Boosting the bone biology. The effect of oral L-citrulline supplementation on mesenchymal stem cell concentration and osteogenic potential of BMAC in healthy humans. A randomized open-label pilot study.

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The objective of this study is to investigate whether oral supplementation of citrulline will improve the amount of MSCs and osteogenic capacity in BMAC.

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON56806

Source
ToetsingOnline

Brief title
Boosting the bone biology

Condition

- Other condition

Synonym
Bone metabolism, osteogenic differentiation

Health condition

Botaandoeningen. fracturen

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Bone Marrow Aspirate concentrate, Citrulline, Mesenchymal stem cells, Osteogenic potential

Outcome measures

Primary outcome

The osteogenic potential of MSCs in the BMAC samples.

Secondary outcome

Cell viability and the amount of MSCs

Adverse events

Study description

Background summary

Non-union is a common complication after a sustained fracture. The treatment of a non-union requires a multidisciplinary approach. Not only mechanical stability and osteoconductive material is needed for an adequate healing response, also osteogenic cells and osteoinductive reagents are crucial. Current approaches are aimed towards transposition of osteogenic cells, like bone marrow aspirate concentrate (BMAC), and the addition of osteoinductive reagents, like bone morphogenic proteins (BMPs) or collagen. However, it is known that the nutritional status of a person also has an impact on fracture healing and the occurrence of non-union. This suggests that improving the nutritional status of a patient can be a valuable part in non-union treatment. Some nutrients, like vitamin D and calcium have already been proven to aid in this process. Non-essential amino acids are described to promote proliferation and differentiation of mesenchymal stem cells (MSCs), leading to increased consolidation of fractures. In 2020 the effect of citrulline on fracture healing was studied in mice and showed an increase in fracture consolidation.

This effect has yet to be studied in human subjects.
When BMAC is used, bone marrow is harvested from the iliac crest of the patient, centrifuged to isolate the MSCs and growth factors, and then added to the fracture site. The idea of improving these MSCs before harvesting, essentially using the body as bioreactor, can be a low-impact and cost efficient way to improve non-union surgery.

Study objective

The objective of this study is to investigate whether oral supplementation of citrulline will improve the amount of MSCs and osteogenic capacity in BMAC.

Study design

The study will be performed as a single center randomized open label pilot study.

Intervention

The control group will receive no supplementation. The two intervention groups will receive either once or twice 5 grams of oral L-citrulline supplementation 14 days prior to the surgery to remove the OSM. Bone marrow will be harvested from the iliac crest during surgery and centrifuged to create BMAC.

Study burden and risks

From the study supplement, citrulline, no risks or burden is to be expected. Persons participating in the study will undergo a bone marrow puncture in the iliac crest. This procedure will be performed under general or spinal anesthesia. From this puncture some postoperative pain can be expected, long term complaints only rarely reported. Complication rates of bone marrow punctures of the iliac crest are low, up to 0.3% is reported.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Age >18 years
- Patients are planned for the removal of OSM under general anaesthesia or spinal anaesthesia where the iliac crest is anesthetized.

Exclusion criteria

- Age <18 years
- Patients with a reported allergy for L-citrulline.
- Chronic use of NSAIDs or use of NSAIDs 14 days prior to surgery
- Chronic use of immunosuppressant medications or use 14 days prior to surgery
- The use of bisphosphonates
- Inability to stop therapeutic anticoagulants prior to surgery
- Surgery under general anaesthesia or spinal block not possible
- Unmanaged comorbidities known to effect bone metabolism: Such as diabetes, osteoporosis, recent polytrauma
- Subject has (had) an active infection or fever in the weeks prior to the surgery
- Malnutritional state based on The Simplified Nutritional Appetite Questionnaire (SNAQ).

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2024
Enrollment:	30
Type:	Anticipated

Medical products/devices used

Registration:	No

Ethics review

Approved WMO

Date:	07-06-2024
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL84409.068.23