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How can synthetic proteins help premature babies?

Authors:
Frans Walther, Monik Gupta, Michael Lipp, Holly Chan, John Krzewick, Larry Gordon, Alan Waring

Associate Editors:
Elitsa Panayotova and Lisa Woodruff

Abstract

Sometimes babies are born *premature* – three weeks or more before they are due. Premature babies often have health problems. One of the most common issues is breathing problems, because the lungs haven't fully developed yet. The immature lungs lack a specific mixture of lipids and proteins, called *surfactant*, which allows the lungs to expand. The current treatment for this condition is the introduction of animal surfactant through a tube in the baby's windpipe. This method is often successful, but it's expensive and sometimes dangerous. This is why we wanted to test a new possible way: letting the baby inhale *synthetic* lung surfactant. We developed dry powders containing synthetic surfactant and tried them both in the lab and on animal models – rabbits and lambs lacking lung surfactant. Our results show that the delivery of a surfactant powder through the windpipe gives better results, but that two inhalation doses of the synthetic surfactant are a safe and effective method to improve lung function.

Introduction

Have you ever heard of *respiratory distress syndrome*? It can occur in premature babies, whose lungs haven't developed enough for them to breathe by themselves. The problem is that they lack a mixture of specific lipids and proteins, called lung surfactant, which would allow their lungs to expand so that they can breathe. Modern medicine has found a way to help these babies breathe. Doctors usually introduce animal surfactant into the baby's windpipe (trachea). While this method is most often successful, it has some drawbacks: animal surfactant is hard to produce and sterilize, it costs a lot, and most of all – doctors have to introduce it through the windpipe with a process called *intubation*. This is problematic because research has shown that intubation leads to a higher risk of chronic lung injury.

To reduce the risk of lung injury in premature babies, healthcare providers now prefer to use breathing machines that don't enter the windpipe but use a mask and *continuous positive airway pressure* (*CPAP*) instead (Figure 1). Additionally, the high cost and complex production of animal surfactant have led to the testing of synthetic lung surfactant. Is the synthetic lung surfactant efficient, though? And can we deliver it as a dry powder that babies can inhale? These are the questions we wanted to answer.

Figure 1:
Baby with a CPAP machine.
Source: Amsterdam University Medical Center

Methods

- First, we synthesized *analogs* of the natural surfactant proteins and obtained pure surfactant lipids.
- We then designed various dry powders, which contained synthetic surfactant.
- We chose three variations of the synthetic surfactants.
- To deliver the powders, we created a special device which disperses the dry powders through the CPAP machine.

To test our dry powders with synthetic surfactant:

- We first checked the structure of the synthesized surfactant proteins through *spectroscopy.*
- A specific device, called *captive bubble surfactometer,* allowed us to test the ability of the dry powders to reduce surface tension in the lab.
- We also tested the activity and efficiency of the dry powders on live animal models – 39 rabbits and 19 premature lambs, all of which lacked surfactant.

We wanted to compare delivery through intubation to delivery through inhalation (CPAP). To do this we delivered the powder to 13 of the rabbits and 6 lambs through a tube and to the others through CPAP. To test whether two doses of the dry powder have a positive effect on lung function, we gave two doses to 6 lambs and just one dose to 7 lambs to inhale.

Finally, to test the lung function after delivery of the powders, we measured the amount of oxygen in the blood vessels and we monitored the lungs' ability to expand.

Results

The tests in the lab – the spectroscopy and the captive bubble surfactometer – showed good results. All three surfactant variations were able to minimize the *surface tension* (so the lungs can expand).

What about our animal models?

In the rabbits we observed:

- The ability of the lungs to expand and the levels of oxygen in the blood vessels improved quickly after delivery of surfactant through intubation.
- Surfactant delivery through CPAP also led to an improvement in lung function but not as great as through intubation.
- One of the three variations showed slightly better results than the rest; that's why we tested only this one in the lambs.

In the lambs the results were the same as with the rabbits:

- The intubation delivery showed better results.
- Two doses of dry surfactant powder improved lung function more than one dose (Fig. 2).

Which method shows the best result?

