Detection of sentinel lymph nodes in laryngeal cancer by injection of patent blue dye via flexible laryngoscopy as a new technique

Published: 23-04-2021
Last updated: 07-12-2024

Primary Objective: After ex vivo confirmation that BD injected around LC in a laryngeal surgical specimen is not spreading into tissues beyond the tumor, the detection of SLN by a technique of injecting BD via a flexible laryngoscope using a working…

Ethical review	Approved WMO
Status	Will not start
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON49436

Source
ToetsingOnline

Brief title
Patent blue dye in laryngeal cancer

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Laryngeal cancer, Laryngeal carcinoma

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Laryngeal cancer, Methylene blue dye, Sentinel lymph node

Outcome measures

Primary outcome

Applicability of the used technique and diagnostic accuracy (sensitivity,

specificity, positive and negative predictive value and diagnostic accuracy)

for detection of SLN will be calculated by using histopathological results as

gold standard.

Secondary outcome

We want to analyse the difference in BD spreading in primary TL and salvage TL

for detection of SLN by using histopathological results as gold standard.

Study description

Background summary

Worldwide laryngeal carcinoma (LC) is in the top 25 most common cancers with an annual incidence of more than 175.000 and around 90.000 deaths each year (13). In the Netherlands each year around 700 patients will develop LC. Five years overall survival is 60% and in advanced stage supraglottic LC, this is approximately 30%. The recurrence rate of LC increases with an advanced T-stage: patients with T1-T2 stage have a recurrence rate of up to 30%, while in T3-T4 this is 50% (1). The treatment consists of nonsurgical, surgical, radiation or chemoradiation modalities. The presence of lymph node metastases or the likelihood of a tumor spread to the lymph nodes are important for the treatment selection (2). According to international guidelines, elective treatment of clinically and radiologically confirmed N0 regional lymph nodes is indicated in cT1-T3 supraglottic and T2b-T4b glottic cancer (i.e. without clinical signs of lymph node metastases).

Improving the detection of the SLN in LC
In general, the sentinel lymph node (SLN) is the primary site which receives lymphatic drainage from metastasizing tumor tissue. Previous treatment in second primary tumors or recurrent LC could possibly influence the lymphatic drainage and metastatic behavior (14). With the identification of the SLN due to BD injection around tumor tissue the individual tumors drainage pattern gets visible (14). This SLN sampling technique turned into the standard care in malignant breast cancer and melanoma (3-6). In the UMCG, the SLN procedure using BD is applied for breast cancer and melanoma (7). Also, the SLN procedure using BD has been studied in vulva cancer and colon cancer in the UMCG (8, 9). A confirmed negative SLN could lead to avoid unnecessary treatment of the neck and decrease swallowing problems, fibrosis or lymphedema as complications of treatment of the neck. After an ex vivo first pilot study, the aim of this second in vivo part of this pilot study (feasibility and validation) is to analyze [*] the applicability and diagnostic accuracy of BD for detection of the SLN in LC in vivo by injection via the working channel of a flexible laryngoscope around the tumor (in vivo). The flexible laryngoscope with the working channel is routinely used in patient care in the UMCG since 2017 and has received the European certification mark (CE) which shows that the product meets the safety, health and environmental requirement for selling and using in the European Union (10). The injection by using the working channel is conform the intended use (11). For injection of BD we will use the single use injector needle (injector force max. model number NM-401L-0425, Olympus). We hypothesize that BD locates accurately at SLN by injecting BD around tumor tissue. This could result in a prevention of patients receiving an unnecessary treatment of the neck.

Study objective

Primary Objective: After ex vivo confirmation that BD injected around LC in a laryngeal surgical specimen is not spreading into tissues beyond the tumor, the detection of SLN by a technique of injecting BD via a flexible laryngoscope using a working channel has to be tested.

Secondary Objective: We want to analyze the difference in BD spreading for detection of SLN in primary TL and salvage TL.

Study design

After previously tested spreading of BD around the LC ex vivo in prospectively collected laryngeal surgical specimens, we will prospectively include ten patients who will undergo a TL with planned neck dissection to inject BD in vivo.
Duration: Study period of 18 months
Setting: In total, around 20 total laryngectomies are performed at the department of Otolaryngology / Head and Neck Surgery of the University Medical

Center Groningen each year.

In this study we will analyze if BD distributes accurately to the SLN in vivo in ten patients who will undergo a TL with planned neck dissection. Secondary, we want to analyze the difference in BD spreading in primary TL and salvage TL. Therefore, 0.5-1 ml BD will be injected around laryngeal tumor tissue at the beginning of the planned TL under general anaesthesia by using a standard injection needle via the working channel of a routinely used flexible laryngoscope. Applicability and diagnostic accuracy (sensitivity, specificity, positive and negative predictive value and diagnostic accuracy) for detection of SLN will be calculated by using histopathological results as gold standard.

Study burden and risks

BD is widely used in several medical studies and turned into standard care for SLN sampling technique in malignant breast cancer and melanoma (3-6). Adverse reactions reported to BD subcutaneous administration are allergic reactions (3, 12). In approximately 1% of the patients it causes hypersensitivity reactions and the risk of anaphylactic shock is the highest within the first 30 minutes (3, 16). The risk of the side effects is higher in patients with hypersensitivity reactions to BD earlier and to trifenylmethan pigment. Therefore, we will exclude patients with this hypersensitivity in medical history. Also, we will administer BD during general anaesthesia in the operation theatre. The patient is under constant supervision and the vital parameters are controlled. In the rare case of (the first signs of an anaphylactic allergic reaction medical support is given instantly. Next to this, the urine of the patient can be coloured blue within the next 24-48 hours after injection (3). Adverse effects reported by using BD intravenously are next to allergically reactions and anaphylaxis also oedema of the larynx and angio-oedema (4). Other side effects are urticaria, erythema, itching and skin rash (4). At the side of injection, BD can colour the skin blue. We will not inject BD intravenously but subcutaneously. Therefore, we do not expect these side effects in our study. Due to staining lymphatics we are able to localize the spreading of BD. We will exclude pregnant woman because it is advised to only use BD in strict indications during pregnancy (3).

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL

Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713 GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- proven carcinoma of the larynx
- > 18 yrs of age
- undergo a total laryngectomy with planned neck dissection.
- informed consent

Exclusion criteria

- partial laryngectomy
- no planned neck dissection
- pregnancy
- earlier hypersensitivity reaction to BD or to trifenylmethan pigment (which is used in cosmetics or food)

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

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

Ethics review

Approved WMO

Date:	23-04-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Not approved

Date:	21-03-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
CCMO	NL74127.042.20

Study results

Actual enrolment: 0

Summary results
Trial never started