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Numerical Investigation of Aerosol Deposition at the Eyes When Using a Hood Inhaler for Infants—a 3D Simulation

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ABSTRACT

A numerical investigation of a hood inhaler is presented, aiming at the assessment of the amount of aerosol that reaches the eyes of the patient when administrating medications with such a device. Using a hood for aerosol therapy for infants was already found to be effective and friendly to handle over the commonly used face mask. Using a hood device may adversely deliver unwanted medications to the eyes of the infant. The current study addresses the extent of aerosol deposition at the infant's eye zone. We describe the development and utilization of a numerical simulation for studying the transport and fate of the aerosol particles within a 3D realistic representation of the hood and the infant's head, with a focus on the eye zone. The governing equations were solved using the commercial software, FLUENT 6.1, which is based on the finite volume method. The computational domain was created using the GAMBIT package. The computational geometry was built separately for each configuration of the hood and the infant. It is shown that under optimal working conditions (i.e., when the infant's head is aligned to the funnel) the percentage of aerosol reaching the eye zone is 0.48%. However, when the funnel is tilted toward the eyes the amount of aerosol reaching the eyes zone is predicted to be 4.7%. In general, the results obtained in this study are in good agreement with available *in vitro* data. It can be concluded that using the hood for aerosol therapy results in minimal deposition at the infant's eye area

Key words: nebulizer, aerosol therapy, breathing function

INTRODUCTION

AEROSOL DELIVERY TO INFANTS using a face mask is known to have several disadvantages in terms of patient's tolerance and efficient handling by nonprofessionals. A major drawback is the difficulty of achieving a good mask face seal when the infant is screaming and crying.[1,2] Moreover, nebulizer treatments take about 10 min, much longer than most infants readily tolerate when us-

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ing a mask. The infant's impatience further reduces the efficiency of drug delivery to the lungs.[3,4] Recently, aerosol therapy to wheezy infants using a hood interface has been reported as efficient as using a mask.[5] As expected, the hood was preferred by parents and better tolerated by the infants. This has led to the development of a hood-shaped device in the form shown in Figure 1.

During the hood operation some of the drug may not reach the respiratory system. The amount lost varies with the funnel and the face position with respect to each other. The efficiency of this apparatus to administer drug to the respiratory system has been investigated and reported previously.[6,7] However, the possibility that inhaled drugs could be deposited on the face, and especially in the eyes, gives rise to safety concerns. A former research[8] that quantified facial and eye deposition in a model simulating drug delivery to a young child using commercially available facemasks in combination with jet nebulizers found that all face masks leaked aerosol with significant facial and eye deposition. Ocular deposition should be avoided for any inhaled drug, and more specifically, for anticholinergic and corticosteroid agents[9] because of ocular effects including cataracts, precipitation, or worsening of narrow-angle glaucoma, eye discomfort, or temporary blurring of vision. Knowledge of the amount of drug that deposits near the eye region, together with information about the amount that enters the respiratory system, can lead to devising optimal aerosolized drug administration protocols using the hood system.

This work further utilizes a numerical model that was reported in a previous study.[7] The model is comprised of a detailed 3D configura-

