Computers in Biology and Medicine 77 (2016) 40–48

Contents lists available at ScienceDirect

Computers in Biology and Medicine

journal homepage: www.elsevier.com/locate/cbm

Effects of nasal drug delivery device and its orientation on sprayed particle deposition in a realistic human nasal cavity

Xuwen Tong, Jingliang Dong, Yidan Shang, Kiao Inthavong, Jiyuan Tu*

School of Engineering, RMIT University, PO Box 71, Bundoora, VIC 3083, Australia

ARTICLE INFO

Article history:
Received 12 May 2016
Received in revised form
1 August 2016
Accepted 1 August 2016

Keywords:
Nasal spray
Atomization
Deposition fraction
Medications delivery

ABSTRACT

In this study, the effects of nasal drug delivery device and the spray nozzle orientation on sprayed droplets deposition in a realistic human nasal cavity were numerically studied. Prior to performing the numerical investigation, an in-house designed automated actuation system representing mean adults actuation force was developed to produce realistic spray plume. Then, the spray plume development was filmed by high speed photography system, and spray characteristics such as spray cone angle, break-up length, and average droplet velocity were obtained through off-line image analysis. Continuing studies utilizing those experimental data as boundary conditions were applied in the following numerical spray simulations using a commercially available nasal spray device, which was inserted into a realistic adult nasal passage with external facial features. Through varying the particle releasing direction, the deposition fractions of selected particle sizes on the main nasal passage for targeted drug delivery were compared. The results demonstrated that the middle spray direction showed superior spray efficiency compared with upper or lower directions, and the 10 μm agents were the most suitable particle size as the majority of sprayed agents can be delivered to the targeted area, the main passage. This study elaborates a comprehensive approach to better understand nasal spray mechanism and evaluate its performance for existing nasal delivery practices. Results of this study can assist the pharmaceutical industry to improve the current design of nasal drug delivery device and ultimately benefit more patients through optimized medications delivery.

1. Introduction

The nasal route for therapeutic agent delivery is an attractive proposition due to the possibility of obtaining a systemic and local response, especially when rapid absorption and effect are desired [5,33]. Nasal sprays are seen as a more efficient way compared with injection or pills to transport drugs with potential use in bypassing the blood-brain barrier [2]. Due to the filtration effect of anterior nostril, majority of sprayed droplets deposits in the anterior nasal cavity [1,14,21,31]. A number of nasal spray studies have reported the low targeted area deposition rate using conventional nasal spray devices. For example, the deposition fraction in the olfactory region only accounts 0.5% of the total delivered therapeutic agents when the particle size is in submicron range [28,34], and this value even becomes negligible for inertial particles [29]. Therefore, comprehensive understanding of nasal spray characteristics and its interaction with the human nasal cavity play essential roles in the design of nasal spray devices and their performance assessment when need.

The nasal cavity is a convoluted anatomy with its primary function to humidify and filter foreign aerosols from the inhaled air before it reaches the lungs (Fig. 1). The main nasal passage may serve as an efficient absorption surface for topically applied therapeutic agents due to the rich vascularization and large surface area proportion [5]. In particular, the olfactory region located at the uppermost of the nasal cavity is the only site in human body where the central nervous system (CNS) is in direct contact with the environment. Intranasally administered drugs once deposited in the olfactory region can migrate across the olfactory mucosa and reach the CNS within minutes, resulting in quick therapeutic onset [10]. However, the nasal anatomy exhibits narrow passageways highlighted by the anterior nasal valve, which limits the transport of sprayed droplets during intranasal spray. This triangular valve-like region has the smallest cross-sectional area located approximately 2–3 cm posterior from the nostril inlet [4] and acts as a flow limiting region [5] before expanding into the main nasal passage. Large aerosols that are unable to navigate through this narrow section can be captured easily. Therefore, the nasal valve presents a major obstacle for effective drug delivery into the main nasal passage where rapid absorption across the mucosa into the blood stream can occur.

* Corresponding author.
E-mail address: jiyuan.tu@rmit.edu.au (J. Tu).

http://dx.doi.org/10.1016/j.compbiomed.2016.08.002
0010-4825/

List of Figures

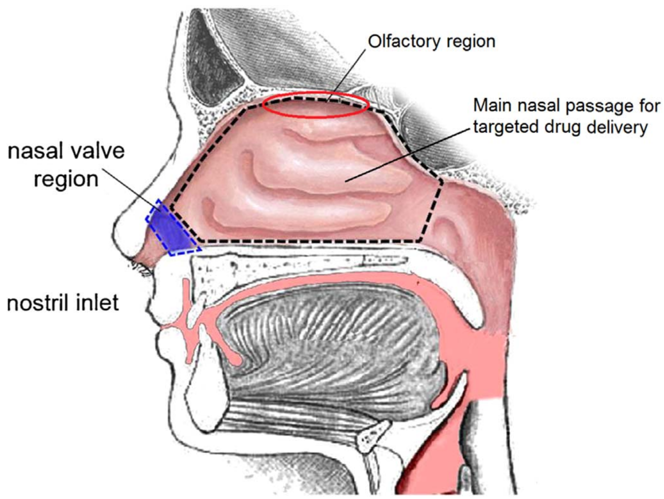

Fig. 1. Schematic diagram of nasal cavity showing region for targeted drug delivery for absorption through the mucosa and into the blood stream, where the most obstructive region nasal valve is highlighted by blue. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Various nasal spray studies adopting human nasal cavity have found the main influences on spray particle deposition involve the nasal cavity geometry and spray parameters (such as droplet size, injected velocity) controlled by the design of nasal spray devices. The aqueous spray pump is the dominant delivery device in the nasal drug delivery market [22] which relies on an actuation force to atomize the drug formulation as it is discharged from the device. The underlying objective of the device is to deliver sufficient drug formulation to the target site.

