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Assessment of facial and ocular deposition of nebulized aerosol using a color-based method

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Abstract

Purpose: The objective of this investigation was to develop an inexpensive and uncomplicated color-based method to rapidly assess undesirable facial and ocular deposition of aerosolized droplets on the surface of a 3D rigid replica of a 4-year-old child's face. *Methods*: Sar-Gel®, which changes color on contact with water, was evenly coated on the face model through which air was drawn using two breathing patterns (representing moderate and shallow inhalations) or a constant rate of 0, 10, and 20 L/min. A standard and two proprietary (one shaped to resemble a fish face, the other shaped to resemble a dragon face) pediatric facemasks were evaluated. A nebulizer was charged with 3 mL of normal saline before connection to the facemask. The mask was held in contact with the face using 300 g-F determined by instrumenting the mounting strap using a force gauge. The nebulizer was operated for 5 minutes. The region of color change was captured using a digital camera and analyzed using Adobe® Photoshop. *Results*: Facial and ocular deposition with all the facemasks was affected by breathing pattern. Compared to the standard and dragon masks, the fish mask resulted in significantly reduced facial and ocular deposition at all breathing patterns. *Conclusions*: This simple screening method allows quantification of droplet deposition outside the facemask and may be a useful tool for designing masks that result in reduced facial and ocular deposition.

Key words: *Breathing pattern; facemask; face model; nebulizer; pediatric*

Introduction

Nebulizers are commonly used to deliver aerosolized medication using a facemask, which is typically the interface between a nebulizer and a patient for both pediatric and elderly groups, for whom the task of retaining a mouthpiece between their lips for a full treatment period is difficult.

Many studies have indicated that aerosol therapy using facemasks can result in facial and ocular deposition and that facemask design may affect drug delivery. In a study by Sangwan et al., they demonstrated that facial and ocular deposition varied in the range of 0.44–2.34% and 0.09–1.78%, respectively, with seven commercially available facemasks in combination with three jet nebulizers[1]. There are several in vitro studies that have looked at the effect of a facemask leak on aerosol delivery and demonstrated that only a small proportion of aerosolized drug reaches the lungs of spontaneously breathing small children[2–7]. In an in vitro study by Everard et al., a 50% and 80% reduction in drug delivery was found when the mask of a nebulizer was displaced 1 and 2 cm from the face, respectively[8]. Furthermore, in an in vivo study by Erzinger et al. in volunteers, they demonstrated that nebulizers interfaced with ill-fitting facemasks for aerosolized treatment resulted in undesirable deposition on the face and in the eyes[9]. In addition, the facemask design, and in particular the face seal, is a key factor affecting aerosol delivery efficiency that was confirmed by a study by Sangwan et al., where they reported that although a tight-fitting mask improves delivery efficiency, ocular deposition was enhanced[1]. This combination of wasted drug and its potential to elicit undesirable ocular side effects, including pupillary dilatation and glaucoma, is driving interest in the development of new mask designs, which creates a need for rapid screening methods to assess them.

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Facial deposition characteristics of different facemask designs can be assessed using clinical and scintigraphic techniques, but these methods each have limitations and are expensive and time-consuming. The purpose of this study was to develop an inexpensive and uncomplicated in vitro method to rapidly visualize and quantify undesirable facial and ocular deposition of aerosolized droplets on the surface of a 3D replica of a 4-year-old child's face, and to demonstrate the utility of this approach by comparing different commercially available facemask designs for facial and ocular deposition of nebulized aerosols under different air flow conditions.

Materials and methods

Sar-Gel® (Sartomer Company Inc., West Chester, PA, USA), a commercially available water level indicating paste which changes from white to purple on contact with water was used to visualize deposition of nebulized droplets on the surface of a white, 3D rigid replica of a 4-year-old child's face (PA Consulting Group, Cambridge Technology Center, Melbourn, Royston, UK). We evaluated three commercially available facemasks. A standard facemask (Hudson RCI, Durham, NC, USA), a mask resembling dragon shape (Dragonmask, KidsMED, Hinsdale, IN, USA), and a mask resembling fish shape (Modified version of the Pari Bubbles the Fish, PARI Respiratory equipment, Monterey, CA, USA), all of which were used in conjunction with a Hudson Updraft II jet nebulizer (Hudson RCI). The nebulizer was operated with a Pulmo-Aide compressor (Sunrise Medical Respiratory Products Division, Somerset, PA, USA). Aerosol generated through jet nebulizer was drawn into the mask using either a piston pump (Harvard Pump, South Natick, MA, USA) or a regulated vacuum pump connected to an opening in the face model that represented the mouth. All the images were captured using a digital camera (Canon PowerShot SD100 6.1MP Digital ELPH Camera w/3× Optical Zoom) and were quantified using Adobe Photoshop (CS3 Version).

