ISRCTN74608958 https://doi.org/10.1186/ISRCTN74608958

Evaluation of a treatment for incontinence associated dermatitis

Submission date
26/04/2012

Recruitment status
No longer recruiting

Registration date
04/05/2012

Overall study status
Completed

Last Edited
27/11/2015

Condition category
Skin and Connective Tissue Diseases

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

Plain English summary of protocol

Background and study aims
This initial study is being performed to test a new type of skin treatment (barrier cream) for a skin disease known as incontinence-associated dermatitis (IAD) (inflammation of the skin that occurs when urine or stool comes in contact with the skin). If successful, this work may provide a new treatment for a range of other skin conditions (such as eczema) which are caused by exposure to chemicals in the work or domestic environment. The aim of this study is to assess the effectiveness of a new barrier cream product for the prevention and treatment of incontinence-associated dermatitis.

Who can participate?
The study will be performed on up to 32 volunteers (age > 17 years) willing to attend up to three, five day sessions.

What does the study involve?
The study is divided into three parts.
In part 1, we will determine the optimum thickness of barrier cream to apply to the skin in order to provide protection against a substance called methylnicotinate (MN). This will involve application of the test and compartor products (at up to five different thicknesses) at multiple sites on each volunteers forearms.
Part 2 will involve determining how often the cream needs to be reapplied to maintain effectiveness against MN. Application of MN to the skin causes a temporary redness which we can accurately measure using instruments designed to measure blood flow and skin colour. So, by measuring the reduction in skin redness, we can directly measure the effectiveness of the barrier cream when applied at different thicknesses for different times in order to judge the best conditions for use (or standard dosing regime).
Part 3 of the study will assess the effectiveness of the barrier cream on the skin of volunteers against an irritant solution (synthetic urine). We will use synthetic urine (SU) in order to safely replicate the disease state (incontinence-associated dermatitis). The effectiveness of the cream will be quantified using measurements such as blood flow and skin colour.
Each volunteer gets each treatment (control, comparator and test product)

What are the possible benefits and risks of participating?
There will be no immediate direct benefit to those taking part, but there should be future benefits to those who suffer from incontinence-associated dermatitis if the study demonstrates that the new barrier cream is effective.
The risk of participating relates to the compounds being applied to each volunteers skin. In particular, synthetic urine (SU) will cause some minor irritation in the form of redness and possibly some itching and mild swelling.

Where is the study run from?
University of Hertfordshire in the UK.

When is the study starting and how long is it expected to run for?
It is anticipated that recruitment will start in August or September 2012. The study will take approximately three months to complete.

Who is funding the study?
Bracco Imaging S.p.A.

Who is the main contact?
Professor Robert P Chilcott
r.chilcott@herts.ac.uk

Contact information

Type(s)
Scientific

Contact name
Prof Robert Chilcott

ORCID ID
https://orcid.org/0000-0002-8845-9400

Contact details
University of Hertfordshire
College Lane
Hatifled
United Kingdom
AL10 9AB

Additional identifiers

Protocol serial number
SER RD1 2012-01

Study information

Scientific Title
Assessment of a topical skin protectant (barrier cream) for the prevention and treatment of incontinence-associated dermatitis (IAD).

Study objectives
A new type of barrier cream, based on a chemically inert formulation, will reduce the signs of exposure to an irritant solution (synthetic urine).

Null hypothesis:
Cream will not affect the onset of experimentally-induced dermatitis.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Not provided at time of registration

Primary study design
Interventional

Study design
Randomised within subjects double blind study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Incontinence-associated dermatitis

Interventions
The project is organised into four elements. Work Package 1 relates to the ethics application. Initial work with human volunteers (Work Package 2) will establish the actual thickness of RD1433 required for optimum protection, with Work Package 3 providing a measure of the duration over which it retains efficacy. The latter will provide information upon which to base the topical reapplication frequency. Collectively, the required thickness and frequency of application contribute to the development of the standard dosing regime. The outputs of WP2 and WP3 will provide relevant information to facilitate a preliminary evaluation of the efficacy of RD1433 (versus a standard treatment; Vaseline™) within Work Package 4. This experimental approach will enable an efficacy assessment for both prevention and treatment strategies. The corresponding data would be collated into a final report for delivery to the sponsor (WP5) with a request to publish the results in a peer-reviewed journal.

Note that all experiments involving the use of RD1433 and Vaseline™ will be performed in a double-blind manner: the Clinical Investigation Team will not be present when the test and comparator products are applied and the volunteers will not be aware of what treatment (if any) each skin site receives. The treatment each individual skin site receives will be according to a Latin square design (and so pre-determined). However, the assignment of each volunteer to a particular Latin square treatment allocation will be random.

