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Does the current pneumococcal vaccine prevent experimental nasal carriage with pneumococcal bacteria?

Submission date
18/11/2013

Recruitment status
No longer recruiting

Registration date
18/11/2013

Overall study status
Completed

Last Edited
24/06/2021

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
We are interested in developing new and better ways to protect the body against a bug, or bacterium, called Streptococcus pneumoniae (also known as pneumococcus). In most people pneumococcus can occasionally be found harmlessly inhabiting the nose where it does not cause any problem (pneumococcal carriage). About 10% of adults carry pneumococcus at any one time, and almost all adults experience an episode of carriage at least once per year. Carriage acts as a natural vaccine, boosting immunity against pneumococcal infection in adults and children. There is already a vaccine against pneumococcus called Prevenar-13. It is licensed for use in children and adults aged over 50 and helps prevent sepsis and meningitis, but the vaccines effect on nasal pneumococcal carriage is not understood. The purpose of our study is to understand the impact of Prevenar-13 on pneumococcal carriage in healthy adults.

Who can participate?
Fit and healthy volunteers, not a current regular smoker, and between the age of 18 50 years old.

What does the study involve?
If you agree to take part you will be participating for up to 21 weeks. Over this period you will be asked to visit the clinical research facility up to 10 times. Initially we will screen volunteers for natural carriage of pneumococcus and take samples of blood (up to 40 ml = eight teaspoons), saliva and urine (up to 50 ml = ten teaspoons). These samples will be compared with consequent samples. Volunteers will be randomly allocated to receive the Pneumococcal Conjugate Vaccine (Prevenar-13) [test group] or the hepatitis A vaccine (Avaxim) [control/comparator group]; you will not be informed which vaccine you receive until the end of the study. You will be offered a complete course of the hepatitis A vaccine at the end of the study if you wish. We will inoculate small doses of bacteria into the nostrils of volunteers. We will then collect samples from these volunteers in order to answer questions about immune defence and then use the information in our work to develop a better vaccine to protect against pneumonia. The samples we collect will

include upper airway (nasal wash, throat swab and saliva) and systemic (blood, urine) samples relevant to defence against infection. Lower airway (bronchoscopy and lavage) samples may be collected (optional).

What are the possible benefits and risks of participating?
The only direct medical benefit of taking part in this study is that you will have the opportunity to receive a full course of hepatitis A vaccine free of charge. You will be a valuable part of a research study that we hope will eventually lead to the development of a new vaccine against pneumonia. Both vaccines used in this study are licensed vaccines; however, Prevenar-13 is not licensed for use in healthy adults aged 18-50. The current license is only for children and adults over 50. The safety of these vaccines has been assessed in different clinical studies in which several thousand healthy adults received the vaccines. If you receive the hepatitis A vaccine, around 10% of people who receive this vaccine experience mild reactions. The most commonly reported adverse reactions include headache, mild fever and muscle ache. If you receive Prevenar-13, the most commonly reported adverse reactions include swelling and redness at the injection site (10%) and low-grade fever (1%). A rare but important adverse reaction is bronchospasm (wheezing and breathlessness) and facial oedema; this may require treatment and possible hospitalisation. No other serious side effects have been reported. Since the effects of the Prevenar-13 and Avaxim on the unborn child are not known, for this reason you or your partner must not become pregnant whilst taking part in this study. Women who are pregnant may not participate in this study. We do not expect that carrying the bacteria in your nose will cause any illness in you or your contacts but this is one of the reasons we want to make sure you are healthy (with a good immune system) before taking part and we will not recruit people in close contact with young children or vulnerable adults.

Where is the study run from?
The study is run from the clinical research facility at the Royal Liverpool University Hospital trust, Liverpool, UK.

When is the study starting and how long is it expected to run for?
The study started in September 2013 and is expected to run for 9 months.

Who is funding the study?
The study is funded by the Bill and Melinda Gates Foundation Grand Challenges Expedition II.

Who is the main contact?
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Contact information

Type(s)
Scientific

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Clinical Trials Information System (CTIS)
2012-005141-20

Protocol serial number
13932

Study information

Scientific Title
Pneumococcal Conjugate Vaccine (PCV-13) and Experimental Human Pneumococcal Carriage Study (EHPC) Study

Acronym
PCV and EHPC

Study objectives
The purpose of our study is to refine a research model for vaccine effect testing. In our previous studies, we demonstrated that nasal pneumococcal carriage could be reproducibly achieved in healthy adult volunteers without adverse events. The dose-response curve allowed prediction of a 30-60% endpoint enabling combined testing for benefit and harm for our future vaccine studies.

Healthy non-smoking volunteers, who meet the study inclusion / exclusion criteria are recruited, then randomised to receive either protein-conjugated pneumococcal polysaccharide-13 (referred to as PCV) or Hepatitis A (Avaxim) vaccination. This vaccine has been chosen due to its safety profile, preparation (contains alum as does PCV which may be immunogenic), lack of effect on nasal colonisation/immunity and health benefit for those involved in the study if the volunteer travels to endemic areas in the future.