Face model

Facial and ocular deposition of aerosol was studied in vitro using a Sar-Gel-coated 3D face replica, which allowed visualization of deposited nebulized aqueous droplets under simulated conditions of breathing (Figure 1). The face model was evenly coated with Sar-Gel using a brush and was connected to a Harvard pump that simulated a 15-breath/min breathing pattern with a ratio of inspiration to expiration of 40/60, and tidal volume of 700 mL (which we considered a moderate inhalation) or 50 mL (which we considered a shallow inhalation), or to a vacuum pump to simulate constant air flows of 0, 10, and 20 L/min as confirmed by a calibrated flow meter. For a given breathing pattern, both the compressor and the Harvard pump/Vacuum pump were started simultaneously. A filter was placed in the air flow path downstream of the face to protect the pump. The filter was not intended to allow drug capture and quantification in this study, but this would obviously be possible.

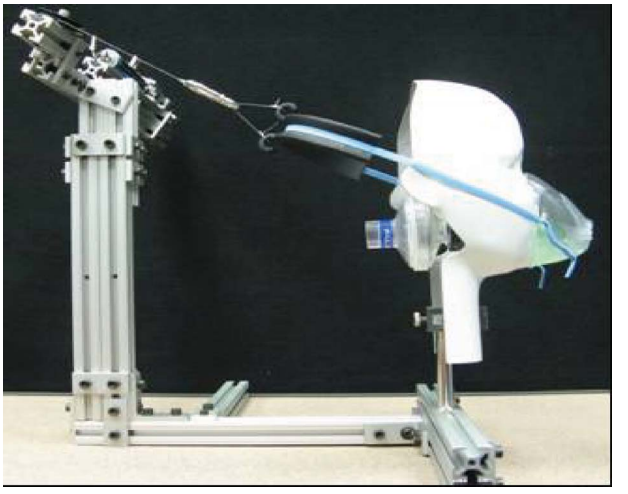

Figure 1. Experimental apparatus for standardized assessment of facial and ocular deposition.

Nebulizer and facemasks

A Hudson Up-draft II jet nebulizer was attached to a standard facemask or a dragon mask or a fish mask in alternating order. Five individual nebulizer of the same type were used to evaluate all three mask types. To ensure the pressure of the mask against the face that remained constant, the facemask was attached to the face model with a known tension (300 g-F) using a mounting strap connected to a force gauge. The nebulizer charge (amount of normal saline placed in the nebulizer to start with) was 3 mL, and the nebulizer was then operated for a fixed period of 5 minutes.

Quantification

Before and after images of the Sar-Gel-coated face were captured using a digital camera under standardized photographic conditions with respect to lighting, camera position, and magnification. Sequential photographs were taken approximately 10 seconds apart and the deposition area was measured from the first photograph in each series. The region of color change was quantified using Adobe Photoshop using the procedure detailed by Kundoor et al.[10]. To correct for variations in the starting image size and the deposition area that

result from the use of different camera-to-face model distances, we incorporated a 1 cm^2 purple square that served as an area standard and was imaged simultaneously with deposition area in all face model photographs. The variations in starting image size could then be corrected using the known area of the reference square. We considered the idea of quantitative water analysis, but it is technically difficult to directly relate the color change to dose delivered to the face/eyes because of confounding variables such as coating thickness.

Statistical analysis

All experiments were performed in triplicate. All data are presented as mean ± standard deviation (SD). A Kruskal–Wallis one-way analysis of variance test was used to identify significant differences in facial and ocular deposition for the three facemasks at the three constant breathing rates and two breathing patterns. *P*-values < 0.05 were judged to represent statistical differences.

Results

There was a significant and quantifiable change from white to purple when nebulized droplets came into contact with Sar-Gel. Deposition area was quantified from the first image in a series of sequential photographs taken for the three masks at three constant airflow rates (0, 10, and 20 L/min) and two simulated breathing patterns (moderate and shallow inhalations). Deposition area of the second and third photograph was similar to the deposition area of the first photograph indicating no postdeposition migration of nebulized aerosol on the face model within the timeframe of interest.

Facial and ocular deposition area varied widely depending on the mask design and the airflow regimens (Figures 2 and 3). At 0 and 10 L/min (Figures 4 and 5, respectively), compared to standard and dragon masks, the fish mask showed significantly ($P < 0.001$) reduced facial and ocular deposition. Moreover, droplet deposition was seen only on the face, in contrast to deposition on the face and in the eyes with the standard and dragon masks. No significant differences were observed between standard and dragon masks at these flow rates. Facial deposition was lowest and no ocular deposition was observed for all the three masks at 20 L/min (Figure 6). No significant differences were observed between the three masks at this flow rate. Using the simulated shallow breathing pattern (Figure 7), deposition on the face and in the eyes was significantly ($P < 0.001$) less for the fish mask when compared to standard and dragon masks. No significant differences were observed between standard and dragon masks using the simulated shallow breathing pattern. Minimal facial and ocular deposition was observed with standard and dragon masks using the simulated moderate breathing

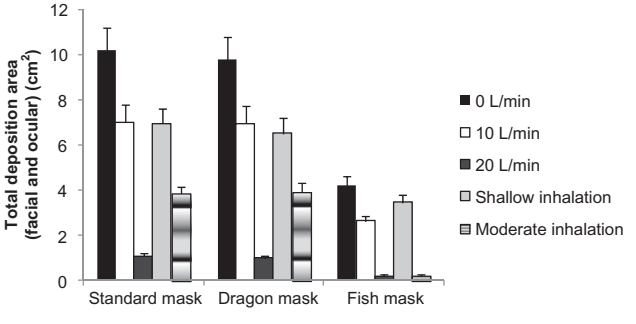

Figure 2. Comparison of facial and ocular deposition of facemasks at different breathing patterns.

