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Low- or high-intensity patching for lazy eye

Submission date
22/01/2021

Recruitment status
No longer recruiting

Registration date
11/02/2021

Overall study status
Completed

Last Edited
11/02/2021

Condition category
Eye Diseases

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

Plain English summary of protocol

Background and study aims
Amblyopia (or lazy eye) is an eye and brain condition that affects about 230,000 children under 7 years in the UK. It affects the way eyesight develops, causing blurred vision. It is commonly caused by misalignment of the eyes (squint) and/or a need for glasses. Amblyopia usually only affects one eye. Commonly, children aged 4-5 years in the UK are tested through school-entry vision screening. Children with reduced vision are then referred to a hospital or community eye service. Treatment is most effective in children under 8 years. The first stage of treatment involves prescribing glasses, if required, and monitoring if vision improves over time (usually 3-6 months) as the brain adapts to a clear image.
In children whose vision does not improve to normal levels with glasses alone, further treatment is required. This is most commonly achieved by covering the better-seeing or normal eye for a number of hours per day, called “patching” or “occlusion therapy”. Patching is often difficult for children and many suffer from bullying. Treatment is often unsuccessful.
Research over the last 20 years has focussed on investigating the minimum number of hours of patching required each day to achieve a treatment effect. Evidence shows 2 hours daily patching (low-intensity treatment) works, but usually takes a number of months, and sometimes years. Adherence to treatment drops dramatically over time.
It costs the NHS about £314m to treat 230,000 children with amblyopia. Full-time patching (high-intensity treatment) could produce faster improvements in vision and better final outcomes, shortening treatment and reducing costs, but there isn’t enough information about the treatment to appropriately design a clinical trial to compare low with high-intensity patching. Patients, their parents and the public have been involved in the design of the proposed study, and will provide oversight of all future work. This study will compare low with high treatment doses for patching (occlusion therapy) children with lazy eye (amblyopia) to support the design of a future study.

Who can participate?
Children with mild/moderate amblyopia in one eye aged 4-17 attending Moorfields Eye Hospital NHS Foundation Trust for their care

What does the study involve?
Children will be randomly allocated into two groups and asked to either undertake low-intensity patching (2 hours per day – ‘treatment-as-usual’) or high-intensity patching (full-time). Each group will be monitored routinely and have their vision tested (by reading letters on a chart)

every 8-12 weeks for the low-intensity group and every 5 weeks for the high-intensity group, for up to 1 year or until vision improves. Participants and their families will be asked to use electronic dose monitors to measure how much time the patch is worn. The first 20 participants and their families will be invited to take part in interviews to discuss how they found treatment. Interviews will take place at the start, middle and end of treatment, and will take about 30 minutes.

What are the possible benefits and risks of participating?
Children will either receive the best treatment currently available or one the researchers think may be faster and/or produce a better result. The study is designed to find out in a 'head-to-head' comparison the feasibility and acceptability of different patching doses. The researchers will then use the information to run a larger trial to look at the treatments in detail. Patching in children 4 years and older is generally a very safe treatment. If there are any concerns about potential side effects (e.g. double vision or worsening of vision in the 'good' eye) these will be discussed with families fully at each visit by their managing Orthoptist. By taking part in this study children and their families will be making a valuable contribution to this area of research.

Where is the study run from?
UCL Great Ormond Street Institute of Child Health (UK)

When is the study starting and how long is it expected to run for?
January 2018 to December 2023

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
266637

Protocol serial number
CPMS 43423, IRAS 266637

Study information

Scientific Title
Low- vs high-intensity occlusion therapy for mild/moderate amblyopia: a randomised, controlled feasibility trial

Study objectives
In children with previously untreated strabismic, anisometropic, meridional or mixed amblyopia after full refractive adaptation, aged 4 years and older, full-time (high-intensity) occlusion produces a better visual outcome than current 'gold- standard' care (low-intensity occlusion).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 27/05/2020, London - Bloomsbury Research Ethics Committee (HRA RES Centre Manchester, Barlow House 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8063, +44 (0)207 104 8285, +44 (0)207 104 8196; bloomsbury.rec@hra.nhs.uk), REC ref: 20/LO /0093

Study design
Randomized; Interventional; Design type: Treatment, Other

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Amblyopia (lazy eye)

Interventions
Aim 1:
A randomized, controlled, multi-centre (within a single Trust) feasibility trial, comparing low (treatment-as-usual (TAU)) to high-intensity (full-time (FTO)) patching.

