‘Electrosol’ – Electrostatic Aerosol Surfactant

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References:

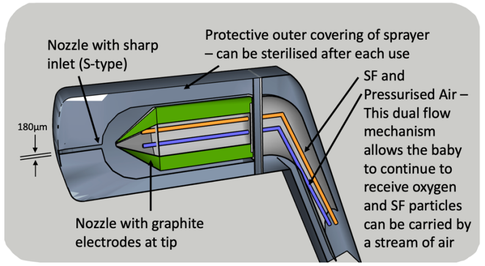
‘Electrosol’ is an electrostatic aerosol surfactant, developed with the aim to achieve uniform distribution of surfactant throughout the lung, minimising adverse effects and the cost of surfactant administration procedures to be more affordable and available in all healthcare environments. This product consists of an electrostatic spray and an electromagnetic collar. It aims to treat Infant Respiratory Distress Syndrome (RDS) and also work as a preventative treatment for premature babies at risk of RDS, overcoming surfactant (SF) deficiencies to alleviate symptoms. Over half of all babies born between 28 and 32 weeks of pregnancy develop RDS, and although there are other medical alternatives to treat RDS symptoms and other methods of SF administration, side effects can be fatal and the risk of barotrauma of the alveoli are high. Theoretically there is a feasibility of our product as an alternative, but clinical trials would have to be performed to thoroughly understand its mode of action.

Acute Respiratory Distress Syndrome

RDS is the most common complication of prematurity leading to significant morbidity in late preterm neonates and even mortality in low-birth-weight infants.
The main hallmark of RDS is insufficient lung surfactant production. This causes difficulty in breathing which can become fatal due to hypoxia.
The deficiency of surfactant causes difficulty to resist surface tension.
The delicate balance of pressures at the air-fluid interface is essential to prevent the alveolar collapse or the filling of the alveolus with fluid.
Apart from prematurity at birth, another main cause of RDS is gestational diabetes of the mother. The mother becomes hyperglycaemic hence the foetus becomes hypoglycaemic, with increased insulin in the blood. This inhibits the expression of surfactant protein A (SP-A), the major surfactant-associated protein, in lung epithelial cells, leading to the insufficient production of lung surfactant and therefore RDS.

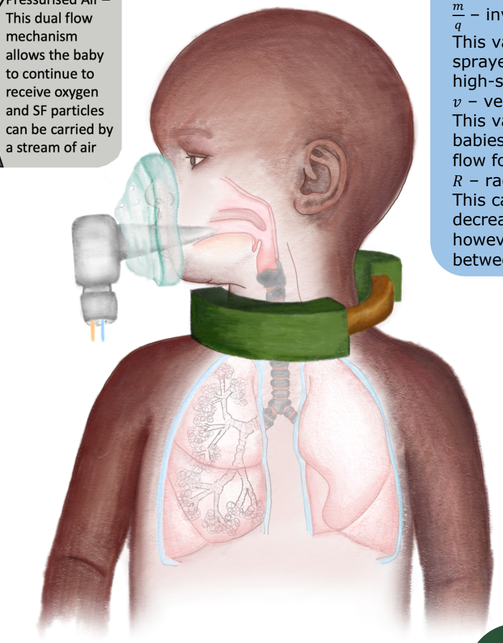
Unmet Needs

Complications arising from premature birth is the leading cause of neonatal death in the UK. RDS is the most common complication of prematurity leading to significant morbidity in late preterm neonates and even mortality in low-birth-weight infants.
This requires the intervention of corticosteroids, (e.g., dexamethasone) which improves pulmonary compliance with mechanical ventilation.
Whilst this treatment has proved beneficial in ventilated neonates, it is ineffective on oxygen-dependant babies, ignoring the needs of a certain patient demographic. However, there are several serious issues that pertain with early steroid treatment, such as anaemia, metabolic derangements, and effects on plasma caffeine concentrations.
In terms of current methods for SF transplantation, tracheal instillation has been utilised, which involves the dripping of SF into alveoli. Whilst this has been termed the less invasive surfactant administration (LISA) the introduction of SF via a catheter leads to uneven distribution of SF particles, making its overall advantages significantly muted.
Non-invasive modalities, such as aerosol SF administration, are preferred as they decrease the risk of mortality, and bronchopulmonary dysplasia (BPD) compared to invasive ventilation with or without SF.
However, under 10% of aerosol administrated drugs reach the upper lobes of the lungs, leading to several undertreated alveoli. Uneven distribution can result in barotrauma of alveoli, decreasing the beneficence of treatment. Hence, the issues of SF administration and overcoming RDS in premature babies is a significant issue.



