Hyaluronidase for Enhancement of Tissue Perfusion: A Pilot Study

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We do not currently have enough knowledge about the potentially beneficial effect that hyaluronidase might have on skin flap angiogenesis.

Ethical review	Not approved
Status	Will not start
Health condition type	Skin vascular abnormalities
Study type	Interventional

Summary

ID

NL-OMON53369

Source
ToetsingOnline

Brief title
Pilot Hyaluronidase

Condition

- Skin vascular abnormalities
- Skin and subcutaneous tissue therapeutic procedures

Synonym
Transposition flaps

Research involving
Human

Sponsors and support

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

Intervention

Keyword: flap reconstruction, hyaluronidase, perfusion, vascularisation

Outcome measures

Primary outcome

The primary outcome is tissue perfusion of the perforator flap which is visualized using fluorescence imaging.

Secondary outcome

The color (white/pale/pink/red/black), time of capillary filling, texture (hard/soft), temperature (cold/normal/warm), Doppler sound (absent/poor/normal), flap color and any complications (such as wound infection, necrosis and pain) will be checked

Study description

Background summary

Traumata, pressure ulcers and oncologic treatments can cause severe tissue defects. The plastic surgeon can restore the contour and function of tissue defects. The success rate of a perforator flap depends on the quality of the blood flow. In 20-30% of cases, there is skin and fat necrosis, meaning that parts of the flap die because of insufficient blood flow. This often involves the fragile, most distal parts. The challenge is to reduce the risk of circulation problems during and after the procedure. We want to investigate whether hyaluronidase could help to reduce this risk. Hyaluronidase is a drug that has been studied several times. It is used to improve systemic effects of injectable drugs, for local anesthesia in ophthalmic surgery, keloid scar treatment and cosmetic facial fillers. The effect of the substance hyaluronidase relies on the dissolution of hyaluronic acid and monopolysaccharides in connective and epithelial tissues. The enzymatic breakdown of hyaluronic acid occurs directly, breaking subcutaneous tissue connections and allowing diffusion of the extravasated fluid over a 3-5 times larger interstitial space. The dissolution of the ground substance thus changes the viscosity and increases interstitial perfusion. In this way, hyaluronidase may possibly contribute to improve blood flow in the perforator flap and thus

could reduce the risk of fat necrosis.

Study objective

We do not currently have enough knowledge about the potentially beneficial effect that hyaluronidase might have on skin flap angiogenesis.

Study design

The procedure will start according to the standard surgical protocol. After preparation of the flap, the flap will be measured and a special camera system will be set up to visualize the tracer. Next, 7.5 mg of indocyanine green (ICG) will be administered intravenously. The NIR fluorescence intensity in the perforator flap will be recorded for 5 minutes using the Quest Spectrum platform. This becomes the baseline fluorescence. Then after 20 minutes, 150 IE hyaluronidase will be injected intradermally. Immediately afterwards, another intravenous 7.5 mg indocyanine green (ICG) will be administered and another fluorescence measurement will follow. During the camera recording, the time to staining and intensity of the signal will be recorded.

Intervention

The procedure will start according to the standard surgical protocol. After preparation of the flap, the flap will be measured and a special camera system will be set up to visualize the tracer. Next, 7.5 mg of indocyanine green (ICG) will be administered intravenously. The NIR fluorescence intensity in the perforator flap will be recorded for 5 minutes using the Quest Spectrum platform. This becomes the baseline fluorescence. Then after 20 minutes, where the surgeon normally takes a break, 150 IE hyaluronidase will be injected intradermally. Immediately afterwards, another intravenous 7.5 mg indocyanine green (ICG) will be administered and another fluorescence measurement will follow. During the camera recording, the time to staining and intensity of the signal will be recorded.

Study burden and risks

Like any drug, hyaluronidase can have side effects, although not everyone experiences them. The following side effects could occur: existing infections may worsen, an allergic reaction and injection pain. Indocyanine green, has been used for decades, is very safe and side effects are very rare. The only possible side effect is a treatable allergic reaction. Moreover, this reaction has only been seen in people who received a higher amount of indocyanine green (about 10-15 times higher).

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 who will undergo reconstructive surgery at the LUMC in the period May 2023 to Oct 2023 using a perforator flap.

Exclusion criteria

Exclusion criteria included patients with known hyperthyroidism, autonomic thyroid adenoma, lactation, terminal renal insufficiency, congenital heart defects, congestive heart failure, symptoms of shock or hypersensitivity to indocyanine green, sodium iodide, iodine, hyaluronidase, seafood, bovine proteins and/or gelatin hydrolysate.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	10
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	hyaluronic acid
Generic name:	Hyason
Registration:	Yes - NL outside intended use

Ethics review

Not approved

Date:	22-02-2023
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTRnet-NL
CCMO	NL83595.058.23