ISRCTN16827947 https://doi.org/10.1186/ISRCTN16827947

A Study of Concerta XL on reducing ADHD symptoms and behavioural problems in adult offenders with ADHD

Submission date
18/05/2016

Recruitment status
No longer recruiting

Registration date
31/05/2016

Overall study status
Completed

Last Edited
20/09/2023

Condition category
Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
Attention deficit hyperactivity disorder (ADHD) is a common disorder that affects behaviour. ADHD can present in a number of ways, but common symptoms include a short attention span, restlessness, hyperactivity and impulsiveness. These symptoms often overlap with and could be better explained by other common mental health disorders seen in offenders. A particular concern for children with ADHD is the high risk for developing antisocial behaviour during adolescence and young adulthood. Previous studies have shown that around 30% of adolescent and 26% of adult prisoners have ADHD. Currently, the drug methylphenidate is the first line treatment recommended for ADHD with severe impairment in the UK. Despite known effects of methylphenidate on ADHD symptoms, it is uncommon for offender mental health teams to diagnose and treat ADHD. The reason is uncertainty over the effects of methylphenidate on ADHD and behavioural outcomes in offender populations, where ADHD is often accompanied by conduct problems, substance abuse and stress related disorders. The aim of this study is to investigate the effects of methylphenidate in young male prisoners with ADHD.

Who can participate?
Male prisoners aged between 16 and 25 years with ADHD.

What does the study involve?
Participants are randomly allocated to one of two groups. Those in the first group are treated with a placebo (dummy pill) for eight weeks. Those in the second group are treated with methylphenidate for eight weeks. This involves gradually increasing the dose to find the best balance of symptom improvement against side effects for the first five weeks and then maintaining the dose for a further three weeks. At the start of the study and then after eight weeks, participants complete a number of questionnaires in order to find out if their ADHD symptoms, well-being and attitudes towards violence have changed. The prison officers and education staff also complete a questionnaire to find out if the prisoner's level of aggressive behaviour has changed.

What are the possible benefits and risks of participating?
Study participants may benefit from receiving the diagnosis of ADHD and treatment for the disorder, as all participants will be offered treatment once the 8 week trial is completed. Common side effects from medication such as appetite reduction and sleep disturbance are usually minor and reduce with time, but can lead to some participants withdrawing from treatment. Serious side effects are rarely reported in ADHD treatment trials and so are likely to be rare and unexpected.

Where is the study run from?
The study is run from King's College London and takes place in two prisons, one in England and one in Scotland (UK)

When is the study starting and how long is it expected to run for?
May 2014 to August 2019

Who is funding the study?
This project is funded by the Efficacy and Mechanism Evaluation (EME) programme, a partnership between the Medical Research Council (MRC) (UK) and the National Institute for Health Research (UK). Janssen-Cilag Ltd. supplied Concerta XL

Who is the main contact?
Professor Philip Asherson
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Contact information

Type(s)
Scientific

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Prof Philip Asherson

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Additional identifiers

Clinical Trials Information System (CTIS)
2015-004271-78

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CPMS 30391

Study information

Scientific Title
Randomised controlled trial of the short term effects of OROS-methylphenidate on ADHD symptoms and behavioural outcomes in young male prisoners with attention deficit hyperactivity disorder

Acronym
CIAO-II

Study objectives
Current study hypothesis as of 22/01/2021:
The overall aim of the trial is to investigate the effects of Methylphenidate extended release (OROS MPH) in young male prisoners (age 16-25) meeting DSM-5 diagnostic criteria for ADHD.

Hypotheses:
1. OROS-MPH is better than placebo in reducing inattention and hyperactivity-impulsivity in young male prisoners meeting diagnostic criteria for DSM-5 ADHD
2. OROS-MPH is better than placebo at reducing secondary outcomes that are key indicators of behavioural and functional impairments used in the management of young prisoners in the UK (including emotional dysregulation, antisocial behaviour in the prison, violent attitudes)
3. Improvements in secondary behavioural outcomes due to OROS-methylphenidate are mediated by improvements in ADHD symptoms or emotional dysregulation

Previous study hypothesis:
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Hypotheses:
1. OROS-MPH is better than placebo in reducing inattention and hyperactivity-impulsivity in young male prisoners meeting diagnostic criteria for DSM-5 ADHD
2. OROS-MPH is better than placebo at reducing secondary outcomes that are key indicators of behavioural and functional impairments used in the management of young prisoners in the UK (including emotional dysregulation, antisocial behaviour in the prison, violent attitudesand the number of recorded positive Incentives and Earned Privileges)
3. Improvements in secondary behavioural outcomes due to OROS-methylphenidate are mediated by improvements in ADHD symptoms or emotional dysregulation