Nozzle -

The SF is electrostatically charged as it passes through an electrostatic field produced between the electrode on the front of the nozzle. A sharp inlet is used as opposed to rounder edges to keep the spread of the spray narrow as it is carried by the electromagnetic field through the airway, but still allowing SF to spread out and coat the alveoli as distance increases. This is because the jet from a sharper inlet has minimum breakup while that from a round inlet has a broader spatial distribution in the near-nozzle region.
One of the tubes within the nozzle supplies pressurised oxygen, not only allowing ventilation of the baby to be maintained, but also enabling the constant flow of SF droplets (supplied via the other tube in the nozzle) down the airway. If the alveoli are first sprayed with oxygen given an opposite charge, then the next jet of SF droplets will be attracted to them. Due to the SF droplets all having the same charge, they will repel from each other, giving an even, thin coating on the alveoli.

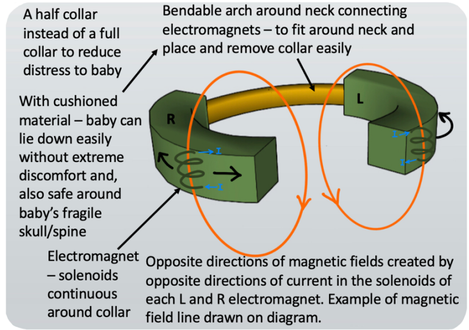


$$\Phi = \frac{m}{q} \times \frac{v}{R}$$

$\emptyset$ - magnetic field strength [T] to be calculated to manufacture electromagnetic collar
$\frac{m}{q}$ – inverse of specific charge of particle [kgC^{-1}]
This value is to be determined – the electrostatic sprayer and collar on a CPR model of a baby using a high-speed camera could be used to investigate this.
v – velocity of air flow [ms^{-1}]
This value is the flow rate of ventilators used on babies, which will act as an average velocity of air flow for all babies.
R – radius of electromagnetic field [m]
This can be adjusted to each baby by increasing or decreasing the current through the solenoid, however there should not be too much variation between all premature babies.

Collar –

In comparison to the most used method of SF administration (LISA), *Electrosol* will not require a catheter or other tubing into the lungs, reducing invasiveness as much as possible. Hence, to direct as much of the charged SF down the trachea and into each mainstem bronchi, an electromagnetic collar will be placed around the baby’s neck. The solenoids will accelerate the charged particles into the lungs, so particles do not accumulate at the back of the throat and will enable a greater coverage of SF on the alveoli and bronchioles. The circular magnetic field of each solenoid should accelerate particles into the bronchi as shown in Figure X. Since the left mainstem bronchi is higher than the right, the collar will not be even – the left solenoid will be slightly higher than the right for the particles to accelerate and flow successfully into each bronchus. The difference in height of the solenoids can be investigated during the development stages of manufacturing the collar.



Suitability of ‘Electrosol’ and Feasibility

The use of electrostatically charged SF particles accelerated and directed into to the lungs by electromagnets will ensure an even, greater coverage of SF over alveoli, via a non-invasive technique, decreasing risks of co-morbidities.
Electrosol is a suitable approach to overcome RDS as it can reduce the risk of BPD and other complications of SF administration, whilst overcoming SF deficiencies. This can limit the occurrence of RDS as well as the mortality rate. As a result, the idea of premature birth and survival would have a changed societal outlook. The simple, non-invasive design means that SF administration can occur in any healthcare setting by clinicians with minimal skill. *Electrosol* can resolve respiratory issues in premature babies in areas of low income, reducing disparities in the outcomes of premature birth and RDS. The cost of *Electrosol* should not expensive, as it can be manufactured by adapting existing technologies (e.g., electrostatic insecticide sprayers and, solenoids), and the collar and the sprayer can be sterilised and reused. But SF must be purchased which may be costly – *Electrosol* can use any SF (allogenic or animal-derived). *Electrosol* aims to be more efficient and use less SF per procedure hence, compared to other methods, this should be cheaper overall.
The main apprehension with using *Electrosol* would be the risk of interfering with cardiac conduction – this could lead to arrythmias or cardiac arrest. However, this risk is low since the magnitude of charges would not be significantly high to cause a current above 50mA, and precautions would be taken during the procedure, such as earthing the sprayer and the baby via a metal wire connected to the ground.

