Exploring underlying mechanisms of paediatric growth disorders using human ex vivo growth plates.

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Endocrine and glandular disorders NEC
Study type	Observational non invasive

Summary

ID

NL-OMON52513

Source
ToetsingOnline

Brief title
Growth plate collection during routine epiphysiodesis

Condition

- Endocrine and glandular disorders NEC
- Tendon, ligament and cartilage disorders

Synonym
Tall stature

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Beurs van St Anna fonds is toegekend

Intervention

Keyword: chondrocytes, epiphysiodesis, growth plate, tall stature

Outcome measures

Primary outcome

1. Can we harvest viable growth plate tissue from patients undergoing routine percutaneous epiphysiodesis?

2. Can we use these growth plate biopsies to make ex vivo explant cultures, perform histology, characterize molecular processes from RNA and DNA of different cell types of the human growth plate?

3. Can we perform functional studies with in vitro and ex vivo cells/explants to test the effects of current growth-promoting or -inhibiting compounds such as GH, GH-receptor antagonists and C-natriuretic peptide?

To our knowledge this study would provide the first collection of biospecimen to systematically study pharmaceutical effects directly at the level of the human growth plate.

The ultimate goal of this study is to form a multidisciplinary research line that will develop human growth plate models and apply molecular epidemiology such as proteomics, metabolomics, and molecular profiling (genome, transcriptome, and epigenome). This will open the way for novel models to study determinants of growth plate function and eventually medical therapies in

growth disorders and several paediatric orthopaedic conditions.

Secondary outcome

N/A

Study description

Background summary

Human growth plate tissue would be extremely valuable to elucidate underlying mechanisms of severe short stature and the degenerative joint disease osteoarthritis (OA). Furthermore in the field of articular cartilage regeneration a knowledge gap of cell fate decisions towards articular chondrocytes precludes deposition of high quality neo-cartilage. Studying dynamic changes in growth plate chondrocyte signalling will provide critical insight into functional determinants of both growth plate and articular chondrocytes.

Study objective

The current study is designed to collect viable growth plate tissue of tall statured individuals that undergo percutaneous epiphysiodesis (PE). With this collected biomaterial we will be able to characterize dynamic changes in growth plate chondrocyte signalling during endochondral ossification and maturation and set up a human ex vivo growth plate model. Such a model could greatly enhance our ability to study underlying mechanisms of growth-related problems, osteoarthritis and apply regenerative medicine while providing a tailored human disease model to test effects of current and novel compounds e.g. GH, GH-receptor antagonists and C-natriuretic peptides.

The following objectives are formulated:
1. Harvest viable growth plate tissue from paediatric patients undergoing routine orthopaedic removal of their growth plates.
2. Isolate viable growth plate cells at different stages of maturation.
3. Characterize, at the molecular level, growth plate cells at different stages of maturation.
4. Set up a human ex vivo explant model of growth plate tissue.

Study design

In this observational study we aim to establish a collection of growth plate tissues from 100 patients with tall stature undergoing routine PE.
Growth plate tissue will be collected (and not discarded) by the surgeon during

surgery in containers with a study number. Within 4 hours after collection containers will be transferred to the department of Biomedical Data Sciences, section Molecular Epidemiology. Here biomaterials will be processed and stored according to a previously established protocol. The biomaterial will be used to answer the main study objectives as outlined above. In case future (new) research questions on the collected material are developed, an amendment to this protocol, will be submitted to the CME LUMC for approval.

We propose to divide the study into two phases. The first phase will consist of the sequential inclusion of 10 patients, to test the usefulness and feasibility of our proposed in vitro research model. If we are able to preserve viable chondrocytes in the majority of these first 10 patients, we will automatically proceed to the second phase of the study, which is the sequential inclusion of approximately 100 patients for further in vitro analysis.

Study burden and risks

Percutaneous epiphysiodesis (PE) is deemed a routine orthopedic procedure with a low complication rate in general. The risk of post-operative complications as a result of the study is extremely low as no additional surgical techniques need to be employed. The caliber of the biopsy needle (8 Gauge) is smaller or similar to generally used drills and curettes. Orthopedic biopsy has been proven to be safe in the hands of an experienced orthopedic surgeon. The trajectory of the biopsy needle is the same as the trajectory used for the drill in a standard epiphysiodesis

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

Male or female pediatric patients (< 18 years of age) with idiopathic or familiar tall stature with a predicted adult height > 205 cm (boys) or > 185 cm (girls), and/or evidence of syndromic condition with predisposition for tall stature.

Male or female pediatric patients undergoing PE because of idiopathic or post-traumatic limb length discrepancy or transgender patients (male to female) who have a predicted adult height in the normal male range but choose to undergo epiphysiodesis to prevent female tall stature.

Exclusion criteria

General or other standard contra-indications for PE surgery.
Inability to read Dutch and/or verbalize understanding of the study information

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial

Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-10-2020
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO

Date:	30-07-2020
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	06-09-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	31-03-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL71533.058.19