

Dr Ronan MacLoughlin

(1) Aerogen (2) School of Pharmacy, Royal College of Surgeons, Dublin, Ireland (3) School of Pharmacy and Pharmaceutical Sciences, Trinity College, Dublin, Ireland.

Design considerations for aerosol delivery to Children and Infants

Children and infants are not simply small adults and require special consideration when planning aerosol-mediated inhalation drug therapy. Further, the variety of presentations in children and infants is vast, and includes a disparate range that includes ~0.5kg premature infants with respiratory distress syndrome (RDS), term infants with (RSV) infection and older children with complications associated with lung infection or Pulmonary Hypertension as examples. With continual advances in formulation, aerosol generator technology, patient interventions and patient interfaces, several options are now available to both designers of drug/device combination products, and caregivers at the bedside tasked with the selection and use of these products.

Anatomical features, breathing profiles, a tendency towards nasal breathing, patient compliance and the use of 'one size fits all'- type products all conspire to reduce the efficacy of aerosol mediated drug therapy, and despite the obvious need, relatively little has been done in attempting to design systems specifically for these populations. These advances have been hindered by the difficulty in conducting trials in children and infants and rely heavily on surrogate animal models, which may share similar breathing patterns, but the effect of differences in upper airway geometries is unknown.

Droplet size is known to have a significant bearing on the ability to target drug to the airways. Smaller particles or droplets are considered better on the basis that they are less likely to see impactational losses in the nasal passages. The majority of work determining optimal MMAD has focused on adults and children greater than 9 – 10 months, with reported bench and mathematical modelling predicting that 5 micrometers remains the upper target in infants ^[1,2], however, more studies are now beginning to be published using anatomical models that should provide more specific size ranges ^[3,4].

As no aerosol generating devices were specifically designed for use with children, devices designed for adults are frequently modified by attaching small infant or child size masks, with little evidence of provided to support efficacy or benefit ^[5]. Face masks, nasal cannula, hoods and spacers are the most commonly used interfaces with selection dependent on age, patient's tolerance, and patient's preference. Each facilitate delivery of some aerosol, but that dose varies between each ^[6,7].

Choice of device is also of paramount importance. Considerations such as the effect of supplemental gas flow rate (8 to 13 LPM for a jet nebuliser for example) on the small lung must be taken into account. With the increased risk of volutrauma or barotrauma during concurrent use of a jet nebuliser during invasive mechanical ventilation, the list of appropriate and effective devices is limited. Softer considerations must also be made, for example, noise. Noise emitted from a device during therapy can result in physiological responses that can affect breath patterns, and consequently the inhaled dose ^[8-10].

These and several other factors shall be the focus of this presentation, which shall draw from the current literature in an effort to provide guidance on design and selection options for optimised aerosol-mediated therapy in these patients.

References

1. Delvadia RR, Longest PW, and Byron PR: *In vitro tests for aerosol deposition. I: Scaling a physical model of the upper airways to predict drug deposition variation in normal humans*. Journal of aerosol medicine and pulmonary drug delivery. 2012;25:32-40
2. Martonen T: *Mathematical model for the selective deposition of inhaled pharmaceuticals*. Journal of pharmaceutical sciences. 1993;82:1191-1199
3. Janssens HM, De Jongste JC, Hop WC, and Tiddens HA: *Extra-fine particles improve lung delivery of inhaled steroids in infants: a study in an upper airway model*. CHEST Journal. 2003;123:2083-2088.
4. Ruzycki CA, Golshahi L, Vehring R, and Finlay WH: *Comparison of in vitro deposition of pharmaceutical aerosols in an idealized child throat with in vivo deposition in the upper respiratory tract of children*. Pharmaceutical research. 2014;31:1525-1535.
5. Everard ML: *Inhalation therapy for infants*. Advanced drug delivery reviews. 2003;55:869-878.
6. Amirav I, Balanov I, Gorenberg M, Groshar D, and Luder A: *Nebuliser hood compared to mask in wheezy infants: aerosol therapy without tears!* Archives of disease in childhood. 2003;88:719-723.
7. Réminiac F, Vecellio L, Loughlin RM, Le Pennec D, Cabrera M, Vourc'h NH, Fink JB, and Ehrmann S: *Nasal high flow nebulization in infants and toddlers: An in vitro and in vivo scintigraphic study*. Pediatric pulmonology. 2017;52:337-344.
8. Erzinger S, Schuepp KG, Brooks-Wildhaber J, Devadason SG, and Wildhaber JH: *Facemasks and aerosol delivery in vivo*. Journal of Aerosol Medicine. 2007;20:S78-S84.
9. Janssens HM, Van Der Wiel EC, Verbraak AF, De Jongste JC, Merkus PJ, and Tiddens HA: *Aerosol therapy and the fighting toddler: is administration during sleep an alternative?* Journal of aerosol medicine. 2003;16:395-400.
10. Zahr LK and Balian S: *Responses of premature infants to routine nursing interventions and noise in the NICU*. Nursing research. 1995;44:179-185.