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Comparison of four inhalation training methods in healthy adult volunteers when they inhale salbutamol through a pressurized inhaler

Submission date
28/11/2017

Recruitment status
No longer recruiting

Registration date
06/12/2017

Overall study status
Completed

Last Edited
22/08/2022

Condition category
Respiratory

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The pressurized metered dose inhaler (pMDI) is the most commonly prescribed inhaler device. Although the pMDI appears simple to use, the deceptive simplicity of the pMDI technique may result in a sub-optimal treatment outcome as many patients misuse their inhalers. Verbal training on the correct pMDI technique improves patients' inhaler use. However, patients do forget the correct inhaler use with time after the training session. The aim of this study is to evaluate and compare the impact of four inhaler technique training methods. These are the Trainhaler (TH), Flo-Tone CR (FT), Able Spacer (AS) and Verbal pMDI technique counselling (VC) methods. The Ventolin® Evohaler® will be used as the study pMDI. It contains a drug named salbutamol that increases the size of the narrowed air passages in certain lung diseases so that patients can breathe comfortably.

Who can participate?
Male adult (age 18-55) non-smoking healthy volunteers

What does the study involve?
Participants attend four study periods 1 week apart. In each of the study periods, the participants are confined to the clinical study site (ACDIMA BioCentre, Amman, Jordan) 12 hours before drug administration and until 24 hours after. At the start of each study period, each participant inhales two puffs from a Ventolin Evohaler separated by 30-60 seconds using one of four randomly allocated inhalation methods. Immediately after each puff, the participant washes /gargles their mouth and throat with water which is collected and analysed for salbutamol levels. The participant provides urine samples shortly before and 30, 60 and 120 minutes after drug administration. The participant pools their urine into a special container until 24 hours after salbutamol inhalation. At the end of each study period, the collected urine samples are stored and analysed.

What are the possible benefits and risks of participating?
The study results are expected to help healthcare providers choose the best inhalation method for their patients when they use this type of inhalers so that the patients can benefit the most

from their medicine. Since the participants are healthy, it is not expected that they will get any treatment benefits. However, participants are reimbursed financially for their time spent during participation. As with any other medicine, inhaled salbutamol might cause some side effects. Although rare, these include fast heart rate (tachycardia), headache, tremor, dry mouth and discomfort. As participants take one small dose of the study drug at each period, this is not expected to put the participants at risk of unwanted side effects.

Where is the study run from?
ACDIMA BioCentre (Jordan)

When is the study starting and how long is it expected to run for?
February 2017 to June 2018

Who is funding the study?
1. Al-Ahliyya Amman University (Jordan)
2. Clement Clarke International Ltd

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
Protocol Code: 694-2017, V.03 / Project Code: BC-SAL-16/547

Study information

Scientific Title
Relative lung and systemic bioavailability and oropharyngeal deposition of inhaled salbutamol: evaluation of Trainhaler, Flo-Tone CR, Able Spacer and verbal pMDI counselling

Study objectives
The pressurized metered dose inhaler (pMDI) is the most commonly prescribed inhaler device worldwide. Although the pMDI appears simple to use, the deceptive simplicity of the pMDI technique may result in a sub-optimal therapeutic outcome as many patients misuse their pressurized inhalers. Verbal training on the correct pMDI technique improves patients' inhaler use. However, patients do forget the correct inhaler use with time after the training session which mandates repeated inhaler technique reinforcement and re-training.
A report by the European Aerosol Drug Management Improvement Team (ADMIT) has stated that inhalation devices enhanced with feedback mechanisms to reassure the patients and their caregivers that the performed inhalation technique via an inhaler is sufficient should improve the overall correct inhaler use and ultimately disease control.

The current research study evaluates the impact of three pMDI inhalation training devices; the Trainhaler (TH), Flo-Tone CR (FT) and Able Spacer (AS), on the relative lung and systemic bioavailability of salbutamol inhaled by healthy adult volunteers. These inhalation tools will be compared to the Verbal pMDI technique counselling (VC) method.

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. ACDIMA BioCenter Institutional Review Board (IRB), 12/03/2017
2. Jordan Food and Drug Administration (JFDA) Clinical Studies Committee, 25/07/2017, ref: 01/30/2017

Study design
Investigational four-treatment four-period randomized crossover pharmacokinetic study

Primary study design
Interventional

Secondary study design
Randomised cross over trial

Study setting(s)
Other

Study type(s)
Other

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Testing ways of improving inhaler technique in healthy volunteers

Interventions
The study will evaluate and compare the impact of using the Trainhaler (TH), Flo-Tone CR (FT), Able Spacer (AS) and Verbal pMDI technique counselling (VC) methods on the relative lung and systemic bioavailability of salbutamol inhaled by healthy adult volunteers. Additionally, oropharyngeal deposition will be assessed immediately post inhalation.

