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Dynamics of endocrine and inflammatory changes during critical illness

Submission date 09/07/2010	**Recruitment status** No longer recruiting	[_] Prospectively registered [_] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 12/08/2010	**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

Contact name
Prof Greet Van den Berghe

Contact details
Director of the Department of Intensive Care Medicine
Catholic University Leuven University Hospitals
and Chair of the Division of Acute Medical Sciences
Catholic University Leuven
Herestraat 49
Leuven
Belgium
3000

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
S52376

Study information

Scientific Title
Dynamics of endocrine and inflammatory changes during critical illness: An observational trial comparing patients and healthy volunteers

Study objectives
During critical illness, cortisol levels are often high in spite of low ACTH levels. Indeed, apart from centrally regulated cortisol production, cortisol can also be regenerated from its inactive form cortisone in peripheral tissues, or its clearance may be reduced. Furthermore, cortisol can also be produced in an ACTH-independent manner via the action of cytokines. We therefore hypothesized that during critical illness, cortisol levels are driven by one or more of these alternative mechanisms.

Please note, as of 25/10/2011 the trial record has been updated in accordance with protocol amendments. The changes can be found under this date of update in the relevant fields below. The original end date was 31/12/2010. The expanded study is now expected to end by 31/12 /2011.

Ethics approval required
Old ethics approval format

Ethics approval(s)
The Institutional Review Board of the Catholic University Leuven School of Medicine approved on the 5th of July 2010 (Belgian reference number B32220108999)
Approval of the amendments to the protocol was provided on 4th of January 2011 (intervention 2), 7th of February 2011 (intervention 3) and 22nd of August 2011 (intervention 4).

Study design
Observational cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Other

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

Health condition(s) or problem(s) studied
Critical illness

Interventions

1. At the second day after admission to the ICU, patients will be evaluated on their appropriateness for the study and written informed consent will be obtained from the closest family member or legal guardian. Patients that do not meet the selection criteria will be re-evaluated on day 3 and day 4.
Written informed consent will also be obtained from the healthy volunteers.
During 9 hours (9 p.m. - 6 a.m.) a blood sample (2 ml) will be taken every 10 minutes via an arterial catheter connected to the VAMP (Venous Arterial blood Management Protection) system to avoid unnecessary blood waste.
For the critically ill patients, blood will be sampled via the arterial catheter that is in place as part of their standard intensive care. In the healthy volunteers, an arterial catheter will be inserted into the arteria radialis.

Added 25/10/2011:

2. To quantify urinary cortisol metabolites as a measure for the activity of cortisol metabolizing enzymes, we will perform 24h-urine collections. To obtain a group of 60 patients comparable to the ones included for intervention 1, we will cross-sectionally collect urine once a week during 6 weeks, from all patients admitted to the ICU who do not receive exogenous glucocorticoids.
In addition, we will collect urine from all healthy control persons included for intervention 1.
3. From patients comparable to those included for interventions 1 and 2 who die in the intensive care unit and who undergo an autopsy, adrenal glands will be prelevated to study the effect of the endocrine changes during critical illness on the adrenals. As controls, we will use autopsy material from non-critically ill persons who died in the emergency unit.
4. To perform deconvolution analysis, the half-life of cortisol during critical illness must be known.
In 20 critically ill patients receiving a bolus injection of hydrocortisone, serial blood samples will be taken. The first sample will be taken immediately after infusion, then every ten minutes during one hour, and then every hour until 5 hours post-infusion. Again, blood will be sampled via the arterial catheter that is in place as part of their standard intensive care, connected to a VAMP system.
In addition, we will collect serial blood samples from 5 healthy volunteers receiving a single bolus injection of 100mg hydrocortisone, according to the same time scheme as mentioned above. Blood samples will be collected via a superficial venous line.

Intervention Type

Other

Phase

Not Applicable

Primary outcome measure

1. Comparison between the secretion dynamics of cortisol and ACTH, and comparison with time series of inflammatory markers, will allow us to identify the main driving mechanisms for cortisol production during critical illness.