Pre-randomisation
Moorfields operates a Trust-wide opt-out process for patients being approached for

participation in research studies. Thus, the researchers will only consider the eligibility of patients who have not opted out to be contacted for research.
Eligible patients will be identified by the Fellow (DEP), managing clinicians and NIHR BRC staff and will be approached, with their parents, to participate during their routine clinical visit. They will be provided with written information about the study, including age-appropriate information for children, and offered an opportunity to ask questions. Informed, written consent will be sought by the Fellow from parents/guardians who choose to participate.

Randomisation and masking
Computer-generated permuted block randomisation, stratified by site and age. Children will be asked to perform the required occlusion dose by the Fellow (either TAU or FTO). To facilitate communication about treatment adherence, examiners will be not be masked to the treatment group. It is not possible to mask children/their parents to their treatment allocation.

Procedure
Participants will remain in standard clinics, with routine orthoptic measurements taken every 5 weeks (± 1 week) for 25 weeks for those undertaking FTO, and every 8-12 weeks for TAU. TAU matches current standard care exactly.

Parents will be asked to fit Theramon® dose monitors when undertaking occlusion. Data will be taken from dose monitors at each visit.

All clinical data will be recorded inpatient medical records and extracted for analysis. These will be stored securely on NHS Trust networks, and pseudo-anonymised before analysis at UCL. Data will be collected on: age at presentation, diagnosis, refractive error, initial visual acuity, and binocular status. At each visit, further data will be collected, until treatment completion, on time between visits, VA, stereopsis and objective and subjective (as a proportion of prescribed dose to the nearest 10%) adherence to treatment.

Interviews
Interviews are being conducted to provide information about barriers to, and facilitators of, treatment adherence to inform the design of an intervention to improve adherence in future research/practice.

The first 20 participants and their families (approximately 10 from each trial arm) will be invited to interview. Interviews will be conducted by the Fellow on the same day as routine clinical appointments to reduce the travel burden on families. If necessary, families will be offered the opportunity for video/telephone interviews. Consent will be sought for audio recording.

The attached topic guides (Appendices I and II) show the topic areas and sample questions for each Theoretical Domains Framework (TDF) domain. Questions will be refined after consulting Moorfields YPAG.

Interviews will be conducted at recruitment (to capture patient/parental concerns at treatment outset), after 1-2 visits to capture reported barriers to treatment adherence, methods for mitigating problems and barriers to participation in the full trial, and at treatment completion to capture views on the entire treatment course and determine out-of-pocket costs. Other care providers (such as grandparents and nannies) will be asked to either be present or provide information for this final interview.

Due to the narrow focus of each interview, they are expected to last approximately 30 minutes at most, but children and their parents will be given as much time as is necessary to fully capture their views.

At the end of 'year 3', Orthoptists at MEH (n=15) will be invited to interview separately, covering views about treatment regimens, patterns of practice, methods for managing treatment adherence, barriers to incorporating research findings into practice and exploring opinions on high-intensity occlusion and the likelihood of uptake into clinical practice.

Thus, in total, the researchers will capture 60 interviews with patients/families and 15 with clinicians, generating data to be used by focus groups to create interventions to improve treatment adherence. Data will be analysed concurrently with data collection, and the decision to recruit more/less families will be based on whether saturation of concepts has been reached.

Additional data capture:

At commencing treatment:
1. Waking hours/sleep patterns

At final visit:
1. Out-of-pocket costs
2. Parental completion of an implementation survey (Appendix III).

Assessment of HRQoL:
At each visit, parents will be asked to complete the Amblyopia Treatment Index (ATI) questionnaire. The ATI is designed to capture parental concerns about patching.
At the beginning, middle and end of treatment, participants will be asked to complete an age-appropriate version of the PedsQL survey.

At 25 weeks:
It is expected that many children undertaking 2 hours occlusion will have residual amblyopia at 25 weeks. Those who demonstrate a plateau in improvement will then be asked to increase occlusion to 6 hours daily (in line with current recommendations). Those with residual amblyopia undertaking FTO will also continue treatment until no further improvement is seen.

