DEVELOPMENT OF NASAL SPRAY DELIVERY SYSTEM TARGETING AT THE POSTERIOR NOSE FOR MUCOSAL IMMUNIZATION

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Abstract

Delivering vaccines to the posterior nose has been proposed to induce mucosal immunization. However, conventional nasal devices often fail to deliver sufficient doses to the posterior nose. This study aimed to develop a new delivery protocol that can effectively deliver sprays to the caudal turbinate and nasopharynx. High-speed imaging was used to characterize the nasal spray plumes. Three-dimensional-printed transparent nasal casts were used to visualize the spray deposition within the nasal airway, as well as the subsequent liquid film formation and translocation. Influencing variables considered included the device type, delivery mode, release angle, flow rate, head position, and dose number. Apparent liquid film translocation was observed in the nasal cavity. To deliver sprays to the posterior nose, the optimal release angle was found to be 40° for unidirectional delivery and 30° for bidirectional delivery. The flow shear was the key factor that mobilized the liquid film. Both the flow shear and the head position were important in determining the translocation distance. A supine position and dual-dose application significantly improved delivery to the nasopharynx, i.e., 31% vs. 0% with an upright position and one-dose application. It is feasible to effectively deliver medications to the posterior nose by leveraging liquid film translocation for mucosal immunization. Spray formulations of varying viscosities were also tested, and their posterior nose delivery efficiencies were quantified.

Figure

Liquid film translocation can significantly affect the nasal spray dosimetry in the nose [1]. High-speed imaging techniques were used to visualize the aerosol generation from soft mist and squeeze bottle sprays (Fig. 1). The soft mist spray bottle generated smaller aerosols could reduce the front nose deposition and increase spray dispensing beyond the nasal valve.

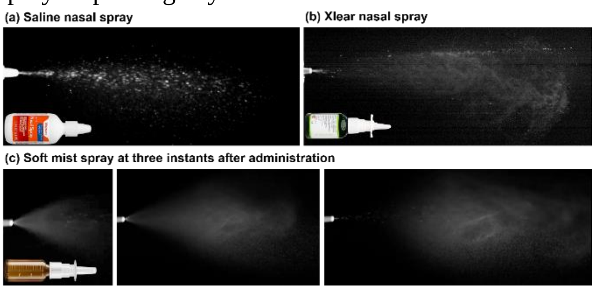

Figure 1: High-speed imaging of the three types of nasal sprays: (a) saline nasal spray, (b) Xlear, and (c) soft mist spray (at three instants after administration).

Considering that the liquid-holding capacity of the turbinate furrows is sensitive to the head orientation, two head positions were evaluated that tilted up and down from the flat supine position by 20º, respectively. As shown in Fig. 2a, when titling the head up by 20º (equivalent to head on a pillow), most of the spray droplets were deposited in the inferior turbinate and nasal floor. This was because the vestibule was aligned with the inferior turbinate along the gravity in this case. Moreover, the liquid film traveled a shorter distance than the supine position, because titling the head up by 20º changed the turbinate furrow from vertical to a 70º slope. Applying the second dose delivered significantly more doses to the caudal turbinate, but negligible dose was observed in the nasopharynx, as displayed in the middle panel of Fig. 7a. The posterior nose dose (i.e., caudal turbinate and nasopharynx) with one-dose and dual-dose applications was 2.9 mg and 34.0 mg, respectively (Fig. 2b). It was also noted that the same factors (gravity and flow shear) that helped mobilizing the liquid film could also reduce the maximal liquid film thickness, thus slightly decreasing the dose adhering to the same region.

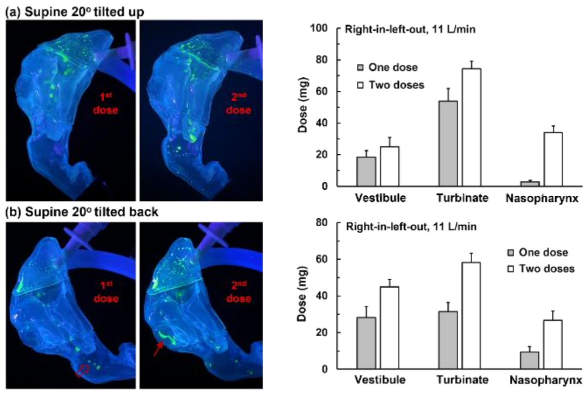

Figure 2: Head orientation effects on nasal spray deposition distribution: (a) supine 20º titled up (head on a pillow), and (b) supine 20º titled back.

References

1. Si, X.A.; Sami, M.; Xi, J. Liquid film translocation significantly enhances nasal spray delivery to olfactory region: a numerical simulation study. *Pharmaceutics* **2021**, *13*, 903.