INFLUENZA VIRUS INFECTIONS IN TRANSPLANT RECIPIENTS: A MULTICENTER REGISTRY

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Viral infectious disorders
Study type	Observational invasive

Summary

ID

NL-OMON35721

Source
ToetsingOnline

Brief title
AST Influenza

Condition

- Viral infectious disorders

Synonym
Influenza infection, virus infections

Research involving
Human

Sponsors and support

Primary sponsor: University of Alberta
Source(s) of monetary or material Support: Grant van de Canadese overheid

Intervention

Keyword: Antiviral resistance, Antiviral therapie, Influenza, Organ transplant

Outcome measures

Primary outcome

The primary study endpoint is value of the Quantitative influenza PCR assay

from NP swabs at the 6 measuring points as a measure for viral shedding after

infection.

Secondary outcome

Secondary endpoints include

- immune response to Influenza at 4 and 6 weeks after infections

- viral resistance testing at first and last positive swab

- Subtyping of influenza virus

Study description

Background summary

There is limited prospective data on influenza infections in transplant recipients. However, influenza can be a significant cause of morbidity and mortality in some organ transplant populations. Reported attack rates have varied considerably and are likely due to differences in transplant populations, immunosuppression protocols, exposures, and type and virulence of circulating influenza viruses. Complications of influenza infection appear to be common in hematopoietic stem cell transplant (HSCT) and solid organ transplant (SOT) populations. There appears to be a relatively high rate of progression to viral pneumonia in some reports especially in lung transplant recipients and HSCT recipients. In one study of organ transplant recipients over a 10-year period, the rate of influenza infection ranged from 2.8 cases/1000 person years (liver transplant) to 41.8 cases/1000 person years (lung transplant). Complications including secondary bacterial pneumonia (17%) as well as extrapulmonary complications such as myocarditis, and myositis were observed. This is in contrast to a report by Ljungman et al. of 12 influenza cases in renal transplant recipients. Only one patient developed viral

pneumonia and one had bronchitis. The remaining 10 patients recovered without complications.

The largest study in the SOT population was done during 2009-2010 outbreak of pandemic H1N1 by the American Society of Transplantation (AST) H1N1 Collaborative Group. This was a retrospective review of 237 patients with pandemic H1N1 infection and included both adults and pediatric patients. The majority of the patients reported in the study were hospitalized (70%) and 15% were admitted to the intensive care unit. Approximately one-third of patients had pneumonia at presentation. Death occurred in 4% of patients. Early initiation of antiviral therapy was associated with decreased hospitalization, ICU admission and a lower risk of death.

Despite the recognized importance of influenza in transplant patients, there is actually very limited prospective data. This registry will represent the largest prospective data collection on influenza in transplant patients and will provide invaluable data on the clinical presentations, antiviral efficacy and other parameters related to influenza.

Study objective

• Our purpose is to prospectively characterize influenza infections over a 3 year period in transplant patients using a registry system.
• We plan to generate robust data on clinical features of upper and lower respiratory disease, antiviral therapy and its effects on disease outcome, as well as quantitative virologic data on shedding and antiviral resistance.
• We also will study the long term sequelae of influenza infections and look at development of rejection.

Study design

This will be a prospective, multi-center study conducted at investigator sites who comprise the Influenza in Transplant collaborative study group. This includes over 30 centers from across North America and Europe. The co-ordinating center will be the University of Alberta. We will aim to enrol 300 patients in the registry over a 3 year period.

The following information will be gathered:

a) Clinical Information
- Baseline demographic information about the transplant (including immunosuppression, graft function)
- Comorbidities such as diabetes, obesity, chronic lung disease
- Symptoms of infection, radiologic features of infections
- Antiviral use
- History of vaccination

- Outcomes such as hospitalization, ICU admission, mechanical ventilation, death
- Long term outcomes: allograft function, chronic respiratory disease
- Laboratory parameters including lymphocyte count, immunoglobulin levels, renal function
- Adverse events - all serious adverse events occurring during the study (till day 180) will be reported. These include: a) hospitalization; b) congenital deformity; c) death; d) disability; and e) other adverse events the investigator considers serious. Pregnancy during the follow-up period will also be reported.

b) Virology
- Method of diagnosis (DFA, viral culture, PCR)
- Subtype of influenza virus (ie HxNx)
- Viral Shedding by serial NP swabs at day 0 (diagnosis), 3, 6, 11, 18, 28 (weekly thereafter if shedding persists)
- Quantitative PCR of NP swabs (centrally at University of Alberta)
- Antiviral resistance testing at first and last positive swabs

c) Immunology
- Serum collection at disease onset and 4-6 weeks afterwards for
o Serology against circulating influenza viruses
o Production of HLA alloantibodies

Study burden and risks

Possible Benefits:
It is not known whether there will be direct benefit from being in the study. However, the information learned in this study may help other patients with similar conditions in the future.

Possible Risks:
Taking blood is briefly uncomfortable, but not dangerous. When having blood drawn, participant may have some bruising where it is taken. This may take several days to go away. Every effort will be made so that blood will be collected for the study at times when subjects are having other routine blood tests.

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

Liver transplanta patients on at least one immunosuppressive medication

Exclusion criteria

Unable to provide informed consent

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	20
Type:	Anticipated

Ethics review

Approved WMO

Date:	22-12-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	NL38285.058.11