The influence of peroperative dobutamine infusion on the blood flow of the DIEP-flap

Published: 15-10-2013
Last updated: 15-05-2024

Primary Objective: To investigate in a prospective randomized controlled trial whether intravenous infusion of low doses dobutamine solely peroperative or for 18 more hours postoperative in women undergoing a breast reconstruction by means of a DIEP...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Therapeutic and nontherapeutic effects (excl toxicity)
Study type	Interventional

Summary

ID

NL-OMON38526

Source
ToetsingOnline

Brief title
Influence of dobutamine on blood flow

Condition

- Therapeutic and nontherapeutic effects (excl toxicity)
- Breast neoplasms malignant and unspecified (incl nipple)
- Breast disorders

Synonym
breast reconstruction with own tissue, DIEP-flap reconstruction

Research involving
Human

Sponsors and support

Primary sponsor: Orbis Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: blood flow, DIEP-flap, Dobutamine, peroperative

Outcome measures

Primary outcome

Increase in microcirculatory blood flow after dobutamine infusion and measured by means of laser Doppler flowmetry.

Secondary outcome

1. Is the incidence of partial or total flap necrosis lower after peroperative intravenous dobutamine infusion as compared to placebo [clinical judgement: the amount of visible necrotic (black) tissue, measured and calculated as percentage of the total flap]?

2. Is the incidence of fat necrosis lower after peroperative intravenous dobutamine infusion as compared to placebo (postoperative ultrasound)?

3. Is the incidence of partial or total flap necrosis and fat necrosis lower when dobutamine is given 18 hours post-operative as compared to peroperative?

4. How often has the escape been used to keep the blood pressure at level?

5. Quality of life (measured by means of a questionnaire sent after 2 weeks, 6 weeks and 3 months)

Other study parameters which might intervene with the main study endpoints are body weight, chemotherapy, radiation therapy, previously abdominal surgery,

diabetes and smoking.

Study description

Background summary

Breast cancer is the most common form of cancer in women. In 2008 the amount of new cases of an invasive form of breast cancer was 1.56 per 1.000 women (absolutely 13.005 new cases), in 2009 this amount was already 13.177. [BRON: NATIONAAL KOMPAS].

With the increasing percentage of breast cancer, the amount of women who want a breast reconstruction increases as well, specifically the reconstruction with own tissue in the form of a DIEAP-flap for its natural, soft result. The negative publications about silicone implants attributes to this increase.

In de DIEAP-flap is the blood flow in the microanastomosis most crucial for flap survival. Of previously performed studies we know that dobutamine increases the blood flow. This data however comes forth out of cardiologic or small, non-randomized nor controlled trials. Dobutamine is standardly used in performing DIEP-flap reconstruction although till now no randomized controlled trial has proven its effectiveness or even its ineffectiveness. For this reason this research will be performed. Hence, it is not an experimental treatment.

Study objective

Primary Objective:
To investigate in a prospective randomized controlled trial whether intravenous infusion of low doses dobutamine solely peroperative or for 18 more hours postoperative in women undergoing a breast reconstruction by means of a DIEP flap, increases the blood flow in arterioles and decreases the amount of fat necrosis postoperative after dobutamine infusion as compared to placebo (NaCl 0.9% infusion) measured by means of laser doppler for the blood flow and ultrasound for the fat necrosis?

Study design

A double-blind, randomized placebo-controlled pilot study with a duration of at least one year performed in the hospital during DIEP-flap reconstruction. The control group has the same characteristics as the investigational group en will receive the placebo on the same time as the investigational product is given to its group.

In case of severe hypotension (<80mmHg systemic pressure) which can not be

corrected with fluid infusion and is not related to the dose of anesthesia, one can use the escape medication (ephedrine). If the tension remains low in the placebo group dobutamine can be given and these patients will be left included due to the intention-to-treat analysis performed. The rationale for this analysis is to estimate the effect of allocating an intervention in practice instead of the effect in the subgroup of the participants who adhere to it. In case of ongoing low tension in the intervention group despite dobutamine and ephedrine given, the anesthesiologist can give phenylephrine or noradrenalin.

Intervention

1. Dobutamine 5microgram/kg/min peroperative, 18hours postoperative 0.9% NaCl infusion
2. Dobtuamine 5microgram/kg/min until 18hours postoperative
3. 0.9% NaCl infusion both per- and 18hours postoperative

One investigational group will receive intravenous dobutamin in a dose of 5migrogram/kg/min, while the other investigational group will receive dobutamine 5 microgram/kg/min until 18hours postoperative. This catecholamin can stimulate the *1-, *2- and **adrenergic receptors. The combined *1- and *1*adrenergic receptor stimulation leads to an inotropic effect, while *2-receptor stimulation induces a peripheral vasodilatory effect. Dobutamin will be given during dissection of the artery and during the performed microanastomosis.

The comparator (placebo) group will not receive dobutamine infusion, but NaCl 0.9% solution. Blood flow will be measured at the same time as done in the investigational group.

The patients in all the groups will receive medication infusion at the same time, so in the postoperative hours that one investigation group receives dobutamine, the other groups receive placebo infusion. This to preserve blinding. The medication preparation and distribution is done by the clinical pharmacologist.

With the Laser doppler the blood flow will be measured during the operation on standard moment (by dissecting the inferior epigastric artery, before the micro anastomosis, during the micro anastomosis, after the micro anastomosis and at the end of the operation. Postoperative the blood flow will be measured at 18.00hrs, 00.00hrs and 8.00hrs in the morning. 24hours postoperative patient are on the ICU where the nursing staff can do the measurement and note it on the research status of the patient.

Study burden and risks

The potential value of the research * namely increasing the rate of flap

survival * is in proportion to the potential risk to and burden for the patient. The potential risk is mainly related to the use of dobutamine (among them increased heart frequency, increased blood pressure, supraventricular extra systole, ventricular tachycardia, chest pain, bronchospasm, dyspnoea).

The most feared risk of the DIEP-flap operation is flap failure due to problems with the anastomosis. Since dobutamine is thought to increase the blood flow in the anastomosis making it easier to perform the anastomosis and increasing the flap survival rate, this study is expected to be beneficial to the patient.

This is in proportion to the risks which are restricted to the already cardiologic registered medicine dobutamine with a known vasodilatory action.

In conclusion: the theoretically action of dobutamine should lead to the desired effect but it still has to be proven for this specific research population and 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

- women
- age between 30 and 65 years old
- breast carcinoma in the history
- mastectomy in the history
- planned secondary reconstruction by means of a DIEP-flap

Exclusion criteria

- cardiac history (i.e. atrial fibrillation)
- clotting disorders (deep venous thrombosis or pulmonary embolus in the history)
- smoking
- allergic reaction to dobutamine or bisulfate

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-11-2013
Enrollment:	60
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	15-10-2013
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

ID: 26226
Source: Nationaal Trial Register
Title:

In other registers

Register	ID
EudraCT	EUCTR2013-002840-96-NL
CCMO	NL42897.096.13
OMON	NL-OMON26226