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INFORMATION LEAFLET AND CONSENT FOR PARENT/GUARDIAN

RESEARCH TITLE: Myopia Outcome Study of Atropine in Children

MOSAIC
Myopia Outcome Study of Atropine In Children

Please read carefully.

Myopia (shortsightedness) is caused by the eye growing too long resulting in distant objects such as the whiteboard in school becoming blurred. Other signs and symptoms of myopia include squinting, eyestrain and headaches.

While the exact cause of myopia is unknown, genetics and our daily lifestyle have been associated with the development or progression of shortsightedness. In Ireland, Europe and the USA, the prevalence of myopia has doubled to close to 50% of people affected by the time they leave education. Progression of shortsightedness results in more frequent trips to the Optometrist to update your glasses. The higher the glasses prescription, the thicker and heavier the glasses are. There is also an increased risk of sight threatening eye disease with higher degrees of myopia.

WHAT IS THE PURPOSE OF THE STUDY?

Background

Today, rather than preventing shortsightedness, we only treat the optical consequences of it by wearing glasses and contact lenses or opting for laser refractive surgery. By controlling and possibly preventing myopia we will not only reduce the burden of glasses/contact lens wear but we will also prevent the sight threatening diseases associated with myopia - retinal detachment, myopic maculopathy, glaucoma and cataract.

Research Aims

1. To investigate new ways to prevent, treat and control the progression of shortsightedness in children
2. To deepen our understanding of myopia and its risks.

Please ask if there are any aspects of this document you do not understand, or you would like more information on a particular aspect.

INVITATION TO PARTICIPATE

We are inviting myopic children to participate in a clinical trial using a low dosage of an eye drop called atropine. Atropine is currently used in the treatment of amblyopia ("lazy eye"), and is used effectively in Asia to stop the progression of shortsightedness in children. A randomised, placebo-controlled clinical trial will be conducted in the Centre for Eye Research Ireland at Technological University Dublin (TUD), Grangegorman Campus Grangegorman Lower, Dublin 7. The trial will investigate the capacity of atropine to reduce the rate of progression of myopia amongst eligible European children. The study will be conducted under the supervision of Prof Flitcroft and Prof Loughman.

WHO IS ORGANISING THE RESEARCH STUDY?

This research study will be conducted by the following 3 investigators:

Principal Investigators: Prof. Ian Flitcroft (Consultant Ophthalmic Surgeon, Mater Hospital) and Prof. James Loughman (Professor of Optometry, Head of the Centre for Eye Research Ireland, Technological University Dublin)

Investigator: Dr. Saoirse McCrann, FAOI (Centre for Eye Research Ireland, Technological University Dublin)

The duration of the study is 36 months for the treatment and the control group.
Treatment Group- 24 months treatment with atropine and an additional 12 month follow up (washout period).
Control group- 24 months treatment with placebo eye drop. Following this all placebo control participants will then have the option to crossover to atropine treatment for 12 months.

WHAT WILL HAPPEN TO ME IF I TAKE PART?

At the baseline visit, we will ensure your child is eligible to take part in the trial.

The Inclusion Criteria is as follows:

- Children must be aged between 6 and 16 years old
- Children must have a myopic prescription of -1.50D or worse
- There must be a myopic progression of at least -0.50D over the last year
- Astigmatism must be less than -2.50D
- It is required the difference in spherical equivalent between the two eyes is less than 1 diopter.
- The child's corrected visual acuity must be better than logMAR 0.2 (6/9.5 in conventional units)
- The difference between the non-cycloplegic and cycloplegic spherical refraction must be less than -1.00 diopter
- The child's ocular health and intraocular pressures must be normal
- The child must have good general health and no history of cardiac/respiratory diseases

The Exclusion Criteria is as follows:

- Ocular/systemic diseases affecting vision or refractive error

- Any ocular/systemic condition wherein atropine is contraindicated
- Defective binocular vision, amblyopia or strabismus
- Allergy to atropine or the preservative
- Pregnancy

The eligible participants will have a detailed assessment of their vision and an ocular health examination at each visit. The assessments will be identical to what is currently standard practice in an eye examinatioin with the addition of a number of additional non-invasive tests. (please note children should still attend their Optometrists/Ophthalmologist for their routine eye examinations during trial participation)

The additional tests are as follows:

- Amplitude of Accommodation (the ability to focus up close)
- Reading Speed
- Pupil diameter and pupillary reflexes
- Measurement of the size of the eye (including length and other dimensions)
- Height and Weight measurement
- Heart Rate
- Pregnancy test if girls are of childbearing potential

Each participant will visit the Centre for Eye Research Ireland a minimum of 7 occasions. This will include a baseline visit followed by a visit at 6, 12, 18, 24, 30 and 36 months. Each visit will take approximately 90 minutes. If the participant is eligible the parent/guardian will be given atropine or placebo eye drops to take home and instill one drop every night into both eyes for a given duration.

