Release of endogenous ligands of Toll-like receptors type 4 during mechanical ventilation in surgical patients with healthy lungs

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Primary objective is to show the presence of endogenous ligands of TLR4 in the lung of patients being mechanically ventilated in a standardised way with clinical parameters. Secondary objective is to investigate the amount of endogenous ligands of...

Ethical review	Approved WMO
Status	Pending
Health condition type	Immune disorders NEC
Study type	Observational invasive

Summary

ID

NL-OMON32393

Source
ToetsingOnline

Brief title
Release of endogenous ligands for TLR4 during mechanical ventilation.

Condition

- Immune disorders NEC
- Lower respiratory tract disorders (excl obstruction and infection)

Synonym
ventilator-induced lung injury

Research involving
Human

Sponsors and support

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

Intervention

Keyword: endogenic ligands, mechanical ventilation, TLR4

Outcome measures

Primary outcome

The studied variable is the IL-8 concentration of the HEK293-TLR4 reporter

assay after exposure to bronchotracheal aspirate.

Secondary outcome

Not applicable.

Study description

Background summary

Mechanical ventilation (MV) is commonly used in general anesthesia during surgery or in the critically ill patient at the Intensive Care. Besides the obvious beneficial effects of MV there is increasing evidence that MV worsens lung injury, but can also induce lung injury in healthy lungs. This has been termed Ventilator Induced Lung Injury (VILI). Animal and human research revealed that MV can induce an inflammatory reaction with cytokine release and activation of the innate immune system. Results from our own experimental studies support these findings. Recently it has been demonstrated that the intrapulmonary cytokine release is triggered by the activation of Toll-like receptor 4 (TLR4). This receptor can be triggered by certain endogenous ligands. In animal studies we have found that endogenous ligands of TLR4 are released in response to MV. However, the release of endogenous ligands after MV has never been demonstrated in humans. Finding endogenous ligands of TLR4 after MV gives support to the hypothesis that MV in humans leads to the release of endogenous ligands which triggers the cytokine release.

Study objective

Primary objective is to show the presence of endogenous ligands of TLR4 in the

lung of patients being mechanically ventilated in a standardised way with clinical parameters. Secondary objective is to investigate the amount of endogenous ligands of TLR4 in relation to the duration of mechanical ventilation.

Study design

At defined time points perioperatively (t=0, t=60, t=90, t=120 minutes) the lung is flushed with 10 mL of saline via a suction catheter inserted in the endotracheal tube via a special conduit. Bronchotracheal aspirate is obtained and analysed for the presence of endogenous ligands for TLR4 using a HEK293-TLR4 reporter assay.

Study burden and risks

This study can be completely integrated in regular healthcare. There is no extra time burden for the participating patient. Extra risks for the patient are minimal. A lung lavage with a similar small amount of saline will not impair lung function, especially considering the ASA class (1 or 2) of the participating patients. Furthermore, this procedure is part of regular care at the Intensive Care Unit and is performed by nurses regularly. A standard bronchoalveolar lavage as performed by pulmonologist is done with a volume of up to 400 mL in a specific lobe. Therefore, we deem the risk for patients participating in this study to be minimal.

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

Between 18-65 years old, American Society of Anesthesiologists (ASA) status 1 or 2, ability to speak Dutch, no (N)SAID intake within 36 hours prior to surgery, no history of drug dependency or abus, body weight between 60-100 kg with a BMI <30 kg/m2.

Exclusion criteria

Patients with pulmonary, cardiac, hepatic or renal disease or significant or instable disease of the central nervous system, patients that smoke, use of (N)SAIDs within 36 hours prior to surgery, history of drug dependence or drug abuse, BMI > 30 kg/m2 or <20 kg/m2.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2008
Enrollment:	10

Type:	Anticipated

Ethics review

Approved WMO Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL21222.091.07