More about Surfactant, Oxygen, Caffeine and Chronic Lung Disease

The 29th International Workshop on Surfactant Replacement was held in Valencia in Spain from May 30 to 31, 2014. It is with great regret that the Scientific Committee reports the recent death of Adolf Valls-i-Soler (Bilbao, Spain), who regularly attended and contributed to our surfactant workshops for many years. With the meeting being in Spain this year, he would undoubtedly have loved to be present to support our president Máximo Vento.

Valencia was founded 2,000 years ago by the Romans, in a privileged location on a large gulf on the Mediterranean, providing the city with a very mild climate, perennial sun and a blue sky. Today, Valencia is a modern university city with over 60,000 students on 3 campuses. The beauty of the city and the friendliness of its inhabitants will surely encourage return visits from visiting delegates.

The theme for this year’s Workshop was somewhat less focused than in previous years, with presentations not only on surfactants, oxygen therapy and chronic lung disease but also on the ethical pitfalls in neonatal trials, caffeine treatment and clinical pharmacology as applied to the neonate. The Workshop comprised the 6th Bengt Robertson Memorial Lecture and 5 other excellent overview presentations, 16 orally presented free communications and 28 poster presentations, all selected from a record total of 84 submitted abstracts.

The 6th Bengt Robertson Lecture was delivered by Máximo Vento from Valencia, Spain. This review dealt with the new paradigm in the use of oxygen in neonatal medicine. Máximo Vento’s review dealt with the practical issues raised in Ola D. Saugstad’s 4th Bengt Robertson Lecture in 2012 [1]. Since the Resair 2 study was published in the late 1990s [2], experimental and clinical research on oxygen metabolism and toxicity in the neonatal period have grown exponentially. This body of evidence is helping us to develop more appropriate ways of both supplementing and monitoring oxygen in the newborn [3, 4], in order to obtain the best possible clinical outcomes while minimizing short- and long-term morbidities [5]. Máximo Vento concluded that the state-of-the-art management of oxygen therapy in the delivery suite consists of allowing preductal oxygen saturation to spontaneously increase in the first minutes of life. If oxygen is needed, it should be titrated according to pulse oximeter readings kept within the standard nomogram. Thereafter, oxygen saturation targets should be maintained in the range of 90–95% for optimal outcomes [3, 4, 6].

Caffeine, the wonder drug in neonatology, was the topic of the lecture given by Dirk Bassler, previously from Tuebingen, Germany, but now based in Zurich, Switzerland. Caffeine, as the title indicates, has proved to be a wonder drug in neonatology. Methylxanthines have been used in neonatology for more than 40 years, but it was not until 2006 that doubts about the safety of caffeine were dispelled [7]. Caffeine’s effectiveness as a stimulator of respiratory drive in apnea of prematurity and weaning from mechanical ventilation were widely recognized before this time. However, the Caffeine for Apnea of Pre-
maturity (CAP) trial has found other unexpected positive outcomes such as a reduction of bronchopulmonary dysplasia [8] and improved long-term neurodevelopmental outcome [9], rendering caffeine one of the most useful and widely used drugs in the neonatal armamentarium today [10].

The molecular era of surfactant biology was the topic developed by Jeffrey Whitsett from Cincinnati, Ohio, USA. He is one of the greatest experts in the world in the field of lung biology and control of perinatal maturation [11]. His profound knowledge of the signaling pathways and transcriptional mapping that control surfactant homeostasis [12] enlightened the audience and facilitated their comprehension of this fascinating and rapidly developing field of lung development. He noted that mutations in the genes that regulate alveolar epithelial cells and surfactant homeostasis cause severe lung disease in newborn infants and older patients. Other gene mutations are now known to play an important role in the pathogenesis of chronic lung diseases.

Neonatal pharmacology has always been an important, if sometimes ignored, issue for the clinical neonatologist. Too often, off-label drugs developed for adults are prescribed for neonates and doses are extrapolated from those used for children or adults. Neonatologists often lack a real knowledge of the basic pharmacodynamic and pharmacokinetic properties of the drugs that they administer. Karel Allegaert from Leuven, Belgium, emphasized the unique features of neonatal pharmacology [13] in his presentation and discussed how pharmacokinetic modelling tools were helping to reverse this lack of knowledge. He mentioned the interplay between drugs used in neonatal medicine and the renal function of preterm infants [14] as well as stressing the importance of performing follow-up studies in order to exclude unanticipated long-term adverse effects [6, 15].

Neena Modi from London, UK, addressed the very important and topical issue of ethical pitfalls in neonatal comparative effectiveness trials. Recent criticism of the SUPPORT trial [16] by the US ‘Office for Human Research Protections’ on the grounds of inadequate consent procedures threatens all future randomized clinical trials in newborns. Neena Modi, amongst others, has spoken out strongly against this unfair criticism [17], just as she has been critical of neonatologists who overinterpret evidence from clinical trials [18]. Her presentation was followed by a wide-ranging panel discussion on this topic. The exponential advances in neonatal care and technology have been due to carefully conducted randomized clinical trials and it is hoped that unfair criticism of their ethical standards will not deter research-orientated neonatologists from continuing these advancements [17].

Jesus Perez-Gil from Madrid, Spain, gave a masterly talk on how knowledge of the biophysics of the surfactant system has helped the development of effective surfactant therapies [19].

Bronchopulmonary dysplasia remains a major problem in neonatal care and it can cause a heavy burden on healthcare services and medical resources throughout childhood and even in adulthood. However, these consequences of long-term respiratory morbidity are often unknown or are ignored by neonatologists. Eugenio Baraldi from Padova, Italy, an international authority in pediatric pulmonology, has performed very interesting and informative studies on pulmonary function and outcomes for neonates with chronic lung disease when they are of school age and in adolescence [20, 21]. The most severe cases of bronchopulmonary dysplasia remain symptomatic in adulthood and the severity of airflow obstruction is probably worsened by smoking [20].

To conclude, there was a postconference workshop dealing with noninvasive ventilation during postnatal stabilization with contributions from Arjan te Pas from Leiden, The Netherlands, and Eric Shinwell from Rehovot, Israel, both outstanding international experts in the field of lung physiology and ventilation. Finally, Rangaswamy Ramanathan from Los Angeles, Calif., USA, spoke about a burning issue: ‘graded oxygen saturation targeting and ROP’. The audience had plenty of time to discuss the contents of both these sections of the Workshop and actively interacted with questions addressed to the speakers.

The program of the 29th International Workshop on Surfactant Replacement covered a wide range of relevant issues related to lung biology, physiology, pathophysiology, therapeutics and ethics, all delivered by international experts in these fields. This issue of Neonatology contains the overviews and orally presented abstracts from the Workshop. The Scientific Committee would like to honor and remember Bengt Robertson [22] who founded this series of workshops in 1986 and was the architect of our understanding of neonatal RDS and its treatment with surfactant.

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References