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 31/05/2016, East of England – Essex Research Ethics Committee, ref: 16/EE/0117

Study design

Randomised; Interventional; Design type: Treatment, Screening, Diagnosis, Process of Care, Drug, Psychological & Behavioural

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Current condition as of 22/01/2021:
Specialty: Mental Health, Primary sub-specialty: Learning disorders; UKCRC code/ Disease: Mental Health/ Behavioural and emotional disorders with onset usually occurring in childhood and adolescence, ADHD

Previous condition:
Specialty: Mental Health, Primary sub-specialty: Learning disorders; UKCRC code/ Disease: Mental Health/ Behavioural and emotional disorders with onset usually occurring in childhood and adolescence

Interventions
Current interventions as of 22/01/2021:
Participants will be randomised to receive 8-weeks treatment with either OROS-MPH or placebo, titrated over 5 weeks to balance ADHD symptom improvement against side effects and then maintained for a further 3 weeks. 200 participants will be recruited with 1:1 ratio of drug to placebo. Randomisation will be conducted by the King's CTU with blinding of both investigators and participants.

Randomisation will take place once informed and signed consent has been obtained, eligibility checks have been completed and before the treatment is started. We will use the King's Clinical Trials Unit's Independent Randomisation Service, ensuring reliability and credibility in the randomisation process. Random block sizes will be used to control the numbers of subjects allocated to each group, stratified by site and in a 1:1 drug-placebo ratio. Patient characteristics will not be taken into account in the randomisation process, but we expect a balanced ratio of cognitive ability, ADHD symptom severity and co-occurring psychosocial and mental health problems across the drug treatment and placebo groups.

Both active medication (Concerta XL 18 mg tablets) and matched placebo will be titrated weekly for 5 weeks and then kept at stable maintenance dose for 3 weeks. The maximum titrated dose (or matching placebo) is as follows: Week 1 = 18 mg (1 tablet); Week 2 = 36 mg (2 tablets); Week 3 = 54 mg (3 tablets); Week 4 = 72 mg (4 tablets); Week 5 = 72 mg (4 tablets); Week 6 = 72 mg (4 tablets); Week 7 = 72mg (4 tablets); Week 8 = 72mg (4 tablets). Titration of dose is conducted by the study psychiatrist. Both the trial investigators and participants are blinded. The titration protocol is followed in the same way for both active medication (IMP) and placebo. Treatment will start at an initial dose of 18 mg (1 tablet) for 1 week, and be increased weekly in 18 mg increments to a maximum of 72 mg (4 tablets) (i.e. 18 mg (1 tablet), 36 mg (2 tablets), 54 mg (3 tablets) and 72 mg (4 tablets). Medication will be reduced by 18 mg (1 tablet) if there is a limiting adverse event, in which case there will be no further increase in medication for the duration of the trial. Medication may be provided either once or twice daily up to the maximum daily dose. Titration upwards will be stopped if all 18 ADHD symptoms are scored as negligible (score of 0 or 1 on the CAARS-O) or absent. Unacceptable levels of adverse effects on the lowest dose of

18mg might lead to a cessation of treatment in a few cases; if this occurs we will ask participants to remain in the trial for the remaining trial assessments.

Participants in both groups are followed up at eight weeks.

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Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
methylphenidate (Concerta XL)

Primary outcome(s)

Current primary outcome measure as of 22/01/2021:
Level of ADHD symptoms measured on the investigator rated Connors Adult ADHD rating scale (CAARS-O) measured at baseline and after 8-weeks of treatment.

Previous primary outcome measure:
Level of ADHD symptoms measured on the investigator rated Connors Adult ADHD rating scale measured at baseline and after 8-weeks of treatment.

Key secondary outcome(s))

