The effect of ARTISS on latissimus dorsi donor site seroma formation after breast reconstruction: a randomised controlled trial.

Published: 23-01-2017
Last updated: 13-04-2024

The aim of this study is to investigate the effect of ARTISS compared with our standard care on total volume of donor site seroma after harvesting a LD in immediate breast reconstruction. Seroma is diagnosed, when >= 20 mL can be punctuated after...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Soft tissue therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON41295

Source
ToetsingOnline

Brief title
The use of ARTISS to prevent seroma: a randomized controlled trial

Condition

- Soft tissue therapeutic procedures

Synonym
(wound) fluid collection, Seroma

Research involving
Human

Sponsors and support

Primary sponsor: Isala Klinieken

Source(s) of monetary or material Support: Zwols Wetenschapsfonds Isala Klinieken

Intervention

Keyword: ARTISS, Fibrin sealant, latissimus dorsi, Seroma

Outcome measures

Primary outcome

The aim of this study is to investigate the effect of ARTISS compared with conventional care (i.e., only vacuum drains after wound closure) on the formation of total volume of donor site seroma after harvesting a LD for immediate breast reconstruction.

During hospitalization drainage volumes will be measured starting on day one. The drains will be removed if measured output is less than 50 mL per 24h. The duration of drainage will be recorded (i.e., in days). When the drains are removed and when the patient does not have fever, pain (VAS score <= 2), or signs of an infection, the patient can be discharged. Clinical examination will be performed at one, two, six, and twelve weeks after discharge. Evidently, when the patient reports discomfort caused by seroma in-between the standard moments afore-mentioned, he or she will visit the hospital and these visits will also be counted. It will also be evaluated how many times the seroma has to be punctuated (when the patient reports discomfort caused by seroma or if the size of the seroma is >= 20mL, diagnosed with clinical examination and/ or by ultrasound).

Secondary outcome

In addition to the formation of seroma, other complications will be taken into account. That is, the total volume of drainage during hospitalization, duration

of drainage, donor-site pain, length of stay in the hospital, and costs.

Study description

Background summary

Yearly the plastic surgery department of the Isala Clinics performs about 23 pedicle-based musculocutaneous latissimus dorsi flaps (LD) used in immediate breast reconstruction surgery. One of the most frequent and dreaded complications of these interventions is production of seroma. The incidence of donor-site seroma is seen up in 80% of the patients. The amount of seroma can differ from 0mL until almost 3500 mL. Seroma can occur at the donor site at the back, but also in the chest wall after mastectomy. Formation of seroma can result in seroma related morbidity such as infection, formation of a capsule around seroma resulting in deformity, skin flap necrosis or impaired wound healing. As a consequence, patients suffer from increased postoperative pain, delay of adjunctive treatments, longer hospital stays and therefore increased costs. Potential treatments for seroma are frequent needle aspiration, *benign neglect*, and even doxycyline or bleomycine sclerotherapy.
Avoiding seroma production seems to be of great importance for both patients and plastic surgeons. Since a couple of years, ARTISS© (Baxter Healthcare Corporation, Utrecht, NL), a human fibrin sealant, is available as a treatment option to reduce or even prevent donor site seroma formation. ARTISS is a mixture of fibrinogen, human thrombin, aprotinin and calcium chloride solution. Therefore, it facilitates haemostasis, seal leaky lymph vessels, and manage tissue adherence2. In a rodent model, after harvesting the LD and using fibrin sealant, seroma formation was even decreased from 90% to 20%.
So far, no large randomized controlled trials are conducted describing the effectiveness of ARTISS on seroma production after LD procedures in breast reconstruction surgery. Therefore, this prospective, single-blinded randomized controlled trial aims to determine the effect of ARTISS in preventing donor site seroma production compared with the current standard care.
*

Study objective

The aim of this study is to investigate the effect of ARTISS compared with our standard care on total volume of donor site seroma after harvesting a LD in immediate breast reconstruction. Seroma is diagnosed, when >= 20 mL can be punctuated after fine needle aspiration or when >= 20 mL can be diagnosed with the help of ultrasound, after removal of all drains.

Study design

A prospective, single-blinded, randomized controlled trial in one teaching hospital (Isala Clinics, location Zwolle) will be carried out from 1st July 2015 until 1st July 2020. The recruited patients will be allocated in one of the two groups: ARTISS and suction drains or suction drains alone. The program *research manager* will allocate the patients in groups.