The Trainhaler (TH), Flo-Tone CR (FT), Able Spacer (AS) are manufactured by Clement Clarke International, UK.
Ventolin® Evohaler® (100 µg/puff), GlaxoSmithKline, will be used as the salbutamol pMDI. The 30-min urinary excretion pharmacokinetic method will be used to determine the relative lung and systemic bioavailability following salbutamol inhalation. The salbutamol oropharyngeal deposition will be assessed by analysing mouthwash aqueous samples collected immediately post-inhalation.

Enrolled healthy volunteers will be randomized into a four-period, four-treatment (TH, FT, AS and VC) based on a randomization table constructed prior to study recruitment.

Intervention Type
Mixed

Primary outcome measure
1. Relative lung bioavailability of inhaled salbutamol, assessed by determining salbutamol concentration using a developed and validated HPLC-MS/MS analytical method in urine sample given 30 minutes post inhalation from Ventolin Evohaler using the assigned inhalation technique method
2. Relative systemic bioavailability of inhaled salbutamol, assessed by determining salbutamol concentration using a developed and validated HPLC-MS/MS analytical method in urine samples given at 60, 120 minutes and in urine subsequently pooled for 24 hours post inhalation from Ventolin Evohaler using the assigned inhalation technique method

Secondary outcome measures
Salbutamol oropharyngeal deposition, assessed using a developed and validated HPLC-MS/MS analytical method in mouthwash aqueous samples collected immediately post-inhalation

Overall study start date
01/02/2017

Completion date
30/06/2018

Eligibility

Key inclusion criteria
1. Non-smoker
2. Male aged 18 – 50
3. The subject is within the limits for his height & weight as defined by the body mass index range (18.5 – 30.0 kg/m2) or as judged acceptable by the principal investigator/clinical investigator
4. The subject is willing to undergo the necessary pre- & post- medical examinations set by this study

5. The results of medical history, vital signs, physical examination & conducted medical laboratory tests are normal as determined by the clinical investigator
6. The subject tested negative for hepatitis (B & C) viruses and Human Immunodeficiency Virus (HIV)
7. There is no evidence of psychiatric disorder, antagonistic personality, and poor motivation, emotional or intellectual problems likely to limit the validity of consent to participate in the study or limit the ability to comply with protocol requirements
8. The subject is able to understand and willing to sign the informed consent form
9. The subject has normal cardiovascular system and ECG recording

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Male

Target number of participants
16

Total final enrolment
16

Key exclusion criteria
1. The subject has suffered an acute illness one week before dosing
2. The subject has a history of or concurrent abuse of alcohol
3. The subject has a history of or concurrent abuse of illicit drugs
4. The subject has a history of hypersensitivity and/or contraindications to the study drug and any related compounds.
5. The subject has been hospitalized within three months before the study or during the study
6. The subject is vegetarian
7. The subject has consumed caffeine or xanthine containing beverages or foodstuffs within two days before dosing and until 24 hours after dosing in either study period
8. The subject has taken a prescription medication within two weeks or even an over the counter product (OTC) within one week before dosing in each study period and any time during the study
9. The subject has taken grapefruit containing beverages or foodstuffs within seven (7) days before first dosing and any time during the study
10. The subject has been participating in any clinical study (e.g. pharmacokinetics, bioavailability and bioequivalence studies) within the last 80 days prior to the present study
11. The subject has a history or presence of cardiovascular, pulmonary, renal, hepatic, gastrointestinal, hematological, endocrinal, immunological, dermatological, neurological, musculoskeletal or psychiatric diseases

Date of first enrolment
15/12/2017

Date of final enrolment
30/01/2018

Locations

Countries of recruitment
Jordan

Study participating centre
ACDIMA BioCentre
Amman
Jordan
19328

Sponsor information

Organisation
Al-Ahliyya Amman University

Sponsor details
Zip Code 19328
Amman-Jordan
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Sponsor type
University/education

ROR
https://ror.org/00xddhq60

Funder(s)

Funder type
University/education

Funder Name
Al-Ahliyya Amman University

Funder Name
Clement Clarke International Ltd

Results and Publications

Publication and dissemination plan
The protocol has not been published. No additional documents (such as study protocol, statistical analysis plan, other) will be available. However, the study methodology, procedures and statistical analysis (already in protocol) will be published in future journal articles. Planned publication of the results in a high-impact peer reviewed journal.

Intention to publish date
30/06/2019

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed in this study will be included in the subsequent results publication. For publication purposes, each volunteer will be identified by unique code number if individual results to be published.

IPD sharing plan summary
Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	30/04/2020	11/09/2020	Yes	No
Results article		18/08/2022	22/08/2022	Yes	No