Current secondary outcome measures as of 22/01/2021:
1. Emotional dysregulation rated by the investigator and measured using the Wender-Reimherr Adult Attention Deficit Disorder Scale (WRAADDS) at baseline, 5, and 8 weeks
2. Critical incidents (adjudications) measured from prison records during the 8-week period before randomisation to the 8-week assessment
3. Aggressive behaviour rated by prison officer and education staff using the Modified Overt Aggression Scale (MOAS) at baseline and 8 weeks
4. Behaviour measured using behaviour report cards from prison staff (BRC-P) and education staff (BRC-E) at baseline and at week 8
5. Engagement in education, occupational, and rehabilitation programs measured from prison records during the 8-week period before randomisation to the 8-week assessment
6. Attitudes towards violence self-rated using the Maudsley Violence Questionnaire (MVQ) at baseline, week 5 and 8
7. Subjective well-being measured using the CORE Outcome Measure (CORE-M) at baseline and 8 weeks
8. Spontaneous mind wandering self-rated using the mind excessively wandering scale (MEWS) at baseline, 5, and 8 weeks
9. General psychopathology measured using the Brief Symptoms Inventory (BSI) at baseline, 5, and 8 weeks
10. Symptoms of irritability measured using the Affective Reactivity Index - Self Report (ARI-S) at baseline, 5, and 8 weeks
11. Overall health measured using Clinical Global Impression (CGI) at baseline, 5, and 8 weeks

Previous secondary outcome measures:
1. Emotional dysregulation is rated by the investigator and measured on the Wender-Reimherr Adult ADHD Diagnostic Scale at baseline and 8 weeks
2. Number of negative Incentives and Earned Privileges (IEPs) and adjudications for antisocial behaviour and rule breaking reported in the prison records at baseline and 8 weeks
3. Aggressive behaviour is rated by prison officer and education staff using the Modified Overt Aggression Scale at baseline and 8 weeks
4. Number of positive incentive and earned privileges (IEPs) for positive engagement in education, occupational and rehabilitation programs recorded in the prison records at baseline and 8 weeks
5. Attitudes towards violence are self-rated using the Maudsley Violence Questionnaire at baseline and 8 weeks
6. Subjective well-being is measured using the CORE Outcome Measure (CORE_OM) at baseline and 8 weeks

Completion date

27/08/2019

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 22/01/2021:
1. Male, aged between 16 and 25 years
2. English speaking
3. Able to provide informed consent (understand the information sheet and make an informed decision taking into account pros and cons of study participation)
4. Meet clinical diagnostic criteria for DSM-5 ADHD: 5 or more current symptoms of ADHD in either the inattentive or hyperactive-impulsive symptom domains; 6 or more symptoms of ADHD in either the inattentive or hyperactive/impulsive symptom domains before the age of 12 years; Where it is not possible to gain sufficient clinical information to score childhood symptoms of ADHD, the operational criteria will be adapted to include evidence of several ADHD symptoms with impairment starting before the age of 12 years, and 5 or more symptoms currently with moderate to severe impairment
5. Persistent trait like (non-episodic) course of symptoms
6. Impairments in two or more clinical or psychosocial domains and two or more settings from symptoms of ADHD
7. Onset of symptoms before the age of 12 years

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6. Impairments in two or more clinical or psychosocial domains and two or more settings from symptoms of ADHD
7. Onset of symptoms before the age of 12 years

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
16 years

Upper age limit
25 years

Sex

Male

Key exclusion criteria
Current participant exclusion criteria as of 22/01/2021:
1. Lack of capacity to give informed consent
2. Moderate or severe learning disability, defined as an IQ <60
3. Serious risk of violence to the researcher
4. Current major depression, psychosis, mania or hypomania
5. Past history of bipolar disorder or schizophrenia (such as those with a clear history of episodic mania/hypomania or psychosis unrelated to acute drug intoxication. Excluding chronic emotional dysregulation such as irritability, frustration, anger or emotional-mood instability)
6. Medical contraindications to the use of stimulants (e.g. glaucoma, hypertension, cardiovascular disease or structural heart problem)
7. Drug-seeking behaviour or craving (defined as drug-seeking behaviour that is unusually severe and likely to affect the titration protocol due to unusual and excessive demands for drugs; or where there is a current withdrawal syndrome from an addition disorder with drug dependency)
8. Taking contraindicated medication (e.g. Clonidine, Courmarins, Monoamine oxibase inhibitors, Moclobemide, Rasagline) during the four weeks prior to randomisation
9. Receiving any ADHD medication between consent for screening and randomisation

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Date of first enrolment
17/10/2016

Date of final enrolment
02/04/2019

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
HMP YOI ISIS
Western Way
London

United Kingdom
SE28 0NZ

Study participating centre
HM YOI Polmont
Polmont
Falkirk
United Kingdom
FK2 0AB

Sponsor information

Organisation
King's College London

ROR
https://ror.org/0220mzb33

Funder(s)

Funder type
Government

Funder Name
National Institute for Health Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

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 available from the corresponding author on reasonable request

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article	protocol	02/12/2019	04/12/2019	Yes	No
Basic results		24/09/2020	16/06/2022	No	No
HRA research summary			20/09/2023	No	No