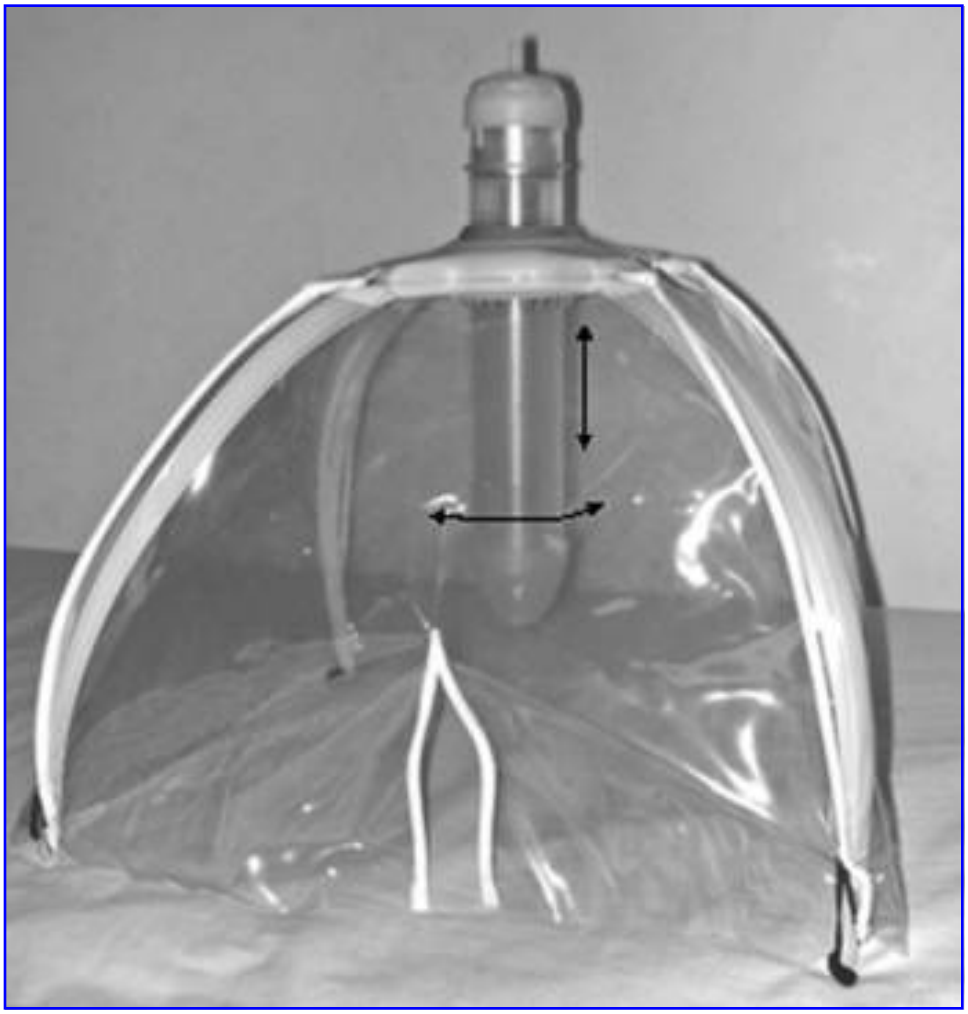

FIG. 1. The nebulizer hood inhaler. The arrows show possible modifications of the funnel.

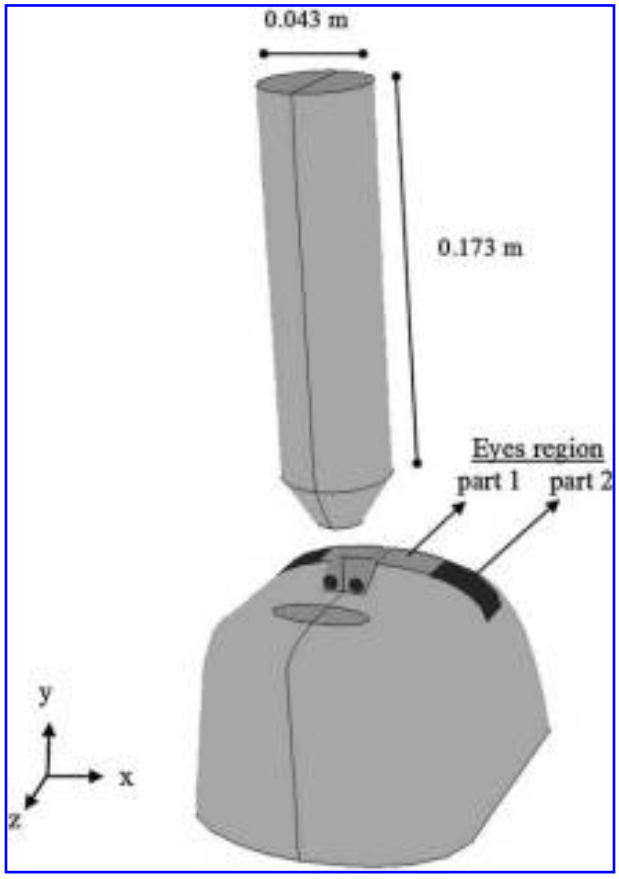

FIG. 2. A 3D representation of the nebulizer hood inhaler and the infant's head. The eyes region is divided into two parts.

