THE EFFECT ON DELIVERED DOSE WHEN USING AND MISUSING NEBULISER FACE MASKS

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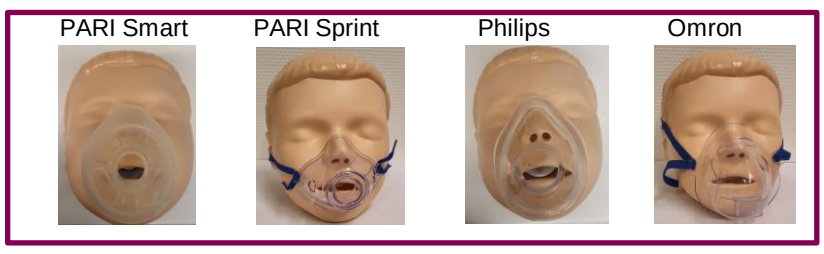
Introduction

- There is a trend to move from **jet to mesh** nebulisers, including breath-controlled nebulisers, to get a more efficient dose delivery to the lung[1]. This is of particular importance when nebulising expensive biologics.
- Use of **face masks may significantly reduce the lung dose**[2,3]. If not used correctly or if there is a leakage between skin and mask, the dose will be affected even more.
- The **face mask design differs for different brands**, e.g. material flexibility, inlet, inclusion of air vent holes[4] or one-way exhalation valves, which **may impact the patient dose**. See Fig 1 for examples of face masks tested.



►Fig. 1. Examples of face masks tested together with a Copley child face

Methods

Materials:

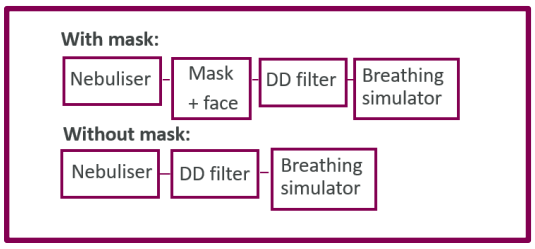
- **Jet nebulisers**: LC Sprint blue, PARI and NE-C900, Omron
- **Mesh nebulisers**: Innospire Go, Philips Respironics and Micro Air U100, Omron.
- **Test substance**: Bricanyl Respules
  - 2mL terbutaline sulphate solution, nominal dose = 5000 µg
- **Moulded face models**: Copley (adult, child, infant) and plastic face models[2]
- **Face masks**: A wide range of face mask in sizes adult, child, infant
- **Breathing patterns** representing adult, child and infant: Copley BRS3100 breathing simulator. See Table 1 for the breathing patterns used.

Testing:

- **Delivered dose**: Collected on Respirgard filters and obtained throughout the full nebulisation time. Terbutaline sulphate was extracted from the filters and analysed using High Performance Liquid Chromatography. See Fig. 2 for the lab set-up.
- **Leakages**: Visually observed

Breathing pattern parameter	Adult	Child	Infant
Tidal Volume (mL)	500	155	50
Frequency (breathing cycles/min)	15	25	30
Inhalation time: Exhalation time ratio	1:1	1:2	1:3

►Table 1 Breathing patterns for adult, child and infant



►Fig. 2 Lab set-ups with or without a face mask

Objectives

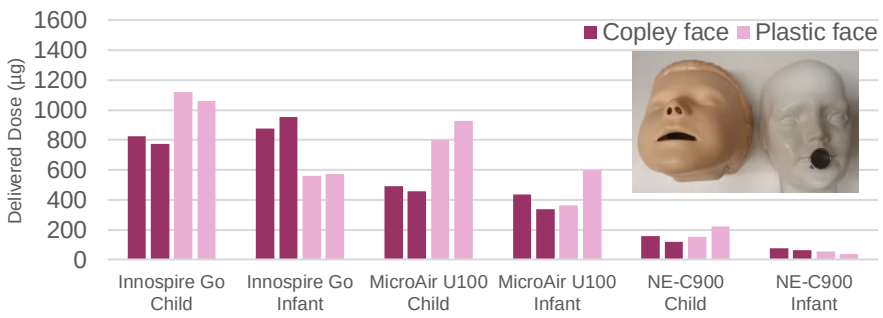
To investigate the impact on the delivered dose when using jet and mesh nebulisers in combination with different face mask brands (adult, child and infant)