Intervention

Firstly, the general surgeon will perform a mastectomy. One drain will be inserted in the cavity of the amputated breast. Hereafter, the LD flap is harvested by a qualified plastic surgeon using the following technique. Beside the latissimus dorsi musle, a transverse skin paddle will be included in the LD flap. The LD flap size is designed in reference to the removed breast tissue. Dissection of the flap is performed using electrocautery. All adipose tissue is included in the flap and the thoracodorsal nerve is dissected. Therefore, the flap could be transposed anteriorly. A mamma prothese can be used in breast reconstruction. Haemostasis is performed using electrocautery. The wound site is irrigated with saline solution. Before closure, two suction drains are inserted at the same location at the back in every patient. In the ARTISS group, the entire cavity is dried and than sprayed with ARTISS. Pressure is applied for three minutes to ensure the obliteration of the cavity. The drains are not activated before these three minutes after the fibrin sealant is sprayed, to avoid disturbing the gluing process. Hereafter, the wound is closed using vicryl and monocryl sutures. Our control group will have the same wound closure technique, besides the ARTISS spraying in the cavity.
Starting on day one, all volumes and duration of wound drainage will be recorded. Suction drains are removed if drainage < 50 cc/ 24hours. When the drains are removed, seroma formation is diagnosed with clinical examination of the back and/ or with ultrasound. Seroma can be aspirated with fine needle aspiration and the aspirated volume will be recorded if aspiration had occurred. Standard out clinic examination will be performed at one, two and six weeks after discharge. At six weeks after discharge, an ultrasound will be performed of the donor site in our included cases, to objectivize the volume of seroma formation. Our last measurement will be at 12 weeks postoperative.
In case of discomfort caused by donor site seroma, patients will visit our out clinic department more often than our check-ups at 1, 2, 6 and 12 weeks. The volume and frequency of these aspirations are also recorded during these extra examinations.
Our secondary outcomes are drainage volume and duration of drainage, length of hospital stay of a patient, other postoperative complications besides donor site seroma (such as infection), pain measured by the Visual Analog Scale (VAS), and costs in euros.

Study burden and risks

All included patients in the ARTISS group can experience the benefits of the

fibrin sealant. So, patients can experience less donor site seroma and seroma related complications.
In line with the manufacturer*s guide, a few risks are associated with the use of ARTISS:
a. Hypersensitivity Reactions
Hypersensitivity reactions, including anaphylaxis, can occur. Cases have been reported in post-marketing experience with fibrin sealant. In specific cases, these reactions have progressed to anaphylaxis. Such reactions may especially be seen if product is applied repeatedly over time or in the same setting, or if systemic aprotinin has been administered previously; however, these reactions may also occur in patients receiving ARTISS for the first time. Even if the first treatment was well tolerated, a subsequent administration of ARTISS or systemic aprotinin may not exclude the occurrence of an allergic reaction. Symptoms associated with allergic anaphylactic reactions include: Flush, urticaria, pruritus, nausea, drop in blood pressure, tachycardia or bradycardia, dyspnea, severe hypotension and anaphylactic shock.
The product contains aprotinin for its antifibrinolytic properties. Aprotinin, a monomeric polypeptide, is known to be associated with anaphylactic reactions. Even in the case of strict local application of aprotinin, there is a risk of anaphylactic reactions to aprotinin, particularly in the case of previous exposure.
Discontinue administration in the event of hypersensitivity reactions. Remove the already applied, polymerized product from the surgical field. Mild reactions can be managed with antihistamines. Severe reactions and reactions involving hypotension require immediate resuscitative intervention.
b. Air or Gas Embolism
Air or gas embolism has occurred with the use of spray devices employing pressure regulator to administer fibrin sealants. This event appears to be related to the use of the spray device at higher than recommended pressures and in close proximity to the tissue surface.
When using a spray device, be sure to use the pressure within the pressure range recommended by the spray device manufacturer. In the absence of a specific recommendation avoid using pressure above 20-25 psi. Do not spray closer than the distance recommended by the spray device manufacturer. In the absence of a specific recommendation avoid spraying closer than 10-15 cm from the surface of the tissue. When spraying, changes in blood pressure, pulse, oxygen saturation and end tidal CO_2 should be monitored because of the possibility of occurrence of air or gas embolism. When using the Easyspray device, or an equivalent spray device cleared by FDA, use the pressure within the pressure range recommended by the spray device manufacturer. Spray only on to visible application sites.
c. Protein Denaturation
The sealer protein and thrombin solutions can be denatured by alcohol, iodine or heavy metal ions (e.g., antiseptic solutions). If any of these substances have been used to clean the wound area, the area must be thoroughly rinsed before application of ARTISS and made as dry as possible.
d. Transmission of Infectious Agents

ARTISS is made from human plasma. Because this product is made from human blood, it may carry a risk of transmitting infectious agents, e.g., viruses, the variant Creutzfeldt-Jakob disease (vCJD) agent, and theoretically, the Creutzfeldt-Jakob disease (CJD) agent. All infections thought by a physician possibly have been transmitted by this product should be reported by the physician or other healthcare provider to Baxter Healthcare Corporation, telephone no. 1-866-888-2472.
Some viruses, such as parvovirus B19, are particularly difficult to remove or inactivate at this time. Parvovirus B19 most seriously affects pregnant women (fetal infection), immune-compromised individuals or individuals with an increased erythropoiesis (e.g., hemolytic anemia).

Contacts

Public
Isala Klinieken

Dokter van Heesweg 2
Zwolle 8025AB
NL
Scientific
Isala Klinieken

Dokter van Heesweg 2
Zwolle 8025AB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

All female patients older than 18 years, who will undergo a breast reconstruction with a LD flap will be included. All participating patients have to sign a written consent, before they can be included in our study.

Exclusion criteria

Patients who are pregnant, have a pre-operative on-going infection, history of systemic anti-coagulant use, known hypersensitivity to ARTISS or postoperative haemorrhage will be excluded.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-07-2015
Enrollment:	121
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	ARTISS
Generic name:	ARTISS - fibrin sealant
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	23-01-2017
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	28-03-2017
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)

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	EUCTR2014-000727-25-NL
CCMO	NL47582.075.15