The Perioperative ADministration of Dexamethasone and Infection trial

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We plan to conduct a large, pragmatic, multicentre, randomised non-inferiority trial to determine whether the use of intraoperative dexamethasone, a widely used antiemetic in perioperative medicine, is associated with an unacceptable increased risk...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Bacterial infectious disorders
Study type	Interventional

Summary

ID

NL-OMON47052

Source
ToetsingOnline

Brief title
The PADDI trial

Condition

- Bacterial infectious disorders

Synonym
surgical site infections, wound infections

Research involving
Human

Sponsors and support

Primary sponsor: Alfred Health
Source(s) of monetary or material Support: Vergoeding per patient geincludeerd in het UMC Utrecht. De studie als geheel is gefinancierd door de NHMRC (overheidssubsidie Australie)

Intervention

Keyword: dexamethasone, infection, surgery

Outcome measures

Primary outcome

Surgical Site Infection at 30 days

Secondary outcome

PONV OUTCOMES

1. Nausea (0-24 hours)- Nausea as measured on a numerical rating scale (NRS) in the first 24 hours following surgery

2. Vomiting (0-24 hours)- Vomiting (occurrence and number of events) within first 24hours following surgery

PAIN OUTCOMES

3. Highest pain score (NRS) at rest and on movement in the first 24 hours

4. Chronic Post-Surgical Pain (at 6 months)- defined as pain over the surgical site, for at least three months after surgery, that cannot be explained by other causes, such as disease recurrence or a pre-existing pain syndrome.

OTHER OUTCOMES

5. Hospital stay: from the start (date, time) of surgery until actual hospital discharge.

6. Quality of recovery: QoR-15 score on days 1, and 30

7. C-reactive protein (CRP) concentration- Days 1 and 2 postop.

8. Proportion of patients requiring insulin

9. Hypoglycaemia rates

10. Hyperglycaemic rates

11. Other infections (i.e. non-SSI) at 30 days - see *Infections Diagnostic Definitions*

12. Sepsis- see *Infections Diagnostic Definitions*

13. Wound Dehiscence- partial or total disruption of any or all layers of the operative wound.

14. The relationship between diabetic status, glycaemic parameters (preoperative blood glucose, glycated haemoglobin (HbA1c)) and infective outcomes

Study description

Background summary

Dexamethasone is a synthetic glucocorticoid with potent anti-inflammatory and metabolic effects. It is frequently administered in the perioperative period, most commonly for prophylaxis and treatment of postoperative nausea and vomiting (PONV). The growing concern about the routine administration of dexamethasone in the perioperative period is due to a lack of safety data in relation to infection risk, particularly in vulnerable populations such as patients with diabetes and children. Proposed mechanisms of infective risk include a) the potential for immunosuppression, b) the theoretical impairment of wound healing and c) induced hyperglycaemia. Any or all of these may contribute to an increased risk of perioperative infection.

Study objective

We plan to conduct a large, pragmatic, multicentre, randomised non-inferiority

trial to determine whether the use of intraoperative dexamethasone, a widely used antiemetic in perioperative medicine, is associated with an unacceptable increased risk (2%) of postoperative infection in 8880 adult surgical patients. There is biological plausibility that dexamethasone may alter our defined primary and secondary outcomes (see below). The trial has been endorsed by the Australian and New Zealand College of Anaesthetists (ANZCA) Clinical Trials Network and the Australian Society for Infectious Diseases Clinical Research Network, representing the first collaboration between these two organizations

Study design

International, multicentre, prospective, randomised, double blind, placebo-control, parallel assessment, stratified, non-inferiority safety and effectiveness study.

Intervention

Patients will be randomised to receive dexamethasone 8 mg or saline placebo, administered intravenously within 5 minutes after induction of anaesthesia.

Study burden and risks

The intervention in this trial is a common prophylactic intervention to prevent postoperative nausea and vomiting following general anaesthesia. In daily clinical practice, whether or not this intervention is used depends on the attending anaesthetist, and varies between anaesthetists. The risks of participation in this trial is therefore not different from that of other patients undergoing a surgical procedure.

The burden for the participants consists of 4 blood samples (most of these are taken regardless within the context of routine care), and the completion of a number of short questionnaires: once before the operation, and on 2 occasions in the 6 months following the operation.

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 *18 years of age
* American Society of Anesthesiologists (ASA) physical status 1-4
* Elective or Expedited non-cardiac surgery of at least 2 hours duration under general anaesthesia (± regional block)
* At least two hours* duration
* Requiring a hospital stay of at least one postoperative night
* A surgical skin incision > 5 cm in length or multiple incisions with a total incision length of 5 cm.

Exclusion criteria

* Poorly controlled type 1 diabetes (HbA1c > 9.0%)
* Endovascular procedure with a small (< 5 cm length) skin incision
* Ophthalmic surgery
* Planned dexamethasone (or other corticosteroid) therapy (e.g. history of intractable PONV, maxillofacial surgery, intracranial neurosurgery)
* Recent (< 2 weeks since end of treatment) infective episode requiring treatment with antibiotics
* Chronic antibiotic therapy (e.g. for bronchiectasis, cystic fibrosis etc)
* When surgery is indicated for an infective process (e.g. infected joint prosthesis)
* A history of allergy or adverse reaction to glucocorticoids

* Planned postoperative intubation or ventilation
* Concurrent immunosuppressive therapies
* Current or recent (within preceding 1 month) systemic use of glucocorticoids
* Surgical procedures within the preceding 2 months
* Known immunosuppressed state
* Known moderate or severe liver disease (Hepatitis A, B, C, with cirrhotic liver states, primary biliary cirrhosis, sclerosing cholangitis - any of these with portal hypertension and/or variceal bleeding)
* Dialysis-dependent renal failure
* When the index surgical procedure is expected to require a further surgical procedure within the subsequent 30 days.
* Metastatic cancer

Study design

Design

Study phase:	4
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	125
Type:	Anticipated

Medical products/devices used

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

Ethics review

Approved WMO Date:	26-07-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	05-12-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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
Other	ACTRN12614001226695
EudraCT	EUCTR2016-003431-37-NL
CCMO	NL58984.041.17