tion of the hood, funnel, and the infant's head, including the chin, shoulders, mouth, nose, nostrils, and the eye region (Fig. 2). The model enables investigation of drug delivery while the funnel and the head are both tilted. Moreover, a full transient solution has been implemented, which is necessary when dealing with realistic time-varying breathing functions, like those used in this study, to describe the conditions at the inlet of the respiratory system. Because the model was described in detail previously, we focus in this study on its application to the assessment of the risk to the eyes when administrating drugs with the hood inhaler.

MATERIALS AND METHODS

The nebulizer hood

The nebulizer hood shown in Figure 1 (manufactured by Baby's Breath Advanced Inhalation Technologies, Israel) has been described by Shakked et al.[6] In short, the hood system includes a funnel (with an effective volume of 238 cm^3), a pneumatic nebulizer, a hemispherical and flexible plastic cape that encloses the infant's head, and four folding legs. The funnel delivers the aerosolized drug to the infant. It can be manually adjusted by the caregiver for better performance by shifting it up and down and by tilting it at a wide range of angles. In the simulation, 5000 particles were injected in each time step.

Governing equations

The governing equations, boundary conditions, computational domain and mesh generation were described in detail in the author's previous work.[6] Specifically, the flow field of the air and the discrete phase were accounted for as nonsteady, although the injection of the aerosol was assumed continuous throughout the cycle. In contrast to previous studies where a constant flow was modeled, the present study implemented various, realistic breathing patterns at the openings of the respiratory system (the mouth and the nostrils). The flow field was obtained by solving the mass and momentum conservation equations. A commercial computational fluid dynamics (CFD) software[10] (FLUENT 6.1, Fluent Inc., Lebanon, NH), which is based on the finite volume method, was used to solve the governing equations. The computational domain was created using the GAMBIT package.[11]

Breathing functions

Common infant breathing patterns are modeled here via breathing functions derived using the POLYMATH software package (a computational software that allows the user to apply effective numerical analysis techniques during interactive problem solving on personal computers). The breathing functions represent regular tidal breathing (2-sec total breath length) with inspiratory duty cycle of 0.4, based on a sinusoidal waveform.[12] IDC's equal to 0.35, 0.45, and 0.5 were also implemented. The tidal volume was set to 50 mL, to be consistent with the experiment.

Numerical approach

In order to model the transient problem properly, the time step for the transient simulation was set to 0.05 sec. Particle size was set to 1.78

microns. Trajectories of the discrete phase were calculated by stepwise integration over discrete time steps, with the integration time step set by FLUENT to obtain a minimum error. Integration of the force balance equation, using a trapezoidal scheme, yields the velocity of the particle at each point along its trajectory.

Operating conditions

Four typical configurations of the funnel relative to the infant's head (Fig. 3) were analyzed: (1) the funnel being perpendicular to the infant face, (2) the head being tilted to the funnel, (3) the funnel being tilted in several angles relatively to infant head, and (4) both the funnel and head being tilted. Hence, simulation results are classified according to the spatial relationships between the funnel and the infant's head. In the base-case scenario, the funnel is perpendicular to the infant's face while nasal breathing. The second scenario considers nasal breathing when the funnel is tilted relative to the infant's face. Subcases include the funnel being tilted in the x direction (sideways), in the z direction (in the sagital plane), and at a general inclination. The third scenario considers the funnel in a vertical orientation, whereas the head is tilted relative to the funnel (in the x direction). The last scenario considers nasal breathing when the head and the funnel are in a general noncollinear orientation. The two subcases studied are (1) the head and the funnel are tilted sideways (in the x direction) and (2) the head is tilted sideways (in the x direction) while the funnel takes a general orientation.

