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A programme to develop a skin patch containing two medicines (physostigmine and hyoscine), Study 6: Assessment of blood levels of the two medicines and any associated symptoms in healthy female participants.

Submission date
13/01/2020

Recruitment status
No longer recruiting

Registration date
20/01/2020

Overall study status
Completed

Last Edited
14/01/2020

Condition category
Injury, Occupational Diseases, Poisoning

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
A skin patch containing two medicines (physostigmine and hyoscine) has been developed. The skin patch releases these medicines enabling them to cross the skin into the bloodstream. The aim of this study was to measure the amount of physostigmine and hyoscine in the blood at different times and assess any associated symptoms with two different patch sizes (21cm² and 25cm²). The participants in the study are healthy female participants. All the previously conducted studies on the skin patch involved healthy men.

Who can participate?
Study participants are females aged between 18 and 45 years.

What does the study involve?
Each participant in period 1 of the study will wear an active F11 transdermal patch (21 cm²) for 72 hours. Each participant in period 2 will wear a larger size F11 transdermal patch (25 cm²) for 72 hours. Each participant in period 3 will wear three consecutive active or placebo F11 transdermal patches (21 cm²) for 9 days. Each patch will be applied for a period of 72 hours. Blood samples are taken before and after patch application to measure the amounts of the two medicines (physostigmine and hyoscine). In addition the activity of the enzyme acetylcholinesterase (AchE) is measured in these blood samples. The condition of the skin under the patch is recorded at set times and any symptoms experienced while it is worn are noted. Heart rate, blood pressure, electrical activity of the heart (ECG), tests of vison and cognitive function are also recorded at set times.

What are the possible benefits and risks of participating?
There are no direct benefits for the individuals participating in this study. However, the information collected from the study will add to the scientific knowledge about the

physostigmine and hyoscine patch. All medicinal products may cause side effects. The most common side effects known about the medicines in the patch are nausea and vomiting due to physostigmine and blurred vision and dry mouth due to hyoscine. Single and multiple applications of the F-11/21 patch are considered to be well-tolerated.

Where is the study run from?
The study was conducted at Simbec Research Limited, UK.

When is the study starting and how long is it expected to run for?
September 2006 to November 2008.

Who is funding the study?
UK Ministry of Defence

Who is the main contact?
centralenquiries@dstl.gov.uk

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

Clinical Trials Information System (CTIS)
2006-006809-90

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
RD 209/24426

Study information

Scientific Title

A study to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of a single
application (one or two dose levels) and multiple applications (one dose level) of the transdermal patch formulations of physostigmine and hyoscine in healthy female subjects

Study objectives
The aim of this study is to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of single (two dose levels) and repeat application (one dose level) of a transdermal patch containing physostigmine and hyoscine, in healthy female participants.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 19/03/2007, South East Wales Local Research Ethics Committees (LREC) (Churchill House, 17 Churchill Way, Cardiff, CF10 2TW, UK; +44 (0)2920402402; no email address provided), ref: 07/WSE04/24

Study design
Single centre 3-part randomized double-blind placebo-controlled study of 2 dose levels

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
Potential risk of poisoning by nerve agent

Interventions
Generic drug name- physostigmine and hyoscine (transdermal patch)
Dosage - period 1: a single 72 hour application of active 21 cm^2 patch formulation F-11 (F11/21)
Dosage - period 2: a single 72 hour application of active 25 cm^2 patch formulation F-11 (F11/25)
Dosage- period 3: three consecutive 72 hour applications of active or placebo 21cm^2 patch formulation F-11 (F11/21)

Randomisation:
A sequential three-digit subject (randomisation) number was assigned once subjects were enrolled in the study. In the randomised, placebo-controlled, part of the trial (Period 3) active or placebo patches were allocated according to the randomisation schedule produced by the CRO.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
Physostigmine and hyoscine

Primary outcome(s)
The safety and tolerability of physostigmine/hyoscine transdermal patches assessed by monitoring vital signs, ECG, ocular function (near point), patch application site assessment, using digital photography. Tests performed at intervals for up to 96 hours after patch application and at follow up after periods 1 and 2. In period 3 these safety measures are conducted at up to 240 hours after first patch application and at follow up.

