ISRCTN16859029 https://doi.org/10.1186/ISRCTN16859029

A programme to develop a skin patch containing two medicines (physostigmine and hyoscine), Study 3: Assessment of blood levels of the two medicines and any associated symptoms in healthy male participants wearing four prototype skin patches.

Submission date
05/09/2019

Recruitment status
No longer recruiting

Registration date
19/09/2019

Overall study status
Completed

Last Edited
08/10/2019

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
Several different versions (called formulations) of a skin patch containing two medicines (physostigmine and hyoscine) have 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. In the first part of the study four groups of six participants were given one of four different formulations for 72 hours. Following review of the results of the first part of the study, one formulation was selected to be given to 12 participants for three consecutive 72 hour periods.

Who can participate?
Study participants were healthy males aged between 18 and 45 years

What does the study involve?
Each participant was allocated a specific formulation of patch for 72 hours in period 1 of the study. One of the four formulations was allocated to each participant on a random basis. In period 2 participants were randomly allocated to receive the selected patch formulation or placebo for three consecutive 72 hour periods.
Blood samples were 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) was measured in these blood samples. The effects of the patch were assessed by recording the condition of the skin under the patch at set times and any symptoms that were experienced. Heart rate, blood pressure, electrical activity of the heart (ECG), tests of vison and cognitive function were also recorded at set times.

What are the possible benefits and risks of participating?
There were no direct individual benefits for the participants participating. However, the information collected from these individuals added to the scientific knowledge about the physostigmine and hyoscine patch. All medicinal products have a risk of causing 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. Overall all formulations tested were 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?
Study has been completed.

Who is funding the study?
The study was funded by UK MoD

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

Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number
2005-003851-10

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
RD 209/24142

Study information

Scientific Title
A Two-part Study to Investigate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Single and Multiple Applications of Four Transdermal Patch Formulations of Hyoscine and Physostigmine in Healthy Male Participants

Study objectives
The aim of this study was to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of single and multiple applications of a four transdermal patch formulations of hyoscine and physostigmine in healthy male participants.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 12/10/2005, South East Wales Local Research Ethics Committees (Churchill House, 17 Churchill Way, Cardiff, CF10 2TW; 02920402402), ref: 04/WSE04/115

Study design
Single centre two-part randomised double-blind single-dose study
of four patch formulations (F8, F9, F10, F11)
Period 2 - A Randomised, Double-Blind, Placebo-Controlled multiple-dose Study of a single patch formulation (F 11)

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Other

Participant information sheet
No participant information sheet available

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

Interventions
(i) Generic drug name- physostigmine and hyoscine (transdermal patch)
(ii) Dosage - In the study 4 patch formulations were tested.

Period one:
Method and frequency of administration- design was a randomised, double- blind, parallel, two-part study. Period one was a double-blind assessment of four formulations (F8, F9, F10, F11) of the transdermal patch, with each participant being randomised to receive a single application of one patch. Six participants were allocated to each of the four formulations.

Period two:
A double-blind, randomised, placebo-controlled assessment of repeat doses of the selected patch formulation (F11) to be administered to 18 participants (12 participants received active patch formulation and six received placebo patches).

Randomisation:
A sequential three-digit subject (randomisation) number was assigned once eligibility for the study had been confirmed. Treatment was allocated according to the randomisation schedule produced by the CRO.

Intervention Type
Drug

Phase
Phase II

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

Primary outcome measure
Safety and tolerability of drugs tested was assessed by monitoring vital signs, ECG, near point ocular function and patch application site assessment using digital photography. In period 1 these parameters were measured at baseline and at pre-determined intervals up to 84 hours after patch application, prior to discharge on day 5 and at follow up. In period 2 they were measured at these times and also at additional time points up to follow up at Day 42 after the first patch application

Secondary outcome measures
1. Pharmacokinetic measures:
Plasma concentration of physostigmine and hyoscine tested at following intervals. Period 1: pre-dose and at intervals up to 96 hrs after the patch application. Period 2: pre-dose and at intervals up to 240 hours after application of the first patch. (test method for PK measures was liquid chromatography tandem mass spectrometry (LC-MS-MS) method).
2. Pharmacodynamic measures:
Blood measurement of red cell acetylcholinesterase (AChE) activity tested at the following intervals. Period 1: pre-dose and at intervals up to 96 hrs after the patch application. Period 2: pre-dose and at intervals up to 240 hours after application of the first patch. (test method for PK measures was validated spectrophotometric method).

Overall study start date
06/09/2005

Completion date
17/01/2007

Eligibility

Key inclusion criteria
At screening for period 1:
1. Ability to give written informed consent prior to study participation

2. Healthy Caucasian male participants aged between 18 and 45 years (inclusive)
3. Body Mass Index (BMI) within the range of 21 and 30 kg/m2
4. Vital signs within the following ranges:
4.1 Pulse rate 40-90 bpm
4.2 Systolic blood pressure 90-140 mmHg
4.3 Diastolic blood pressure 50-90 mmHg
5. Ability to communicate well with the Investigator and to comply with the requirements of the study.

Baseline (Period 2):
1. Successful completion of Part 1.
2. Randomisation to take part in Part 2.
3. Willing and able to continue in the study.

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Male

Target number of participants
Period 1 - 24 healthy male participants

Key exclusion criteria
Does not meet inclusion criteria

Date of first enrolment
12/10/2005

Date of final enrolment
07/11/2005

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Simbec Research Limited
Merthyr Tydfil
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Sponsor information

Organisation
Defence Science and Technology Laboratory (Dstl)

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Sponsor type
Government

ROR
https://ror.org/04jswqb94

Funder(s)

Funder type
Government

Funder Name
Study conducted on behalf of UK Ministry of Defence

Results and Publications

Publication and dissemination plan
Our intention is to submit the results of this study for publication in an academic journal later in the development programme.

Intention to publish date
09/09/2020

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