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Comparison of the equivalence of ceftriane plus azithromycin or doxycycline for the treatment of pelvic inflammatory disease

Submission date 11/12/2005	**Recruitment status** No longer recruiting
Registration date 18/01/2006	**Overall study status** Completed
Last Edited 03/07/2007	**Condition category** Urological and Genital Diseases

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

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
03-006

Study information

Scientific Title

Acronym
DAZ

Study objectives
1 g of azithromycin once a week for two weeks is equivalent to 14 days of 200 mg doxycycline per day.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Hospital de Clinicas de Porto Alegre (HCPA) Institutional Review Board (ref: IRB0000921)

Study design
Randomized double-blinded placebo trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Pelvic inflammatory disease

Interventions
Eligible patients were invited to participate in the doxycycline azithromycin protocol (DAZ). After giving written consent, a standardized interview, examination and specimen collection techniques were taken. Only three researchers will perform the physical exams. Whenever possible, the researcher that performed the first clinical examination on the first visit also did follow up on that patient.
A standardized screening examination, including a visual pain scale (0-10), and the McCormick modified pain scale was performed in the same sequence by the three researchers. A complete blood count, endometrial biopsy, urinalysis, and erythrocyte sedimentation rate will be performed on the first visit.
Endometrial samples will be divided into two equal amounts. One will be snap frozen in liquid nitrogen for Polymerase Chain Reaction (PCR) analysis and the other will be fixed in

formaldehyde for histological analysis.
After the initial interview, the patient will receive a parenteral 250 mg ceftriaxone injection and will be randomly allocated to one of two treatment groups.

Randomization and treatment:
A restricted randomization sequence list was generated by computer, and was kept concealed from the researcher until the moment of assignment. We will consider subjects in blocks of four at a time to create the allocation sequence. After the patient is enrolled in the protocol, she will be blindly assigned to a coded treatment, either 14 days doxycycline or 1 g of azithromycin per week for two weeks. To avoid bias, the medication will be manipulated by the hospital pharmacy and will be put in identically coded blisters (treatment A, treatment B). To confirm compliance, a treatment of just seven days will be given to the patient, forcing her to return in seven days to receive the rest of the treatment. Because of the difference in the amount of capsules in each treatment, the azithromycin blister was filled up with placebo.
In the first visit, the patient will receive 250 mg intramuscular ceftriaxone and a blister for seven days treatment. The first dose of the medication (1 g of azythromycin, or 200 mg of doxycycline) will be taken in front of the physician. She will receive a leaflet and instructions of how she should take the rest of the medication. Special attention was taken about warning against taking the medication on an empty stomach, using analgesics, and abstaining from sexual intercourse until the treatment was completed. All women will be advised to have their partner treated with 1 g of azithromycin.

Endometrial biopsy and definition of endometritis:
The endometrial biopsy was performed at the office using a Karman plastic curette (MedGyn Products Inc., Lombard, IL, USA). Histopathological endometritis was defined by the presence of ≥1 plasma cell per X120 field in the endometrial stroma plus ≥5 neutrophils per X400 field in the endometrial surface.
PCR techniques will be used to investigate the presence of Neisseria gonorrhea and Chlamydia trachomatis in the endometrial samples.

Follow-up and adherence:
Participants will be monitored with in-person visits at 2, 7, 14 and 30 days. In each visit, the gynecological examination and the assessment of the pain will be registered. On day 7, the patient will return the first blister and receive the second one. Again, the first dose will be taken in front of the physician. On day 14, she will return the second blister. Adherence will be checked by absence of capsules in each blister. On day 30, another endometrial biopsy will be performed to measure histological cure and blood tests will be repeated.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
Ceftriane, azithromycin and doxycycline

Primary outcome measure
The primary outcome for the trial is clinical cure, defined as improvement or absence of the initial pain at day 14 compared to baseline.

Secondary outcome measures
1. A clinical cure, defined as 70% or greater reduction in the total tenderness score at day 14 compared to baseline
2. Histological cure defined as absence of plasma cell per X120 field in the endometrial stroma and <5 neutrophils per X400 field in the endometrial surface
3. Absence of Neisseria gonorrhea and Chlamydia trachomatis on endometrial samples on day 30 by PCR techniques

Overall study start date
10/08/2003

Completion date
10/05/2006

Eligibility

Key inclusion criteria
1. A history of pelvic discomfort for a period of 30 days or less
2. Findings of pelvic organ tenderness (uterine or adnexal) on bimanual examination
3. Leukorrhea and/or mucopurulent cervicitis and/or untreated known positive gonococcal or chlamydial cervicitis

Participant type(s)
Patient

Age group
Adult

Sex
Female

Target number of participants
112

Key exclusion criteria
1. Current pregnancy as demonstrated by beta-Human Chorionic Gonadotrophin (HCG) or ultrasonography
2. Inability to tolerate an outpatient oral regimen as demonstrated by the vomiting of eight ounces of water one hour after taking 10 mg of metoclopramide
3. Presence of tubo-ovarian abscess, appendicitis or hemorrhagic ovarian cysts confirmed by ultrasound or laparoscopy
4. Pelvic pain over 30 days duration
5. Allergy to ceftriaxone, azithromycin or doxycycline
6. Antimicrobial therapy within seven days of recruitment
7. Delivery, abortion or gynecological surgery within 30 days
8. Prior hysterectomy or bilateral salpingectomy
9. Homelessness
10. Fever
11. Abdominal rebound tenderness

Date of first enrolment
10/08/2003

Date of final enrolment
10/05/2006

Locations

Countries of recruitment
Brazil

Study participating centre
Rua Ramiro Barcelos, 2350/1125
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Sponsor information

Organisation
Foundation for the Incentive of Research (Fundacao de Incentivo a Pesquisa) (FIPE) (Brazil)

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Sponsor type
Charity

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ROR
https://ror.org/040y74d88

Funder(s)

Funder type
Charity

Funder Name
Foundation for the Incentive of Research (Fundacao de Incentivo a Pesquisa) (FIPE) (Brazil)

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?
Results article	Results	01/07/2007		Yes	No