Pamidronate for Pain in Sternocostoclavicular Hyperostosis: a double-blind randomized placebo-controlled trial

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Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27475

Source
Nationaal Trial Register

Brief title
PAPS

Health condition

Sternocostoclavicular Hyperostosis

Sponsors and support

Primary sponsor: Leiden University Medical Center
Source(s) of monetary or material Support: ReumaNederland

Intervention

Outcome measures

Primary outcome

Change in score of maximal pain on BPI (NRS 0-10) from baseline to 6 months.

Secondary outcome

- Change in range of motion - Number of patients with mild pain (maximal pain as measured with NRS score in BPI ≤4) - Number of patients with 50% reduction in maximal pain (NRS score in BPI) - Change in shoulder rating questionnaire and facets of SFA score (among which are ability to dress) - Change in general health, quality of life, fatigue, work activity score, physical activity, and partner burden - Change in standard dose of analgesics (including NSAIDs) possible during course of the study as evidence for efficacy of treatment. - Evaluation of confounding factors for outcome of treatment such as delay in diagnosis and the amount of baseline tracer uptake, pain and range of motion - Evaluation of a possible neuropathic component of the reported pain - Change in biochemical markers of inflammation - Amount of tracer uptake of SCCH lesions on Na18F-PET/CT - Spinal involvement - Cost-effectiveness

Study description

Background summary

Background: sternocostoclavicular hyperostosis (SCCH) is a rare inflammatory disorder of the axial skeleton, mainly affecting sternum, clavicles and upper ribs. Patients present with swelling and pain in the affected areas and impaired movement of the shoulder girdle. Disease burden is high, and impaired quality of life common as well as inability to keep working. Diagnosis is often delayed as awareness for SCCH is low. There is no approved therapy for SCCH. In our center, we have been effectively and safely treating patients with SCCH with intravenous bisphosphonates for over two decades, with an observed favourable outcome of reduction in pain, improvement in shoulder mobility, and prevention of disease progression in a majority of patients. However, there is a need to confirm these observations by means of RCT, using validated tools for evaluation of changes in pain, shoulder girdle function and quality of life in response to treatment. Objectives: we aim to investigate in SCCH patients whether 3-monthly pamidronate decreases locally increased bone turnover (measured by Na18F-PET scans) and thereby decreases pain (primary endpoint), and leads to improvement in shoulder girdle function, quality of life, physical and work activity (secondary endpoints) in de active treatment arm compared to placebo. Study design: double-blind placebo controlled 6 months intervention study followed by a 6 months open-label study. Study population: Patients over 18 years old with an established diagnosis of SCCH on the basis of characteristic clinical and radiological features and persistent pain at the site of lesions with a maximum pain score of ≥6/10 as measured by the Brief Pain Inventory (BPI). Intervention: Eligible patients will be randomized to receive two courses of pamidronate,

administered intravenously at a dose of 30 mg daily on 3 consecutive days 3-monthly, or placebo. After these 6 months, the trial is continued in an ‘open label’ design for the following 6 months, with pamidronate being administered to all patients with a maximum pain score of 4/10 or higheras measured by BPI. Main study parameters/endpoints: pain scores (measured by brief pain inventory (BPI)).

Study objective

We hyopthesize that in SCCH patients 3-monthly pamidronate decreases locally increased bone turnover (measured by Na18F-PET scans) and thereby decreases pain, and leads to improvement in shoulder girdle function, quality of life, physical and work activity compared to placebo.

Study design

Baseline, 3 months, 6 months, 9 months, 12 months (total study period being 12 months)

Intervention

Eligible patients will be randomized to receive two courses of pamidronate, administered intravenously at a dose of 30 mg daily on 3 consecutive days 3-monthly, or placebo. After these 6 months, the trial is continued in an ‘open label’ design for the following 6 months, with pamidronate being administered to all patients with a maximum pain score of 4/10 or higher as measured by BPI. Every 3 months patients will be requested to complete the following questionnaires: BPI to assess pain and interference of pain with daily life, Pain-DETECT to assess neuropathic pain, shoulder rating questionnaire and shoulder function assessment to assess shoulder complaints. Also requested to be completed is a questionnaire to assess work activity. IPAQ will be used to evaluate physical activity both during work and leisure time, sf-36 for general health, and CarerQol for partner burden. Patient Global Impression of Change will be used to evaluate changes in well-being. Patients will be asked to keep a pain and fatigue diary. Use of analgesics is to be recorded in these forms as well. For economic evaluation the iMCQ questionnaire and iPCQ questionnaire will be evaluated to measure healthcare use and productivity respectively. Laboratory investigations at every visit include measurement of parameters of inflammation (CRP, leucocytes, BSE, IL-1, IL-6, TNFalpha, DKK1, sclerostin, RANKL), kidney function (creatinine, to check whether pamidronate dose is safe; in case of eGFR < 30 ml/min, pamidronate will not be administered, conform Farmacotherapeutisch Kompas), electrolytes (potassium, sodium). Bone markers will be measured after an overnight fast, as it represents bone remodelling activity (alkaline phosphatase and P1NP as markers for osteoblast activity, and beta crosslaps as marker for osteoclast activity).Vitamin D, PTH, calcium and albumin will be measured to check whether levels are within normal range, as needed before pamidronate infusion. Na18 F-PET/CT will be performed (intravenous 18 F-sodium fluoride injection followed by scan) at baseline, 6 months and end visit to monitor tracer uptake and radiologic appearance.

Contacts

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Eligibility criteria

Inclusion criteria

- Adult patients with an established diagnosis of SCCH based on clinical and radiologic features and increased radioactive tracer uptake on 99mTc scan - Reported maximum pain score of 6/10 or higher - No treatment with bisphosphonates for the previous 6 months

Exclusion criteria

- Patients under 18 years of age - Active pregnancy wish, pregnancy or nursing - Generalized pain without SCCH related pain - Bisphosphonate use 6 months before study entry - Bisphosphonate allergy - Estimated glomerular filtration rate < 30 ml/min - Uncontrolled endocrine abnormalities - Active cancer treatment - Language barrier, severe co-morbidity, mental disability, poor mobility and other causes preventing attendance for control visits, In case of poor dental hygiene or inadequate dental care, patients will only be enrolled after oral maxillary surgeon consultation.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-12-2020
Enrollment:	90
Type:	Anticipated

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Positive opinion

Date:	01-02-2021
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 52471
Bron: ToetsingOnline
Titel:

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

No registrations found.

In other registers

Register	ID
NTR-new	NL9233
CCMO	NL68020.058.20

Register	ID
OMON	NL-OMON52471

Study results