Clinical Trial Selection

Trials to identify sufficient dosage, time frame for administration, duration of treatment, and potential side effects are necessary to ensure safe implementation of *Electrosol* in NICUs and PICUs.

1. The trials will begin on animals, where we would use baboons, due to their similar anatomy and surfactant levels compared to neonates. The effectiveness of treatment will be measured by studying for overall improvements in surfactant metabolism, where radioactive isotopes would be used to identify the half-lives of a dipalmitoyl phosphatidylcholine, a major component in surfactants.
2. Following this, once rough boundaries are set in each of the factors, trials will be moved to adults and eventually neonates. To ensure a lack of heterogeneity in results, trials will be repeated several times, with varying severities of respiratory distress, to identify concrete guidelines for implementation.
3. Eventually long-term trials will commence, to identify any other morbidities that may rise from treatment as well as to gauge the long-term benefits of administrating *Electrosol*.

We understand the longevity of trialling a novel product, and that we may face several hurdles in the process, such as gathering premature babies to partake in our experiment. However, with sufficient preliminary testing in the animal and adult testing period, a clearer idea to the viability and potential of *Electrosol* will prevail.

Implementation into NHS

Electrosol constitutes as a ‘new clinical procedure’ (NCP) as it is a clinical intervention involving new techniques which have not been previously undertaken, using new equipment.

1. Proposal given to clinician who receive approval from clinical directors
2. Consultations whether NCP complies with existing NICE guidance. Our NCP does not relate to medicine.
3. Since new equipment is involved, Health, Safety and Security Committee (HSSC) would consider product for any potential issues and adverse side effects.
4. If NCP is approved, NCP will be submitted to specific Trust Executive Committees
5. If NCP is approved, clinicians willing to use product must ensure that:

- All relevant staff receive necessary training – must identify training needs of staff who will be involved with procedure and how the needs will be met
- Appropriate patient consent and information are available – Information given prior to consent must include specific reference to the fact that the technique is new. Patients must understand the safety and efficacy of NCP is uncertain and must be informed of anticipated benefits and potential side effects.

Acceptance by Stakeholders

Inevitably, there will be some hesitation from all stakeholders as *Electrosol* would be a new clinical procedure and uses electrostatic charged particles in treatment which are not used regularly in practice.
Regarding the public, misconceptions about the technology can be anticipated, particularly since there will be concerns about long term effects.
With clinical trials showing the safety of *Electrosol* and the potential side effects, public trust can be improved, however at the time of proposal, distrust and doubt are expected. Since babies would not be able to provide consent, parental consent is necessary. Parents may be concerned about using charged particles on babies, who have already fragile respiratory systems, and the risk of charges causing further strain on the baby. Clinicians, who prioritise patient safety and well-being, also require concrete evidence about benefits and side effects.
To date, there are few studies published that verify the potential effects of electrostatic particles in treatment and the public views on such procedures. To ensure our product is keeping with beneficence, we will issue more trials to test activity specific to the use of electrostatic activity, whilst also sending out surveys at every stage of the trial, so the public stay informed. This will ensure public trust, leading to better uptake later on.

Future Technologies:

Dosage guidelines must be established prior to implementation, which will vary depending on the severity of RDS. A lack of dosage comprehension has led to alveolar rupture in other previous treatments. But technologies to track the phospholipid levels of lung surfactant can be used. SP-A and SP-D proteins impact the biophysical function of surfactant and regulate phospholipid secretion/re-uptake. These can be markers for restoration of surfactant levels. Following the implementation into NHS, preventative measures to reduce the likelihood of developing RDS as an adult can be taken using *Electrosol*.
Considering the aftermath of treatment by tracking surfactant levels will ensure optimum use of the product.