Coagulation parameters in patients with rheumatoid arthritis, ankylosing spondylitis and psoriatic arthritis during and after dose reduction of biologicals

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To measure the effect of lowering or stopping biologicals on various coagulation parameters in patients with rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Coagulopathies and bleeding diatheses (excl thrombocytopenic)
Study type	Observational invasive

Summary

ID

NL-OMON43241

Source
ToetsingOnline

Brief title
Effects of dose reduction of biologicals on coagulation

Condition

- Coagulopathies and bleeding diatheses (excl thrombocytopenic)
- Joint disorders

Synonym
auto-inflammatory joint diseases, Rheumatism

Research involving
Human

Sponsors and support

Primary sponsor: Jan van Breemen Instituut

Source(s) of monetary or material Support: Reade

Intervention

Keyword: Biologicals, Cardiovascular disease, Coagulation, Rheumatoid arthritis

Outcome measures

Primary outcome

Additional blood samples will be taken during three consecutive visits to the

'biopoli'. These will be stored at a temperature of -80 ° C. The following

biomarkers of coagulation activation will be determined:

F1 + 2, prothrombin fragments1 and 2

TAT, thrombin-antithrombin complexes

PAP, plasmin-a2-antiplasmin inhibitor complex

TGA, trombin generation analysis

Secondary outcome

Not applicable.

Study description

Background summary

Inflammation and cardiovascular risk
RA is associated with increased morbidity and mortality, primarily as a result of cardiovascular complications. This increased risk is only partly explained by an increased prevalence of traditional risk factors such as dyslipidemia, hypertension, smoking, obesity and diabetes mellitus. In addition to these traditional cardiovascular risk factors, inflammation contributes significantly to the increased cardiovascular risk. Several markers of active inflammation, such as CRP and disease activity scores have been associated with cardiovascular risk. This relationship between inflammation and increased cardiovascular risk is not only present in RA, but also in other rheumatic diseases such as AS and PsA.

Pro-thrombotic phenomena
Another important link between inflammation and risk of cardiovascular disease is formed by increased clotting activity. Inflammation can lead to the activation of the coagulation system and vice-versa activity of the coagulation system can also influence inflammatory activity. Previous studies reported various blood parameters that reflect an increased coagulation activation in patients with RA. For example, elevated levels of thrombin-anti-thrombin complexes (TAT), prothrombin fragments 1 and 2 (F1 + F2), plasmin-a2-antiplasmin inhibitor complex (PAP), D-dimer an increased number of platelets have been found in patients with active disease. Impaired fibrinolysis in combination with an elevated antithrombin levels have also been reported in RA. In summary, RA (and other autoimmune inflammatory disorders such as AS and PsA), can be regarded as a pro-thrombotic state, which partially explains why patients with RA have an increased risk of thromboembolic cardiovascular events.

Effects of anti-rheumatic therapy
Inflammatory cytokines, particularly TNF-* and interleukins such as interleukin-6 (IL-6), are able to stimulate endothelial cells, which leads to a pro-thrombotic state. Cytokines induce the expression of tissue factor, inhibit the protein C system and inhibit fibrinolysis, thereby promoting a pro-thrombotic state. It is therefore very likely that biologicals have a beneficial effect on the hemostatic status in auto-inflammatory diseases. Biologicals indeed result in a reduction of cardiovascular risk in patients with RA. Up to now, only small studies have examined the effects of biological agents on coagulation factors, and they suggest an association between therapy with biologicals and normalization of thrombotic biomarkers.

Today biologicals are increasingly being tapered, but how this effects the coagulation activation is unknown. Given the mounting evidence of increased cardiovascular morbidity and mortality in patients with rheumatic disease, treatment strategies should not only focus on relieving symptoms, but should also have a beneficial effect on cardiovascular risk factors, such as clotting activation. Although modest, there are indications that biologicals have a beneficial effect on the haemostatic status. Unfavorable changes in haemostatic markers can thus (re)occurt as the biological is tapered or stopped.

Study objective

To measure the effect of lowering or stopping biologicals on various coagulation parameters in patients with rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis.

Study design

In Reade, all patients using biologicals are seen regularly at the 'biopoli',

were they are monitored systematically. In patients with disease activity, the dosage of the biological is gradually reduced, and if possible, the biological is completely stopped. During this tapering period patients are seen regularly at our biopoli, and during that visits disease activity and current medication use (among others) are registered. Furthermore, these visits include laboratory evaluations. In order to study biomarkers of coagulation, we are going to draw a small extra amount of blood on some of this visits, consisting of 2 tubes (2 x 4.5 mL). This extra blood collection is combined with the blood tests that are done already, so that the additional load is minimal for the patient.

Additional blood tests will take place on three occasions: prior to tapering of the biological, and after 6 and 12 months after dose reduction.

Study burden and risks

Not applicable.

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

Diagnosis RA, AS or PsA
Use of biologicals
Reducing biological due to low disease activity (to be determined by the treating rheumatologist)

Exclusion criteria

Insufficient understanding of the Dutch language to be able to sign informed consent

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-07-2016
Enrollment:	300
Type:	Actual

Ethics review

Approved WMO

Date:	08-06-2016
Application type:	First submission

Review commission: METC Amsterdam UMC

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	NL57580.048.16