Active vitamin D for secondary hyperparathyroidism after bariatric surgery: a multicenter randomized controlled trial.

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This study has been transitioned to CTIS with ID 2023-510312-40-00 check the CTIS register for the current data. Main objective- to investigate the effect of alfacalcidol on the treatment of secondary hyperparathyroidism in patients after RYGB...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Parathyroid gland disorders
Study type	Interventional

Summary

ID

NL-OMON53666

Source
ToetsingOnline

Brief title
ActiVitD-trial

Condition

- Parathyroid gland disorders
- Bone, calcium, magnesium and phosphorus metabolism disorders

Synonym
increased parathyroid hormone lever

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: bariatric surgery, secundairy hyperparathyreoidism, vitamin D

Outcome measures

Primary outcome

Primary outcome parameters: normalization of PTH (and thus recovery of secondary hyperparathyroidism) at 1 and 2 years after diagnosis and start of treatment in one of the study groups. Secondary hyperparathyroidism will be defined as PTH at the upper limit or above the labs reference value combined with a normal or decreased serum calcium level (in patients with 25(OH)D >50 nmol/L).

Secondary outcome

Secondary outcome parameters: decrease in BMD (defined as 3% decrease in T-score at the lumbar spine and 5% decrease in T-score at the hip / forearm), measured at 1 and 2 years after inclusion. As DEXA BMD measurements at regular sites (hip, spine) depend on body weight and circumference to a certain extent, BMD measurement of the forearm will be performed because this site is known to be less influenced by surrounding tissue. For a reflection on bone turnover, serum bone turnover markers (P1NP, b-crosslaps, alkaline phosphatase) will be measured.

Quality of life is measured after inclusion and thereafter every 6 months with

the OBESI-Q (https://dica.nl/dato/documenten) questionnaire, a relatively new questionnaire which is validated and endorsed by the Dutch Society of Metabolic and Bariatric Surgery (DSMBS) and the Dutch society for Internal Medicine (Nederlandse Internisten Vereniging; NIV) and the patients society (Stichting OverGewicht). This questionnaire is part of Dutch Audit for Treatment Of Obesity (DATO) which aims to registrate the results of all bariatric procedures performed in the Netherlands.
The EQ5D questionnaire will be completed every 6 months to asses generic health status for health economic benefits.
Medication adherence will be measured every 6 months with the validated Promise questionnaire, which includes the MARS (Medication Adherence Report Scale) questions which are used by pharmacists to screen for adherence and side effects.

Study description

Background summary

Observational studies show a 5-8% decrease in bone mineral density (BMD) after bariatric surgery. Significant associations are found between increase in PTH level and percentage decline in femoral neck BMD. Moreover, calcium absorption, as measured by urine calcium excretion, is decreased by a mean of 73% after bariatric procedures that exclude the duodenum and jejunum from the gastro-intestinal tract. The decrease in calcium excretion is associated with enhanced bone resorption markers. These data suggest that secondary hyperparathyroidism, caused by calcium malabsorption and relative calcium deficiency could be an important factor in postoperative bone loss.

In current practice in the Netherlands, if vitamin D deficiency and secondary hyperparathyroidism occurs, oral supplementation with calcium and cholecalciferol is increased. There is no strict guideline covering treatment of secondary hyperparathyroidism after surgery, but in general cholecalciferol

intake is increased titrating serum 25OH vitamin D level up to >75 nmol/L. When hyperparathyroidism persists thereafter, calcium intake is increased up to 2000 mgs daily. However, increased calcium and vitamin D supplementation leads to gastro-intestinal side effects, extra costs for patients, and besides that, calcium tablets are chalky and difficult to swallow.
Alfacalcidol, an active vitamin D analogue, suppresses PTH and increases calcium absorption from the gut. Alfacalcidol is a small, easy to swallow tablet, has limited side effects and has little costs. We hypothesize that treatment with alfacalcidol is more effective and results in better therapy adherence in secondary hyperparathyroidism after bariatric surgery.

Study objective

This study has been transitioned to CTIS with ID 2023-510312-40-00 check the CTIS register for the current data.

Main objective
- to investigate the effect of alfacalcidol on the treatment of secondary hyperparathyroidism in patients after RYGB
Secondary objectives:
- to investigate bone turnover and changes in BMD in relation to secondary hyperparathyroidism and its treatment in patients after RYGB
- to investigate quality of life, medication adherence and health economic benefits related to hyperparathyroidism and medication intake in patients after RYGB

Study design

A randomized controlled trial will be performed to compare the effect of adding alfacalcidol to standard postoperative care (with cholecalciferol and calcium but without addition of alfacalcidol) in treatment of secondary hyperparathyroidism after Roux-en-Y-gastric bypass.

The duration of the intervention will be 2 years. We intend to arrange follow-up of patients afterwards to be able to determine long term effects on BMD. The study will be performed in several hospitals in the Netherlands (RKZ Beverwijk, Groene Hart Ziekenhuis Gouda, Rijnstate Ziekenhuis Arnhem, Zuyderland Medisch Centrum, Centrum Overgewicht Noord Nederland, Spaarne Gasthuis Haarlem).

Both groups: bloodsample, 24 hour urine and dexa scan at baseline, 1 year and 2 year follow up.
Intervention group: for patients randomized to treatment with alfacalcidol additional visits will take place to adjust (t=6 weeks, 12 weeks, 18 weeks, 24 weeks) medication. We expect that no more than 3-4 adjustments in medication

dose will be needed. Altogether, inclusion in the study protocol will mean an extra 5-6 visits to the hospital for those patients randomized to alfacalcidol, and 2-3 extra visits for those randomized to standard treatment.
Risks associated with participation: no significant risks are expected in the standard care group. In the intervention group, alfacalcidol conveys a small risk of developing hypercalcemia and hypercalciuria. Therefore the dose will be carefully titrated and serum and urine calcium will be measured.

Intervention

Intervention:
- A. Standard care in case hyperparathyroidism the dose of calcichew-D3 is increased to 1000/800 3dd1
- B: Intervention: calcichew-D3 500/800 3dd1 + stepwise supplementation of alfacalcidol titrated to normalization of PTH levels

Study burden and risks

The appointments in this trial will coincide regular follow up
Within the adjesment fase of alfacalcidol there will be some extra visits with venipuncture
There will be performed 3 extra dexa scans
There will be questionnaires at three extra timepoints

There is a small risc of haematoma after venipuncture
There is a small risc on hypercalciuria after intake of alfacalcidol, this will be controlled.

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

Men and both pre- and postmenopausal women who have had Roux-en-Y-gastric bypass surgery and present with secondary hyperparathyroidism after surgery, with a vitamin D sufficient state (>50 nmol/l), and only on standard supplementation, are included.

Exclusion criteria

- Patients who are already on active treatment for osteoporosis before inclusion
- Patients with chronic kidney disease defined as eGFR < 60 ml/min
- Patients who had a bariatric intervention before and are re-operated
- Patients that are on chronic steroid use, for example for inflammatory conditions
- Patients that appear to have hypercalcemia on screening
- Patients with known inflammatory conditions (i.e. rheumatoid arthritis)
- Patients that have an active pregnancy wish

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:	Recruiting
Start date (anticipated):	01-12-2023
Enrollment:	130
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ethalpha
Generic name:	alfacalcidol
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	20-04-2023
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	20-10-2023
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	23-10-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	27-10-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	29-03-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	02-04-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	09-10-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO Date:	14-10-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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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
EU-CTR	CTIS2023-510312-40-00
EudraCT	EUCTR2022-000178-24-NL
CCMO	NL80100.058.22