Key secondary outcome(s))
1. The pharmacokinetic (PK) and pharmacodynamic (PD) profiles of physostigmine and hyoscine measured in periods 1 and 2 at pre-dose and regular intervals up to 96 hours after patch application. In period 3 the blood levels of these medicines was measured at pre-dose and up to 240 hours after first patch application. Assay by liquid chromatography-tandem mass spectrometry (LC-MS-MS) method. Acetylcholinesterase levels measured at baseline, pre-dose, and intervals up to 240 hours after patch application. Method was validated spectrophotometric method

2. The cognitive and ocular effects of physostigmine and hyoscine measured by a set of attention tests and light responsiveness/ vision accommodation tests respectively

Completion date
12/11/2008

Eligibility

Key inclusion criteria
Screening (all periods):
1. Ability to give written informed consent prior to study participation
2. Healthy Caucasian female subjects aged between 18 and 45 years (inclusive)
3. A female with a documented record of surgical sterilisation, or of child-bearing potential could be enrolled provided she:
3.1. Had a negative pregnancy test prior to entry into the study and agreed not to attempt to become pregnant during the study.
3.2. Is routinely using adequate hormonal contraception (including hormonal implants, depot injections, and hormone-impregnated IUDs when supplemented by a barrier method) which had not been changed in the three months before the study; agreed to continue to do so during the study, and agreed to use an additional barrier method for the duration of the study and for 28 days after study completion
3.3. Is not breastfeeding
4. Body Mass Index (BMI) within the range of ≥21 and ≤30 kg/m²
5. Individual vital signs must be within the following ranges:
5.1. Pulse rate 50-90 bpm
5.2. Systolic blood pressure 100-140 mmHg
5.3. Diastolic blood pressure 50-90 mmHg
6. Ability to communicate well with the investigator and comply with the requirements of the study
7. Subjects intending to take part in two study periods must agree not to take part in another clinical study involving blood sampling for a further 4 months (due to the relatively high amount of blood required for this study)

Participant type(s)

Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Male

Key exclusion criteria
Screening (all periods):
1. Presence of any clinically significant medical condition as determined by the Investigator
2. Any surgical or medical condition which might significantly alter the absorption, distribution, metabolism or excretion of any drug (e.g. renal or liver disease, respiratory, immunological, endocrine or neurological disorders).
3. Any clinically-significant ECG abnormality other than sinus bradycardia or respiratory sinus arrhythmia
4. Evidence of postural hypotension (BP measurement after 5 minutes supine and again after 2 minutes standing, defined as a decrease between the two measurements of more than 20 mmHg (systolic)
5. Known or suspected hypersensitivity or idiosyncratic reaction related to any of the study products
6. Any history of contact dermatitis
7. A dibucaine number of less than 70
8. Any skin disorder, broken skin, scars, tattoos at the sites of patch application (i.e. on both arms, if volunteer planned to take part in more than one patch administration)
9. Glaucoma or a history of glaucoma in first-degree relatives (i.e. parents, siblings or offspring)
10. Presence of Anterior Chamber Narrow Angle (Van Herrick Grade 1 and 2)
11. Intra-ocular pressure exceeding 20 mmHg
12. Uncorrected vision in either eye of worse than 6/9 on the Snellen Scale
13. Corrected vision of 6/9 or better on the Snellen Scale when wearing +2.25 dioptre reading glasses.
14. Require glasses or contact lenses for distance vision
15. History of asthma (within the previous 10 years), exercise induced bronchospasm or relevant seasonal bronchospasm
16. Lung function of less than 80% of predicted FEV1 and FVC values
17. History or evidence of drug abuse (opiates, methadone, cocaine, amphetamines, cannabinoids, barbiturates)
18. Positive test for HIV, Hepatitis B surface antigen or Hepatitis C antibody
19. History or evidence of alcohol abuse defined as an intake of more than 21 units per week (where 1 unit corresponds to 250 ml beer, 20 ml spirits/liqueur or one glass (100 ml) of wine)
20. Positive urine test for alcohol
21. Participation in another clinical study within the last three months
22. Use of any prescription medication within the last 14 days (with the exception of hormonal contraception)
23. Use of non-prescription medication that may have impacted the safety aspects and

objectives of the study, within the last 7 days (apart from paracetamol)
24. Donation of blood or blood products within the last 3 months, or the intention to donate blood or blood products within 3 months after completion of the study if taking part in one study period or donated blood or blood products within 4 months after completion of the study if taking part in two study periods

Baseline (all periods):
1. Evidence of postural hypotension (BP measurement after 5 minutes supine and again after 2 minutes standing, defined as a decrease between the two measurements of more than 20 mmHg (systolic)
2. Development of any exclusion criteria since last visit
3. Positive urine test for alcohol
4. Positive drugs of abuse test
5. Negative pregnancy test (if appropriate)
6. Use of any prescription medication since last visit (with the exception of hormonal contraception)
7. Use of non-prescription medication that may impact the safety aspects and objectives of the study, within the last 7 days (apart from paracetamol)

Date of first enrolment
19/03/2007

Date of final enrolment
20/07/2007

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Simbec Research Limited
Merthyr Tydfil
Merthyr Tydfil
United Kingdom
CF48 4DR

Sponsor information

Organisation
Dstl

ROR
https://ror.org/04jswqb94

Funder(s)

Funder type
Government

Funder Name
Ministry of Defence

Alternative Name(s)
MOD

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to confidentiality.

IPD sharing plan summary
Not expected to be made available