ISRCTN08083905 https://doi.org/10.1186/ISRCTN08083905

In vivo analysis of the 11-beta-hydroxysteroid dehydrogenase activity during critical illness using isotopically labeled cortisol and cortisone

Submission date 30/10/2009	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 23/11/2009	**Overall study status** Completed	
Last Edited 07/05/2013	**Condition category** Other	

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

S51644

Study information

Scientific Title
In vivo analysis of the 11-beta-hydroxysteroid dehydrogenase activity during acute and prolonged critical illness using isotopically labeled cortisol and cortisone: an observational study

Study objectives
Current hypothesis as of 15/02/2012
Cortisol levels remain high in critically ill patients, in spite of low adrenocorticotrophic hormone (ACTH) levels. We hypothesize that hypercortisolism during critical illness is driven mainly by a reduced cortisol metabolism.

Previous hypothesis
Cortisol levels remain high in prolonged critically ill patients, in spite of low adrenocorticotrophic hormone (ACTH) levels. We hypothesize that hypercortisolism during acute critical illness is driven mainly by the hypothalamic-pituitary-adrenal (HPA) axis, whereas during prolonged critical illness regeneration of cortisol in the peripheral tissues in an ACTH-independent way via 11beta-hydroxysteroid dehydrogenase (HSD) becomes predominant.

As of 15/02/2012, the following changes were made to the record.
Public title: Updated from In vivo analysis of the 11-beta-hydroxysteroid dehydrogenase activity during acute and prolonged critical illness using isotopically labeled cortisol and cortisone to In vivo analysis of the 11-beta-hydroxysteroid dehydrogenase activity during critical illness using isotopically labeled cortisol and cortisone
Anticipated start date was updated from 01/01/2010 to 13/02/2012.
Anticipated end date was updated from 31/12/2010 to 01/06/2012.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Institutional Review Board of the Catholic University Leuven School of Medicine approved on the 21st September 2009 (ref: B32220096943)
Adaptations to the original protocol are approved on the 27th of January 2012.

Study design
Observational case-control study

Primary study design
Observational

Secondary study design
Case-control study

Study setting(s)
Hospital

Study type(s)

Screening

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
Critical illness

Interventions
Current interventions as of 15/02/2012
After admission to the SICU, patients will be evaluated on their appropriateness for the study and written informed consent will be obtained from the patient or the closest family member or legal guardian.

11-beta-reductase activity will be assessed by infusion of a deuterated cortisol tracer (D4-cortisol). This is a non-radioactive labelled form of cortisol, the bodys own natural steroid hormone. In addition, a deuterated cortisone tracer (D2-cortisone) will be infused at the same time to obtain information on the directionality of the 11-beta-hydroxysteroid dehydrogenase activity.

Infusion of D4-cortisol/D2-cortisone will occur according to the following schedule:
- 9,11,12,12-D4-cortisol as a bolus of 0.7 mg followed by infusion of 0.35 mg/hour; blood samples are taken at t = -5, +60, +120, +160, +165, +170, +175 min.
- 1,2-D2-cortisone as a bolus of 0.076 mg at t = +100 followed by infusion of 0.1053 mg/hour; an additional blood sample is taken at t = -5 min, +120min,+140 min.
- urine samples are collected at t =0, +60, +120, +180.
- A complete 24h urine collection will be collected started at the moment of study.

For patients, blood and urine samples are taken via the catheters that are present.
Control persons will receive two intravenous catheters for the collection of blood samples; for collection of the urine samples they will be asked to urinate at the appropriate time points.

Previous interventions
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- urine samples are collected at t =0, +60, +120, +180.

For patients, blood and urine samples are taken via the catheters that are present.
Control persons will receive an arterial catheter for the collection of blood samples; for collection of the urine samples they will be asked to urinate at the appropriate time points.
Both patients and control persons will receive an extra intravenous catheter for infusion of the tracers.

In addition to the tracer injection, daily blood samples (4 ml) will be taken from all included patients for characterisation of the HPA axis during critical illness.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Cortisol, cortisone

Primary outcome measure
Current primary outcome(s) as of 15/02/2012
An estimation of the amount of ACTH-driven cortisol production , the amount of cortisol regenerated from cortisone via 11-beta-HSD1and 2 and the activity of the different metabolizing enzymes based on urinary metabolites.

Previous primary outcome(s)
An estimation of the amount of ACTH-driven cortisol production and the amount of cortisol regenerated from cortisone via 11-beta-HSD1, measured at day 2 and 7 after admission.

Secondary outcome measures
No secondary outcome measures

Overall study start date
13/02/2012

Completion date
01/06/2012

Eligibility

Key inclusion criteria
Current inclusion criteria as of 15/02/2012
For patients:
1. Admitted to the surgical intensive care unit (SICU) of the Leuven University Hospital
2. No age limits, either sex

For healthy control persons:
1. Age- and gender-matched to the included patients

Previous inclusion criteria
For patients:
1. Admitted to the surgical intensive care unit (SICU) of the Leuven University Hospital

2. Estimated duration of illness prior to admission less than 48 hours
3. No age limits, either sex

For healthy control persons:
1. Age- and gender-matched to the included patients

Participant type(s)
Patient

Age group
Other

Sex
Both

Target number of participants
A first sample comprising 11 patients and 11 control persons; to be increased as appropriate

Key exclusion criteria
Steroids received during the last 3 months

Date of first enrolment
13/02/2012

Date of final enrolment
01/06/2012

Locations

Countries of recruitment
Belgium

Study participating centre
Director of the Department of Intensive Care Medicine
Leuven
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3000

Sponsor information

Organisation
Catholic University Leuven (Katholieke Universiteit Leuven) (Belgium)

Sponsor details

c/o Professor Dr Ir Koenraad Debackere
Managing Director
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3000

Sponsor type
University/education

ROR
https://ror.org/05f950310

Funder(s)

Funder type
Government

Funder Name
Methusalem (Belgium) - long term structural funding by the Flemish Government

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	18/04/2013		Yes	No