Synovial tissue analysis of factors related to bone-destruction and bone-production in patients with knee arthritis

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON40451

Source
ToetsingOnline

Brief title
SynBone

Condition

- Autoimmune disorders
- Joint disorders

Synonym
joint inflammation

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: arthritis, rheumatoid arthritis, spondyloarthritis, synovial tissue

Outcome measures

Primary outcome

Endpoints of the study are analysis of the immune cells in the synovial

biopsies of 80 patients with knee arthritis, analysis of molecules involved in

osteoblast and osteoclast activation and analysis of the effect of molecules in

synovial fluid on activation of osteoclasts and osteoblasts in vitro.

Secondary outcome

n/a

Study description

Background summary

Many rheumatic diseases affect the joints. The most common forms of chronic inflammatory joint disease are rheumatoid arthritis (RA) and a group of rheumatic diseases collectively known as spondyloarthritis (SpA) which includes diseases like psoriatic arthritis and ankylosing spondylitis. Treatment of these inflammatory rheumatic disease with pharmaceutical agents is comparable with drugs like methotrexate, sulfasalazine and TNF-blockers used in both diseases.
In both diseases irreversible damage of the joints may develop. In general, inflammation of joints often leads to premature osteoarthritis. but different patterns of joint damages occur in RA as compared to SpA and vice versa.
A typical phenomenon observed in RA associated joint destruction is erosion of bone and cartilage. An erosion of bone in RA is an interruption of the bone surface caused by invading inflammatory cells.
In contrast, although erosion may also occur SpA the typical pattern of joint damage in SpA is that of bone deposition. This bone deposition which is the opposite of bone erosion may lead to ankylosis (fusion of bones) and impairment of joint mobility.
So while both RA and SpA are both chronic and potentially destructive joint diseases the way they may damage the joint differs in an extreme way.
Surprisingly , analysis of synovial tissue - soft tissue lining the joint- of

patients with RA and SpA show at first glance more similarities than differences between the two inflammatory diseases. In both disease there is proliferation of synovial cells including macrophages and an influx of T-cells and B-cells. However, RA synovium has a more pronounced intimal lining layer hyperplasia and more synovial T cells compared with SpA.
So, although both RA and SPA are both inflammatory diseases, clear differences exist in the inflammation and we propose that these are likely to influence the outcome of disease in terms of erosions versus bone deposition.
Under physiological circumstances, bone resorption by osteoclasts and bone formation by osteoblasts are tightly coupled processes. In recent years much research has been done on how immune cells influence the balance between osteoclasts and osteoblasts. Most work has been performed on the influence of immune cells including T-cells and NK-cells on differentiation of monocytes into osteoclasts and the role of RANKL and TGF in that process in. More recently mediators produced by macrophages such as BMP and Oncostatin M have been described to induce differentiation of mesenchymal stem cells into osteoblasts.

Study objective

Aim of this study is to obtain synovial tissue and synovial fluid, from 80 patients with non-septic, inflammatory knee arthritis undergoing routine arthroscopy of the knee and analyze inflammatory factors influencing osteoclast and osteoblast activation.

Study design

The study is a cross-sectional, single centre study.

Study burden and risks

Arthroscopy as performed by rheumatologists has a low complication rate. In a recent survey, in which information of 15,682 arthroscopies performed by rheumatologists was collected, the complication rate was 15.1 per 1000 arthroscopies, which is comparable to the figures reported in the orthopaedic literature. The arthroscopy nor the taking of excess synovial fluid mentioned in this protocol is done for study purposes. Only the biopsies performed are procedures that are done solely for the interest of the study. In the the previously mentioned study no complications were reported related to the taking of 2mm biopsies. The synovial fluid collected for this study is waste material of the arthroscopy.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

-Adult (older than 18 years of age)
-Diagnosed with rheumatoid arthritis or peripheral spondyloarthritis according to the treating rheumatologist.
-Undergoing a diagnostic or therapeutic arthroscopy of the knee
-Able to give a written informed consent after reading and understanding the letter of information.

Exclusion criteria

-Patients who fail to meet the inclusion criteria.
-Patients deemed unfit to participate in the study for whatever reason by the physician

performing the study.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	11-12-2014
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO

Date:	29-09-2014
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	11-08-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	13-08-2015

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	NL47565.058.14