Dexamethasone for Cardiac Surgery II trial

Published: 07-07-2017
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The primary objective of this study is to study the effects of intraoperative dexamethasone administration on postoperative recovery following cardiac surgery.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Procedural related injuries and complications NEC
Study type	Interventional

Summary

ID

NL-OMON55453

Source
ToetsingOnline

Brief title
The DECS-II trial

Condition

- Procedural related injuries and complications NEC
- Cardiac therapeutic procedures

Synonym
Cardiac surgery, open heart surgery

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Cardiac Surgery, Dexamethasone, Standard practice

Outcome measures

Primary outcome

The main endpoint for this study is the number of days alive and spent at home

up to 30 days after surgery.

Secondary outcome

Secondary endpoints include major complications (MI, stroke, death), duration

of mechanical ventilation, postoperative troponin (myocardial injury) levels,

and infections.

Study description

Background summary

Open-heart surgery with cardiopulmonary bypass (CPB) is a unique model of systemic inflammation in humans, because treatment can begin before the inflammatory stimulus (surgery, CPB). The inflammatory response associated with cardiac surgery and CPB likely plays an important role in the development of a significant number of adverse outcomes. Deregulated inflammation is associated with haemodynamic instability, respiratory compromise and organ dysfunction leading to a severe systemic inflammatory response syndrome (SIRS). Patient recovery is delayed and the risk of postoperative complications and prolonged hospital stay are greatly increased.

High-dose corticosteroids attenuate the inflammatory response to surgery with CPB and are commonly used in some countries including The Netherlands, but less common in others, such as Australia, the US and Canada. Steroids can reliably attenuate activation of the complement pathways associated with cardiac surgery, but clinical trials measuring clinically relevant outcomes have had mixed results.5 The current evidence is dominated by the results of two large randomised trials: DECS (n=4,494)6 and SIRS (n=7,507). Both DECS and SIRS assigned patients undergoing cardiac surgery to receive either a highintraoperative dose of steroids (dexamethasone 1 mg/kg, or methylprednisolone 500 mg, respectively) or placebo. The point estimates of

both trials suggested a possible reduction in serious complications and mortality. Planned subgroup analyses in the DECS trial found steroids reduced the incidence of respiratory failure (3.0 % vs. 4.3%, P=0.02), infection (9.5% vs. 14.8%, P=0.009), and shortened hospital stay (median 8 [7-13] vs. 9 [7-13] days, P=0.009). Severe renal failure (need for RRT) was reduced, 0.4% vs. 1.0%, P=0.04. But SIRS found methylprednisolone was associated with a higher incidence of myocardial injury (as measured by elevation of CK-MB enzyme). Neither trial identified a higher risk of myocardial infarction (MI). The methylprednisolone-induced elevation of CK-MB may therefore not be a class effect. Another compelling finding in pre-planned subgroup analysis of patient age groups is that when limiting analysis to those aged less than 75 years in the DECS trial, dexamethasone reduced the risk of the primary composite endpoint, RR 0.74 (95% CI: 0.58-0.95), P=0.017; as well as respiratory failure RR 0.62 (95% CI: 0.42-0.91), P=0.014; and possibly mortality RR 0.53 (95% CI: 0.26-1.10), P=0.08.6 This age-interaction effect is supported by the demonstration of increased C-reactive protein concentrations in younger patients enrolled in the DECS trial. Therefore, it is highly plausible that prophylactic steroids can suppress deregulated inflammation and improve outcomes in cardiac surgery, but only when used in a less elderly (i.e. <75 years) patient population.

In the proposed study, a novel trial design will be used in order to improve the efficiency of clinical trials in routine care settings. Such trials must be robust (internal validity) and pragmatic (external validity) in their design if they are to have maximal impact. They typically require enrolment of many thousands of patients, and so are costly and take years to complete, and longer still for their results to be implemented into routine clinical practice. In this context investigator-initiated, public good, clinical trials are under threat. There are growing calls for improved efficiencies in medical research, and this has led to interest in novel trial designs. There is also renewed interest in low-cost, large, simple randomized trials, including registry-nested trials.

We therefore propose to use the *standard practice-preference randomised consent* (SPP-RC) design. In this design, a modified consent procedure will be used in participating centres in The Netherlands. For this, patients will first be asked to participate in the DECS-II cohort, and also to be randomised between use of standard care (in this case, the intraoperative use of dexamethasone as part of the cardiac anaesthesia protocol for cardiac surgery) of use of care that is different from the standard (in this case, not using dexamethasone intraoperatively as part of the cardiac anaesthesia protocol for cardiac surgery). Randomisation will be in a 2:1 ratio favouring standard care. Patients who are randomised tot non-standard care will be approached for additional consent for this alternative treatment.

Study objective

The primary objective of this study is to study the effects of intraoperative dexamethasone administration on postoperative recovery following cardiac surgery.

Study design

The DECS-II study is a pragmatic, assessor-blinded randomised clinical trial of administering a single dose of dexamethasone,1 mg/kg (standard care in the UMC Utrecht), versus no dexamethasone (non-standard care in the UMC Utrecht) as part of anaesthesia care for cardiac surgery.

Intervention

Not giving dexamethasone as part of routine cardiac anaesthesia care. This intervention will be compared to standard care in the UMC Utrecht, which is of administering a single dose of dexamethasone,1 mg/kg.

Study burden and risks

Dexamethasone has been used during many decades for a large variety of indications. In the setting of cardiac surgery, it*s routine use to reliably suppress the perioperative inflammatory response has been common practice already for decades in many of the Dutch cardiac surgical centres, while practice is much more variable across countries around the world. However, both practices (of giving and not giving steroids) are considered safe, with comparable postoperative outcomes. Since both practices are common and considerably safe, the risks for patients to participate in this study are anticipated to be low, and as such acceptable for subjects participating in this study.

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

Adult patients undergoing cardiac surgery
Elective or semi-elective cardiac surgical procedure
On-pump cardiac surgery
Age <= 75 years

Exclusion criteria

Age >75 years
Preoperative use of systemic corticosteroids
Urgent cardiac surgery
Type 1 diabetes
Sepsis
Endocarditis

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial

Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	23-10-2018
Enrollment:	1400
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	07-07-2017
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	21-12-2017
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	25-09-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-12-2020
Application type:	Amendment
Review commission:	METC NedMec

Approved WMO Date:	16-12-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	19-01-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	04-02-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-04-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-04-2021
Application type:	Amendment
Review commission:	METC NedMec

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	ID
EudraCT	EUCTR2017-002494-19-NL

Register	ID
CCMO	NL61864.041.17