Work Package 2 (WP2): Dosing Regime Thickness.
Work Package 2 (WP2) will determine the optimum dose (thickness) of each topical treatment required to protect the skin. Ideally, volunteers recruited for this Work Package will return for subsequent investigations and so this may reduce experimental variation.
The experiment will involve application of the test products (at up to five different thicknesses)

at multiple sites on the volar aspect of each volunteers forearms, with two contralateral control (untreated) sites. Treatments will be allocated using a Latin square design to minimise the effects of chiral preference and variations due to anatomical location (Chilcott and Farrar, 2000). After a period of 15 minutes, each site will be exposed to a (10 µl) droplet of a rubefacient (5 mMol aqueous solution of methylnicotinate; MN) and measurements of blood flow at each site will be acquired at up to 60 minute intervals by laser Doppler imaging (LDI) for a total duration of up to six hours. (Blood flow measurements will also be taken prior to and immediately after application of test products to account for optical interference caused by the presence of test material on the skin surface.) Additional, non-invasive measurements such as skin reflectance spectroscopy (SRS), infrared imaging (IRI), visual observations, tissue viability imaging (TiVi) and acquisition of digital photographs for image analysis may also be taken.

Application of the test and comparator products (RD1433 and Vaseline™) will be achieved by applying a set volume of material within a circular (defined) area of skin marked with an indelible ink pen to provide a nominal thickness of 0.01, 0.02, 0.05, 0.1, and 0.2 mm. Application will be achieved by pre-loading (to excess) an empty 1 ml syringe barrel and subsequently inserting the syringe plunger to the required volume (thus eliminating trapped air). After applying the test products to the skin surface, a pre-weighed finger glove will be used to rub the cream into the skin at each exposure site, after which the finger glove will be reweighed to determine the actual amount of test product applied (and so permit an adjustment to determine actual applied dose per unit area). Application of the two products at five nominal thicknesses with two contralateral control sites will require 12 exposure sites. Therefore, in order to balance the Latin square design , a total of twelve volunteers will be required. As LDI measurements will be taken prior to application of the rubefacient, the study will essentially be a within subjects design. Additional measurements (such as visual observations, SRS, TiVi, IRI and digital photographs for image analysis) may also be acquired.

As the development of erythema (redness) at the site of methylnicotinate exposure is dependent on biochemical activation via an enzyme (cyclooxygenase), it will be important to exclude any volunteers who had taken non-steroidal anti-inflammatory drugs (such as aspirin and acetaminophen) within 24 hours of the start of the study.

The technical output of this first experiment will be to determine the optimum thickness for application of the test products. It is likely that the level of protection afforded by both the test and comparator product will plateau after a certain thickness is exceeded: the point at which this occurs will be identified as the optimum thickness.

Work Package 3 (WP3): Dosing Regime Reapplication Frequency
This work package is designed to determine the duration of effectiveness of both the test and comparator products following application at one (optimal) thickness. The study will essentially be performed as described above, but instead of applying different thickness of topical products, we will apply the optimum thickness as identified in WP2. Application of the rubefacient (10 µl methylnicotinate; 5 mMol aqueous solution) will subsequently be staggered so as to expose each test product at one of five time points (1, 2, 3, 4 and 6 hours after application of the test products). Application of the two products for five durations with two contralateral control sites will require 12 exposure sites. Therefore, a total of twelve volunteers will be required to comply with a Latin square design1. Volunteers from Work Package 2 will not be excluded from participating in Work Package 3 and so the total number of volunteers required for WP 2 and 3 will range from 12 to 24. The combined outputs of WP2 and WP3 will define the optimum dosing regime for Work Package 4.

Work Package 4 (WP4): Efficacy Testing

This Work Package will seek to evaluate the preventative and curative efficacy of the test products (Vaseline™ and RD1433) in an established human model of incontinence associated dermatitis (IAD). The actual study design will be dependent on the dosing regime identified in WP 2 and 3.

It is important to note that it may be necessary to remove the exposure chambers containing the diaper/irritant (synthetic urine) matrix during the intended 6 hour exposure period to enable re-application of the test formulation(s): this current study protocol assumes that one re-application of each test product will be required during the exposure period. Clearly, this may change in light of the output of WP 2 and it should be noted that an amendment to the protocol may be required to accommodate such changes.

A combination of four treatments (A D) will be applied to the arms of each volunteer:

1. RD1322 (applied on one arm as pre-treatment and on contralateral arm as a treatment).
2. Vaseline™ (applied on one arm as pre-treatment and on contralateral arm as a treatment).
3. Positive control (exposure chamber to contain swatch of nappy soaked in appropriate volume of synthetic urine).
4. Negative control (exposure chamber to contain swatch of nappy soaked in 0.9% saline).

