Medical assessment of adverse health outcomes in Dutch childhood cancer survivors; a nationwide project; SKION LATER Q2008 onderzoek:
Growth hormone deficiency in children, after treatment for childhood cancer

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• To assess the prevalence of short stature, in combination with an aberrant IGF-1 in combination with IGF-BP3 in the entire cohort of childhood cancer survivors and the therapy related risk factors.• To assess the distribution of IGF-1 and IGF-BP3...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hypothalamus and pituitary gland disorders
Study type	Observational invasive

Summary

ID

NL-OMON41436

Source
ToetsingOnline

Brief title
SKION LATER Q2008 - growth hormone child

Condition

- Hypothalamus and pituitary gland disorders

Synonym
growth hormone deficiency in childhood cancer survivors, shortage of growth hormone after treatment for childhood cancer

Research involving
Human

Sponsors and support

Primary sponsor: Stichting Kinderoncologie Nederland
Source(s) of monetary or material Support: Quality of life gala

Intervention

Keyword: Growth hormone deficiency, IGF-1, pediatric oncology, survivor

Outcome measures

Primary outcome

* Mean height (in non-disproportional patients) at near final height

* Height distribution (in non-disproportional patients) at near final height

* IGF-1 distribution compared with normal population/sibs

* IGF-BP3 distribution compared with normal population/sibs

* % of cancer survivors with an IGF-1 < 2 SD corrected for age

* % of cancer survivors with an IGF-BP3 < 2 SD corrected for age

Secondary outcome

not applicable

Study description

Background summary

Advances in diagnosis and treatment of childhood cancer over the last decades have dramatically increased long-term survival. As a result, the numbers of childhood cancer survivors (CCS) are growing and it has become increasingly clear that the former disease and its treatment can significantly impair long-term health. The need for long-term follow-up is uniformly recognized. Research focusing on identification and characterization of high-risk populations is an essential foundation on which to build evidence-based recommendations for long-term follow-up. Furthermore, research focusing on more

accurate screening tests and effective interventions is needed to reduce excess morbidity and mortality in CCS. The SKION LATER Q2008 - growth hormone study phocuses on growth hormone deficiency in CCS .
After cranial radiation therapy for childhood cancer, endocrine deficienties are frequently seen. Damage to the hypothalamic-pituitary axis is time and dose dependent. The incidence of problems increases in time. For both the hypothalamus and the pituitary gland, the dose per fraction that is administered is of importance next to the total administered dose. Younger patients are more vulnerable than older patients.
The hypothalamus is more radiosensitive than the pituitary gland; damage can be expected after 40-50 Gy, and after higher doses also the pituitary gland may be damaged. However, also at doses < 40 Gy hypopituitarism may be present due to hypothalamic dysfunction.
Of the production of the pituitary hormones, the synthesis of GH will be affected first, mostly followed by LH & FSH, ACTH, and TSH. Next to a GH deficiency, also GH neurosecretory dysfunction has been described to occur, characterized by a normal GH peak in the stimulation test but a decreased spontaneous 24-hour GH-secretion.
Growth retardation after treatment with chemotherapy has also been described. The glucocorticoids are one of the best known drugs to cause growth retardation and are frequently administered to children during cancer treatment, as anti-emetic or as part of the cytotoxic regimen. Reduced growth velocity in children treated with multiple cytotoxic drugs is common, and it is likely that the effects of underlying disease and the different drugs interact or act additively. The exact influence of chemotherapy on the GH axis is unknown.
The diagnosis of growth hormone deficiency is difficult as there is no golden standard. The diagnosis is always made with the combination of presenting symptoms; short stature with delayed bone-age, low IGF-1 with low IGF-BP3, in absence of other endocrine deficiencies and other diseases such as kidney or liver disease. In this case GH-stimulation tests are performed twice. In case of a maximum peak of GH < 20 mE/L, GH deficiency is made more likely.

Study objective

• To assess the prevalence of short stature, in combination with an aberrant IGF-1 in combination with IGF-BP3 in the entire cohort of childhood cancer survivors and the therapy related risk factors.
• To assess the distribution of IGF-1 and IGF-BP3 in the entire cohort of childhood cancer survivors.

Study design

This study with cross sectional design will consist of a history and physical exam, and a venapuncture. For half of the population, these tests will be part of regular patient follow up as defined by the guidelines for screening for late toxicity in CCS. Data will be collected anonymously in a central database.

Study burden and risks

Half of the survivors (n=200) will have the outpatient visit, and venapuncture as part of their regular follow up based on screening guidelines for CCS. For the CCS treated with chemotherapy, the visit at the outpatient clinic is part of the regular follow up based on screening guidelines for CCS, but the venapuncture is done as part of the study (15 minutes) . There are no risks for the study participants.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)

Inclusion criteria

All patients who were treated for childhood cancer (before age 18) in one of the seven

Pediatric Oncology Centers between 1960 and 2001 and who survived for at least 5 years after diagnosis will be included in the SKION LATER study. Participating centres are located in Amsterdam (the Emma Children's Hospital/ Academic Medical Centre (EKZ/AMC) and the VU University Medical Center (VUMC) and), Groningen (Children's Cancer Center/ University Medical Center Groningen (UMCG)), Rotterdam (Rotterdam Erasmus MC-Sophia (REMC-S), Nijmegen (University Medical Center Nijmegen (UMCN)), Leiden (Leiden University Medical Center (LUMC) and Utrecht (Princess Máxima Center for Pediatric Oncology (PMC)). From this cohort of 575 survivors, 400 childhood cancer survivors will be asked to participate in the growth hormone study.

Exclusion criteria

Diagnosis of childhood cancer with survival less than 5 years, age at diagnosis >17 years or diagnosis while residing in foreign country , abnormal thyroid function tests, kidney or liver values. BMI < -2 SD as these children typically have a combination of poor growth and very low IGF-1 levels; this implies that the plasma concentration of IGF-1 does not reflect the presence of a GH deficiency in these children and thus cannot be interpreted correctly in the context of our study.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	04-05-2016
Enrollment:	400
Type:	Actual

Ethics review

Approved WMO Date:	23-01-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-01-2016
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL34998.018.12