COMPARISON BETWEEN THE MODEL AND THE MEASUREMENTS

The model results were compared to experimental *in vitro* data using a nebulizer hood and a doll simulating drug delivery to an infant's eyes. An isotope-labeled saline solution represented the drug and quantification of drug delivery was carried by gamma counting of absorbing filters, which were placed on the eyes of the doll. The hood nebulizer was charged with 2 mL of 0.9% saline. Radiolabeling was done by the direct addition of technetium-99m DTPA (99mTc) solution to the saline ensuring uniform distribution. Addition of 99mTc has no physical effect on aerosol characteristics.[13–16] An artificial breathing simulator (PARI Respiratory Equipment, Inc., Monterey, CA) situated at the doll's throat exit imitated a real infant breathing parameters: a tidal volume of 50 mL, breath length of 2 sec, and an IDC of 0.4 (0.8-sec inspiration and 1.2-sec expiration). Figure 4 illustrates the experimental configuration of the hood funnel relative to the infant's face, which resembled the base-case model scenario with the funnel perpendicular to the face. The nebulizer was driven by an oxygen cylinder at a flow rate of 8 L/min for exactly 5 min. Under these conditions, the hood nebulizer has a mass output of 0.22 mL/min, and produces particles with a mass median aerodynamic diameter (MMAD) of 1.8 μm and geometric standard deviation 2.2 (measured by an Anderson Cascade Impactor and a Malvern Laser Diffraction device).

Radioactivity counting of the nebulizer and the filters (the latter representing eyes deposition) were measured before and immediately following treatment with a dose calibrator (Capintec; Ramsey, NJ). Fractional eye deposition [radioactivity of filters/(radioactivity of nebulizer before − radioactivity of nebulizer after)] was calculated from these measurements.

To compare the results with conventional face mask delivery, the same settings were used in a similar experiment, this time substituting the hood with an tightly (open-vent) infant face mask (Hudson Respiratory Care Inc., Temecula CA) covering the mouth and nose of the doll.

RESULTS

We examined the fractional amount of aerosol that reaches the eye region at each of the above scenarios. In the base-case, the funnel is vertical and normal to the infant's face, and hence, the computational geometry is symmetrical (Fig. 3a) with respect to a plane that traverses the funnel and between the eyes.

The air accelerates as it moves toward the funnel's narrow exit and the velocity field within the funnel and at short distances away from its exit is not affected by the infant's breathing pattern.[6,7] After a continuous injection of aerosol particles, 0.48 ± 0.01% of the aerosol introduced at the entrance to the computation domain is deposited at the infant's eye region for breathing with IDC = 0.4. For IDC = 0.35, 0.45, and 0.5, the percentage of aerosol deposition in the eye region is: 0.55 ±

0.01%, 0.43 ± 0.01%, and 0.39 ± 0.01%, respectively. Therefore, a linear relation is apparent between the deposition amount and the IDC.

A realistic scenario is when the funnel and head are not colinear. When the funnel is tilted sideways at 10° (along the *x*-axis) while the head is at its base configuration (Fig. 3b), simulation of nasal breathing with IDC equal to 0.4 reveals that the amount of aerosol deposited in the eye region is 0.5 ± 0.01%. Under these conditions (of the funnel being tilted sideways at 10°) a considerable amount of drug is lost, because most of the air that emanates from the funnel does not approach the nostrils but rather drifts away. When the funnel is tilted at 10° along the positive *z*-axis (in the longitudinal direction) while the head is at its base-case position (Fig. 3c), none of the particles reach the eyes of the infant. This is true also for IDC equal to 0.35, 0.45, and 0.5. Again, a considerable amount of drug is lost, because most of the air that emanates from the funnel does not approach the nostrils and is rather drifted away. Similar results are achieved when the funnel is positioned at an angle of 10° to the *x*–*z* plane (Fig. 3d). When the head is tilted sideways (in the *x* direction) and the funnel is kept vertical (Fig. 3e) 0.38 ± 0.01% of the particles introduced to the system deposit near the infants' eyes. An addi-

