Resistance to chemotherapy induced by plasma from healthy volunteers after fish oil consumption

Published: 15-03-2012
Last updated: 26-04-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON38363

Source
ToetsingOnline

Brief title
Fish Oil Volunteer Study

Condition

- Other condition

Synonym
chemoresistance; insensitivity to chemotherapy

Health condition

het gaat hier om gezonde vrijwilligers zonder aandoening.

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Chemotherapy, Fish Oil, Healthy Volunteers, Resistance

Outcome measures

Primary outcome

Primary endpoint:

To determine the level of 16:4(n-3) in plasma withdrawn from volunteers that

have ingested fish oil or fish.

Secondary outcome

Secondary endpoint:

The ability of plasma withdrawn from volunteers that have ingested fish oil or

fish to induce resistance in an in vitro tumor cell culture, or in vivo in

mouse models.

Study description

Background summary

In previous preclinical studies from our lab, mesenchymal stem cells have been shown to be involved in chemoresistance by secreting two specific fatty acids KHT and 16:4(n-3). These fatty acids are present in human plasma and increase after chemotherapy exposure. In a preliminary analysis this increase has been shown to correlate with therapy response. Moreover, patient plasma containing elevated levels of 16:4(n-3) can induce resistance to chemotherapy in an in vitro tumor cell line.

Mass spectrometry analysis has shown that these two fatty acids are abundantly present in fish oil, which is often used by cancer patients due to its presumed beneficial effect. We found that fish oil can induce chemoresistance in

preclinical mouse studies.

Very recently we have also found that certain species of fish contain hight levels of these 'bad fatty acids', specifically herring and mackerel. In this study, we would therefore like to study the effect of fish consumption on plasma levels of these fatty acids.

We hypothesize that consumption of fish oil or fish can induce resistance to chemotherapy by upregulating plasma levels of KHT and 16:4(n-3). The next step to test this hypothesis in a human situation is by performing a study in healthy volunteers.

Study objective

The objective of this study is to determine whether oral intake of commercially available fish oil or fish induces a rise in plasma levels of KHT and 16:4(n-3), and whether this plasma can thereby induce chemoresistance in an in vitro tumor cell culture and in in vivo mouse models.

Study design

Healthy volunteers who are willing to participate and who signed informed consent will receive 5x the advised daily dose of fish oil for oral intake. An infuse will be placed and blood will be withdrawn from the infuse 7 times. The infuse will be removed at the end of the day. The next day, the volunteer will come back to the hospital for a venapuncture 24 hours after fish intake. In total, a volume of 47.5 ml blood will be collected.
Analysis of 16:4(n-3) levels will be performed by mass spectrometry, and plasma will be added to in vitro immortalized tumor cell cultures and in vivo in mouse models, together with chemotherapy, to determine the degree of resistance by counting the number of tumor cells after 24 hours of treatment.

Intake fish oil after t=0 blood sampling
t=0 2 CPT 8 ml 16:4(n-3) levels, KHT levels, resistance in in vitro tumor cel cultures and in vivo mouse models
t=0.5 uur 1 citrate 4.5 ml 16:4(n-3) levels, KHT levels, resistance in in vitro tumor cel cultures and in vivo mouse models
t=1 uur 1 citrate 4.5 ml 16:4(n-3) levels, KHT levels, resistance in in vitro tumor cel cultures and in vivo mouse models
t=2 uur 1 citrate 4.5 ml 16:4(n-3) levels, KHT levels, resistance in in vitro tumor cel cultures and in vivo mouse models
t=4 uur 1 citrate 4.5 ml 16:4(n-3) levels, KHT levels, resistance in in vitro tumor cel cultures and in vivo mouse models
t=6 uur 1 citrate 4.5 ml 16:4(n-3) levels, KHT levels, resistance in in vitro tumor cel cultures and in vivo mouse models
t=8 uur 1 citrate 4.5 ml 16:4(n-3) levels, KHT levels, resistance in in vitro

tumor cel cultures and in vivo mouse models
t=24 uur 1 citrate 4.5 ml 16:4(n-3) levels, KHT levels, resistance in in vitro tumor cel cultures and in vivo mouse models

Total
8 9 47.5 ml

When we find differences in FFA levels, or resistance either in vitro or in vivo in an internal interim analysis, there will be a follow-up with the recommended daily amount of fish oil. In addition, fish intake will be tested. This will be doen in the different volunteers with intervals of at least two weeks.

Intervention

The intervention is this study is intake of fish or fish oil at T0.
Volunteers will be randomly assigned to one of three fish oil brands, or to each of the fish species.

Study burden and risks

The burden for the volunteers is that blood withdrawal will take place in the hospital. This means that the volunteers will have to spend 8.5 hours in the hospital, in which 7 blood withdrawals will be performed via an infuse needle. In case of fish intake, the volunteer will come to the hospital the next day as well for a venipuncture 24 hours after fish intake. This will take approximately 15 minutes.

During the day, the volunteer is not expected to stay in the same location, only at times of blood withdrawal will he/she be expected to be present.

Placing of an infuse needle and venapunction can result in an haematoma. Further risks are minimal.
Fish oil and fish consumption is not expected to lead to any side effects.

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

1. The volunteer must be >= 18 years of age
2. The volunteer must be healthy, meaning:
* no history of diabetes mellitus
* no history of immune disorders
* no history of hypercholesterolemia
* no use of anti-coagulant medication
* no breast feeding
* no allergy to fish or related products
3. The patient may not have used fish oil products within 2 weeks before start of the study
4. The patient may not have eaten a fish meal within 1 week before the start of the study
5. The patient must have given written informed consent

Exclusion criteria

Any other condition by which the volunteer does not meet the inclusion criteria.

Study design

Design

Study type: Interventional

Masking:	Single blinded (masking used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	11-04-2012
Enrollment:	28
Type:	Actual

Ethics review

Approved WMO Date:	15-03-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	29-08-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL37645.041.12