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Responses to booster vaccinations in UK toddlers

Submission date
07/01/2013

Recruitment status
No longer recruiting

Registration date
12/02/2013

Overall study status
Completed

Last Edited
20/05/2016

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
The UK national immunisation schedule is updated regularly as new vaccines are licensed so that the best protection is offered to infants and young children. Currently, in addition to diphtheria, tetanus, pertussis (whooping cough) and polio, infants are also vaccinated against the pneumococcus, Hib and Meningococcal C (MenC) bacteria, which are major causes of serious bacterial infections in early childhood, including meningitis, septicaemia (blood poisoning) and pneumonia. The vaccines against these three bacteria were developed by linking (or conjugating) their outer sugar capsules to a carrier protein, such as inactivated tetanus or diphtheria toxin. Unlike polysaccharide vaccines (which are made of the bacterial sugar capsule only and provide limited, short-term immunity in older children and adults only), conjugated vaccines are able to induce very high antibody levels in infants as young as 2 months old. Currently, all infants in the UK receive the same pneumococcal (Prevenar13) and Hibcontaining (Pediacel) vaccines, but can receive any one of 3 licensed MenC vaccines which contain different conjugate proteins (NeisVacC contains tetanus toxoid, while Menjugate and Meningitec contain inactivated diphtheria toxin), depending on which vaccine stock the GP surgery have acquired from the Department of Health at the time. We have recently found that the immune responses of infants to MenC as well as Hib when measured at 5 months (1 month after completing their infant schedule) depends on the conjugate protein in the MenC vaccine. Because all infants receive a booster dose of both MenC and Hib vaccines at 12 months of age, it is likely that they will all develop adequate long-term protection against these infections. In order to verify this, however, we would like to check the immune responses of infants just before and one month after they receive their 12month booster vaccines.

Who can participate?
The families of infants who have completed their primary immunisations at 2, 3 and 4 months of age, and are due their routine 12month booster vaccinations will be invited to have a blood test just before and around one month after the vaccinations. The infants will all receive the vaccines that they would have received as part of the national immunisation programme. The blood samples are the only way to assess the immune responses to vaccination and, because such responses are age and time specific, it would not possible to conduct the study in any other age group.
Our exclusion criteria are minimal and we aim to recruit a representative population of children

and their families from the community so that our findings can be generalised to the rest of the population.

What does the study involve?
This study involves obtaining a blood sample just before and one month after infants receive their routine booster vaccinations at 12 months of age as part of the national immunisation programme.

What are the possible benefits and risks of participating?
As this study only involves blood sampling from infants by highly experienced nurses, we do not anticipate any risks or burdens. All families will be free to withdraw from participation at any time without giving a reason and without this affecting the ongoing care from the GP surgery (any outstanding vaccinations required would be notified to the participant's GP surgery).We will ensure any discomfort from blood sampling will be minimised by ensuring that the blood samples will be collected by specialist research nurses with excellent experience of working with young infants, who will use local anaesthetic cream or spray to numb the skin and various distraction techniques before and during the blood sampling. Infants who are found to have low Hib or MenC antibody levels after their 12month booster will be offered an extra dose of the appropriate vaccine in order to ensure long term protection against these bacteria.

Where is the study run from?
GP Practices (UK)

When is the study starting and how long is it expected to run for?
We hope to begin the study in March 2013 and will include children for about 6 months.

Who is funding the study?
UK Department of Health

Who is the main contact?
Professor Elizabeth Miller
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Contact information

Type(s)
Scientific

Contact name
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Additional identifiers

EudraCT/CTIS number

2012-005110-18

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
HPA Protocol No: 12/05

Study information

Scientific Title
A prospective study to evaluate the immune responses of UK infants to their routine 12-month booster vaccines following receipt of different meningococcal capsular group C (MenC) conjugate vaccines as part of their primary immunisation schedule (code: P13BOOST)

Acronym
P13Boost

Study objectives
To assess responses to booster doses of conjugated vaccines in UK toddlers who have received the vaccinations in infancy as per the routine UK schedule.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Brent Ethics Committee (UK), 07 December 2012, ref: 12/LO/1875

Study design
Open label phase 4 non randomised study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
GP practice

Study type(s)
Prevention

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

Health condition(s) or problem(s) studied

Responses to vaccinations against Hib, meningococcal serogroup C and 13-valent pneumococcal diseases