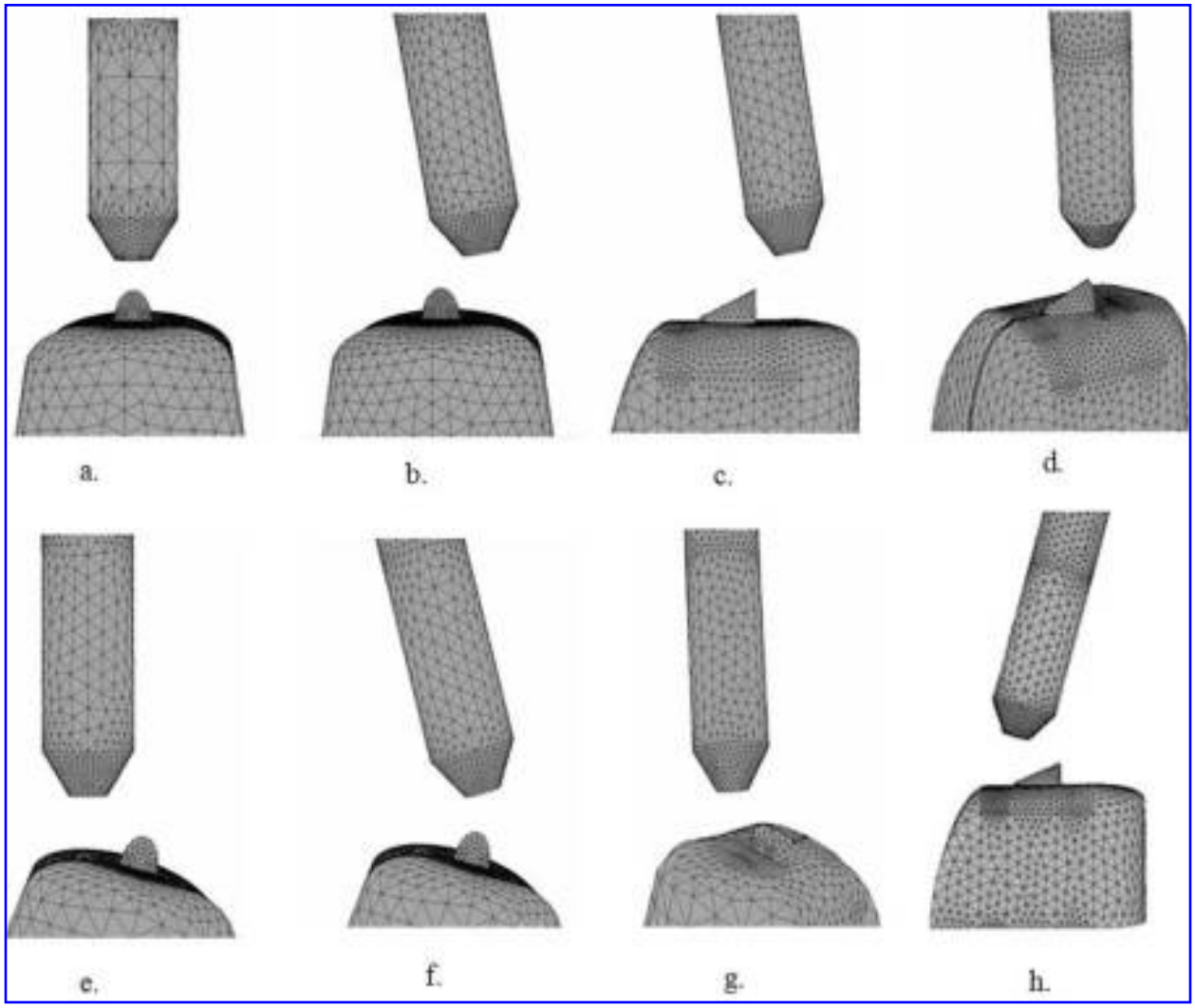

FIG. 3. Different configurations of the funnel and the infant's head. (**a**) Base case—the funnel is normal to the infant's face, (**b**) the funnel is tilted sideways (along the *x* axis), (**c**) the funnel is tilted in the longitudinal direction (along the positive *z* axis), (**d**) the funnel takes a general inclination with respect to the vertical, (**e**) the head is tilted sideways (in the *x* direction) while the funnel is vertical, (**f**) the head and funnel are tilted sideways toward each other, (**g**) the head is tilted sideways (along the *x* axis), the funnel is arbitrarily inclined to the vertical and (**h**) the funnel is tilted in the longitudinal direction (along the negative *z* axis).