Cheng et al. [3] evaluated four nasal spray pumps and found that spray plume angle and droplet size distribution were important factors in deposition. Foo et al. [7] found that insertion angle and plume angle are critical factors in determining deposition efficiency and this was confirmed by a number of computational simulations [15,21,8,9]. Kundoor and Dalby [23] evaluated the effect of formulation and administration related variables and found that the deposition area decreased with increasing viscosity but this was mediated by an increase in droplet size and a narrowing of the spray plume. Frank et al. [8,9] investigated effects of the deviated nasal septum on the distribution of spray particles and demonstrated that septal deviation significantly diminished drug delivery on the obstructed side. Our previous study numerically demonstrated the most important parameter was the particle's Stokes number which affects all other parameters on the deposition efficiency [15].

Based on these studies if a spray device can produce a combination of desirable spray characteristics (e.g. spray plume, viscosity, insertion angle, droplet size distribution) then more efficient drug delivery systems can be produced. Despite numbers of relevant studies have been conducted, majority of them were based on experimental measurements or numerical simulation exclusively, and the airflow obstruction effect due to the insertion of nasal spray devices into vestibule region was rarely considered. Although our latest study [14] numerically modelled this airway blockage at one of the nostrils during nasal spray administration, the nasal spray device was over simplified, and its insertion direction and depth was not well aligned with the nasal vestibule.

In the present study, a more realistic nasal spray administration assessment through a combined experimental and numerical approach was presented. Firstly, the initial particle conditions such as spray plume angle, break up length, particle velocity were acquired from Particle Droplet Image Analyser (PDIA). Then, numerical simulations considered the insertion of nasal spray bottle nozzle and human facial effects were conducted. To optimize the drug delivery performance, a spray nozzle orientation adjustment plane was proposed for spray nozzle-nasal valve alignment.

2. Methods

2.1. Experimental apparatus

The experimental setup for this study is shown in Fig. 2. The main components used in the present study were similar with our previous studies [14,16], which mainly includes the automated actuation system and the visualization system. In our previous studies, the pneumatic actuator was driven by constant pressure through pressure regulator to achieve a relatively steady spray plume, while this driven force failed to represent the human actuation behaviour. In the present study, a programmable logic control (PLC) unit (model: 1760-L12BWB; Allen Bradley, Lumberton, New Jersey) was employed to control the two-way solenoid valve which drives speed controllers for spray device actuation. Thus, the strength of actuation force is controllable during the flow visualization. To represent adult's actuation behaviour, 20 adult volunteers were invited to press the spray bottle with strain gauge sensors attached. In this study, a small strain gauge in rectangular shape was attached to the nasal spray bottle wall. During spray, the nasal spray device is compressed by the applied force, and a slight vertical deformation (compression) occurs. Meanwhile, the firmly attached strain gauge sensor will capture the ratio of compression length to its original chip length and send this information to the recorder in terms of electronic signal. Therefore, the spray bottle deformation characteristics during actuation can be recorded for each person invited. This actuation action was repeated 5 times for each volunteer, and the averaged microstrain profile was presented in Fig. 3. Through adjusting the programmable PLC regulator and input pressure, a programmed realistic actuation strain profile was achieved with reasonably good accuracy.

For capturing of the spray, an Oxford laser PDIA system was used. The CCD camera was mounted on a traversing unit which allowed precise movements in all three coordinates to capture the spray plume in full. A long distance microscope lens providing a magnification of 2.46 was used. This enables to capture a physical region of 192 mm × 120 mm with a resolution of 1280 × 800 for each image. To ensure the camera view can be fulfilled with even bright illumination, a 2000 W spotlight was mounted in line with the camera lens.

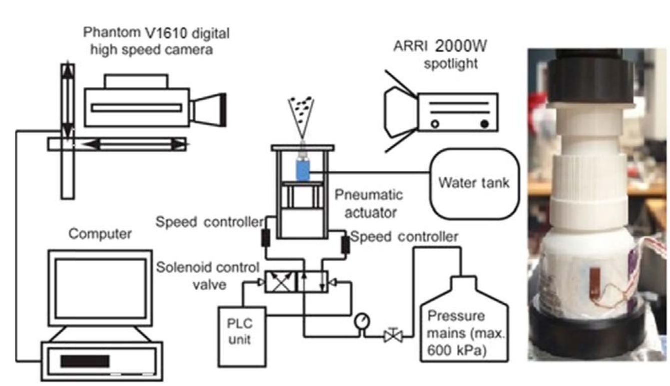

Fig. 2. A schematic of the experimental setup showing the automated actuation system and the visualization system.