Sharing Progress in Neonatology (SPIN): A Critical Appraisal of Our Current Knowledge

Incorporating the Proceedings of the 34th International Workshop on Surfactant Replacement, Parma, June 7–8, 2019

The fourth Sharing Progress in Neonatology (SPIN) meeting incorporating the 34th International Workshop on Surfactant Replacement took place from June 7 to 8, 2019 in Parma, Italy. Parma is a northern Italian city in the Emilia-Romagna region, famous for its architecture, music, art, prosciutto, and parmesan cheese. It is also home to the University of Parma, one of the oldest universities in the world, and the city where the surfactant, poractant alfa is manufactured from porcine lungs [1]. Parma was thus an appropriate city to host the 4th SPIN meeting. Previous SPIN meetings have been held in Naples [2], Dublin [3], and Lübeck [4], where topics beyond neonatal respiratory care and surfactant replacement were discussed. This year the range of topics was expanded by having 14 international invited speakers and a reduced number of free presentations.

The meeting opened with the 11th Bengt Robertson Memorial Lecture given by Eduardo Bancalari from Miami whose excellent talk was entitled “Bronchopulmonary dysplasia: 50 years after the original description” [5]. In his lecture Eduardo Bancalari discussed the evolution of bronchopulmonary dysplasia (BPD) as a complication of neonatal respiratory disease in the more than 50 years since Bill Northway’s first description in 1967 [6]. He made the point that BPD has evolved into a milder disease with lower mortality compared to the classical disease described by Northway et al. [6]. New BPD is the result of complex interactions between altered alveolar and vascular development, injuries occurring pre- and postnatally,

and reparative processes in the lung. A major challenge exists as regards the definition of BPD and the discovery of effective preventive measures. This lecture was a fitting tribute to Bengt Robertson, a pioneer in surfactant research [7] who coordinated these international surfactant workshops which have been held annually since 1986 [1].

Henry Halliday from Belfast discussed “Lessons from the past” highlighting problems that have occurred during more than a century of neonatal care [8]. These include unlimited oxygen therapy, inappropriate thermal care, delayed onset of feeding for preterm infants, and use of many drugs without adequate knowledge of either short- or long-term effects. These drugs comprise some antibiotics, Epsom salt enemas for respiratory distress syndrome (RDS), sodium bicarbonate for acidosis, and postnatal corticosteroids to treat BPD. He also discussed how the management of RDS has evolved over his lifespan of almost half a century in neonatology. From purely supportive care in the past, babies with RDS now receive specific care targeted at their surfactant insufficiency. There are many lessons from the past and we must continue to learn from them.

The third invited speaker was Arjan te Pas from Leiden whose presentation was entitled “The changing landscape in supporting preterm infants at birth” [9]. He discussed non-invasive respiratory support and delayed cord clamping during stabilization of preterm infants. Recent experimental data show that during apnoea at birth the larynx is closed, and this may mean that non-invasive

ventilation is ineffective. The speaker advocated stimulation and supporting spontaneous breathing to ensure successful transition. Animal data also show large swings in blood pressure, blood flow, and oxygenation after immediate cord clamping, which can be avoided by delaying clamping until lung aeration has been established. This new experimental information has been described as a potential “gamechanger” in stabilization of the preterm infant.

Ola D. Saugstad from Oslo gave an update on delivery room management in a talk entitled “The golden minute in the delivery room: what is needed?” In 2015 he had listed the problems facing those managing newborn infants at birth as follows: noting the precise time of birth, antenatal steroid use, delayed cord clamping, need for suctioning, thermal control, use of CPAP, delaying surfactant treatment, and selecting the right oxygen concentration according to gestational age [10]. It was Max Vento who was perhaps the first to use the term “golden minutes” with regard to stabilization of extremely low gestational age neonates [11]. Ola D. Saugstad in his lecture discussed the different resuscitation algorithms for use in the first minute. Furthermore, he underlined the effect on outcome of maternal and antenatal factors such as the mother’s body mass index at the beginning of the pregnancy and mode of delivery.

The fifth invited speaker was Haresh Kirpalani from Hamilton (and Philadelphia) who asked the question “What is new about transfusions for preterm infants?” [12]. An international survey conducted in 2012 showed a wide variation in transfusion practices [13]. Erythropoietin was used by 26% of respondents and delayed cord clamping by 29%, but there was wide variation in haemoglobin values used to transfuse extremely preterm infants regardless of postnatal age. The debate about whether liberal or restrictive transfusion practices are associated with the best outcomes is not settled. A Cochrane review suggests benefits of higher threshold values for transfusion [14], but the evidence is not strong. Two current trials will help answer the question, but there are also emerging potential risks of blood transfusions which should be taken into account. However, Haresh Kirpalani reported that there is insufficient evidence to support a practice recommendation of avoidance of packed red cell transfusion to prevent necrotizing enterocolitis (NEC) [15].

Bill McGuire from York discussed “Immuno-nutrition for preterm infants” [16]. The pathogenesis of NEC and late onset sepsis may be related to the content and mode of delivery of the enteral diet, particularly immunonutrients from human breast milk and their effects on the

microbial and metabolic balance in the immature intestine. Breast milk is protective against NEC, but supplementation with individual immuno-nutrients such as immunoglobulins and lactoferrin [17] is ineffective in preventing NEC. Evidence for probiotics is stronger [18], but concerns exist about the choice, safety, and availability of formulations. The best policy at present is probably to advocate breast milk feeding for very preterm infants [19].