At 52 weeks:
To appropriately design the full trial, it will be important to understand outcomes at 1-year post-baseline, and thus patients will be followed in routine clinical practice until treatment completion, and their data will be extracted from their medical records.

Terminating treatment:
Treatment will be tapered and stopped if children meet the current success criteria during the study. If both eyes do not have equal acuity when criteria are met, children will be given 1 more visit to continue occlusion to attain 'best-achievable' acuity. If during this time, amblyopic eye acuity improves by >0.050 LogMAR, but IOD remains >0.1 LogMAR, occlusion can be continued until no measurable difference (0.050 LogMAR) is seen between 3 visits. At this stage, examiners will be unmasked to the patients' treatment to monitor tapering of occlusion.

Treatment adherence:
Monitored by ODMs and parental report. At each visit parents will be asked to report compliance with prescribed occlusion to the nearest 10%. Compliance diaries do not reflect clinical practice, are known to commonly have >50% missing data, and thus will not be used here.

To reflect the proportion of waking hours with occlusion, parents will be asked to report their children's usual sleeping patterns.

Aim 2: Address barriers to treatment adherence:
Analysis of outcomes from interviews (Aim 1) will be presented to two focus groups. One will comprise parents of patients, the public, a psychologist, implementation scientist, and the Fellow (to facilitate discussions). Patients themselves are likely to be too young to participate in a focus group of this type, though their views will be captured during interviews. A second focus group will comprise a mix of clinicians (orthoptists, ophthalmologists and optometrists (with a psychologist, implementation scientist, and the Fellow to facilitate discussions). Target group size will be eight members. Both groups will be asked to produce methods for improving treatment adherence based on outcomes from interviews. Impact studies of these developed interventions will be assessed separately.

Intervention Type
Other

Primary outcome(s)
Visual acuity measured in LogMAR at 25 and 52 weeks

Key secondary outcome(s))
1. Patient-reported outcomes of interest derived from interviews at the beginning, middle and end of treatment and focus groups at the end of the study
2. Number of eligible patients per hospital/year (for external sites) measured using data collection sheets over a 1-year period
3. Participation rate (number recruited/number approached) measured using a participant logbook over a 1-year period
4. Willingness of participants/families to be randomised, ascertained by interview at their first visit
5. Drop-out/attendance rates measured using data collection sheets at each clinical visit
6. Usability of occlusion dose monitors (ODMs) by patient report at each clinical visit
7. Evaluation of outcome measures to include in a cost-effectiveness model in a fully-powered RCT (e.g. out-of-pocket costs measured using questionnaires at clinical visits)
8. Treatment adherence rates and acceptability of high-intensity occlusion measured using occlusion dose monitors at each clinical visit

Completion date
31/12/2023

Eligibility

Key inclusion criteria
1. Patients attending paediatric clinics at three large Moorfields sites. City Road (Central/East London) sees ~60% of all paediatric cases, Northwick Park (North-West London) has 6.5%, and St. George's Hospital (South-East London) 5.5% of paediatric cases
2. Aged 4-17 years
3. Able to perform crowded LogMAR acuity testing with letters (using a matching card if necessary)
4. Mild/moderate amblyopia, defined as interocular difference in vision ≥0.2 LogMAR, and VA worse than 0.2 LogMAR, but better than 0.7 LogMAR in the amblyopic eye after full refractive adaptation (a minimum of 18 weeks glasses wear, with proven stability (<0.075 LogMAR change

in vision between two separate visits))
5. Cycloplegic refraction within the last 6 months and up-to-date glasses (if required)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
4 years

Upper age limit
17 years

Sex
All

Key exclusion criteria
1. Stimulus deprivation amblyopia
2. Ocular co-morbidities that would affect final visual outcomes (e.g. albinism, nystagmus, coloboma, retinal dystrophies, lens opacities, corneal dystrophies, keratoconus)
3. Previous occlusion therapy
4. Developmental/learning difficulties that preclude accurate assessment of vision

Date of first enrolment
01/04/2021

Date of final enrolment
01/04/2023

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Moorfields Eye Hospital
162 City Road
London
United Kingdom
EC1V 2PD

Sponsor information

Organisation
University College London

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
NIHR Academy; Grant Codes: NIHR300054

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No