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SaDial: the adaptive immune response against Staphylococcus aureus in hemoDialysis patients

Submission date
24/09/2018

Recruitment status
No longer recruiting

Registration date
02/10/2018

Overall study status
Completed

Last Edited
08/05/2019

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Healthy human skin and mucosa is colonized by a variety of protective bacteria and microorganisms. A common component of this skin flora is the bacterium Staphylococcus aureus (S. aureus). Dialysis patients are chronically exposed to S. aureus, due to their frequent stays in dialysis centers, hospitals or rest homes, where this bacterium is common. In dialysis patients, the access point for the dialysis is a potential entry site for S. aureus, in particular when using a central venous catheter instead of an arteriovenous fistula. It has been shown that S. aureus carriers have a lower risk of sepsis in case of an endogenous infection (i.e. by their “own” S. aureus strain).
So far, it has not been possible to develop a vaccine that protects against an infection with S. aureus. The aim of this study is to collect information on the functionality of the immune system in dialysis patients, and a long-term reduction of serious clinical complications due to S. aureus infections.

Who can participate?
Hemodialysis patients in the KfH e.V. outpatient dialysis center in Greifswald, and 20 healthy control patients

What does the study involve?
We will follow a group of 86 hemodialysis patients from an outpatient dialysis center over a 30 month period. We will collect their demographic data and medical history, along with taking blood samples, nasal swabs and swabs from the hemodialysis access site every 6 months. These samples and swabs will be tested for S. aureus. We will then compare this to the results from healthy controls to reveal differences resulting from dialysis. We will also look at connections between demographic data and medical history and S. aureus infection.

What are the possible benefits and risks of participating?
The benefit of participating is that we will identify potential risk factors that make the occurrence of a bacterial infection more likely, especially in dialysis patients. We want to get an overview of the types of bacteria that are involved in infections, and we are also interested in the proportion of resistant S. aureus strains. With this knowledge, we aim to minimize the risk of infection for our patients. There are no known risks of participating in this study.

Where is the study run from?
1. University Medicine Greifswald (Germany)
2. Kuratorium für Dialyse und Nierentransplantation e.V., KfH-Nierenzentrum Greifswald (Germany)

When is the study starting and how long is it expected to run for?
January 2015 to December 2018

Who is funding the study?
1. DAMP Foundation (Germany)
2. University Medicine Greifswald (Germany)

Who is the main contact?
Prof. Dr. med. Sylvia Stracke
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
BB O29/15

Study information

Scientific Title
Mortality and bloodstream infections in hemodialysis patients from an outpatient dialysis center (KfH e.V.) in Greifswald with respect to S. aureus carrier status, colonization density, S. aureus genotyping and host immune response (SaDial-study) compared to the general population of the same geographical region (SHIP-TREND-0)

Acronym

SaDial

Study objectives
1. The S. aureus genotypes in hemodialysis patients differ from the general population due to frequent contact with medical environment
2. Nasal S. aureus colonisation protects hemodialysis patients from fatal outcome in case of bloodstream infection by S. aureus
3. The host immune response against S. aureus in hemodialysis patients predicts the course and the outcome of S. aureus sepsis

Ethics approval required
Old ethics approval format

Ethics approval(s)
University Medicine Greifswald, 17/03/2015, internal registration number: BB O29/15

Study design
Observational prospective cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Other

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Staphylococcus aureus bloodstream infection and S. aureus carrier status in hemodialysis patients

Interventions
A cohort of 86 hemodialysis patients are followed over a 30 month period. Patient demographic data and medical history are collected, followed and statistically evaluated. Blood samples, nasal swabs and swabs from the hemodialysis access site are taken every 6 months for a period of 30 months and are tested for Staphylococcus aureus. The pathogens are cultured and further characterised by spa-PCR and DNA microarrays. Patient samples are analysed for S. aureus-specific antibodies using Luminex, and T-cell responses are analysed using Fluorospot.
20 healthy control patients will receive the same treatment as the cohort of hemodialysis patients; however, swabs and blood and serum samples are only take once in 2015 for this group. There is no follow-up period.

Intervention Type

Other

Primary outcome measure
1. Overall mortality rates, assessed using Kaplan-Meier analysis after the final sampling
2. Course and severity of bloodstream infection, determined by assessing for symptoms such as leukocytosis, fever and systemic inflammatory response syndrome, and a positive test for S. aureus in blood culture. This was assessed at the time of infection, and 7 and 14 days after

Secondary outcome measures
1. S. aureus genotype profiles over time, assessed after each 6 month sampling:
1.1. S. aureus spa-types determined by spa-PCR and out coming sequences classified by Ridom software
1.2. Clonal complexes (CC types) of S. aureus determined using S. aureus Genotyping Kit 2.0 from Alere Technologies (now Abbott)
2. S. aureus specific antibody response over time assessed using a multiplex assay and ELISA, with antibodies isolated every 6 months and stored and overall measurement taken once all samples are collected
3. T-cell response over time, assessed by a Fluorospot assay, with T-cells isolated every 6 months and stored and overall measurement taken once all samples are collected

Overall study start date
01/01/2015

Completion date
31/12/2018

Eligibility

Key inclusion criteria
Patients:
1. Hemodialysis patients of an outpatient dialysis centre (KfH e.V.) in Greifswald
2. Voluntary participation

Controls:
1. Voluntary participation
2. Aged 50-70
3. Renally healthy
4. In hospital for at least 1 week

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
86 hemodialysis patients, 20 renal healthy control patients

Total final enrolment
86

Key exclusion criteria
1. Refusal to participate
2. Moving to another town that is not Greifswald

Date of first enrolment
18/06/2015

Date of final enrolment
01/03/2018

Locations

Countries of recruitment
Germany

Study participating centre
KfH-Nierenzentrum Greifswald
Ferdinand-Sauerbruch-Str.
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Sponsor information

Organisation
Damp Stiftung

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Sponsor type
University/education

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Organisation
University Medicine Greifswald

Sponsor details
Universitätsmedizin Greifswald
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Sponsor type
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Funder(s)

Funder type
Not defined

Funder Name
Damp Stiftung

Funder Name
University Medicine Greifswald

Results and Publications

Publication and dissemination plan
S. aureus carrier rates, genetic studies on S. aureus strains and comparison with the general population are currently being published in a peer-reviewed nephrological journal. Immunological work is planned to be published in the end of 2019 in a high-impact peer-reviewed journal.

Intention to publish date
31/12/2018

Individual participant data (IPD) sharing plan
The data could be made available on request after publication.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	06/05/2019	08/05/2019	Yes	No