Added 25/10/2011:

2. Comparison of the ratios of urinary cortisol metabolites will allow us to detect a difference in activity of the cortisol metabolizing enzymes between critically ill patients and healthy control persons.

3. We will study adrenal morphology and storage of lipid droplets, to detect the effect of critical illness associated endocrine changes on the adrenals.
4. Knowing the plasma half-live of cortisol during critical illness will allow us to gain correct deconvolution data.

Secondary outcome measures
None

Overall study start date
09/08/2010

Completion date
31/12/2011

Eligibility

Key inclusion criteria
Intervention 1:
1. Patients: all patients admitted to the surgical and medical intensive care units of the university hospitals, Leuven, (Belgium), will be screened for inclusion when they are still mechanically ventilated at the 2nd, 3rd or 4th day after admission, provided that they do not meet one of the exclusion criteria below.
2. Healthy volunteers: Age-matched to the average age of the included patient population

Added 25/10/2011:
Intervention 2:
1. Patients: all patients with a urinary catheter, present at the surgical and medical intensive care units of the university hospitals, Leuven (Belgium).
2. Healthy volunteers: age-matched to the average age of the included patient population.

Intervention 3:
1. Patients: critically ill patients who died in the intensive care unit and who undergo an autopsy.
2. Controls: non-critically ill persons who died in the emergency unit and who undergo an autopsy.

Intervention 4:
1. Patients: patients receiving a bolus injection of hydrocortisone based on clinical indications.
2. Healthy volunteers: age matched to the average age of the included patient population.

Participant type(s)
Healthy volunteer

Age group
Adult

Sex
Both

Target number of participants
Updated 25/10/2011: 40 patients and 8 healthy controls for intervention 1; 60 patients for intervention 2; 20 patients and 5 healthy controls for intervention 4

Key exclusion criteria

Intervention 1 and 2:
1. Patients:
1.1. Age < 18 years
1.2. Do not resuscitate order
1.3. No arterial line in place
1.4. Patients expected to die within the next 24 hours
1.5. Pregnancy
1.6. Cerebral disease
1.7. (pan)Hypopituitarism
1.8. Known adrenal disease (Cushing or Addisson)
1.9. Systemic treatment with corticosteroids within the last 3 months
1.10. Etomidate within the last 72 hours
1.11. Dopamine within the last 12 hours
1.12. Vasopressine within the last 12 hours
1.13. Treatment with an azole within the last 24 hours
2. Healthy volunteers:
2.1. Age <50 or >75 years
2.2. Active malignancy
2.3. Pregnancy
2.4. Cerebral disease
2.5. (pan)Hypopituitarism
2.6. Known adrenal disease (Cushing or Addisson)
2.7. Systemic treatment with corticosteroids within the last 3 months

Added 25/10/2011:
Intervention 3:
1. Patients:
1.1. Age < 18 years
1.2. Cerebral disease
1.3. (pan)hypopituitarism
1.4. Known adrenal disease (Cushing or Addisson)
1.5. Systemic treatment with corticosteroids within the last 3 months before death
2. Controls
2.1. Critical illness or chronic disease
2.2. Cerebral disease
2.3. Systemic treatment with corticosteroids within the last 3 months before death

Intervention 4:
1. Patients:
1.1. Age < 18 years
1.2. No arterial line in place
1.3. Ascites
2. Healthy volunteers:
Same as for intervention 1

Date of first enrolment

09/08/2010

Date of final enrolment

31/12/2011

Locations

Countries of recruitment
Belgium

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

Sponsor information

Organisation
IWT Flanders (Agentschap voor Innovatie door Wetenschap en Techniek) (Belgium)

Sponsor details
Koning Albert II-laan 35, box 16
Brussels
Belgium
1030

Sponsor type
Government

Website
http://www.iwt.be

Funder(s)

Funder type
Government

Funder Name
Flanders Agency for Innovation in Science and Technology (Agentschap voor Innovatie door Wetenschap en Techniek [IWT Vlaanderen]) (Belgium) - Strategic Programme for Basic Research (Strategisch BasisOnderzoek [SBO]); long term structural funding Methusalem (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