One arm will be used to assess the preventative efficacy, with the contralateral arm being used to evaluate treatment efficacy (i.e. effects of treatment following development of experimental dermatitis).

Where applicable, the test products will be applied to the skin surface using a 1 ml syringe as described in WP2. All exposure sites will subsequently be covered with a standard, occlusive, plastic exposure chamber (for example, HillTop® chamber). A disc of nappy material will be placed inside each chamber. The material with be wetted with up to 1 ml of either synthetic urine (treatment C) or saline (treatment D). The chambers will be secured to the exposure sites using medical adhesive tape. The study will require a minimum of eight volunteers, with treatments allocated according to a Latin square design for the reasons outlined above.

The study will begin with non-invasive measurements at each exposure site prior to the application of any treatments. Measurements will include one or more of the following: Laser Doppler imaging (LDI), skin reflectance spectroscopy (SRS), transepidermal water loss (TEWL), tissue viability imaging (TiVi), infrared imaging (IRI), skin surface pH, visual observations and Digital photography. Immediately following measurements, the appropriate treatments (A D) will be applied to each participant.

For the assessment of treatment, the first two days will involve provocation of a skin response only and so three sites on the selected forearm will be exposed to the irritant matrix (Treatment C) in the absence of any test product with the fourth site on that arm serving as a control (Treatment D). In contrast, the opposite forearm will be used to assess the preventative efficacy of the test products and so will be pre-treated with RD1433 (Treatment A) or Vaseline™ (Treatment B) prior to exposure to synthetic urine (Treatment C) with the fourth site serving as a control.

Exposure chambers on the forearm used to assess preventative efficacy may need to be removed after an interval conversant with the need for re-application of the test products (as determined in WP2). At this point, all the sites will be washed with a standard (mild) detergent such as Dove soap, dried and the test products reapplied. The dosing chambers will then be replaced at each site. (Additional reapplication may be required and so this process may need to be repeated, as appropriate.) At the end of the 6 hour exposure period, the dosing chambers will

be removed from both forearms and the sites left unclothed for a period of one hour, after which biophysical measurements will be taken.

From day 3 of the study, the protocol will be modified to accommodate the application of test products to all relevant exposure sites. Otherwise, the overall procedure will be similar to days 1 2, with temporary removal and washing of all sites and re-application of treatments followed by removal of chambers and acquisition of non-invasive measurements being taken one hour after removal of the exposure chambers.

The volunteers will be asked to return on day 7 for a final set of non-invasive measurements and will be invited to return two weeks later a post-study appointment with a health care professional.

Work Package 5 (WP5): Reporting
On completion of the trial, the supervisor will be responsible for collating all data and transcribing into an appropriate format for outsourced statistical analysis in blind form. Following statistical analysis, the supervisor will be responsible for unblinding the processed data.

Intervention Type
Other

Phase
Not Applicable

Primary outcome(s)
1. Significant reduction in vascular perfusion (Laser Doppler imaging; arbitrary perfusion units)
2. Significant reduction in erythema (skin reflectance spectroscopy; CIELAB a* parameter)
3. Significant reduction in transepidermal water loss (evaporimetry; mg/cm2/h)
4. Significant reduction in skin surface temperature (infrared imaging; °C)

Key secondary outcome(s)
No secondary outcome measures

Completion date
03/12/2012

Eligibility

Key inclusion criteria
1. Age >17 years
2. Generally healthy
3. Willing to attend up to three, five day sessions

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group

Adult

Sex
All

Key exclusion criteria
1. Dark-skinned volunteers. (This is because darker skin may affect some of the measurements we intend to make, as our instruments rely on being able to detect changes in skin colour and blood flow. The presence of melanin (the substance responsible for darkening the skin) reduces the sensitivity of our equipment. This will not affect the outcome of our study if the treatment is successful, it will work on all skin types.)
2. Pre-existing skin disease such as eczema, dermatitis or skin allergy
3. Concurrent use of aspirin, paracetamol or any other anti-inflammatory drugs

Date of first enrolment
03/09/2012

Date of final enrolment
03/12/2012

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Hertfordshire
Hatifled
United Kingdom
AL10 9AB

Sponsor information

Organisation
Bracco Healthcare (USA)

ROR
https://ror.org/03wjptj96

Funder(s)

Funder type
Industry

Funder Name
Bracco Diagnostics Inc (USA) ref: SER RD1 2012-001

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/02/2015		Yes	No
Other publications		01/01/2015		Yes	No