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Comparative study of the efficacy of "short" and "long" duration levofloxacin-rifampicin combination therapy in the treatment of early postoperative and haemotogenous staphylococcal prosthetic joint infection

Submission date	Recruitment status	[_] Prospectively registered
25/02/2011	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
04/08/2011	Completed	[_] Results
Last Edited	**Condition category**	[_] Individual participant data
04/08/2011	Infections and Infestations	[_] Record updated in last year

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
LR-07

Study information

Scientific Title
Comparative study of the efficacy of "short" and "long" duration levofloxacin-rifampicin combination therapy in the treatment of early postoperative and haemotogenous staphylococcal prosthetic joint infection: a phase IV, multicentre, open trial

Study objectives
In the early postoperative and haematogenous staphylococcal prosthetic joint infection with stable implant, treated with surgical debridement and the antibiotic combination of rifampicin and levofloxacin, a short length of therapy of 8 weeks is non inferior to a longer standard therapy of 3 to 6 months (3 in hip prosthesis, and 6 in knee prosthesis)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethic Committee for Clinical Research (CEIC - Comité Ético de Investigación Clínica. Hospital Universitario de Bellvtige. c/ Feixa Llarga s/n. 08907 L'Hospitalet de Llobregat - Barcelona, Spain) approved on 6th November 2008

Study design
Phase IV multicentre open trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

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
Prosthetic joint infection

Interventions

In the same clinical setting of early postoperative or haematogenous staphylococcal prosthetic joint infection treated with surgical debridement. The intervention consists of administering the same antimicrobial therapy for different lengths of therapy: short duration of 8 weeks vs longer therapy of 3-6 months

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)
Levofloxacin, rifampicin

Primary outcome measure
To assess the efficacy of a treatment consisting in early surgical debridement and antimicrobial therapy with an oral combination of rifampin and levofloxacin during either 8 weeks (Short schedule group) or 3 (hip prosthesis) to 6 (knee prosthesis) months (Long schedule group; standard schedule), in the early-postoperative and haematogenous prosthesis joint infection of staphylococcal etiology (Staphylococcus aureus and Coagulase-negative Staphylococcus)

Secondary outcome measures
1. Success of therapy: absence of fever, inflammatory signs or fistula and absence of radiographic prosthesis loosening during the follow-up (12 months)
2. Failure, defined as:
2.1. Persistence of the infection either during treatment (persistence of inflammatory symptoms and signs which lead to the removal of the prosthesis) or at the end of treatment [(symptoms and signs suggestive of infection, with positive cultures (either from surgical or clinically significant samples]). A high value of C-reactive protein at the end of treatment, without clinical signs of relapse or persistence, is not considered criteria of failure by itself.
2.2. Relapse of the infection: initial remission of inflammatory symptoms and signs with posterior reappearance and positive cultures of the same microorganism responsible of the infection from surgical or clinically significant samples.
2.3. Reinfection: initial remission of inflammatory symptoms and signs with posterior reappearance and positive cultures of a different microorganism from surgical or clinically significant samples.
In cases of persistence or relapse, evaluation of possible development of resistance to either rifampicin or quinolones will be performed.
3. Aseptic prosthesis loosening during follow-up, with no clinical evidence of infection and negative cultures
4. Adverse events. All adverse events will be collected, and the possible relation with the antibiotics will be evaluated. Serious adverse events will be reported to authorities, according to the law (Real Decreto 223/2004). Especial attention will be given to the following adverse events:
4.1. Gastrointestinal adverse events: vomiting, nausea, etc
4.2. Rise in liver enzymes
4.3. Flu-like syndrome secondary to rifampicin (head-ache, chills or rigors, arthralgias, myalgias)
4.4. Lupus-like syndrome secondary to rifampicin
4.5. Myopathy or tendinitis secondary to levofloxacin

Overall study start date
13/04/2009

Completion date
13/04/2013

Eligibility

Key inclusion criteria
1. Diagnosis of prosthesis joint infection: fever, local pain, inflammatory signs or purulent exudate in the surgical wound and/or purulent macroscopic exudate during the debridement surgery. Prosthesis joint infection will be considered early-postoperative if symptoms and signs begin in the first 30 days after the placement of the prosthesis. It will be considered haematogenous when the clinical picture is acute and/or it develops in the setting of bacteremia or concomitant to other distant infection.
2. Diagnosis of staphylococcal etiology: Staphylococcus sp must be isolated from reliable samples, such as blood cultures or purulent exudate obtained during surgery or by arthrocentesis. Polymicrobial cases will be accepted if it is not necessary to add more antibiotics with anti-staphylococcal activity to the oral combination of rifampicin and levofloxacin.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
195

Key exclusion criteria
1. Age less than 18 years
2. Pregnancy or breastfeeding
3. Women who may become pregnant in whom methods of contraception cannot be guaranteed during the period of antibiotic therapy
4. Life-expectancy less than 6 months
5. Unwillingness to parcipate in the study or to give written-informed consent
6. Unwillingness to avoid the use of contact lenses during the period of antibiotic therapy
7. Reasonable doubts about the patients treatment observance
8. Allergy or intolerance to quinolones and/or rifampicin which lead to the antimicrobial(s) withdrawal. Prosthesis joint infection by quinolones and/or rifampicin resistance
9. Administration of antibiotics with anti-staphylococcal activity different from rifampicin or levofloxacin for more than 7 days, during the period of study or during the follow-up
10. Delay in performing the surgical debridement of the prosthesis infection of 21 or more days, counting from the beginning of symptoms and signs of infection
11. Radiographic signs of prosthesis loosening in simple X-ray
12. Prosthesis removal during surgery

Date of first enrolment
13/04/2009

Date of final enrolment
13/04/2013

Locations

Countries of recruitment
Spain

Study participating centre
Hospital Universitario de Bellvitge
Barcelona
Spain
08907

Sponsor information

Organisation
University Hospital of Bellvitge (Hospital Universitario de Bellvitge) (Spain)

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Sponsor type
Hospital/treatment centre

ROR
https://ror.org/00epner96

Funder(s)

Funder type
Government

Funder Name
Carlos III Health Institute (Instituto de Salud Carlos III) (Spain) - Health Research Fund (Fondo de Investigaciones Sanitarias [FIS]) - Ministry of Health ref: Expte EC/08/00113

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