Inhaled Therapy for Small Children, are our Current Inhalation Devices Suitable for Them? - Summary of the Morning Symposium

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European Cooperation in Science and Technology (COST) Actions are science and technology networks that focus on a specific, common research subject. The COST Action MP1404—Simulation & Pharmaceutical Technologies for Advanced Patient-Tailored Inhaled Medicines (Siminhale), has as a main objective to create and maintain a pan-European multidisciplinary scientific network to enhance research and development with the aim of improving efficiency, safety and convenience of inhaled medicines. Work Group 2 of SimInhale, chaired by Sitaram Velaga and Wilbur de Kruijf, has a focus on inhalation devices.

The December 5 morning symposium at DDL 2017 consists of four lectures, each with a different angle on the subject of inhalation therapy and devices for small children.

Wim Vos from FluidDA in Antwerp, Belgium is showing 3D images that illustrate the dramatic changes in the geometry of the airways from newborn to adult. The volume of the lungs changes drastically when growing up, as do the local diameters of the airway. Also the tidal volume of inhalation is much less for small children. Apart from that, small children and babies are obligatory nose breathers, which makes delivery of medication to the lungs a real challenge.

When simulating the use of the exact same aerosol from a pMDI with a spacer from newborns to adults, the lung dose and lung distribution is different for each age group. Compensated for body weight these differences may by chance sometimes balance out, but not for all age groups. More knowledge and awareness of these factors among medical doctors is needed to treat pediatric patients more effectively.

Anne Lexmond from Groningen University in the Netherlands, has researched the capabilities of young children to inhale from DPI devices. A certain peak inspiratory flow and inhalation volume are needed for an efficacious drug delivery from DPIs. To teach them a suitable inhalation maneuver, they shall in general be older than 4 years. Passive DPIs for the age of 4 to 10 can be improved by choosing the right air flow resistance, choose a powder release mechanism that enables a lower peak inspiratory flow and choose an optimal mouthpiece geometry for this age group. Further reading: Lexmond AJ, Hagedoorn P, Frijlink HW, Rottier BL, de Boer AH (2017) Prerequisites for a dry powder inhaler for children with cystic fibrosis. PLoS ONE 12(8): e0183130. https://doi.org/10.1371/journal.pone.0183130

The age group from newborns up to 3 year olds may quite well be served with active DPI devices, that whirl up the powder into a valved holding chamber with a face mask, where the young child can inhale in multiple tidal breaths.

Ronan McLoughlin from Aerogen, Galway, Ireland, has a vast expertise in applying aerosols to hospitalized patients including newborns and neonates. Inhaled therapies for this last group need to deal with extremely small tidal volumes. Bringing medication or e.g. surfactant into these tiny lungs is a real challenge. Apart from face masks, nasal cannulas are being used for these groups. Most equipment was never specifically designed for the younger patients, but special adaptations have been made to serve these patient groups. Sometimes successfully, sometimes less successfully...

Dr. McLoughlin also shows the results of pre clinical research of inhalation therapies with small macaque monkeys, whose inhalation volumes and airway geometry show quite some resemblance with young children.

Herbert Wachtel from Boehringer Ingelheim, Germany, is summarizing BI's experience with the use of Respimat soft mist inhaler devices in children of different age groups. The fact that the inhalable soft mist is generated by the device, irrespective of the patient's inhalation maneuver, makes these devices quite suitable for children of 4 years and older, who can perform an inhalation sequence. For the younger children a spacer with a face mask can be successfully applied to use the soft mist inhaler.

Because of the limited options to do clinical research with children in these age groups, Dr. Wachtel also advocates the use of juvenile throat cast models and idealized juvenile throat models for in vitro assessment of inhalation devices to estimate the applied lung dose for children in different age groups. Further reading: Can Pediatric Throat Models and Air Flow Profiles Improve Our Dose Finding Strategy?

Wachtel H, Bickmann D, Breitkreutz J, Langguth P Respiratory Drug Delivery 2010. Volume 1, 2010: 195-204.

The content of these four talks will be forged into a summary article by Anne Lexmond et al. in early 2018, which pivots around the central question: are our current inhalation therapies and devices suitable for young children?

Most of the currently used inhalation devices, whether nebulisers, pMDIs, DPIs or soft mist inhalers were certainly never specifically designed for young children, except for very few developments like the soother mask, that combines the use of a pacifier (dummy/binky) to hold a face mask in place on a young baby's face. source: Amirav I, Newhouse MT, Luder A, et al. Feasibility of aerosol drug delivery to sleeping infants: a prospective observational study. BMJ Open. 2014;4:e004124.doi:10.1136/bmjopen-2013-004124.

The speakers and moderators of the pre-DDL Symposium strongly advocate that more can be done to design proper inhalation devices specifically for young children, with the characteristics of this age group in mind. Rather than just designing add-ons to existing devices. As a spin-off this may also lead to better and easier-to-use devices for elderly.