventing obstruction that can lead to atelectasis and decreased lung compliance. As suctioning is traumatic (infants may become bradycardic or hypoxaemic, and it can damage the trachea), it should be instituted with great care and only when absolutely necessary, based on clinical findings. It is a sterile procedure. Debate surrounds the use of instilled normal saline prior to suction (McCormack, 2003).

**Weaning from ventilation and intensive care**
As the infant’s condition improves, ventilation can be slowly decreased as per blood gas estimation. Steroids may be administered to improve lung function (Wilman, 2001). The goal is to ultimately extubate (probably via CPAP if fully ventilated) into oxygen via a nasal cannula or ambiently. Oxygen may be required for some time to maintain adequate saturation levels.

Monitoring can also be withdrawn but recording of basic observations and pulse oximetry should continue. An apnoea monitor should be in situ.

Enteral feeds can be slowly increased until full requirements are tolerated, although tube feeding may be required for some time, as decreased lung function may negate sucking. Use of breast milk should be encouraged.

**Parents**
It is vital that the parents feel involved. Their anguish begins as soon as they know they are to deliver a preterm infant who may have RDS, and the moment of birth, which should be a happy time, is fraught with worry. The admission of their baby to the neonatal ICU, attached to a plethora of machinery, can be devastating (Strange, 2002).

Family-centred care is an appropriate framework for
the neonatal ICU (Turrill, 1999) but its implementation in the technological environment is not easy. However, parents should be encouraged to help with the care procedures. They can clean their baby’s mouth, change the nappy, and more, if supported and encouraged by staff.

Most importantly, the mother should be encouraged to express and freeze breast milk both for gut priming and later use. Parents can also be encouraged to talk to their infant and learn ‘positive touch and infant massage’ (Wall, 2002) and kangaroo care, in which the infant is placed on a parent’s chest for two to three hours per day (Brandon, 2003) after the acute stage.

**Complications and sequelae**

Complications of RDS are pneumothorax, pulmonary interstitial emphysema, persistant pulmonary hypertension, necrotising enterocolitis, intraventricular haemorrhage, and patent ductus arteriosis (Johnston et al, 2003b).

The most common sequela of RDS is chronic lung disease or bronchopulmonary dysplasia. This has been defined as the requirement of supplementary oxygen after 28 days from birth, or additional oxygen in a prematurely born infant after 36 weeks postmenstrual age (time since the mother’s last menstruation). Steroids reduce the duration of mechanical ventilation and improve lung function (Speidal et al, 1998).

Oxygen is essential in managing bronchopulmonary dysplasia to reduce apnoea and bronchospasm; inadequate oxygenation can cause heart failure. When infants are discharged while still receiving low-flow oxygen, an apnoea monitor should accompany them, and their parents should be taught how to use it. The parents should also be taught how to perform cardiopulmonary resuscitation (Jevon and Henley, 2002).

Poor growth and poor weight gain are often related to persistent hypoxaemia, so vigorous attention should be paid to optimal nutritional care. Cerebral palsy and learning difficulties are also long-term complications.

**Follow-up**

Infants with RDS and subsequent bronchopulmonary dysplasia must be followed up as outpatients for some time. Decisions will need to be made as to when to discontinue oxygen therapy depending on assessment and progress. Parents should be given opportunities to discuss their concerns in outpatient appointments, as taking home a child who has received intensive care is a daunting prospect. Community support should also be ongoing.

**Conclusion**

Antenatal maternal steroids and neonatal surfactant therapy have significantly reduced the incidence, severity, and mortality associated with RDS. However, despite enormous advances in the management of RDS, respiratory morbidity in the form of bronchopulmonary dysplasia remains a major problem (Rodriguez, 2003).

Excellent neonatal care and subsequent follow-up can maximise the occurrence of optimal outcomes for these potentially sick and fragile infants. ■