Effectiveness in knee osteoarthritis of an intramuscular gluteal corticosteroid injection versus an intra-articular corticosteroid injection in general practice: a multicenter pragmatic randomized trial

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Primary objective: to assess whether an intra-muscular gluteal corticosteroid injection is non-inferior to an intra-articular knee corticosteroid injection on knee pain in patients with knee osteoarthritis in general practice at 4 weeks follow-up....

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Joint disorders
Study type	Interventional

Summary

ID

NL-OMON48857

Source
ToetsingOnline

Brief title
Knee Osteoarthritis Injection Trial

Condition

- Joint disorders

Synonym
knee osteoarthritis

Research involving

Human

Sponsors and support

Primary sponsor: Huisartsgeneeskunde
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: corticosteroid injection, knee, osteoarthritis

Outcome measures

Primary outcome

The primary outcome is patient reported severity of pain measured with the KOOS pain scale 4 weeks after the injection.

Secondary outcome

1)Patients* reported adverse events will be assessed with a questionnaire 2 weeks after injection. Patients will be asked to report hospitalization in the questionnaires at 4, 8, 12 and 24 weeks as a proxy for SAEs.

2)Knee pain (KOOS) at all time points (baseline, 2, 8, 12, 24 weeks);

3)Knee pain severity averaged over last week will be measured with an 11-point numerical rating scale (NRS:0-10; 0=no pain);

4)Severity of global osteoarthritis pain will be measured with the WOMAC pain and will be calculated from the KOOS questionnaire (0-100; 0=extreme pain);

5)Intermittent and constant osteoarthritis pain will be measured with the ICOAP (0-100: 0=no pain);

6)Knee complaint characteristics (duration of symptoms at baseline, sensation of swelling in the knee as an indicator of flare-up)

7)Disability will be measured with the KOOS Function in daily living (0-100;

0=extreme problems).

8)Health related QoL will be measured with the EQ-5D-5L (scores ranging from -0.446=worst health related QoL to 1.0=perfect health related QoL);

9)Patients* perceived recovery measured with a 7-point Likert scale that will be dichotomized in recovered (score 1 *complete recovery* and 2 *much improved) and not-recovered (score 3 *improvement* to score 7 *worse than ever*);

10)Percentage responders is defined by the OMERACT-OARSI criteria: High improvement (*50%) in KOOS pain subscale or in KOOS function in daily living subscale and absolute increase *20 points in KOOS pain subscale or function in daily living subscale, if not then improvement in at least 2 of the 3 following domains: 1) *20% improvement in KOOS pain subscale and *10 points increase in KOOS pain subscale, 2) *20% improvement in KOOS function in daily living subscale and *10 points increase in KOOS function in daily living subscale, 3) *20% increase in global score and *10 points increase in global score. In this study patients* global assessment will be measured with a patients* perceived recovery score measured on a 7-point Likert scale. This domain is considered improved if a patient fills in score 1 *complete recovery*, score 2 *much improved*, or score 3 *slightly improved*;

11)Co-interventions including medication, non-drug therapies such as physiotherapy, referrals and surgery will be measured with the modified iMCQ;

12)Experienced painfulness of injection.

Study description

Background summary

The knee is the most affected joint in osteoarthritis and mainly managed by GPs in the Netherlands. The prevalence of knee osteoarthritis in general practice is estimated at 33.7 per 1000 registered patients (24.2 men; 43.1 women). The recent updated version (2016) of the NHG guideline *Non-traumatic knee complaints* recommends to start with advice and/or counseling regarding the course of knee osteoarthritis, in combination with advice on the importance of regular physical activity and reducing body weight if applicable4. If there is an unsatisfactory effect of these first measures a referral for exercise therapy under the supervision of a physiotherapist may be considered. Analgesics (paracetamol, NSAID) can be prescribed for knee pain. When there is an interim aggravation or insufficient pain relief an intra-articular corticosteroid injection with 20 to 40 mg triamcinolone acetonide is commended.

Intra-articular corticosteroids appear to cause as many adverse events as a placebo. However, there is no precise and reliable information about the adverse events of intra-articular corticosteroids available. Intra-articular injection of both corticosteroid and placebo has a small risk of the serious adverse reaction septic arthritis. This risk of septic arthritis is varying from 1:3000 to1:50000 in literature.
Concerns have been expressed that intra-articular corticosteroids might mask the pain, enabling patients to prematurely mobilize and hereby promoting further destruction of the joint. Moreover, repeated intra-articular corticosteroid injection could lead to loss of cartilage volume due to catabolic effects of corticosteroids.

In a recent study we found a clinical and statistical significant difference between intra-muscular corticosteroid injection compared with placebo in patients with hip osteoarthritis. The effect lasted at least 12 weeks. Also, an intra-muscular injection is easier to perform than an intra-articular injection with lesser risk of severe adverse reactions and no risk of cartilage damage.