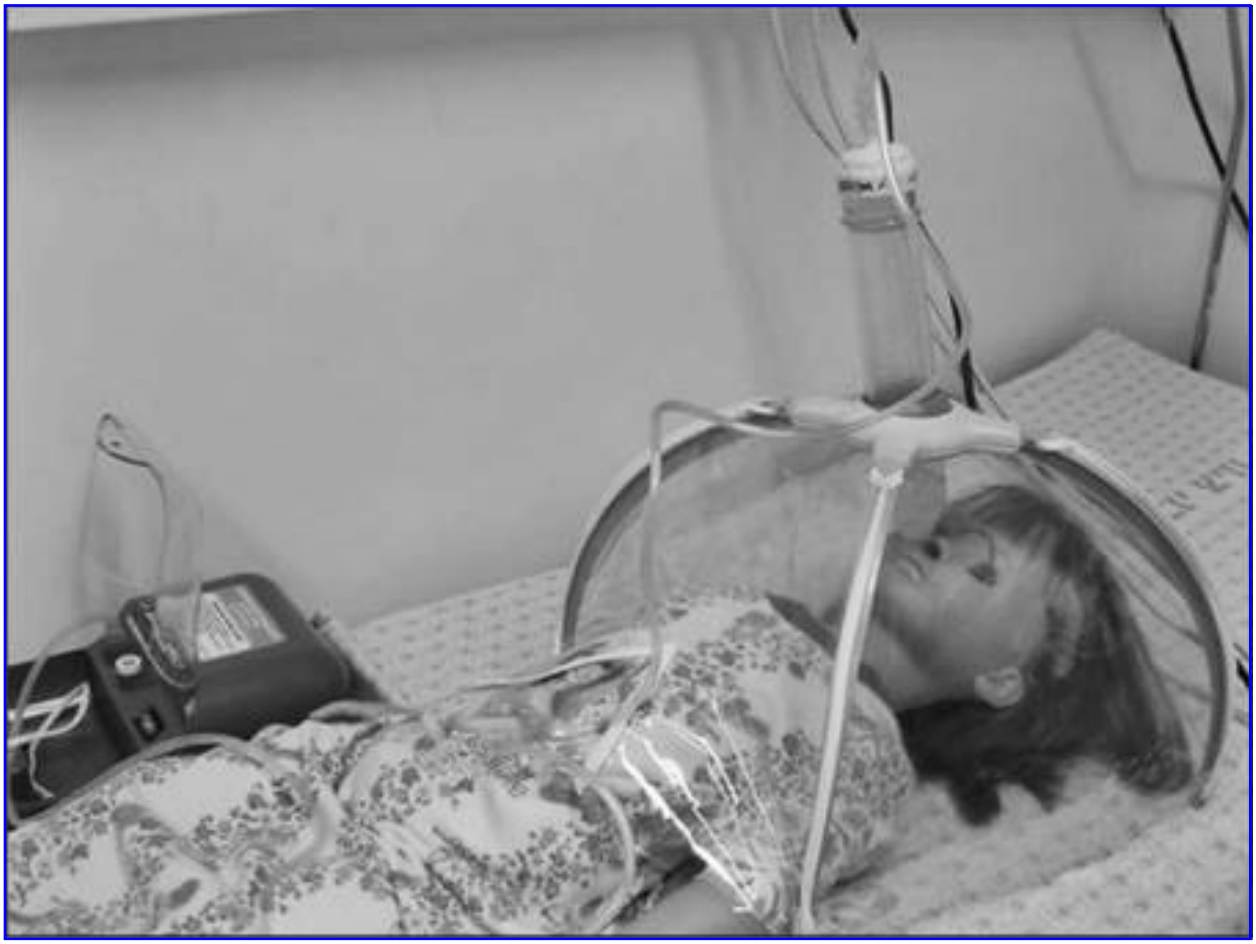

FIG. 4. The *in vitro* experimental configuration.

