An open-label, randomized, single center, crossover study in healthy participants to assess lipoprotein lipase activity and levels, and triglyceride levels after heparin exposure, in both fasted and postprandial state

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Ethical review	Approved WMO
Status	Completed
Health condition type	Vascular disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON50416

Source
ToetsingOnline

Brief title
Investigation of biomarkers after heparin use

Condition

- Vascular disorders NEC

Synonym
cardiovascular disease

Research involving

Human

Sponsors and support

Primary sponsor: Novo Nordisk
Source(s) of monetary or material Support: Pharmaceutical industry

Intervention

Keyword: Biomarker, Heparin

Outcome measures

Primary outcome

To assess lipoprotein lipase (LPL) activity, LPL levels, and triglyceride (TG)

levels after heparin exposure in both fasted and postprandial state.

Secondary outcome

To assess levels of apolipoprotein CII (APOCII), apolipoprotein CIII (APOCIII),

total cholesterol, and free fatty acids (FFAs), and to assess the lipoprotein.

Study description

Background summary

Heparin is no new compound; it is a registered drug that is used to prevent the formation of blood clots. It is used to treat and prevent blood clots caused by certain medical conditions or medical procedures. It is also used before surgeries to reduce the risk of blood clots.

In this study, heparin is used to release more lipoprotein lipase in the blood stream.

Study objective

In this study we will investigate biomarkers in blood after exposure to heparin in the fasted state or after a high-fat meal. Biomarkers are proteins present in the blood. The biomarkers investigated in this study are proteins that are involved in the metabolism and transport of lipids in the blood. Disrupted activity of these biomarkers affects energy balance in the body, insulin

action, body weight maintenance, and cardiovascular disease risk. The main biomarkers that will be investigated in this study are lipoprotein lipase and triglycerides. It is known that following heparin administration, an increased amount of lipoprotein lipase is released in the blood stream which has effects on other specific biomarkers. However, the difference in the effects on lipoprotein lipase and other biomarkers between administration of heparin in the fasted state or after a high-fat meal has not been well-studied up to date. Therefore, the current study will be conducted.

Heparin will be administered as an intravenous injection in this study. In this study, the effects of administration of heparin will be compared with the effects of administration of normal saline which will also be administered as an iv injection. Normal saline is a mixture of salt and water and is commonly used in infusions in hospitals. Normal saline has no effect on the biomarkers that will be investigated in this study. Please note that when the term *study compound* is used in this document, we mean heparin, normal saline, or both.

Study design

For the study it is necessary that the volunteer stays in the research center for 1 period of 7 days (6 nights). The volunteer is expected at the research center at 14:00 h in the afternoon prior to Day 1, the day of first administration of the study compound. The time of entry may be changed. If this happens the volunteer will be informed about it in advance. The volunteer will leave the research center in the afternoon of Day 6 of the study.

Below an overview of the days of visit and stay at the research center:

Screening:
On a day between Day -21 and Day -2

Arrival:
Day -1

In-house stay:
Day -1 up to Day 6

Departure:
Day 6

Telephonic follow-up:
On a day between Day 11 and Day 14

The volunteer will get heparin and normal saline administered as an iv injection in the fasted state and after a high-fat meal.

There will be 2 groups and both groups will receive 6 treatments in a different

order. You will be assigned to 1 of these groups; this will be determined by chance.

The treatments per group per day are as follows:

Group 1
Day
Treatment
When Nutritional state
1 25 international units per kilogram body weight (IU/kg) heparin
Morning After a high-fat meal
2 25 IU/kg
heparin
Morning Fasted
3 Normal
saline
Morning Fasted
4 50 IU/kg
heparin
Morning After a high-fat meal
5 50 IU/kg
heparin
Morning Fasted
6 Normal
saline
Morning After a high-fat meal

Group 2
Day
Treatment
When Nutritional state
1 50 IU/kg
heparin
Morning After a high-fat meal
2 50 IU/kg
heparin
Morning Fasted
3 Normal
saline
Morning Fasted
3 25 IU/kg
heparin
Morning After a high-fat meal
4 25 IU/kg
heparin
Morning Fasted
5 Normal

saline
Morning After a high-fat meal

When the study compound will be administered in the fasted state in the morning (Days 2, 3, and 5), this will take place after you have fasted for at least 10 hours prior to administration of the study compound.