Natural carriage volunteers (screened by nasal wash) will continue in the study. We expect 10-15% to be natural pneumococcal carriers. 5-12 weeks after vaccination (to which both the volunteer and study team are blinded) the volunteers will be inoculated with 0.1ml of a well-characterised penicillin-sensitive pneumococcus (serotype 6B) to each nostril at 80,000 cfu /nostril. The volunteers will be observed for the development of pneumococcal carriage through urine, saliva, blood and nasal wash samples.

Volunteers will be offered bronchoscopy and bronchoalveolar lavage (BAL) to determine lower airway mucosal responses potentially protective against pneumonia.

This model will be used to understand the impact of PCV on pneumococcal carriage in healthy adult humans.

Volunteer samples pre and post vaccination, and comparison of the immune response of colonised versus non-colonised subjects and the PCV vaccinated and alternate vaccinated subjects will provide new information on the innate, cellular and immune response to PCV vaccination and pneumococcal colonisation.

More details can be found at: http://public.ukcrn.org.uk/search/StudyDetail.aspx?StudyID=13932

Ethics approval required
Old ethics approval format

Ethics approval(s)
REC Liverpool East, December 2012, 12/NW/0873

Study design
Randomised interventional trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Topic: Infection; Subtopic: Infection (all Subtopics); Disease: Infectious diseases and microbiology

Interventions
Inoculation, All volunteers will be intranasally inoculated with pneumococcal bacteria (6B 0.1ml per naris)

Vaccination, Volunteers will be randomly allocated to receive either Hepatitis A vaccine (Avaxim) or Pneumococcal Conjugate Vaccine (Prevnar 13).

The study team and volunteer will be blinded to the vaccination.

Follow Up Length: 3 month(s)

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Hepatitis A vaccine (Avaxim) or Pneumococcal Conjugate Vaccine (Prevnar 13)

Primary outcome(s)
Pneumococcal bacteria detected by classical microbiology at either day 2, 7, 14 or 21 post inoculation

Key secondary outcome(s))

1. Pneumococcal bacteria detected by qPCR at either day 2, 7, 14 or 21 post inoculation
2. Pneumococcal bacteria density at day 2, 7, 14 or 21 post inoculation
3. Pneumococcal bacteria duration of carriage as shown by detection at day 2, 7, 14 or 21 post inoculation

Completion date
13/08/2014

Eligibility

Key inclusion criteria
1. Adults, male and female aged 18-50 years old (chosen to minimise the risk of pneumococcal infection post inoculation).
2. Fluent English spoken (to ensure a comprehensive understanding of the research project and their involvement this is predominately for safety reasons).

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
50 years

Sex
All

Key exclusion criteria
1. Previously received PPV or any PCV vaccines (at any age) full vaccine history obtained from General Practitioner as necessary
2. Previously lived in a hepatitis A endemic area
3. Previously received a complete course of hepatitis A vaccination
4. Previous significant adverse reaction to any vaccination/immunisation
5. Close contact with at risk individuals (children, immunosuppressed adults, elderly, chronic ill health) to minimise risk of pneumococcal transmission
6. Current smoker or significant smoking history (>10 pack yrs) to minimise risk of pneumococcal infection and optional bronchoscopy
7. Asthma (on regular medication) or respiratory disease to minimise risk of bronchoscopy or pneumococcal infection
8. Pregnancy to minimise risk of pneumococcal infection and no safety data exists for either vaccine in pregnancy
9. Breast-feeding mothers no safety data exists for either vaccine in pregnancy

10. Women of child-bearing potential (WOCBP) who are deemed not to have sufficient, effective birth control in place for 1 month prior to vaccination and 1 month after the final vaccination
11. Allergic to penicillin/amoxicillin
12. Involved in another clinical trial unless observational or in follow-up (non-interventional) phase
13. Previously been involved in a clinical trial involving experimental human pneumococcal carriage
14. Unable to give fully informed consent
15. Medication that may affect the immune system (e.g. steroids, steroid nasal spray)
16. Current acute severe febrile illness at the time of vaccination/inoculation.

Date of first enrolment
13/08/2013

Date of final enrolment
13/08/2014

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
School of Tropical Medicine
Liverpool
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Sponsor information

Organisation
Royal Liverpool and Broadgreen University Hospitals NHS Trust (UK)

ROR
https://ror.org/009sa0g06

Funder(s)

Funder type
Charity

Funder Name
Bill and Melinda Gates Foundation (UK)

Alternative Name(s)
Bill & Melinda Gates Foundation, Gates Foundation, Gates Learning Foundation, William H. Gates Foundation, BMGF, B&MGF, GF

Funding Body Type
Government organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		22/06/2021	24/06/2021	Yes	No
HRA research summary			28/06/2023	No	No
Other publications	Thorax ;69:A2	01/12/2014		Yes	No