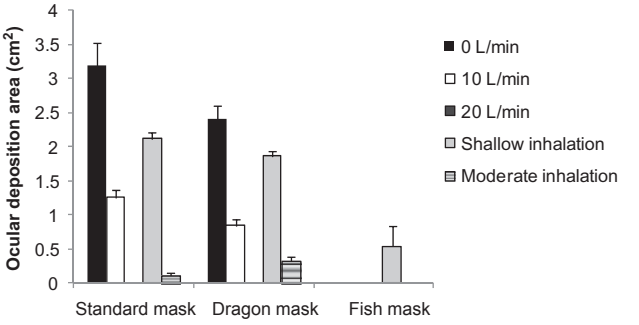

Figure 3. Comparison of ocular deposition of facemasks at different breathing patterns.

Figure 4. Face model after droplet deposition at 0 L/min.

Figure 5. Face model after droplet deposition at 10 L/min.

Figure 6. Face model after droplet deposition at 20 L/min.

Figure 7. Face model after droplet deposition at shallow inhalation.

Figure 8. Face model after droplet deposition at moderate inhalation.

pattern (Figure 8). Similar to all other flow rates, no significant differences were observed between standard and dragon masks at this breathing pattern. The fish mask showed significantly ($P < 0.001$) lower deposition compared to the other two masks.

Discussion and conclusions

In this study, we investigated how facemask design and breathing pattern influences facial and ocular deposition on a 3D replica of a 4-year-old child's face. We found that mask design is a key factor in minimizing facial and ocular deposition. Our results are consistent with previous studies—a well fitting and designed facemask–face seal is important for the efficiency of drug delivery[11–15]. The results in this case were obtained over just a few days enabling rapid screening and precise area quantification with easy identification of undesirable deposition hot spots.

The results of this in vitro study indicate that facial and ocular deposition from the fish mask was significantly reduced compared to dragon mask or standard mask. We suspect that these differences in deposition patterns are partly due to lowered droplet velocities (and correspondingly lower inertial impaction efficiency in undesirable locations) as droplets traverse from the nebulizer exit to the opening simulating the mouth—the fish mask has multiple vents (in the side and bottom of the mask together with 'eye cuts') which collectively serves to reduce acceleration of droplets leaving the nebulizer by providing other routes to air ingress into the mask. The standard and dragon masks lacked eye cuts and vents on the bottom. Furthermore, our results are consistent with the study by Smaldone et al. where they compared three different masks. A prototype tight-fitting nonvented Laerdal mask and two modified versions, one with vent at the bottom of the mask to reduce the inertial effects by reducing the pressure in the mask and the other with eye cuts on the top part of the mask to minimize inertia in the region of eyes. Although the inhaled mass was not significantly different between the three masks, significant decreases in facial and eye deposition were observed with the modified versions compared to the tight-fitting Laerdal mask suggesting the importance of the interaction between the edge of the mask and face in determining facial deposition[16].

A study by Harris et al. reported data that compared tight-fitting, standard, and modified version of Bubbles the fish masks. They found that the combination of fish mask and Pari LC Plus nebulizer was significantly more efficient and had markedly reduced facial and eye deposition although maintaining high inhaled mass than the combination of standard mask and the MistyNeb nebulizer. They concluded that mask design was a key factor in determining drug delivery to lungs, face, and eyes for pediatric patients[17]. In a similar study, Sangwan et al. compared seven commercially available facemasks in combination with three jet nebulizers to study the facial deposition of aerosol. The combination of fish mask and Pari LC Plus nebulizer had the highest inhaled drug mass and also had one of the lowest facial and eye depositions[1].

When tested with different constant and simulated breathing patterns, both facial and ocular depositions were less for all the three masks at higher flow rates. We attribute this to a more efficient entrainment of droplets in streamlines heading toward the simulated mouth opening, such that they get more before being lost to sedimentation. These results are in agreement with the study by Smaldone et al. where they found the inhaled mass from nebulizers was higher with faster breathing patterns[18].

Clearly, our approach has its limitations. First, it measures only the facial and ocular deposition and does

not give any information on the inhaled drug mass. Second, using a single face model to evaluate facial and ocular deposition is not representative of all possible faces or different ethnicities. But uniquely, the color-based approach allows rapid quantification of droplet deposition outside the facemask and is so quick to perform using readily available equipment and software; it potentially allows screening of more prototypes and efficient validation of computational fluid dynamic models which is often not feasible when patient's radiation, or chemical analysis is needed. These evaluative approaches are perhaps better left for later in device development process when designs are approaching finalization.

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this paper.

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