GRAVITY: GLP-1 analogues in craniopharyngioma

No registrations found.

Ethical review	Not applicable
Status	Pending
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27692

Source
NTR

Brief title
GRAVITY

Health condition

Craniopharyngioma

Sponsors and support

Primary sponsor: Erasmus MC
Source(s) of monetary or material Support: Will follow. An application will be done for the Benefit call, and at Novo Nordisk for providing study medication.

Intervention

Outcome measures

Primary outcome

Change in BMI

Secondary outcome

Weight and metabolic related:
- Change in BMI at end of follow-up (approximately 1 year after treatment is stopped);
- Proportion of patients who achieve BMI maintenance (defined as less than 5% change in BMI or 1 SDS
- Change in weight (kg) at end of treatment and last follow-up
- Change in body fat percentage as measured by Dual X-ray Absorptiometry;
- Obesity rates after 54 weeks of treatment and at end of follow-up (obesity is defined as BMI ≥30 kg/m2) (53)
- Change in (systolic and diastolic) blood pressure
- Presence of diabetes mellitus
- Presence of cardiovascular disease
- The Metabolic Syndrome and its components after end of treatment and after 2 years of follow-up (the Metabolic Syndrome is defined according to the IDF consensus, with 3/5 criteria for obesity, high triglycerides, low HDL-cholesterol, hypertension and hyperglycaemia) (54)

Quality of life related:
- Change in physical functioning score (Short Form 36) and its subcomponents
- Health related quality of life by EQ5D-5L

Safety related:
- Number of and reason for discontinuation and lack adherence of treatment/placebo
- Number of (serious) adverse events (with distinction grade 3-4 adverse events and relation to the treatment)

Efficacy related:
- Number of and reason for discontinuation and lack adherence of treatment/placebo
- (genetic) differences between responders and non-responders)

Study description

Background summary

Craniopharyngioma is a rare tumour in the hypothalamic-pituitary region, which is associated with increased mortality (with an average 20-year survival rate of 62%), comorbidities and impaired quality of life of patients. It has an incidence of 0,5-2,5 cases per 1 million population per year globally, has its peak incidence at ages 5-15 and 45-60 years, and is mainly treated with neurosurgery and radiotherapy. Due to its localization, these patients suffer from hypothalamic/pituitary dysfunction, which is important for weight homeostasis, and obesity rates in these patients are found in up to 75%. Obesity is an important risk factor for obstructive sleep apnea syndrome (OSAS) which occurred in 46% in a study in patients with craniopharyngioma, diabetes mellitus type II (T2DM), and the metabolic syndrome, which occurred in 45-51% and in turn doubles risk on cardiovascular disease and increases mortality. For T2DM, a standardized incidence ratio was found of 4.4 (95% confidence

interval 2.8-6.8) in our craniopharyngioma study population. Weight gain in patients with craniopharyngioma occurs mostly in the first year after treatment. This is a big issue in patients with craniopharyngioma, as they are at risk of cardiovascular disease and are impaired in their mobility and quality of life.
Until now, no proper treatment has been found for hypothalamic obesity: lifestyle changes are essentially useless (6). Bariatric surgery in the form of Roux-en-Y gastric bypass, as a last resort, seems effective in small studies in up to two years of follow-up, but is an invasive intervention, and questions on safety issues for the medication are raised. Reliable, less invasive options to treat obesity in patients with craniopharyngioma, are basically not available at this point, but highly desirable in patients with this rare disease. Key to the effectiveness of bariatric surgery in the general obese population, is a decrease in appetite, which is caused by changes in gut hormones like glucagon-like peptide-1 (GLP-1). GLP-1 activates POMC neurons: these are neurons of the first order that regulate neurons of the second order, who have their influence on satiety, feeding, the sympathetic nervous system and the pituitary. GLP-1 analogues have been introduced in patients with diabetes mellitus, and studies have proved the efficacy of weight loss by GLP-1 analogues such as liraglutide in the obese non-craniopharyngioma population. As bariatric surgery appears to be an effective treatment in patients with craniopharyngioma and hypothalamic obesity, this suggests that the gut-hypothalamic feedback still effective. Therefore GLP-1 analogues could be effective as well. Our aim is to find an option to prevent obesity in patients diagnosed with craniopharyngioma. This may increase their quality of life, and decrease comorbidities (such as OSAS, the metabolic syndrome and T2DM) and mortality. We hypothesize that GLP-1 analogues be used to lower the prevalence of obesity in patients with craniopharyngioma if implemented early after first treatment. Our objective is to investigate whether GLP-1 analogue semaglutide is effective on treating obesity in patients with craniopharyngioma aged 16 years or older. Therefore, we will perform a randomized controlled trial with one year of semaglutide versus placebo. Both groups will receive lifestyle advices through general care and will be followed-up two years after stopping the study medication.

Study objective

We hypothesize (hypothalamic) obesity can be treated with GLP-1 analogues in patients with craniopharyngioma.

Study design

Endpoints wil be determined at end of treatment (after 56 weeks). Follow-up will be continued until 107 weeks and endpoints will be determined again.

Intervention

Semaglutide once weekly in increasing dosis, versus placebo, for ~1year.

Contacts

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Eligibility criteria

Inclusion criteria

• Patients with craniopharyngioma, aged ≥16 years;
• BMI ≥30 kg/m2;
• No surgical intervention for craniopharyngioma one year before inclusion;
• Adequate hormone replacement therapy (with or without growth hormone) in the past 4 weeks.

Exclusion criteria

• Pregnancy (wish);
• Breastfeeding or plan to breastfeed during treatment;
• Allergy or oversensitivity for GLP-1 analogues or components;
• Multiple Endocrine Neoplasia syndrome 2 (MEN2 syndrome);
• Up to second degree family members with medullary thyroid carcinoma;
• Gastroparesis or severe digestive problems;
• History of or current pancreatitis;
• Amylase or lipase above 2 times the upper normal range;
• Active gallbladder disease;
• Current depression or suicidal thoughts;
• Liver failure;
• Renal impairment measured by Glomerular Filtration Rate (GFR) value less than 30 ml/min/1,73 m6 (less than 60 ml/min/1,73 m^2 in subjects treated with Sodium-glucose Cotransporter 2 Inhibitors);
• NYHA class IV heart failure;
• Insulin-dependent diabetes mellitus;
• Use of another GLP-1 analogue;

• Succeeded bariatric surgery (≥10% weight loss);
• Extreme fear of needles.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2022
Enrollment:	104
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Plan description
NA

Ethics review

Not applicable

Application type:	Not applicable

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
NTR-new	NL8514
Other	Will follow : Will follow

Study results

Summary results
NA