We suspect that part of the GPs currently feel incompetent to administer intra-articular injections due to lack of training and experience. This is why the alternative of intra-muscular injection could increase the number of patients with knee osteoarthritis receiving timely injections in general practice.
Therefore, we consider an intra-muscular corticosteroid injection a valuable and innovative treatment option for patients with knee osteoarthritis. Additionally, if we can demonstrate clinically relevant effect after 8 to 12 weeks mid-term follow-up of a systemic corticosteroid injection for patients with knee osteoarthritis not responding well to paracetamol/NSAIDs treatment, GPs, orthopedic surgeons and rheumatologists will have an alternative for the short-term effective intra-articular injection.

We hypothesize that an intra-muscular gluteal corticosteroid injection is non-inferior to an intra-articular corticosteroid injection in reducing knee pain measured with the KOOS 4 weeks after injection, with possibly a longer lasting effect for at least 12 weeks.

Study objective

Primary objective: to assess whether an intra-muscular gluteal corticosteroid injection is non-inferior to an intra-articular knee corticosteroid injection on knee pain in patients with knee osteoarthritis in general practice at 4 weeks follow-up.

Secondary objectives:
1) What are the differences in reported adverse events frequency and co-interventions of patients allocated to an intra-articular knee corticosteroid injection, and to an intra-muscular gluteal corticosteroid injection?
2) What is the non-inferiority of an intra-muscular gluteal corticosteroid injection compared to an intra-articular knee corticosteroid injection on knee function, OARSI/OMERACT responder criteria and perceived recovery in patients with knee osteoarthritis at 4 weeks, and over 2, 8, 12 and 24 weeks follow-up?

Study design

The design of the study will be a pragmatic (not blinded) randomized controlled trial with two parallel groups and a follow-up of 24 weeks after the corticosteroid injection.

Intervention

Patients will be allocated to either intra-articular corticosteroid injection or intramuscular corticosteroid injection.

Study burden and risks

Local infections after intramuscular injection, including cellulitis, subcutaneous abscesses, and necrotizing fasciitis have been reported in literature. Additionally, case reports on fatal systemic infection following intramuscular (corticosteroid) injection have been published. Intramuscular injection of NSAIDs is known to lead to higher risk of infection due to their local immunosuppressive effect. An even stronger local immunosuppressive effect can be expected after administration of corticosteroids.
In a previous RCT conducted by our research group (MEC-2011-115) about intramuscular gluteal corticosteroid injection for hip osteoarthritis, no local or systemic infections after intramuscular injection of corticosteroids or placebo were observed.

Moreover, intramuscular gluteal injection can cause damage to the sciatic nerve. This risk can be minimalized by using proper injection technique (injection in ventrogluteal region). In the previous RCT (MEC-2011-115) no sciatic nerve injury was reported.
Another possible risk of intramuscular injection is formation of a hematoma. To reduce this risk, patients with coagulopathies and patients using anticoagulants are excluded from participating in this study.
Intra-articular corticosteroid injection in any joint has a risk varying from 1:3000 to1:50000 to cause septic arthritis. However, intra-articular injection is recommended as part of the standard care according to the NHG guideline. Therefore, the study population will not be exposed to additional risk of adverse reactions.

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

1) contacted their general practitioner (consultation and/or repeat pain medication prescription) due to knee osteoarthritis (ICPC L90 or L15 with unequivocal diagnosis of osteoarthritis) during the past five years;
2) aged 45 years and over;
3) symptomatic knee osteoarthritis for at least 3 months prior to enrolment;
4) a minimum score of 3 on the numerical rating scale asking about the severity of knee pain averaged over the last week (0-10; 0<=no knee pain);
5) corticosteroid injection is indicated in this patient;
6) signed informed consent form., If a patient has bilateral knee osteoarthritis, the most painful knee according to the patient will be selected as the study knee.

Exclusion criteria

1) use of oral corticosteroids;
2) intra-articular injection in a knee in the previous 6 months;
3) allergy to corticosteroids;
4) local or systemic infection, after recent vaccination with live attenuated vaccine;
5) diabetes mellitus type 1, diabetes mellitus type 2 on insulin therapy, poorly controlled diabetes mellitus type 2;
6) presence of inflammatory rheumatic diseases (such as rheumatoid arthritis, psoriatic arthritis, spondylartropathies);
7) coagulopathy, use of anticoagulants, use of dual antiplatelet therapy;
8) a history of gastric/duodenal ulcer or a present gastric/duodenal ulcer;
9) under the care of an orthopaedic surgeon for osteoarthritis of the hip and/or knee;
10) corticosteroid injection is not indicated in this patient;
11) unable to complete questionnaires in Dutch;
12) unable to give informed consent.

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-06-2018
Enrollment:	140
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Kenalog-40
Generic name:	triamcinolone acetonide
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	07-12-2017
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	19-01-2018
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	08-03-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	19-04-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-06-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	18-07-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	21-09-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-12-2018
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-02-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-02-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-06-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	29-08-2019
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
EudraCT	EUCTR2017-003513-25-NL
CCMO	NL63816.078.17