- Participants will be dispensed 0.01% atropine eye drops or a placebo

A parent/guardian will also fill out a questionnaire entailing their thoughts/attitudes to glasses, eye drops and sight tests as well as their daily routine activities and their time spent outdoors.

The enrolment into this study will be on a voluntary basis and you will not be paid. There is no obligation to participate in the study, and the study can be cancelled at any point. The vision-related tests and questionnaires will not cause any distress to the participant.

This is a randomised, double-masked trial. It means that participants will be put into groups and compared. The reason for this is to prevent bias in the study. The computer will randomly assign each participant into the groups. A double-masked trial means that neither the participant, the parent/guardian nor the Optometrist will know which treatment group you are in. This will only be revealed at the end of the study. Participants are more than twice as likely to be on the active treatment (atropine). The placebo will be a dummy eye drop that contains no active ingredient but looks exactly like atropine. The participants who do not receive atropine initially will start on atropine treatment later, meaning all participants will ultimately receive atropine treatment.

WHAT ARE MY RESPONSIBILITITES AS A PARENT/GUARDIAN?

You will be asked to visit the Centre for Eye Research Ireland with your child a minimum of 8 separate occations. Vision tests will be carried at the baseline visit and repeated at 6, 12, 18, 24, 30 and 36 months. If you are initially given a placebo eye drop you will be monitored for a further 12 months after using atropine.

You will also be asked to insert eye drops into your child's eyes every night for 2 years. All participants will have to be compliant with the treatment so that the data we get can be interpreted accurately.

WHAT IS ATROPINE

The active ingredient in topical ophthalmic atropine is atropine sulphate, and is available as a drop or ointment form. This clinical trial will use atropine 0.01 which is 100-times more diluted than the usual clinical dosage. This is to misimise side effects such as glare and difficulty focusing up close, which can be experienced with higher concentrations of atropine.

HOW DO PARENTS DISPOSE OF THE EYEDROP VIALS?

Small garbage disposal cans are provided to you, along with the treatment kits to collect the used vials. The unused vials should be returned on all visits. Therefore you are required to return all vials and boxes at the next study visit, to be replaced with a fresh 6-month supply

when appropriate.
Each vial can only be used once ie. 1 drop in eye eye nightly before disposal

ARE THERE ANY DISADVANTAGES IN TAKING PART IN THIS RESEARCH STUDY? WHAT ARE THE POSSIBLE RISKS OF TAKING PART?

No, there are no disadvantages in taking part in this study. There are no risks associated with the tests administered for the purpose of this study over those of a normal eye examination. They are all completely non-invasive. Regarding atropine eye drops, there are associated possible risks including the following:

- An increase in pupil size (which may cause glare) and a lesser ability to accommodate (which may lead to difficulty reading up close). However with the diluted low dose of atropine used in this trial the risk of glare is minimised
- Uncommon adverse effect to atropine (local skin allergy, eye irritation,conjunctivitis, increased intraocular pressure, swelling of the eyelids, flushing)

If you do develop any symptoms that you are concerned about, you should contact Saoirse McCrann at 087 7783837, Ekaterina Loskutova 01 402 5412 or Prof. James Loughman at 0868589593

Risk Control

- This trial will be fully supervised by an Optometrist, experienced in the art of instilling eye drops, working with children and performing sight tests.
- Detailed pre-trial ocular health examinations will take place for each subject to determine suitability for inclusion in the trial.
- The inclusion and exclusion criteria have been comprehensively defined and will be rigorously implemented.
- The supervision arrangements will facilitate regular health checks throughout the study duration, thus ensuring that any adverse events can be managed according to routine optometric practice protocol.
- The atropine concentration has been previously established as safe in clinical trials.

- Participants/parents will be provided with information describing clinical signs of ocular/systemic side effects and given instruction as to appropriate management.
- Parents will be provided with advice in relation to the importance of safe use and storage of atropine.

WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART?