The next presentation also focused on nutrition when Neena Modi from London spoke on “Preterm nutrition: still controversial after all these years.” Among Neena Modi’s many research interests is body composition of preterm infants following various feeding regimens and after NEC. She reported that the slower weight gain of preterm infants fed breast milk was due to a deficit in non-adipose tissue mass and could reflect lower protein intake [20]. Similar studies in preterm infants who had suffered from NEC showed lower weight at term which was secondary to reduced adipose tissue volume. This suggests that there was adequate nutrition to preserve non-adipose tissue mass, but not to support normal third-trimester deposition of adipose tissue in these preterm infants [21]. The most important point in this presentation was the recommendation that breast milk should be advocated as the best source of nutrition for very preterm infants [19].

Kathleen Wermke from Würzburg gave a fascinating talk on “The vocalist in the crib: decoding neonates’ crying” based on her 30-year research experience. The audience was introduced to the melodic repertoire of infants’ crying [22, 23], including inspiratory phonations [24] and the influence of maternal language during late pregnancy on cry melodies [25]. Human infants are the most proficient of the few vocal learner species. Sex hormones, particularly estradiol during mini-puberty, seem to affect early language development, probably due to organizational and functional effects on the developing brain [26]. These insights provide the basis for clinical studies to identify early risk markers for developmental disorders as regards language.

The next three talks were about surfactant treatment. Tore Curstedt from Stockholm gave an update on the “Development of synthetic surfactant for clinical use.” Six years ago he reported that it seemed that synthetic surfactants containing two peptides and a more complex phospholipid composition will be able to replace natural surfactants in the near future [27]. Today things have moved on, and indeed the first human trials with new synthetic surfactants have begun. The supply of animal-derived

lung surfactants is limited so that not all babies with RDS worldwide can be treated. There is a need to develop well-defined synthetic replicas based on key components of natural surfactant (SP-B and SP-C) enabling cost-efficient production and also facilitating treatment of other lung diseases [28]. David Sweet from Belfast followed by describing “Clinical trials with synthetic surfactant,” including the one he was directly involved in [29]. In this first study in humans, 40 infants of 27–33 weeks’ gestation with RDS needing >35% oxygen were given a single dose of CHF5633 (a synthetic surfactant containing SP-B and SP-C analogues) within 48 h of birth. There were rapid and sustained improvements in oxygen requirements in all but one infant who did not respond to either CHF5633 or two doses of poractant alfa. These encouraging data provide the basis for ongoing randomized controlled trials.

Roger Soll from Burlington discussed “Novel surfactant administration techniques: will they change outcome?” [30]. Surfactant has traditionally been administered through an endotracheal tube with continued mechanical ventilation. This approach may be associated with complications such as pulmonary air leaks and BPD. Several methods of less invasive surfactant administration have been developed including INSURE, pharyngeal deposition, laryngeal mask airway, aerosol, and thin catheter administration. After performing a systematic review with meta-analyses, Roger Soll concluded that there may be meaningful clinical benefits from these new methods of surfactant administration. However, except for aerosolization none is truly non-invasive, and further trials will be needed to refine both appropriate patient selection and the treatment modality to optimize the approach for infants with or at risk of developing RDS.

“Lung growth in preterm infants” was the title of the talk given by Virgilio Carnielli from Ancona. In 2016 he reported use of stable isotope tracer studies to evaluate neonatal respiratory diseases [31]. This year’s presentation was based on the assessment of lung growth in preterm infants by measuring oxygen diffusion during hospital stay. Oxygen diffusion was measured using the non-invasive oxygen saturation/fraction of inspired oxygen ratio [32]. Factors associated with this ratio included gestational age, being small for gestational age, sepsis, human milk feeding, and presence or absence and type of early respiratory disease. Preterm infants with and without BPD had a spectrum of oxygen diffusion impairment that was inversely associated with gestational age [32].

Boris Kramer from Maastricht gave a talk entitled “Necrotizing enterocolitis, gut microbiota, and brain development: role of gut-brain axis” [33]. Microbiota are

thought to play a major role in the development of NEC. Emerging evidence supports the contention that microbiota are also of importance in brain function and development. Microbiota characterization has the potential to diagnose NEC and act as a biomarker to monitor brain development. Analysis of faecal volatile organic components which shape the volatile metabolome and reflect microbiota function and host reaction may help with the diagnosis of NEC and late-onset sepsis. There is a complex interplay between microbiota, NEC, and brain development.

The final section of the meeting comprised the SPIN updates during which Jatinder Bhatia from Augusta discussed the “New ESPGHAN guidelines for total parenteral nutrition in neonates” [34]. Preterm infants and especially those that are of extremely low birth weight (<1,000 g) are susceptible to postnatal growth failure if nutritional demands are not met. Poor postnatal growth is associated with adverse neurodevelopmental outcome. Early parenteral nutrition is necessary to provide appropriate protein and energy when enteral nutrition is not feasible or is suboptimal [35]. The final speaker was David Sweet from Belfast, who presented a summary of the 2019 update of the European Guidelines for the Management of Respiratory Distress Syndrome [36]. After these presentations there was a lively discussion from the large audience.

The meeting also included 10 short oral presentations, and 8 of these are published as abstracts in this issue together with some of the invited lectures. Fourteen poster presentations from many countries, including Turkey, Romania, Brazil, the USA, Belgium, Sweden, Italy, Spain, and Germany, also provided opportunities for interaction for the 300 plus attendees at SPIN 2019.

Tore Curstedt, Stockholm
Henry L. Halliday, Belfast
Mikko Hallman, Oulu
Ola D. Saugstad, Oslo
Christian P. Speer, Würzburg

Disclosure Statement

The scientific program was arranged by the Scientific Committee without interference from the sponsors. All members of the Scientific Committee are or have been consultants to Chiesi Farmaceutici. The content of the meeting and workshop reflects the scientific opinions of the individual presenters and not the view of the sponsors.

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