Pulmonary Pharmacology & Therapeutics 50 (2018) 62–71

Contents lists available at ScienceDirect

Pulmonary Pharmacology & Therapeutics

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

Modeling and optimization of nebulizers' performance in non-invasive ventilation using different fill volumes: Comparative study between vibrating mesh and jet nebulizers

Haitham Saeed[a], Ahmed M.A. Ali[b,c], Ahmed A. Elberry[e], Abeer Salah Eldin[d], Hoda Rabea[a], Mohamed E.A. Abdelrahim[f,*]

[a] Clinical Pharmacy Department, Faculty of Pharmacy, Beni-suef University, Beni-suef, Egypt
[b] Pharmaceutics Department, Faculty of Pharmacy, Beni-suef University, Beni-suef, Egypt
[c] Pharmaceutics Department, Faculty of Pharmacy, Taif University, Taif, Saudi Arabia
[d] Respiratory Department, Faculty of Medicine, Beni-suef University, Beni-suef, Egypt
[e] Clinical Pharmacology Department, Faculty of Medicine, Beni-suef University, Beni-suef, Egypt
[f] Clinical Pharmacy Department, Faculty of Pharmacy, Modern University for Technology and Information, Cairo, Egypt

ARTICLE INFO

Keywords:
Non-invasive ventilation
Modeling
Nebulizer
Neural networks
Fill volume

ABSTRACT

Backgrounds: Substituting nebulisers by another, especially in non-invasive ventilation (NIV), involves many process-variables, e.g. nebulizer-type and fill-volume of respirable-dose, which might affect patient optimum-therapy. The aim of the present work was to use neural-networks and genetic-algorithms to develop performance-models for two different nebulizers.

Methods: In-vitro, ex-vivo and in-vivo models were developed using input-variables including nebulizer-type [jet nebulizer (JN) and vibrating mesh nebulizer (VMN)] fill-volumes of respirable dose placed in the nebulization chamber with an output-variable e.g. average amount reaching NIV patient. Produced models were tested and validated to ensure effective predictivity and validity in further optimization of nebulization process.

Results: Data-mining produced models showed excellent training, testing and validation correlation-coefficients. VMN showed high nebulization efficacy than JN. JN was affected more by increasing the fill-volume. The optimization process and contour-lines obtained for in-vivo model showed increase in pulmonary-bioavailability and systemic-absorption with VMN and 2 mL fill-volumes.

Conclusions: Modeling of aerosol-delivery by JN and VMN using different fill-volumes in NIV circuit was successful in demonstrating the effect of different variable on dose-delivery to NIV patient. Artificial neural networks model showed that VMN increased pulmonary-bioavailability and systemic-absorption compared to JN. VMN was less affected by fill-volume change compared to JN which should be diluted to increase delivery.

1. Introduction

Modeling and optimization of multivariate and complex domains require use of sophisticated mathematical and statistical models and the results are not always easy to interpret. Artificial neural networks (ANNs) belong to data mining technology and are considered a powerful tool to model and optimize these kinds of data with fast and easy interpretation of the results. In many studies previously performed in the field of pharmaceutical development, data mining technology in the form of artificial neural networks and neurofuzzy logic were successfully applied for modeling, optimization and prediction of formulation and/or in-vitro/in-vivo performance of various dosage forms and medical devices [1–3]. It is well known that ANNs superseded conventional mathematical and statistical modeling methodologies, for their ability to model non-linear data and unnecessary establishment of equations to describe relationship between input and output variables [4]. In addition to the above advantages, ANNs can be used for evaluation of historical data and new models can be updated with added new experiments [5]. In similar studies, ANNs were also applied for building predictive models to evaluate the relationship between in-vitro aerosol characteristics and pulmonary bioavailability of inhaled drugs [6,7].

In our previously published work, data mining was employed in many area related to drug delivery e.g. dry powder inhaler delivery [8];

* Corresponding author.
E-mail address: mohamedemam9@yahoo.com (M.E.A. Abdelrahim).

https://doi.org/10.1016/j.pupt.2018.04.005
Received 13 February 2018; Received in revised form 5 April 2018; Accepted 6 April 2018
Available online 07 April 2018
1094-5539/

