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Surfactant Therapy

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A report on the Surfactant Therapy for Adult Respiratory Distress Syndrome.

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Adult Respiratory Distress Syndrome (ARDS) is such a pathological situation in which, the surfactant present inside the alveoli gets inhibited due the entrance of the foreign material in the alveoli due to certain reasons. This is called as secondary deficiency of the lung surfactant. Lung surfactant mainly consists of 90 percent of lipids and 10 percent of proteins.

Surfactant isolated from lung of healthy mammals consists of about 90 percent lipids and 10 percent proteins. Dipalmitoyl phosphatidyl choline (DPPC) is the main component which prevents the alveolar collapse during expiration. Other lipid components like, phosphatidylglycerol (PG), Cholesterol, Palmitoyl oleoyl phosphatidyl choline (POPC) etc. and lung surfactant specific proteins (SP-A, B, C and D), help in adsorbing the DPPC to the air-water interface.

Unlike Neonatal Respiratory Distress Syndrome (NRDS) the main cause of the disease, is not the lack for surfactant but, the lack of surfactant activity. There are mainly two main categories of the surfactants based on the mechanisms by which they

inhibit surfactant activity: chemical inhibitors and physical inhibitors. The examples for physical inhibitors are: blood and plasma proteins, unsaturated lipids and degraded lipids etc. Chemical inhibitors include: lipases and protieases etc.

Therapy available till now

The management and therapy for the treatment of ARDS includes positive end-expiratory pressure (PEEP), lung surfactant replacement and steroid treatment. Many other options are becoming available on the basis of the understanding of the cause of the disease such as: Anti-inflammatory strategies, Anticoagulants, Growth factors and Haemodynamics based therapy. This article is focused on the surfactant replacement options available for the treatment of NRDS and ARDS.

Surfactant replacement therapy, with the popular surfactants products available in the market: Exosurf, ALEC and Curosurf etc. for NRDS, is not found to be successful for ARDS. In very few cases Curosurf and other natural surfactant preparations were found to improve the situation up to some extant.

In 1980, Fujiwara et al. first demonstrated high therapeutic efficiency of PL extract from bovine lung with the addition of palmitic acid (PA) and DPPC in NRDS. Similar approach was tried for the treatment of ARDS also and the first attempt of surfactant application for ARDS treatment was made in 1987 (Lachmann et al). The products which have been used for NRDS are always been tried for the treatment of ARDS.

The most promising surfactants are the natural unmodified surfactants: Alveofact and Surfactant-BL. Uncontrolled multi-center study showed that bronchoscopic application of a high dose of Alveofact in patients with severe ARDS and septic shock is both feasible and safe, resulting in pronounced improvement in gas exchange and far-reaching, though incomplete, restoration of the severely changed biochemical and biophysical surfactant properties. Multicenter uncontrolled clinical trials of Surfactant-BL have been carried out in the patients with ALI and ARDS of different etiology such as sepsis, multiple trauma, multiple transfusion, aspiration of gastric content, thrombo-embolism of lung artery, severe pneumonia, thermo chemical burns of respiratory tracts, and post bypass lung injury. Surfactant administration, at a dose of 6 to 12mg/kg per course reduced significantly the duration of CMV and 28-day mortality rate (from 60 percent to 23.2 percent). The mortality rate in the patients who responded to surfactant administration was 15 percent. Seven patients with severe burns of respiratory tracks treated by Surfactant-BL survived compared to 1 survivor of 15 patients in the control group.

Difficulties in the way

The difficulty which is not allowing this therapy to be as successful in case of ARDS is that, the surfactant given as an replacement is not only have to work in the place of the natural lung surfactant but, it has also to overcome the inhibition caused by the foreign material entered into the alveoli. BoncË†uk-Dayanikli et al. described the requirements for ideal therapeutic surfactant, which include the attributes of any ideal preparation and characteristics specific for surfactants: mimic effect of pulmonary surfactant in vitro, nonimmunogenicity, ability to improve gas exchange, lung mechanics and functional residual capacity, resistance to inactivation, optimal distribution characteristics, known clearance mechanisms, and minimal, toxicity. Furthermore, the preparation must possess such properties of lung surfactant in situ as host defense ability and innate immunity.

Possible reasons for failure can be the following:

- Late administration of surfactant preparations
- Incorrect therapeutic dose and methods of preparation administration
- The injustice of EBM principle usage in patients in critical conditions
- Great variety in surfactant compositions

In spite of the introduction of new LS and some modern techniques for ARDS treatment such as "safe" conventional mechanical ventilation, usage of the concept of "open lung", and so on, the mortality rate due to ALI and ARDS is still very high, so the development of new approaches for ALI and ARDS treatment is well-justified.

Further research in progress

Scintist have been trying various other approaches as well for the treatment of ARDS. For example Xinmin et al (2005) tried corticoids. There is very little evidence of improvement in case of seawater drowning induced acute lung injury/acute respiratory distress syndrome (ALI/ARDS))

Two novel C16:0 sulfur-linked phosphonolipids (S-lipid and SO2-lipid) and two ether-linked phosphonolipids (C16:0 DEPN-8 and C16:1 UnDEPN-8) were studied for surface behavior alone and in mixtures with purified bovine lung surfactant proteins by Chang et al 2005.

N-acetylcysteine was tried Chuang et al recently (2007) significantly attenuated the severity of Acute Lung Inury.

Surfaxin and Venticute are those surfactant preparations, whose clinical trials are in process at the moment. Phase II of clinical study of recombinant SP-C (Venticute) in patients with ARDS showed marked improvements in the oxygenation index, ventilator-free days, and the percentage of successfully weaned patients. However, mortality rate in this group was 29 percent compared to 33 percent in the control.

Several ways of improving surfactants are under study. The investigators have been developing some substitutes for natural surfactant components: first, either synthetic or recombinant surfactant proteins or their analogues to generate proteins that are free of animal contaminants; second, PL analogues that may improve surface activity of surfactant and be resistant to phospholipase and, third, the substances to prevent surfactant inactivation, for example, such nonionic polymers as dextran or polyethylene glycol.

Although there are still a lot of questions regarding feasibility, efficiency, and methods of surfactant therapy for the diseases others than NRDS, the future of surfactant preparations seems to be quite promising. The application of surfactant preparations in patients with direct lung injury is more efficient than in the patients with indirect lung injury. Surfactant application can be fearlessly recommended for the patients with aspiration of gastric content, severe burns of respiratory tracts, severe pneumonia, lung contusion, and others. In any case, the analysis of the efficiency of surfactant therapy should be carried out in homogenous groups of patients as the definition of ARDS is too broad and includes the variety of patients with different and extremely complex pathophysiologies.

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