Steroid-induced reduction of surgical stress

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Does dexamethason reduce the levels of plasma inflammatory proteins in patients undergoing coronary artery bypass graft (CABG) surgery who have a normal or disturbed ejection fraction such that proapoptotic pathways are inhibited?Does a...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Coronary artery disorders
Study type	Interventional

Summary

ID

NL-OMON32372

Source ToetsingOnline

Brief title StReSS StTudy

Condition

• Coronary artery disorders

Synonym CABG, coronary bypass surgery

Research involving Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum **Source(s) of monetary or material Support:** Ministerie van OC&W,European Society of Anaesthesiology

Intervention

Keyword: Apoptosis, Cardiac function, Coronary artery bypass graft surgery, Dexamethasone, Inflammation

Outcome measures

Primary outcome

Expression of p38 in cultured cells and cardiac tissue

Secondary outcome

Pro-apoptotic signaling in atrial biopsies and cultured cells

Blood will be sampled for the measurement of Tumor Necrosis Factor-alpha (TNF-*), IL-6, IL-8, IL-10 and IL-4 and CRP before induction of anesthesia and at the end of surgery.

Plasma samples will be investigated for the presence of novel biomarkers: precursor peptides of ANP (proANP), vasopressin (Copeptin), Endothelin-1 (proET-1) and Adrenomedullin (proADM).

Demographic variables: Age, gender, length, body weight, preoperative and postoperative hematocrit, hemoglobin, leukocyte count.

Surgical characteristics: Surgery time, clamp time, CPB time

Study description

Background summary

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The stress response as induced by myocardial cellular damage during cardiac surgery may lead to myocardial stunning and apoptosis, and could therefore impair postoperative patient recovery. Surgical trauma typically induces the liberation of cytokines. Some of these cytokines are strongly associated with the initiation of intracellular proapoptotic pathways through activation of tyrosine kinases and integrins. The latter are known for their deteriorating effects on cardiac function and are strongly involved in cardiac remodeling. Dexamethasone is typically administered prior to cardiac surgery in order to especially reduce the release of proinflammatory cytokines. It has however never been investigated whether this additionally reduces proapoptotic signaling in the human heart, thereby eliminating risk factors for the induction of cardiac dysfunction. In the present study, we therefore aim to investigate whether dexamethasone inhibits proapoptotic pathways in patients undergoing cardiac surgery. Furthermore, we would like to elucidate whether this proposed effect of dexamethasone is related to the reduction of the stress response in the heart or indirectly by suppression of cytokine release. For this purpose we will obtain cardiac biopsies and plasma from patients, who are randomly assigned to placebo or dexamethasone treatment and undergo on and off-pump coronary artery bypass grafting (CABG) surgery.

Study objective

Does dexamethason reduce the levels of plasma inflammatory proteins in patients undergoing coronary artery bypass graft (CABG) surgery who have a normal or disturbed ejection fraction such that proapoptotic pathways are inhibited?

Does a dexamethasone-induced alteration in plasma inflammatory markers lower proapoptotic signaling in atrial biopsies of CABG patients?

Study design

Single-blinded, placebo controlled, randomized single center clinical trial.

The study will be performed in the VUmc.

Patients will be randomly assigned into two study groups:

- (A) Placebo
- (B) High dose of dexamethasone

In both the following patients will be included:

- (a) Use of cardiopulmonary bypass (on-pump), ejection fraction > 50%
- (b) Use of cardiopulmonary bypass (on-pump), ejection fraction < 50%
- (c) No use of cardiopulmonary bypass (off-pump), ejection fraction > 50%
- (d) No use of cardiopulmonary bypass (off-pump), ejection fraction < 50%

Intervention

0.05 ml/kg dexamethason, i.v. (20 mg/ml, clear fluid) or placebo

Study burden and risks

Dexamethasone: By suppression of the inflammatory response by dexamethasone the occurrence of postoperative infections and postoperative hyperglycemia is slightly increased. These risks are however minimal. Moreover, the attending anesthetist has the possibility to treat all possible complications and may start any treatment that is necessary to guarantee an optimal patient health condition.

Blood sampling from an intravenous catheter: Peripheral intravenous catheter placement is standard perioperative procedure in all surgical patients, and will therefore not add up to patient discomfort in the present study. Patients with anemia will be excluded from the present study (Hb < 5 mmol/l).

Atrial biopsies: Atrial biopsies will be taken from the right atrial appendage during on-pump surgery. Since part of the appendage will be removed for cannulation of the right atrium, the biopsy will not increase patient risk.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age Adults (18-64 years) Elderly (65 years and older)

Inclusion criteria

Patients undergoing coronary artery bypass surgery (CABG) Use of cardiopulmonary bypass (CPB) Age 18-75 years Informed consent

Exclusion criteria

Re-operations Emergency operation Body surface area (BSA) 1.7 > BSA < 2.3 Patient with anemia (Hb < 6.0) Patients with insulin-depended diabetes mellitus

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Placebo
Primary purpose:	Other

Recruitment

NL	
Recruitment status:	Recruitment stopped
Start date (anticipated):	24-06-2009

Enrollment:	108
Туре:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Dexamethasone
Generic name:	dexamethasone
Registration:	Yes - NL intended use

Ethics review

Approved WMO	
Date:	27-11-2008
Application type:	First submission
Review commission:	METC Amsterdam UMC

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register
EudraCT
ССМО

ID EUCTR2008-002739-34-NL NL23266.029.08