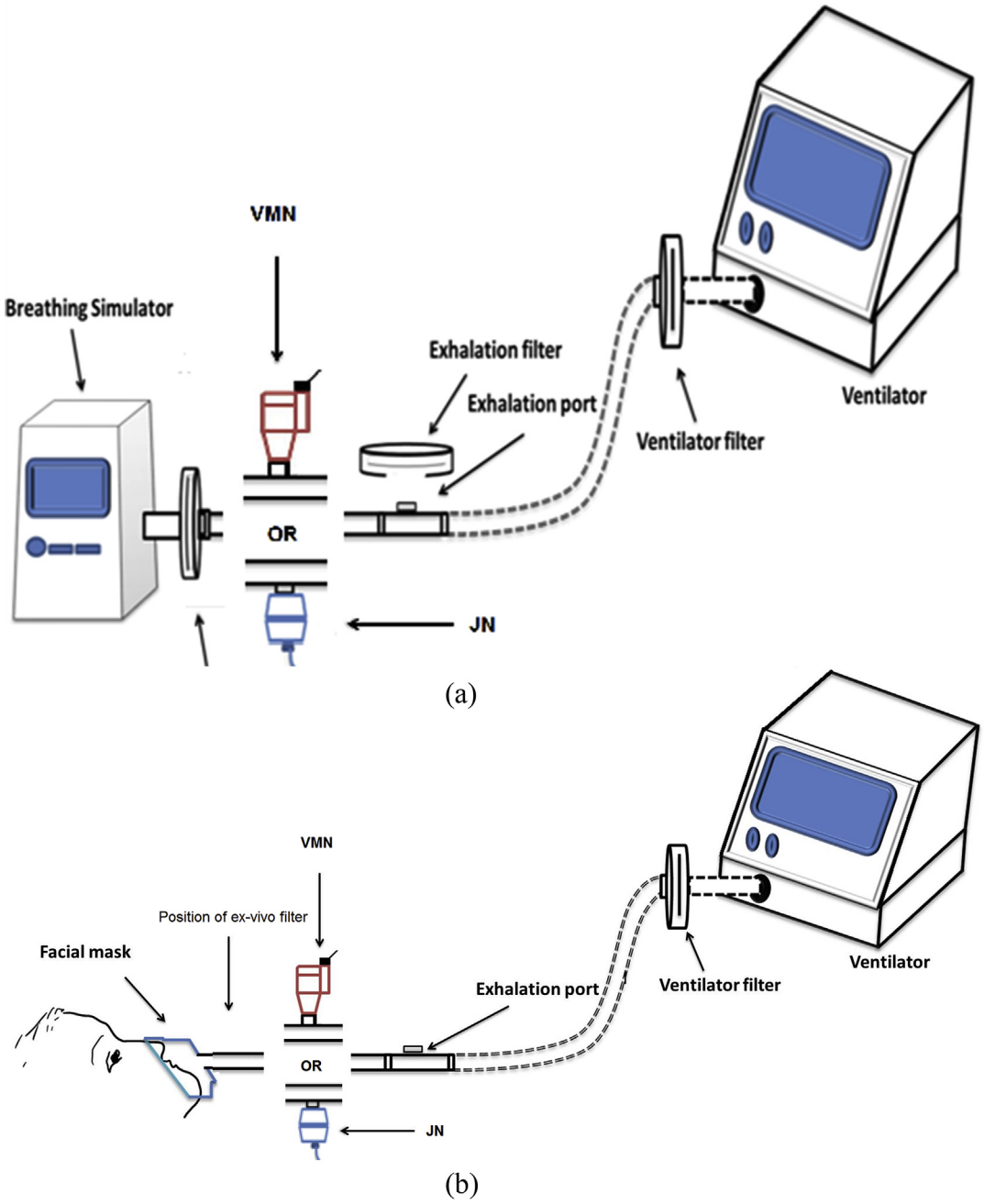

Fig. 1. Schematic design of the nebulizers positions within the non-invasive ventilation circuit. (A) In-vitro setting to determine the fate of the aerosolized dose. (B) In vivo and ex-vivo setting. The inspiratory filter was placed between the patient and nebulizer in the ex-vivo part of the study only.

Table 1
Mean (SD) demographic data of the 4 groups.

	Age (Years)	Wight (kg)	Height (cm)
Group 1	62.3 (6.0)	70.7 (7.9)	173 (4.7)
Group 2	65.0 (5.3)	74.4 (8.5)	170.6 (7.2)

different formulation preparation and optimization [9,10] and they proved to be an effective tool. We extend the use of such a methodology to optimize metered dose inhaler (MDI) delivery with spacers [2] and vibrating mesh nebulizers delivery [1] in non-invasive ventilation (NIV) and again they proved to be an effective and good tool. The modeling study of the VMNs recommended inclusion of other variables in the NIV circuit to optimize the model e.g. nebulizer type and fill volume of the respirable solution.

Hence, this study aimed to evaluate the effects of nebulizer type, fill volume of the respirable solution, placed in the nebulization chamber, on effective drug delivery. The modeling and optimization was carried out using ANNs and neurofuzzy logic based data mining technology.

2. Materials and methods

2.1. Experimental method

Study consisted of three models (in-vitro, ex-vivo and in-vivo) using two type of nebulizers, vibrating mesh nebulizer (VMN, Aerogen Solo, Aerogen Limited, Ireland) and the Oxycare jet nebulizer (JN, Ceren Uretim A.S., Istanbol, Turkey) attached to a compressor (PortaNeb, Philips Respironics, UK) set at 6 L/min. The three parts of study was