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A programme to develop a skin patch containing two medicines (physostigmine and hyoscine), Study 1: Assessment of blood levels of the two medicines and any associated symptoms in healthy male participants wearing prototype skin patches

Submission date
23/07/2019

Recruitment status
No longer recruiting

Registration date
30/07/2019

Overall study status
Completed

Last Edited
26/07/2019

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
Three different versions of a skin patch containing two medicines (physostigmine and hyoscine) have been developed. The patch allows these medicines to cross the skin into the bloodstream. The aim of this study is to measure the amount of physostigmine and hyoscine in the blood at different times over a 72 hour period and assess any associated symptoms.

Who can participate?
Healthy male volunteers aged 18 to 40

What does the study involve?
Each participant wears each formulation of the patch in turn for 72 hours occasions separated by a period of 4 days between removal and new application. On each occasion 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 acetylcholiesterase (AchE) is measured in these blood samples. The effects of the patch are assessed by recording the condition of the skin under the patch at set times and any symptoms that are experienced. Heart rate, blood pressure, electrical activity of the heart (ECG), tests of vision and cognitive function are also recorded at set times.

What are the possible benefits and risks of participating?
There are no direct individual benefits for the participants. However, the information collected from these individuals adds 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.

Where is the study run from?
PPD Development Clinic (UK)

When is the study starting and how long is it expected to run for?
July 2003 to December 2004

Who is funding the study?
Ministry of Defence (UK)

Contact information

Type(s)
Public

Contact name
Dr Medical Advisor

Contact details
Dstl
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Additional identifiers

Clinical Trials Information System (CTIS)
2004-000146-20

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
1700171

Study information

Scientific Title
A randomised, double-blind, three-way crossover study to investigate the pharmacokinetics, pharmacodynamics, safety and tolerability after single applications of three transdermal patch formulations of physostigmine and hyoscine in healthy males

Study objectives
The aim of this study was to investigate the safety, tolerability, pharmacokinetics and pharmacodynamics of single applications of three formulations of a transdermal patch containing hyoscine and physostigmine when administered to healthy male subjects.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 06/04/2004, PPD Development Clinical Independent Ethics Committee (72 Hospital Close, Evington, Leicester, LE5 4WW, UK; Tel: +44(0) 1162733553), ref: PPD 1700171

Study design
Randomised double-blind three-way crossover study

Primary study design
Interventional

Study type(s)
Other

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

Interventions
1. Generic drug name: physostigmine and hyoscine (transdermal patch)
2. Dosage: study planned as single dose (72-hour application) three-way crossover
3. Method and frequency of administration: design was a randomised, single-centre, double-blind, single-dose (72-hour application), three-way crossover study
4. Follow up: safety monitoring, blood sampling for pharmacokinetics and pharmacodynamics, patch adhesion and irritancy assessments, ECG, ocular function assessments and cognitive function assessments were performed for 72 hours after the application of the patch (this included 24 hours after patch removal)

The PHP formulations tested were F1, F2 and F3. The patches were identical in size (37 cm2) and shape and only differed in the adhesive used for each group. The plan was for each subject to wear each formulation of the patch in turn for 72 hours occasions separated by a washout period of 4 days between removal and new application. On each occasion, 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 acetylcholiesterase (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 vision and cognitive function were also recorded at set times.

Intervention Type
Drug

Phase
Phase I

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

Primary outcome(s)

1. Plasma concentrations of hyoscine and physostigmine measured by liquid chromatography-tandem mass spectrometry (LC-MS-MS)): blood samples collected at the following times: 0 hours (pre-dose) and 2, 4, 6, 8, 10, 12, 24, 36 and 48 hours after patch application on Day 1, 2, 4, 6, 8, 10, 12 and 24 hours after patch removal
2. Acetylcholinesterase activity measured by spectrophotometry: blood samples collected at the following times: Day –1, 0 hours (pre-dose) and 2, 4, 6, 8, 10, 12, 24, 36 and 48 hours after patch application on Day 1; 2, 4, 6, 8, 10, 12 and 24 hours after patch removal

Key secondary outcome(s))
Adhesion score measured by visual inspection of degree of patch adhesion to skin at 24 and 48 hours after application

Completion date
13/12/2004

Eligibility

Key inclusion criteria
1. Healthy male participants
2. Aged between 18 and 40 years inclusive
3. Body Mass Index (BMI) ≥ 18 and ≤ 31 kg/m2, and body weight ≥ 60 and ≤ 110 kg
4. Able to understand the informed consent discussion, which included information about potential risks and effects of the test materials, and signed the informed consent form
5. Medical history without major pathology (e.g. cardiac, immunological, endocrine or neurological disorders, cancer or other wasting diseases)
6. Human immunodeficiency virus (HIV), hepatitis B and hepatitis C negative
7. No clinically significant abnormalities at the pre-study screening, and subject’s GP had not advised against inclusion
8. Computerised 12-lead ECG recording without clinically relevant signs of pathology and conductance disturbances as judged by the investigator

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
Male

Key exclusion criteria
1. Presence of any clinically significant medical condition as determined by the investigator
2. Known or suspected hypersensitivity or idiosyncratic reaction related to any of the test materials

3. Homozygous or heterozygous for the atypical (dibucaine resistant) allele of butyrylcholinesterase
4. Any skin disorder, broken skin, scars, tattoos at the site of application
5. Glaucoma or a history of glaucoma in first degree relatives (i.e. parents, siblings and offspring)
6. Presence of Anterior Chamber Narrow Angle (Van Herrick Grade 1 and 2)
7. Intra-ocular pressure exceeding 20 mm Hg
8. Uncorrected vision (or contact lens corrected vision) in either eye worse than 6/9 on the Snellen scale
9. History or evidence of drug abuse (including opiates, methadone, cocaine, amphetamines, cannabinoids, barbiturates)
10. History or evidence of alcohol abuse defined as intake of more than 21 units per week (3 units per day), where 1 unit corresponds to 250 mL beer, 20 mL spirits/liqueur or one glass (100 mL) of wine
11. Participation in another clinical trial within three months prior to the start of the study
12. Use of any prescription medication within two weeks, or non-prescription medication (e.g. acetylsalicylic acid/paracetamol) within 48 hours, prior to dosing
13. Regular drug intake during the month prior to the start of the study
14. History or suspicion of inability to co-operate adequately
15. Donation of blood or blood products for a period of four weeks prior to and four weeks after completion of the study
16. History of asthma (or history of asthma within the previous 10 to 15 years, at investigator's discretion)
17. History of exercise-induced bronchospasm, or relevant seasonal bronchospasm
18. Lung function (FEV1) less than 80% of predicted spirometry criteria

Date of first enrolment
28/04/2004

Date of final enrolment
02/06/2004

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
PPD Development Clinic
72 Hospital Close
Evington
Leicester
United Kingdom
LE5 4WW

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 as subject consent for their release was not obtained.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes