Emitted Dose and Lung Deposition from Certain Inhalation Device

Thesis

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Abstract

Keys words: salbutamol, pressurized metered dose inhaler, Spacer, urine, mean median aerodynamic diameter, fine particle dose, fine particle fraction, relative lung bioavailability.

The main aim was to use a urinary pharmacokinetic method for salbutamol to determine the relative lung and systemic bioavailability following inhalation through the usage of high performance liquid chromatography (HPLC) with ultraviolet (UV) detector and to measure the in-vitro characteristics of the emitted dose by these inhalation methods.

Two new, accurate and sensitive high performance liquid chromatography methods for the determination of salbutamol in aqueous and urine samples were validated. Salbutamol was extracted using solid phase extraction with bambeterol as internal standard. The accuracy, precision, lower limit of detection and recovery for both methods were within recognized limits.

The in-vitro characteristics of salbutamol sulphate emitted from Ventoline® pressurized metered dose inhaler(p MDI) were measured according to standard methodology as well as adaptation of this methodology to routine patient use. The dose emission of salbutamol sulphate from a Ventoline® pressurized metered dose inhaler was determined using an inhalation flows of 28.6L min-1. The particle size distribution was measured using an Anderson Cascade Impactor (ACI).

The in-vitro dose emission characteristics of salbutamol sulphate from Ventoline® pMDI were measured according to the standard compendial methodology at a flow of 28.3 L min-1 . The total emitted dose (TED) and particle size distribution of salbutamol sulphate from the Ventoline® MDI were determined with different spacers (Aerochamber MV, Aerochamber Vent and Aerochamber Mini spacers). The MDI with Aerochamber MV spacer resulted in the smallest mass median aerodynamic diameter (MMAD) and the highest fine particle fraction (FPF). The pMDI with Aerochamber MR resulted in the highest fine particle diameter (FPD).

Twelve non- invasive mechanically ventilated patients (6 females) completed in-vivo urinary salbutamol pharmacokinetic study to determine the relative bioavailability following inhalation. The amount of salbutamol excreted 30 minutes post inhalation can be used as an index of the lung deposition. The amount of salbutamol excreted 24 hour post inhalation can be used as an index of the systemic bioavailability. One dose of 1200 mcg salbutamol sulphate found in 12 puffs from Ventoline® pMDI through the usage of Aerochamber MV, Aerochamber Vent and Aerochamber Mini spacers fitted from one side to the continuous pressure airway pressure (CPAP) as non-invasive ventilator and the other side was sealed to the facemask of the patient and amounts of urinary salbutamol excreted 0.5 and 24 hour post dosing were measured This thesis was an extension for the urinary pharmacokinetic method to be used for comparing the efficacy of three different spacers in vitro and in vivo.

This work is dedicated to
my parents, my husband, and my sons.

List of Publication

Sections of this thesis have already been published in the following form:

1.**Raghda R.S. Hussein**, Ahmed Hassan, Hoda Rabea, , Randa Salah Eldin, Maha M Abdelrahman, Amira S.A. Said, Heba F. Salem Mohamed E. Abdelrahim , In-vitro characterization of the aerosolized dose during non-invasive ventilation: JOURNAL OF AEROSOL MEDICINE AND PULMONARY DRUG DELIVERY Volume 28. Presented as poster in 20th Congress of the International Society of Aerosol in Medicine, Munich Holiday Inn-City Center, Germany,2015.

2**. Raghda R.S. Hussein**., Ahmed Hassan, Hoda Rabea, , Randa Salah Eldin, Maha M Abdelrahman, Amira S.A. Said, Heba F. Salem Mohamed E. Abdelrahim , In-vitro characterization of the aerosolized dose during non-invasive ventilation(in press for publication in J Aerosol Med)

3.**Raghda.R.S.Hussein,Mohammed.E.A.Abdelrahim,AmiraS.A.Said,Maha.A.Abdelrahman,Heba F.Salem ,**In-Vivo Comparison of Aerosol Drug DeliveryIn Patients Receiving Noninvasive Positive Pressure Ventilation Through Pressurized Metered Dose Inhaler with Different Spacer Devices(in press for publication)

4. **Raghda R.S. Hussein, paper of correlation of in-vivo to in vitro**

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