The participant may or may not receive any direct benefit from taking part in the research study. However, information obtained during the course of the research study may help us better understand myopia. We hope that the treatment the child receives may prevent the progression of their myopia. However, this cannot be guaranteed. The information we get from this research study may help us to reduce myopia progression in future subjects.

IS MY DOCTOR BEING PAID FOR INCLUDING ME IN THE RESEARCH STUDY?

No

WILL PATIENT EXPENSES BE MET?

The enrolment into this study will be on a voluntary basis and you will not be paid.

WHAT HAPPENS WHEN THE TRIAL ENDS?

You will be informed whether you were treated with atropine or placebo. The placebo group will then be given the opportunity to receive atropine treatment. A summary of the general trial results and the implications for future myopia control will be distributed to all participants.

WHAT IF SOMETHING GOES WRONG?

0.01% atropine has been previously established safe in previous clinical trials. The investigators and your GP are there to assist you in the unlikely event of any difficulty. If you have any cause to complain about any aspect of the way you have been approached or treated during the course of this research study, the normal Health Service complaints mechanisms are available to you.

CONFIDENTIALITY – WHO WILL KNOW I AM TAKING PART IN THE RESEARCH STUDY?

All information, which is collected about you during the course of the research will be kept strictly confidential and will be obtained and processed in keeping with the Data Protection Act 1988 and the amended Data Protection Act of 2003. All data will be analysed collectively as a group and coded by data link to ensure participants confidentiality. The anonymous results of this study may be published in the medical literature.

STORAGE, RENTENTION AND DESTRUCTION OF CLINICAL TRIAL DATA

The study will maintain strict measures to protect confidentiality. Access to data will be restricted to the investigators, password protected and encrypted.
Participants will be distinguished using a personal identification number. Participants name and any other identifying detail will not be included in any study data electronic file.
The clinical data will be stored for five years. The data will however be used only for the duration of the current study. The data will then be destroyed under confidential conditions.

GP NOTIFICATION

Your GP will normally be informed that you are taking part in this clinical trial. If this is a problem for you, you should discuss it with your study researcher.

HOSPITAL RESEARCH ETHICS COMMITTEE APPROVAL

This clinical trial/research study has been approved by the Mater Hospital Research Ethics Committee and the Research Ethics Committee of Technological University Dublin

WHAT WILL HAPPEN TO THE RESULTS OF THE RESEARCH STUDY?

The results will be published in a peer-reviewed ophthalmology journal. If you wish to receive a copy of the published results, please inform the study researcher.

PROCEDURE TO BE USED IF ASSISTANCE OR ADVICE IS REQUIRED

In the event of a research related injury or any other problems, you can contact Saoirse McCrann at 087 7783837, Ekaterina Loskutova 01 402 5412 or Prof. James Loughman at 0868589593

VOLUNTARY PARTICIPATION

It is up to the participant (with parental consent) to decide whether to take part or not. Even if it is decided to take part, the participant is free to withdraw at any time and without giving a reason. This will not affect the standard of care the participant will receive. Your doctor will not be upset if you decide not to take part.

If the participant has already been involved in previous pharmaceutical or optical myopia control interventions they are not eligible to take part in this reasearch study.

We thank you for taking time to read this information leaflet and sincerely appreciate your contribution in this research study. **If you require any further information or have any query regarding this study, please do not hesitate to ask Ian Flitcroft at the Mater Private Hospital or Saoirse McCrann from the Centre for Eye Research Ireland (CERI) at 087 778 3837.**

How to find us

If driving search for Technological University Dublin, Grangegorman Road Lower
The only available parking is in a red car park zone on the Grangegorman Road Lower
LUAS RED LINE **Smithfield stop** is 10-minute walk from the Grangegorman Lower exit
LUAS GREEN LINE **Grangegorman stop** is a 5 minute walk from Grangegorman Lower exit
BUS stop **37, 39, 39A, 70** is a 5-minute walk from the Prussia St exit
BUS stop **46A is** 1-minute walk from the North Circular Road exit

CONSENT FORM

Protocol Number: PJ21069

Title of Research Study: Myopia Outcome Study of Atropine in Children (MOSAIC)

Participant Name:

Name of Optometrist and Telephone Number:

To be completed by the parent/guardian

1. I confirm that I have read and understood the information leaflet for the above research study and received an explanation of the nature, purpose, duration, and foreseeable effects and risks of the research study and what my involvement will be ☐

2. I have had time to consider my child taking part in this research study. My questions have been answered satisfactorily and I have received a copy of the Patient Information Leaflet ☐

