ISRCTN16993271 https://doi.org/10.1186/ISRCTN16993271

The effect of live attenuated inactivated influenza vaccine on experimental human pneumococcal carriage study

Submission date
02/09/2015

Recruitment status
No longer recruiting

Registration date
04/09/2015

Overall study status
Completed

Last Edited
21/10/2019

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
Secondary bacterial infections such as pneumococcal pneumonia are a leading cause of death during influenza epidemics. Individuals recently infected with influenza become more susceptible to pneumonia, an effect associated with an increased number of pneumococcus (bacteria causing pneumonia) in the nose (pneumococcal carriage) and uncontrolled inflammatory immunological responses. The interaction between influenza virus and pneumococcus has been known and well documented. Recent works have shown that the Live Attenuated Influenza Vaccine (LAIV) increases pneumococcal carriage in murine models (mice /rats). These results highlighted the potential effect of mass immunization of children with LAIV on pneumococcal carriage. Increased carriage could lead to increased pneumococcal disease in people vaccinated with LAIV as well as increased bacterial transmission within the population. LAIV has been licensed for use in children since 2011 in Europe, and has been increasingly administered in children and adults in the USA. This study looks at the effect of LAIV on pneumococcal carriage and compares it with the Quadrivalent Inactivated Influenza Vaccine (QIV).

Who can participate?
Adults aged 18-50, able to speak fluent English and able to give informed consent.

What does the study involve?
Participants are randomly allocated into one of two groups. Those in group 1 are given Fluenz nasal vaccine (LAIV) and a placebo injection. Those in group 2 are given Fluarix vaccination (QIV) as an injection and a placebo nasal spray. All participants are inoculated with pneumococcal bacteria in the nose. Clinical symptoms and pneumococcal carriage between the two groups are then compared.

What are the possible benefits and risks of participating?
The benefit to volunteers when taking part in this study will be that they will all receive a flu vaccination. The risks associated with taking part in the study relate to the vaccination, inoculation with pneumococcus, blood sampling and nasal cell sampling. Risks associated with

the influenza/ placebo vaccinations include: Pain and tenderness at the site of injection; Muscle aches; Fatigue; Nausea; Diarrhoea; Tiredness; Swelling at injection site; Headache; Runny, stuffy nose; Anaphylaxis (very rare 1: 1000000). Risks associated with blood sampling: feeling faint, bruising
Risks associated with pneumococcal inoculation: pneumococcal infection however this very unloikely, we have experienced inoculating over 400 volunteers and we have not had one case of pneumococcal infection. Risks associated with nasal cell sampling: minor temporary discomfort, irritation, eyes watering and minor bleeding.

Where is the study run from?
Royal Liverpool University Hospital (UK)

When is the study starting and how long is it expected to run for?
August 2015 to November 2017

Who is funding the study?
Bill and Melinda Gates Foundation (USA)

Who is the main contact?
Miss Angela Wright

Contact information

Type(s)
Scientific

Contact name
Miss Angela Wright

Contact details
Royal Liverpool University Hospital
Research & Development
4th Floor, Linda McCartney Centre
Prescot Street
Liverpool, Merseyside
United Kingdom
L7 8XP

Additional identifiers

Clinical Trials Information System (CTIS)
2014-004634-26

ClinicalTrials.gov (NCT)
NCT03502291

Protocol serial number
18994

Study information

Scientific Title
The effect of live attenuated inactivated influenza vaccine on experimental human pneumococcal carriage: a randomised controlled trial

Acronym
LAIV and EHPC

Study objectives
This study looks at the effect of live attenuated inactivated influenza vaccine (LAIV) on pneumococcal carriage dynamics and compares it with the Quadrivalent Inactivated Influenza Vaccine (QIV).

Ethics approval required
Old ethics approval format

Ethics approval(s)
NRES Northwest- Liverpool East REC, ref: 14/NW/1460

Study design
Randomised; Observational; Design type: Clinical Laboratory Study

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
1. Influenza Vaccination: Volunteers are randomised to receive Fluenz nasal vaccine (LAIV) plus placebo injection OR Fluarix vaccination (QIV) via injection and placebo nasal spray
2. Pneumococcal Inoculation: All volunteers are inoculated with pneumococcal bacteria in the nose

Study Entry : Single Randomisation only

Intervention Type
Other

Primary outcome(s)
1. We will define the effect of LAIV on pneumococcal colonisation using the EHPC model in order to assess the potential effects of mass influenza vaccination. We will measure colonisation acquisition, density and duration.
2. Pneumococcal colonisation will be monitored using microbiological cultures of nasal wash samples. Nasal wash samples will be taken at pre-vaccination/ preinoculation*, day 2, 6*/7, 9, 14, 21*/22 and 27*/29 post inoculation in study one and study two*.

Key secondary outcome(s))
1. To evaluate changes in commensal and potential pathogenic species in nasopharyngeal microbiome associated with influenza vaccination
2. To evaluate inflammatory responses at the nasal mucosa using mucosal nanosampling method (lining fluid and cells)
3. To evaluate cellular responses in the lung after LAIV and EHPC co-infection
4. To evaluate symptoms associated with influenza vaccination and EHPC

Completion date
14/11/2017

Eligibility

Key inclusion criteria
Participants will be eligible to participate in this study provided they:
1. Have capacity to give informed consent
2. Aged 18-50 yrs - ages chosen to minimise the risk of pneumococcal infection
3. Speak fluent English to ensure a comprehensive understanding of the research project and their proposed involvement, in order to minimise any communication issues to maximise participant safety

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. Currently involved in another study unless observational or in follow-up phase (noninterventional)
2. Received any influenza vaccine in the last 2 years
3. Egg allergy (as per influenza vaccines patient leaflet)
4. Previous significant adverse reaction to any vaccination/immunisation
5. Close contact with at risk individuals (children under 5 years, immunosuppressed adults, elderly, chronic ill health) – to minimise risk of pneumococcal transmission and transmission of virus for those receiving the LAIV
6. Current regular smoker (smokes daily)
7. Significant smoking history [defined as someone who has previously smoked more than 20

cigarettes per day for 10 years or the equivalent (>10 pack yrs)] – to minimise risk of bronchoscopy or pneumococcal disease
8. Asthma (on regular medication) or respiratory disease – to minimise risk of bronchoscopy or pneumococcal disease
9. Pregnant to minimise the risk of pneumococcal disease
10. Women of childbearing potential (WOCBP) who are not deemed 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/ gentamicin
12. On medication that may affect the immune system in any way e.g. steroids, steroid nasal spray
13. Are regularly taking acetylsalicylic acid (aspirin) – as per LAIV guidance to reduce the risk of Reye's syndrome
14. Been involved in a clinical trial involving EHPC over the last 3 years
15. Unable to give fully informed consent
16. Current acute severe febrile illness - to avoid vaccination and inoculation in participants that may have current infection

Date of first enrolment
26/08/2015

Date of final enrolment
30/04/2017

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Royal Liverpool University Hospital
Research & Development
4th Floor, Linda McCartney Centre
Prescot Street
Liverpool, Merseyside
United Kingdom
L7 8XP

Sponsor information

Organisation
Royal Liverpool and Broadgreen University Hospitals NHS Trust

ROR
https://ror.org/009sa0g06

Funder(s)

Funder type
Government

Funder Name
Bill and Melinda Gates Foundation

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
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Basic results				No	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes