Immunity after yellow fever vaccination in travelers using immunosuppressive medication-YETI study

Published: 10-07-2012
Last updated: 15-05-2024

To compare: - the rate of local and systemic adverse events- height and duration of antibody presence using the plaque reduction neutralization test; - The number of yellow fever specific CD8+ T cells in peripheral blood mononuclear cells (PBMCs);...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Viral infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON37037

Source
ToetsingOnline

Brief title
YETI

Condition

- Viral infectious disorders

Synonym
Yellow Fever infection

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Immunosuppressive medication, Travelers, Yellow Fever vaccination

Outcome measures

Primary outcome

The number of yellow fever specific CD8+ T cells in peripheral blood

mononuclear cells (PBMCs)

Secondary outcome

Height and duration of antibody presence using the plaque reduction

neutralization test;

Rate of local and systemic adverse events

Study description

Background summary

The 17D-Yellow Fever vaccine is a live attenuated vaccine. The vaccine has been proven safe and effective; however, in the immunosuppressed, there is a theoretical risk of severe adverse events (SAEs), such as neuroinvasion and encephalitis (1,2). The exact pathogenicity of these SAEs has not been elucidated up to date. Possibly, they are the result of an impaired immunologic host response, resulting in an increased replication of the virus.

Two recent studies on immunocompromised patients who received yellow fever vaccinations showed that a total of 89 patients using immunosuppressive drugs did not experience adverse events at a higher rate compared to healthy vaccinees (3, 4).
However, SAEs happen at very low rates; 0.4/100.000 vaccinees develop yellow fever vaccine associated viscerotropic disease (YEL-AVD), which resembles the clinical course of yellow fever infection, and 0.8/100.000 develop yellow fever vaccine associated neurotropic disease (YEL-AND) (5). Therefore, the numbers of vaccinees in these studies are too small to draw any conclusions from.

Antibody responses were not measured in these studies. Previous studies on HIV positive patients show lower rates of those with protective neutralising antibodies (NA), and lower geometric mean titers (GMTs) of antibodies compared

to healthy controls (6).

We know that in the response to yellow fever 17D infection, a cascade of immunologic responses ensues. This is initiated by the formation of TNF alpha and type I interferons after binding to toll like receptors (TLRs) 2,7,8 and 9 (7, 8, 9, 10). Through stimulation of TLRs, both cellular (through Th1 cells) and humoral (through Th2 cells) responses are triggered. Immune suppressive medication interferes with this immune response in various ways.
In healthy vaccinees, we know that antibodies are present for several decades (Plotkin). However, this response is possibly of a shorter duration in patients using medication which suppresses the immune response. Depending on the type of immune suppressive, immunologic memory might be supressed as well.

Local as well as systemic adverse events were lower in a population of elderly vaccinees compared to young vaccinees (11), even though severe adverse events are known to occur more often in the group of elderly subjects. Possibly, an impaired initial response results in lower rates of local adverse events.

In this study we set out to retrospectively investigate the immunologic response and the rate of adverse events in those using immunosuppressive medication who have inadvertently received a yellow fever vaccination.

Study objective

To compare:
- the rate of local and systemic adverse events
- height and duration of antibody presence using the plaque reduction neutralization test;
- The number of yellow fever specific CD8+ T cells in peripheral blood mononuclear cells (PBMCs);
in various groups of immune suppressive medication to healthy vaccinees, vaccinated with the 17D-YF vaccine, so that:
- an assessment of the duration and height of immunologic response can, and thus the effect of the immune compromising condition on the vaccination, be made,
- advice can be formulated for future accidental vaccinations, and
- insight in the immunologic responses of various groups of immunosuppressive medication can be gained.

Hypotheses

- The height and duration of the immune response, the longevity of immunologic memory and the rate of adverse events differ more from that of the healthy control group as the dose of immunosuppressive medication rises.

- Patients using low-doses of immunosuppressive medication (prednisolone (<20 mg/day), but also methotrexate, (<0.4 mg/Kg/week), azathioprine (<3.0

mg/Kg/day), or 6-mercaptopurine (<1.5 mg/Kg/day)), have an equal height and duration of antibodies and an equal immunologic memory response, and a comparable rate of adverse events. These groups can be regarded as healthy vaccinees.

Study design

Observational case-control study.

Study burden and risks

Burden and risks:
Volunteers have a risk of bruising/a sore arm following venapunction, and they shall be asked to visit the hospital which will cost time.
Benefit and group relatedness:
Volunteers shall be aware of their immune status (whether or not they are protected against yellow fever).
In the long term, larger groups of patients using immunosuppressives shall be better informed of their duration of protection after a yellow fever vaccination.

Contacts

Public
Academisch Medisch Centrum

Meibergdreef 9
1100 DD Amsterdam
NL
Scientific
Academisch Medisch Centrum

Meibergdreef 9
1100 DD Amsterdam
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

> 18 years
Having been administered a Yellow Fever vaccination

Exclusion criteria

< 18 years
Vaccination admnistered > 20 years prior

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	06-08-2012
Enrollment:	75
Type:	Actual

Ethics review

Approved WMO Date:	10-07-2012
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

ID: 20476
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL40560.018.12
OMON	NL-OMON20476