Intranasal LMWH against COVID-19

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON28133

Source
NTR

Brief title
Intranasal LMWH against COVID-19

Health condition

COVID-19

Sponsors and support

Primary sponsor: ZonMW
Source(s) of monetary or material Support: ZonMW

Intervention

Outcome measures

Primary outcome

Primary endpoints: We investigated whether inhalation of enoxaparin by human study participants blocks binding of SARS-CoV-2 to human nasal epithelial cells. Binding of both SARS-CoV-2 pseudovirus (pg/mL) and the authentic virus, hCoV-19/Italy (TCID/ml) to nasal epithelial cells obtained from volunteers after their nasal cavity was exposed to either LMWH enoxaparin or placebo (saline NaCl 0,9%).
Pseudovirus binding was detected by p24 ELISA whereas authentic SARS-CoV-2 binding was detected by RT-PCR measurement of ORF1b/GAPDH.

Timepoints: Virusbinding happens on the same day as cells are obtained from study participants to ensure maximum viability of cells, virus exposure happens for 4 hours at 4C after which all cells are lysed to prevent further infection.

Secondary outcome

Secondary endpoints: We characterized the nasal cell populations and the effect on inhalation on lymphocyte influx, as well as on expression of ACE-2 and heparan sulfates. We investigated the effectiveness of inhalation of enoxaparin by comparing inhalation with in vitro addition of enoxaparin prior to SARS-CoV-2 binding.

Timepoints: Phenotyping happens the same day that cells are obtained from study participants to ensure maximum viability of cells.

Study description

Background summary

SARS-COV-2 utilise various receptors on the human cell surface to facilitate virus-binding and cellular entry. While angiotensin converting enzyme 2 (ACE-2) has been known for a long time little is understood about other receptors. Syndecans are transmembrane receptors that have, according to published work in the AMC, a role in viral-binding and cellular infection similar to ACE-2 (for SARS-CoV-2 they are required as a co-receptor for infection via ACE-2). Syndecans are (made up of) heparansulfates, which provides with an interesting mechanism for potential virus block.
Low molecular weight heparins (LMWHs), which have been extensively used in the clinic as anticoagulants are chemically speaking very similar. Previous (unpublished) works by the department of experimental immunology in the AMC Amsterdam has shown that on cell lines LMWHs can be used to prevent virusbinding by SARS-CoV-2 through competitive agonism. We hypothesise that LMWHs can offer a similar protection in vivo when applied to the nasal epithelium, thereby providing an effective, cheap and safe prevention against infection from SARS-CoV-2, or similar virusses.

Study objective

Low molecular weight heparins able to block virusbinding from SARS-CoV-2 ex-vivo through competitive agonism, our hypothesis is that applying LMWHs using a spray to the nasal epithelium offers similar protection as has been previously observed in primary cells and cell lines.

Study design

Medication is given sequentially every 10 minutes over a period of 30 minutes.
Cells are withdrawn after 30 minutes, stored in medium to keep the populations healthy and

brought to a BSL-3 lab where virus exposure occurs. Viral binding occurs for 4 hours after which all cellular material is lysed to prevent further binding.

Intervention

Intervention medication: 4500IE enoxaparin (in 300uL solution)
Control medication: NaCl 0,9% (in 300uL water)

Contacts

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Eligibility criteria

Inclusion criteria

In order to be eligible for participation, a participant must:
- be able to provide written informed consent (Verbal informed consent or deferred informed concent will be used for the initial screening visit, where written informed consent will be obtained).
- be physically healthy (as defined by not suffering from any illness or disease obstructing general daily functioning)
- be aged between 18 – 65 years
- be sufficiently well versed in the Dutch language, subject to the opinion of the Investigator

Exclusion criteria

If any of the following apply to someone wishing to participate, he/she is rendered ineligible for participation, a participant:
- is unlikely to comply with study procedures, as deemed by the recruiting research doctor/nurse

- has mental disorders that in the view of the investigator would interfere with adherence to study procedures or might impair a decision to participate in the study
- has a known allergy or intolerance to LWWH or heparine-related products, as well as a medical history of heparine inducted thrombocytopenia (HIT).
- has any relevant clinical medical condition that is in the opinion of the investigator to make a volunteer unsuitable for participation in the study (under which underlying haematological disorders or bleeding disorder.
- has (anamnestic) evidence of a respiratory infection in the 4 weeks prior to enrolment.
- has a tympanic temperature exceeding 38,5 degrees Celsius during the screening and clinical visits.
- has frequent nosebleeds (>1/ month).

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	20-01-2021
Enrollment:	34
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Plan description
Individual patient data will not be shared to be traceable back to the individual volunteer, this has been chosen to preserve privacy. General patient characteristics will de displayed using a baseline table, as every patient in the intervention group delivers both a placebo and a medication sample diversity between groups is considered to be negligible.

Anonymised viral binding data will be displayed using a patient trial number to, in published

data, compare cells treated with enoxaparin or placebo medication.

Ethics review

Positive opinion

Date:	04-02-2021
Application type:	First submission

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
NTR-new	NL9430
Other	METC AMC : METC 2020_223

Study results

Summary results
none yet