tional possible realistic scenario is when both the head and the funnel are tilted (e.g., at 15°) sideways toward the same direction (Fig. 3f). In this case, only about 0.15 ± 0.01% of the drug reaches the eyes region. Another configuration that we accounted for is when the head is tilted sideways while the funnel is inclined randomly with respect to the *x*–*z* plan. When the head is tilted sideways at 15° and the funnel takes an angle of 15° to the normal to the *x*–*z* plan (Fig. 3g) no deposition at the eyes region occurs (during nasal breathing). It is important to also consider the worst case in that respect, when, by accident, the funnel is tilted toward the eyes (Fig. 3h). Considerable deposition in the eyes region is expected in such a case, and an amount about 10

Table 1. The Percentage of Aerosol Depositing at the Eye Region for Different Scenario Results

Case	*Description*	*Percentage of aerosol depositing at the eye region*
1	Base case: vertical funnel	0.48 ± 0.01%
2	Upright head, funnel tilted sideways at 10°	0.5 ± 0.01%
3	Upright head, funnel tilted longitudinally at 10°	0%
4	Upright head, funnel tilted longitudinally at 15°	4.7 ± 0.01%
5	Upright head, funnel tilted 10° in a general direction	0%
6	Head tilted sideways, vertical funnel	0.38 ± 0.01%
7	Head and funnel tilted at 15° sideways	0.15 ± 0.01%
8	Head tilted at 15° sideways and funnel tilted at 15° in a general direction	0%

times higher than in the base case (4.7 ± 0.01%) is predicted to deposit at the eye region. Implementation of IDC of 0.35, 0.45, and 0.5 does not change that result. A summary of these results is presented in Table 1.

With regard to the *in vitro* experiments, the average amount of radioactivity found in the eye region during 10 repeated sessions with the hood was 0.45 ± 0.34%, similar to those reported in most case scenarios of the mathematical model.

The experiment with a conventional face mask resulted in higher eye deposition (6.54 ± 2.05%), resembling the worst-case scenario in the prediction model when using the hood apparatus.

DISCUSSION

Aerosol therapy to infants who cannot use a mouth piece requires the use of either a face mask or a hood inhaler. In both of these cases, there are important safety concerns, particularly with respect to the amount of unwanted drug that reaches the eye area of the infant. Mathematical models allow overcoming ethical obstacles to solve these concerns. Using a 3D realistic model of an infant and applying a numerical calculation, the present study determined the fractional amount of drug deposition at the infant's eye region for a wide range of operating conditions, reflecting real-life scenarios that parents and caregivers encounter. The results demonstrated that when using the hood device, less than 1% of the drug delivered from the nebulizer reaches the eye region under most situations. With regard to clinical implications, this fractional eye deposition is comparable to that reported by other studies using conventional face masks.[8] Recently, there have been efforts to further reduce eye deposition by design alteration in the face-mask.[17]

Our findings will certainly lead to better administration procedures when using the hood inhaler, and to awareness of the outcome of various positional scenarios. In particular, the amount of aerosol reaching the infant's eye region for the base-case configuration is expected to be less than 1% and comparable to the amount when using a conventional face mask. When the funnel is tilted at a small angle sideways, the results do not change significantly. If the head is tilted together with the funnel (Fig. 3f) a higher amount of drug can enter the respiratory system through the nostrils while deposition at the eye region decreases. When the funnel is set away from the nostrils, along the positive z direction (toward the chin) and in a general inclination (toward the cheek), no deposition at the eye region is apparent because the flow is drifted away from the nostrils and the eyes. Only when the funnel is tilted and directed toward the eyes does the amount of deposition at the eyes greatly increase. This is probably caused by the jet from the nozzle impinging on the eyes. Although this could happen from misuse of the funnel, the amount of aerosol deposition (reported in our study as fraction of delivered dose) is comparable to that reported previously,[17,18] and its clinical significance is yet to be studied.

The effect of different IDCs is found to be of significant when the funnel is perpendicular to the infant's face. As the inspiratory phase is extended to longer times, a larger amount of the medical aerosol reaches the respiratory system and less is deposited near the eyes.

It can be concluded that for normal operating conditions aerosol therapy with the hood interface results in minimal deposition at the infant's eye area. However, parents and caregivers should be advised and be aware of the possibility that when the funnel is tilted toward the eyes of the infant it may cause a significant increase in deposition at that region.

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DISCLOSURE STATEMENT

No conflicts of interest exist.

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