Neurotoxicity of cancer treatment: Neurocognitive dysfunction and underlying mechanisms

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Ethical review	Approved WMO
Status	Pending
Health condition type	Leukaemias
Study type	Observational invasive

Summary

ID

NL-OMON29855

Source
ToetsingOnline

Brief title
Neurotoxicity of cancer treatment

Condition

- Leukaemias

Synonym
acute lymphoblastic leukemia (ALL), blood cancer

Research involving
Human

Sponsors and support

Primary sponsor: Universiteit Leiden
Source(s) of monetary or material Support: KWF Kankerbestrijding

Intervention

Keyword: ALL, late effects, neuroimaging, neurotoxicity

Outcome measures

Primary outcome

Outcomes will be a neuropsychological deficit profile, a profile of structural and functional integrity of neural networks and descriptions of quality of life. Profiles of the different patient groups and controls will be contrasted.

Secondary outcome

Coincidental findings of secundary tumors after radiation will be registered.

Study description

Background summary

Due to improved treatment, over 80% of children with acute lymphoblastic leukaemia (ALL) are now long term survivors. Central nervous system prophylaxis is an essential part of current ALL treatment. Cranial radiation treatment (CRT) has been reported to cause long term neurocognitive and academic deficits among survivors. The literature suggests that also treatment with chemotherapy exclusively * since 1984 the standard type of treatment in The Netherlands * is associated with neuropsychological sequelae, in particular in the domain of executive functions.
Much of the information on long term sequelae of treatment, also from our previous study*, relates to outcomes within the first 5 * 10 years following treatment. Data on long term consequences beyond this time frame are insufficient. In addition, the greatest gap in our knowledge regarding treatment-related cognitive changes is a lack of understanding of the mechanism(s) that account for these sequelae. So far, abnormalities detected by structural (conventional) MRI have not consistently been found to correlate with clinical findings and neurocognitive status. More sensitive imaging measures that have recently been developed, are considered necessary.
As in other countries cranial radiation is still an important option in the treatment of childhood ALL, and because in other diseases CRT is unavoidable, the study of CRT-related consequences may provide important information.

We hypothesize that long-term unfavourable effects of treatment of childhood ALL are reflected in a neuropsychological profile emphasizing executive function (EF) deficits. This deficit profile may be more outspoken in survivors treated with chemotherapy and cranial radiation (vs. treated with chemotherapy only). As the quality of executive functions is, above all, dependent on the integrity of functional networks of the brain, it is hypothesized that EF deficits are associated with disruptions of neural networks. These disruptions may be more severe in survivors treated with cranial radiation in addition to chemotherapy.

* Effects of Chemotherapy on Attention and Information Processing in Survivors of Childhood Cancer (KWF, project number: AZVU 2001 - 2390). De Sonneville LMJ, Veerman AJP (principal investigators), Buizer AI (research physician)

Study objective

With this information we hope to be able provide ex-patients with more detailed information about late effects of treatment. Also it is a very important step towards ajusting current treatment protocol to prevent late effects as much as possible.

Study design

The study will be purely observational. It will include a neuropsychological assessment to determine the neuropsychological deficit profile of long-term survivors of childhood ALL, neuroimaging of the brain to bring out disruptions in the functional integrity of neural networks (MEG, (f)MRI, DTI) and questionnaires on quality of life.

Study burden and risks

Patients will be requested to visit the VUmc twice: the first time for neuropsychological assessment (2 h) and MEG acquisition (1 h 45 min), the second time for an MRI scan (1 h). Furthermore they will be asked to complete a questionnaire at home and bring it on their first visit.
Subjects will be consulted about a convenient time for the appointments.

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

Being treated for ALL according to DCLSG protocol ALL 5 (1979 - 1984) or according to DCLSG protocol ALL 6 (1984 - 1988)

Exclusion criteria

Use of centrally acting drugs, active psychiatric disease or symptoms, pre-existing CNS disorders, insufficient mastery of Dutch language.

Study design

Design

Study type:	Observational invasive
Intervention model:	Other

Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-11-2006
Enrollment:	338
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
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	NL13950.029.06