When the study compound will be administered after a high-fat meal in the morning (Days 1, 4 and 6), this will take place after you have fasted for at least 10 hours prior to the start of the high-fat meal. The study compound will then be administered at 30 minutes after the start of the high-fat meal.

Study burden and risks

Drawing blood may be painful or cause some bruising. The use of the indwelling cannula can sometimes lead to inflammation, swelling, hardening of the vein, blood clotting, and bleeding in the environment of the puncture site. In some individuals, a blood draw can sometimes cause pallor, nausea, seating, low heart rate, or drop in blood pressure with dizziness or fainting.

In total, we will take about 492 mL of blood from the volunteer from screening to discharge. This amount does not cause any problems in adults. To compare: a blood donation involves 500 mL of blood being taken at once each time. If the investigator thinks it is necessary for the safety of a participant, extra samples might be taken for possible additional testing. If this happens, the total amount of blood drawn may be more than the amount indicated above.

Heart tracing
To make a heart tracing, electrodes (small, plastic patches) will be placed on arms, chest and legs. Prolonged use of these electrodes can cause skin irritation (rash and itching).

High-fat meals/Fasting
The volunteer has to be able to consume a high-fat meal completely in the morning of 3 different days. The high-fat meal contains eg, 2 fried eggs, fried potatoes, bacon, and 2 slices of (toasted) (wheat) bread with margarine. The volunteer must consume the whole meal within 20 minutes. It can be difficult to consume the entire meal, particularly for light eaters.

The fasting for a prolonged time during the study may lead to symptoms such as dizziness, headache, stomach upset, or fainting.

Coronavirus test
Samples for the coronavirus test will be taken from the back of the nose and throat using swabs. Taking the samples only takes a few seconds, but can cause discomfort and can give an unpleasant feeling. Taking a sample from the back of the throat may cause the volunteer to gag. When the sample is taken from the

back of the nose, the volunteer may experience a stinging sensation and the eyes may become watery.

Contacts

Public
Novo Nordisk

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DK
Scientific
Novo Nordisk

Novo Allé
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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. Informed consent obtained before any study-related activities. Study-related activities are any procedures that are carried out as part of the study, including activities to determine suitability for the study.
2. Healthy male or female, aged 18 years to 65 years (both inclusive) at the time of signing informed consent.
3. Body mass index 18.0 kg/m2 to 29.9 kg/m2 (both inclusive) at the time of signing informed consent.
4. Body weight >=50 kg at the time of signing informed consent.

5. Considered to be generally healthy as judged by the Investigator, as defined by the absence of any clinically significant, active, or chronic disease evidenced by a detailed medical and surgical history and a complete physical examination including vital signs, 12 lead ECGs, hematology, clinical chemistry, coagulation, urinalysis, and serology.

Exclusion criteria

1. Previous participation in the current study.
2. Employee of PRA or the Sponsor.
3. History of relevant drug and/or food allergies.
4. Known or suspected allergy to study drug-related products, including heparin or pork products.
5. Using tobacco products within 60 days prior to the first drug administration.

Study design

Design

Study type:	Observational invasive
Intervention model:	Crossover
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	17-12-2021
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Heparin

Generic name:	N/A
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	16-11-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-12-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	18-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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
EudraCT	EUCTR2021-005899-18-NL

Register	ID
CCMO	NL79639.056.21
Other	U1111-1270-0957

Study results

Date completed: 16-01-2022

Results posted: 12-10-2022

First publication
02-09-2022