Results

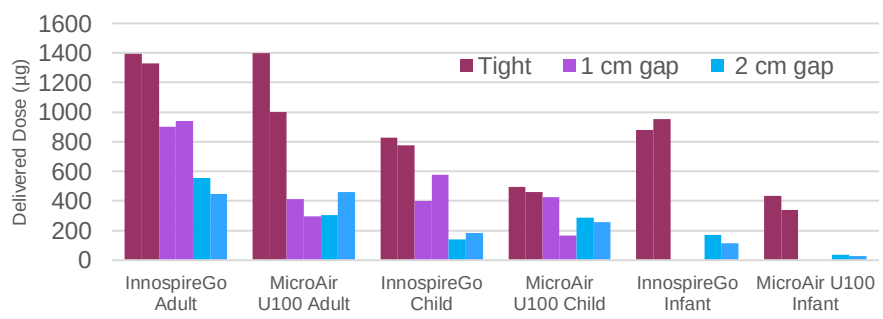
- **Adult face mask and breathing pattern:** Dose (average) range was 332-1361 µg, which corresponds to 51-65% of the dose without a mask (Table 2)
- **Child face mask and breathing pattern:** Dose (average) range was 138-801 µg which corresponds to 45-58% of the dose without a mask (Table 2)
- **Face mask and face shape:** A difference of up to 61% could be seen between the two different face models used (Fig.3)
- **Face mask and fit:** A dose loss of up to 71% for 1 cm gap and up to 91% for 2 cm gap could be seen when the face mask was not held tight to the face (Fig.4)
- **Nebuliser output:** Generally very variable output when comparing different brands, both within jet nebulisers and within mesh nebulisers, as shown in this study. This was also shown in a comparison of 30 different nebulisers when delivering a suspension[5].

Nebuliser	Mask and mask type	Adult DD µg (%nominal dose)		Child DD µg (%nominal dose)	
		With mask	W/O mask	With mask	W/O mask
Innospire Go, mesh	**Std**; no vent holes, soft, front loaded	1329-1392 (27-28%)	2020-2160 (40-43%)	775-827 (15-17%)	1366-1417 (27-28%)
MicroAir U100, mesh	**Std**; vent holes, rigid, bottom loaded	1001-1397 (20-28%)	nt	459-493 (9.2-10%)	1126-1212 (23-24%)
NE-C900, jet	**Std**; vent holes, rigid, bottom loaded	283-381 (5.7-7.6%)	640-675* (13-14%)	121-156 (2.4-3.1%)	300-315* (6.0-6,3%)
LC SPRINT blue, jet	**Sprint**: Vent holes, rigid, front loaded	813-973 (16-20%)	1469-1592 (29-32%)	425-536 (8.5-11%)	683-959** (14-19%)
LC SPRINT blue, jet	**Smart**: One-way inhalation valve, flexible, front loaded	807-871 (16-17%)	1469-1592 (29-32%)	412-621 (8.2-12%)	683-959** (14-19%)

▲Table. 2. Delivered dose (n=2, *n=3,**n=4), full dose, for different breathing patterns, with/without a face mask



▲Fig. 3. Delivered dose (n=2, individual data presented), full dose, using different face models – Copley and plastic face models



▲Fig. 4. Delivered dose (n=2, individual data presented), full dose, mask held 0-2 cm from the face

Conclusions

- Both for jet and mesh nebulisers a significant loss of dose is seen after the addition of a face mask. Face mask properties and handling have a large impact on the patient dose. To make treatment less scary care givers sometimes hold the mask with a gap to the face, here shown to have a large impact on the dose.
- Flexible mask materials seem to be more forgiving e.g., for small mask movements, different face sizes and shapes. The importance of a one-way exhalation valve in the mask needs further understanding, as in this study no difference in delivered dose was seen comparing PARI Sprint and Smart masks.
- A poor fit between face shape and mask design is also a significant factor affecting the dose[3]. Face dimensions vary a lot for the distance between the nasal bridge and tip of the chin as well as for the width of the oral opening[6]. Amirav et al have developed masks based on 3D scanned faces to mitigate this problem[7].

References

[1] J Pritchard, Ross HM Hatley, J Denyer, D v Hollen: Mesh nebulizers have become the first choice for new nebulized pharmaceutical drug developments Ther. Deliv. (2018) 9(2), pp121–136

[2] G C Smaldone, E Berg, K Nikander,: Variation in Pediatric Aerosol Delivery: Importance of Facemask J Aerosol Med (2005) 18(3), pp 354-363

[3] S Erzinger, K G Schueepp, J Brooks-Wildhaber, S G Devadason, J H Wildhaber: Facemasks and Aerosol Delivery In Vivo J Aerosol Med (2007) 20(1), pp S78-S84

[4] A Berlinski: Effect of Mask Dead Space and Occlusion of Mask Holes on Delivery of Nebulized Albuterol Resp Care (2014) Aug 59(8), pp 1228-1232

[5] E Berg, R Picard: In Vitro Delivery of Budesonide From 30 Jet Nebulizer/Compressor Combinations Using Infant and Child Breathing Patterns, Repiratory Care (2009) Vol 54 No 12, pp 354-363

[6] L Goto, W Lee, T Huysmans, J Molenbroek and R Goossens: The Variation in 3D Face Shapes of Dutch Children for Mask Design, Appl. Sci. (2021)11, 6843, pp1-16

[7] I Amirav, A S Luder, A Halamish, D Raviv, R Kimmel, D Waisman, M T Newhouse: Design of Aerosol Face Masks for Children Using Computerized 3D Face J Aerosol Med Pulm Drug Delivery. (2013) 26, pp1-7