3. I understand that my child's participation is voluntary and that he/she is free to withdraw at any time without my medical care or legal rights being affected ☐

4. I have to the best of my knowledge informed the investigator of my child's previous or present illnesses and medication. My child has not participated in any other myopia control intervention ☐

5. I understand that my child's General Practitioner Dr…… will be informed by the study investigator that I am taking part in this research study ☐

6. I understand the results of this clinical trial are likely to be published ☐

7. I agree that my child can take part in the above research study ☐

……. ……
Name of Participant (in block letters) Date

……. …… ……..
Name of Parent (in block letters) Date Signature

……. …….. ……
Optometrist/Researcher Date Signature

1 copy for parent/guardian, 1 copy for researcher.

CONSENT FORM

Protocol Number: PJ21069

Title of Research Study: Myopia Outcome Study of Atropine in Children (MOSAIC)

Participant Name:

Name of Optometrist and Telephone Number:

To be completed by the parent/guardian

1. I confirm that I have read and understood the information leaflet for the above research study and received an explanation of the nature, purpose, duration, and foreseeable effects and risks of the research study and what my involvement will be ☐
2. I have had time to consider my child taking part in this research study. My questions have been answered satisfactorily and I have received a copy of the Patient Information Leaflet ☐
3. I understand that my child's participation is voluntary and that he/she is free to withdraw at any time without my medical care or legal rights being affected ☐
4. I have to the best of my knowledge informed the investigator of my child's previous or present illnesses and medication. My child has not participated in any other myopia control intervention ☐
5. I understand that my child's General Practitioner Dr…… will be informed by the study investigator that I am taking part in this research study ☐
6. I understand the results of this clinical trial are likely to be published ☐
7. I agree that my child can take part in the above research study ☐

…….	……	
Name of Participant (in block letters)	Date	
…….	……	……..
Name of Parent (in block letters)	Date	Signature
…….	……..	……
Optometrist/Researcher	Date	Signature

1 copy for parent/guardian, 1 copy for researcher.

DATA PROCESSING CONSENT

Study title: *Myopia Outcome Study of Atropine in Children (MOSAIC) -PJ21069*

I give informed explicit consent to have my data processed as part of this research study.	**Yes** ☐	**No** ☐
I consent to be contacted by researchers as part of this research study.	**Yes** ☐	**No** ☐

FUTURE CONTACT [please choose one or more as you see fit]		
OPTION 1: I consent to be re-contacted by researchers about possible future research **related** to the current study for which I may be eligible.	**Yes** ☐	**No** ☐
OPTION 2: I consent to be re-contacted by researchers about possible future research **unrelated** to the current study for which I may be eligible.	**Yes** ☐	**No** ☐

STORAGE AND FUTURE USE OF INFORMATION		
RETENTION OF RESEARCH MATERIAL IN THE FUTURE [please choose one or more as you see fit]		
OPTION 1: I give permission for material/data to be stored for *possible future research* ***related*** to the current study ***only if consent is obtained*** at the time of the future research but only if the research is approved by a Research Ethics Committee.	Yes ☐	No ☐
OPTION 2: I give permission for material/data to be stored for *possible future research* ***related*** to the current study ***without further consent being required*** but only if the research is approved by a Research Ethics Committee.	Yes ☐	No ☐
OPTION 3: I give permission for material/data to be stored for *possible future research* ***unrelated*** to the current study ***only if consent is obtained*** at the time of the future research but only if the research is approved by a Research Ethics Committee.	Yes ☐	No ☐
OPTION 4: I give permission for material/data to be stored for *possible future research* ***unrelated*** to the current study ***without further consent*** being required but only if the research is approved by a Research Ethics Committee.	Yes ☐	No ☐
OPTION 5: I agree that some future research projects may be carried out by researchers working for **commercial/pharmaceutical companies.**	Yes ☐	No ☐
OPTION 6: I understand **I will not be entitled to a share of any profits** that may arise from the future use of my material/data or products derived from it.	Yes ☐	No ☐

Patient Name (Block Capitals) Patient Signature Date

Legal Representative/Guardian Name Legal Representative/Guardian Signature
Date

To be completed by the Principal Investigator or nominee.

I, the undersigned, have taken the time to fully explain to the above patient the nature and purpose of this study in a way that they could understand. I have explained the risks involved as well as the possible benefits. I have invited them to ask questions on any aspect of the study that concerned them.

Name (Block Capitals)	Qualifications	Signature	Date