Interventions
There is only one treatment group. All participants will receive a single dose of each of three vaccines - Hib/MenC (Menitorix®), PCV13 (Prevenar13®), MMR (Priorix®/MMRvaxpro®)

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Hib/MenC (Menitorix®), PCV13 (Prevenar13®), MMR (Priorix®/MMRvaxpro®)

Primary outcome measure
1. Immunoglobulin G (IgG) geometric mean concentrations (GMCs) with 95% Confidence Intervals (95% CI) for Hib capsular polysaccharide and proportions of infants achieving antibody concentrations of ≥0.15 µg/mL or ≥1.00 µg/mL (putative antibody levels considered to provide short-term and long-term protection against invasive disease, respectively) immediately before and 21-42 days after the routine 12-month vaccinations in infants who received MCC-CRM followed by MCC-TT in infancy and compare with infants who received other MCC vaccine combinations
2. Achieving SBA titres ≥8 (the putative protective anti-body titre) or ≥128 (more discriminatory antibody titre) immediately before and 21-42 days after receiving the 12-month booster vaccines in infants who received MCC-CRM followed by MCC-TT in infancy and compare with infants who received other MCC vaccine combinations.

Secondary outcome measures
1. Immunoglobulin G (IgG) geometric mean concentrations (GMCs) with 95% Confidence Intervals (95% CI) for Hib capsular polysac-charide and proportion achieving antibody concentrations of ≥0.15 µg/mL or ≥1.00 µg/mL immediately before and 21-42 days after receiving the 12-month booster vaccines in four groups of in-fants receiving different MCC vaccine combinations in infancy.
2. Serum bactericidal antibody (SBA) titres with 95% CI for MenC and the proportion achieving SBA titres ≥8 or ≥128 immediately before and 21-42 days after receiving the 12-month booster vac-cines in four groups of infants receiving different MCC vaccine combinations in infancy
3. IgG GMC with 95% CI and proportions achieving antibody concen-trations of ≥ 0.35 µg/ml for each of the 13 pneumococcal serotypes included in Prevenar13® immediately before and 21-42 days after receiving the 12-month booster vaccines Diphtheria, tetanus and pertussis antigens (PT, PRN, FHA and then FIMS) IgG antibody GMCs with 95%CI and proportions of infants achieving antibody levels ≥0.1 IU/ml or ≥1.0 IU/ml) for diphtheria and tetanus (i) immediately before and (ii) 21-42 days after receiving the 12-month booster vaccines.

Overall study start date
01/02/2013

Completion date
01/08/2013

Eligibility

Key inclusion criteria
Male or female infants:
1. With written informed consent obtained from the parent or legal guardian of the infant to participate in the study and to allow the infants General Practitioner (GP) to be informed of participation in the study and be contacted, if required, for confirmation of the vaccination history
2. Who have received all their primary immunisations by the time they are 6 months old, including:
2.1. Two doses of any MenC vaccine, with a 3-8 week interval be-tween the first and second dose, with the vaccine product identified by product name or batch number from either the parent-held Red Book or the GP records
2.2. Who are available for their routine 12-month booster vaccines and both blood tests as described in Study Schedule (Section 6.2)
2.3. Do not fulfill any of the exclusion criteria

Participant type(s)
Patient

Age group
Neonate

Sex
Both

Target number of participants
200 +/- 20%

Key exclusion criteria
Participant may not be included in the study if any of the following apply:
1. History of invasive Haemophilus influenzae serotype b (Hib), pneumococcal or meningococcal disease
2. Confirmed or suspected immunosuppression or immunodeficiency (including HIV)
3. Receipt of a meningococcal quadrivalent conjugate vaccine prior to the 12-month booster
4. Bleeding disorders and/or prolonged bleeding time
5. Major congenital defects or chronic disease

Date of first enrolment
01/02/2013

Date of final enrolment
01/08/2013

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Health Protection Agency
London
United Kingdom
NW9 5EQ

Sponsor information

Organisation
Health Protection Agency (UK)

Sponsor details
c/o Dr Elizabeth Coates
Research Governance Coordinator
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Sponsor type
Government

Website
http://www.hpa.org.uk

ROR
https://ror.org/03sbpja79

Funder(s)

Funder type
Government

Funder Name
Department of Health (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No