The effect of radiotherapy on glucose metabolism in patients with rectal cancer; a feasibility study

Published: 22-04-2011
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Primary objective:Effect of preoperative radiotherapy on insulin resistance in rectal cancer patients.Secondary objectives:Effect of preoperative radiotherapy on plasma oxidative stress parameters.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Glucose metabolism disorders (incl diabetes mellitus)
Study type	Observational invasive

Summary

ID

NL-OMON36393

Source
ToetsingOnline

Brief title
Radiotherapie en insuline resistentie

Condition

- Glucose metabolism disorders (incl diabetes mellitus)
- Gastrointestinal neoplasms malignant and unspecified

Synonym
Insulin resistance, temporary diabetes

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Centrum Alkmaar
Source(s) of monetary or material Support: Foreest Instituut

Intervention

Keyword: Glucose metabolism, Insulin resistance, Radiotherapy, Rectal cancer

Outcome measures

Primary outcome

Effect of preoperative radiotherapy on insulin resistance in rectal cancer

patients.

Secondary outcome

Effect of preoperative radiotherapy on plasma oxidative stress parameters.

Study description

Background summary

Insulin resistance is a state of insensitivity of tissues for action of insulin leading to hyperglycemia, a situation similar to non-insulin dependent diabetes mellitus. It is well known that insulin resistance occurs after surgery and is related to the severity of the procedure performed. The negative correlation between insulin resistance and postoperative recovery, either by prolonging the capacity of the body to regain normal function, or by increasing the metabolic stress and the risk for complications, has already been confirmed (1,2). The precise mechanism underlying the occurrence of perioperative insulin resistance is unknown, but the latest insights point to an important role for oxidative stress. Oxidative stress is the consequence of an imbalance between the production of oxidant species and their neutralization by antioxidants.

Radiotherapy induces oxidative stress in tissues, an important mechanism of inducing tumor cell apoptosis. However, the oxidative effects of radiotherapy are not limited to the site of radiation but also induce systemic effect as identified by peroxidation of plasma lipids (3, 4). Lipid peroxidation occurs mainly through formation of free radicals and causes membrane damage as well as oxidative modification of critical targets (5). The relationship between radiotherapy and insulin resistance has been described before. Chemaitilly et al. observed frequently insulin resistance in adult survivors of haematopoietic stamcelltransplantation treated with total body irradiation in childhood in their study (6). Furthermore, in 1997 Cicognani already described an impaired insulin response in some patients treated for Wilms* tumour in childhood, mainly in male patients who received abdominal radiotherapy (7). To our

knowledge there are no data on the effect of radiotherapy in adults.

Preoperative radiotherapy in combination with total mesorectal excision is the treatment of choice in rectal cancer reducing local recurrence rate < 5%. Most of the patients with rectal cancer receive short-term preoperative radiotherapy for 5 days (5 x 5 Gy) and some with more extensive tumours receive this dose during 5 weeks.
Insulin resistance is considered a risk factor in the development of complications.

The hypothesis of the present study is that insulin resistance is induced by preoperative radiotherapy in rectal cancer patients and mediated by oxidative stress.
The effects of radiotherapy on the induction of insulin resistance are unknown therefore a feasibility study will be performed using the oral glucose tolerance test (OGTT) before and during the course of radiotherapy. Plasma samples will be taken to measure oxidative stress parameters.

Study objective

Primary objective:
Effect of preoperative radiotherapy on insulin resistance in rectal cancer patients.

Secondary objectives:
Effect of preoperative radiotherapy on plasma oxidative stress parameters.

Study design

Study description
Glucose metabolism of 10 patients, scheduled for radiotherapy as preoperative therapy in rectal cancer, will be studied using the oral glucose tolerance test (OGTT). Oral glucose tolerance testing is a sensitive technique that can detect sub clinical glucose metabolism disorders and discern between increased resistance and impaired insulin production. The test will be performed in the morning after an overnight fast both before and after radiotherapy. Glucose (0.5 g/kg body weight, maximum 75 g glucose) will be administered orally for 4 minutes. Blood samples for measurement of whole blood glucose, C-peptide and insulin will be taken from the opposite arm at t= -15, 0, 5, 10, 15, 20, 30, 40, 50, 60 min.
Insulin resistance will be estimated by the homeostatic model assessment (HOMA-IR), insulin sensitivity by the ratio of fasting glucose (GF) to fasting insulin (IF) (GF/IF), and the quantitative insulin sensitivity check index (QUICKI) (7,8). The calculations are as follows: HOMA-IR=(fasting insulin (mU/ml) X fasting glucose (mmol/l) / 22.5); insulin resistance will be defined as HOMA-IR>2; GF/IF in mg/dl for glucose and mU/ml for insulin; QUICKI=1/[log

(fasting insulin (mU/ ml)) + log (fasting glucose (mg/dl))]; impaired insulin sensitivity was defined as QUICKI<0.339.
To determine oxidative status, plasma samples will be drawn three times during a 5 days session of a 5 X 5 Gy radiotherapy course as preoperative therapy in rectal cancer patients. Plasma samples will be drawn before the start of radiotherapy, on day 3 and day 5 during the radiotherapy course. Samples will be taken after an overnight fast.
The parameters we are interested in are glucose, insulin, C reactive protein, Malondialdehyde, oxidative LDL and HbA1c.
In addition a bio-impedance measurements will be performed to study body composition and monitor fluid shift during radiotherapy.

Study burden and risks

The patients have to undergo 3 times an OGTT. At these moments, some blood will be taken for further analysis.

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

Inclusion criteria
•Age 18 years or older.
•On the waiting list for receiving radiotherapy as preoperative radiotherapy for rectal carcinoma.
•Informed consent

Exclusion criteria

Exclusion criteria
•Diabetes Mellitus.
•Use of corticosteroids or thyroid medication.
•Body Mass Index above 30 kg/m2.
•Participating in another clinical trial.

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-05-2011
Enrollment:	10
Type:	Actual

Ethics review

Approved WMO Date:	22-04-2011
Application type:	First submission
Review commission:	METC Noord-Holland (Alkmaar)

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	NL35378.094.11