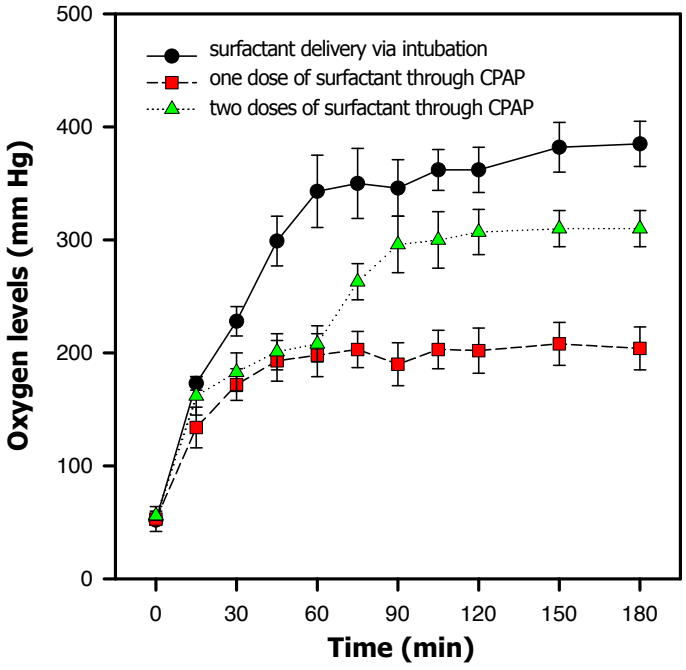

Figure 2:
Oxygen levels in lambs lacking surfactant after synthetic surfactant treatment through intubation or through one or two doses of inhalation.

Discussion

Our results are very promising. All three variations of dry powder synthetic surfactant showed good surface activity – they reduced the surface tension in amounts comparable to a currently used liquid surfactant. Moreover, all three dry powder variations improved lung function in our animal model rabbits, which lack surfactant. Since single delivery of surfactant through intubation showed better results than single delivery through inhalation (CPAP), we tried a two-dosage inhalation approach on the lambs. Indeed, a second dose of dry powder with synthetic surfactant during CPAP greatly increased lung function in the lambs as compared to a single dose. We therefore believe that the delivery of synthetic surfactant through CPAP is an effective method to improve lung function in rabbits and lambs which lack natural surfactant. We hope that our findings will help in future research efforts to improve care for babies with respiratory distress syndrome.

Conclusion

One in 10 babies is born prematurely. Without medical treatment, especially to help them breathe, many of these babies would not survive. Premature birth is the most common cause of death among babies worldwide. Medical research, often using animal models, produces new and better treatments for babies such as these. Though some may feel uncomfortable with using animal models for research, animal research is supervised and approved by specialized ethics committees. Scientists must follow very strict guidelines so that animals are treated carefully and humanely. This research is hopefully a step toward developing treatments to save even more premature babies.

Glossary of Key Terms

Analog – in this case, a synthetic surfactant protein that mimics a natural surfactant protein.

Captive bubble surfactometer – a device which measures surface tension.

CPAP (continuous positive airway pressure) – a method using a breathing machine which provides a mild push of air all the time to help the lungs stay open.

Intubation – the insertion of a tube in the patient's (baby's) windpipe.

Premature – babies that are born three or more weeks before the baby's estimated due date.

Respiratory distress syndrome (RDS) – an illness most common in premature babies who can't produce lung surfactant and thus can't breathe by themselves.

Spectroscopy – a technique which allows you to analyze samples (in this case surfactant proteins) based on the light they absorb at different wavelengths.

Surface tension – a property that exists between fluid (water) and air: the surface of fluid wants to shrink to the minimum area possible. In the case of lungs, when fluids again meet air, there is surface tension which can make your lungs collapse and thus prevent you from breathing. Surfactant reduces this surface tension.

Surfactant (lung) – a specific mixture of lipids and proteins which reduces the surface tension in the lungs where fluids meet air, thus allowing the lungs to expand.

Synthetic – artificial or manmade (i.e. produced in the lab).

Check your understanding

1 What is lung surfactant and why can't some babies produce it?

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2 What are some of the drawbacks of using animal surfactant to treat respiratory distress syndrome?

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3 Why do we experiment in lambs (which lack surfactant) and is it ethical?

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4 Why do we measure oxygen levels in blood vessels?

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