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Determining the effectiveness of Fibrin Sealants in reducing complications in patients undergoing lateral neck dissection

Submission date
04/04/2018

Recruitment status
No longer recruiting

Registration date
16/05/2018

Overall study status
Completed

Last Edited
30/10/2023

Condition category
Cancer

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
A neck dissection is an operation to remove the glands in the neck either because they have cancer in them or they are at risk of cancer spreading to them. Complications after neck dissection can be a significant problem for patients and may affect their quality of life. Research on understanding the feelings of patients who have had head and neck cancer treatment has shown that avoiding complications is very important. Giving patients a substance that copies the blood clotting process, called Fibrin Sealant, may be able to protect them from complications. This is because this substance can seal areas of bleeding and stick the raw surfaces of the wound together, reducing the space for blood to collect in. Fibrin Sealants are natural products derived from the same human blood that is used for blood transfusions and are sprayed directly into the wound. Unfortunately, there is no high quality research that has been able to answer whether Fibrin Sealants can prevent complications after neck dissection. Therefore a clinical trial has been designed to help answer this important question. However, before this can be started a miniature version of the trial (pilot study) needs to be conducted to make sure it has been designed in the best possible way and improve the design of the future trial, which will find out whether or not Fibrin Sealants can really help avoid complications.

Who can participate?
Patients over 18 years old who are due to have a neck dissection

What does the study involve?
Participants are randomly allocated to either receive Fibrin Sealant during their surgery or have their surgery as normal without it. They are followed up for 6 weeks after the date of their surgery. This includes their hospital in-patient stay and two scheduled outpatient clinic appointments. Any unscheduled hospital visits within the 6 week period are also included.

What are the possible benefits and risks of participating?
Taking part in this study does not have an effect on the participants' cancer treatment. They will not be restricted in taking any drugs they may need or in having any further treatment. There are no specific benefits to taking part other than the opportunity to take part in surgical

research. The study has been designed to minimise extra tests and hospital visits so that participation is as easy as possible. Surgeons up and down the country are already using Fibrin Sealants but this is not based on high quality evidence. Participants will be helping to design a 'full' trial that is as effective and efficient as possible. It is hoped that the 'full' trial will answer whether or not Fibrin Sealants are beneficial to patients undergoing neck dissection surgery. Fibrin Sealants are considered to be very safe products and serious risks are very rare. The manufacturer reports the following potential risks:
1. Itchiness of the skin of the neck (between 1 – 10 patients out of a hundred). The doctor may treat this with antihistamines (allergy medicines) depending on how problematic this is.
2. Fluid collection under skin (less than 1 patient out of a hundred). Most fluid collections do not require treatment as the body will eventually absorb the fluid. If the fluid collection is large or problematic, the doctor may drain the fluid. This may be done by either drawing the fluid out using a syringe or formally opening the wound and letting the fluid out.
3. Severe allergic reaction (less than 1 patient out of a hundred). If participants develop a severe allergic reaction it will normally develop during or immediately after the surgery. If signs and symptoms of allergy are noted they will receive treatment as a matter of urgency.
4. If the surgeon holds the spray too close to the blood vessels in the neck, air may enter the blood vessel causing a serious complication known as an "air embolism". Patients who get "air embolisms" are at increased risk of heart attacks, strokes and breathing problems. Fortunately this is very rare as there have only ever been 6 reported cases of life threatening "air embolism" out of many thousands of patients who have already been given Fibrin Sealants over the years. There have been no reported cases of "air embolism" from the type of Fibrin Sealant used (ARTISS, Baxter Healthcare Ltd). Every surgeon who uses the fibrin sealant in this study will be trained on how to avoid this complication.
5. Because the Fibrin Sealant is taken from human blood that is used in blood transfusions, there is a theoretical risk of catching a blood-borne virus (e.g. hepatitis or HIV). People who donate their blood are always carefully selected to minimise the risk of transmitting viruses. Also the Fibrin Sealant has been carefully checked and treated to prevent contamination with viruses. Despite these efforts, it cannot be guaranteed that the Fibrin Sealant is free of viruses. There have been no reported cases of patients catching viruses from Fibrin Sealants. In the very unlikely event that participants do catch a virus, they will be referred to a specialist for treatment.

Where is the study run from?
1. Aintree University Hospital (UK)
2. Queen Victoria Hospital (UK)

When is the study starting and how long is it expected to run for?
October 2017 to September 2020

Who is funding the study?
National Institute for Health Research (NIHR) (UK)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
37896

Study information

Scientific Title
DEFeND: Determining the effectiveness of Fibrin Sealants in reducing complications in patients undergoing lateral neck dissection: a randomised external pilot trial

Acronym
DEFeND

Study objectives
A neck dissection is an operation to remove the glands in the neck either because they have cancer in them or they are at risk of cancer spreading to them. Complications after neck dissection are a significant problem for patients and may affect their quality of life. Research on understanding the feelings of patients who have had head and neck cancer, has shown that avoiding complications is very important to them.

We have found evidence that by giving patients a substance that copies the blood clotting process called Fibrin Sealant, we may be able to protect them from complications. This is because this substance can seal areas of bleeding and stick the raw surfaces of the wound together. Unfortunately, there is no high quality research that has been able to answer whether Fibrin Sealants can prevent complications after neck dissection. Therefore we have designed a clinical trial to help us answer this important question. However, before this can be started we need to conduct a miniature version of the trial to make sure it has been designed in the best possible way. The main questions we aim to answer are:

1. Can we recruit patients?
2. Do all aspects of the study design work well together?
3. How many patients do we need in the 'full' trial?

Ethics approval required
Old ethics approval format

Ethics approval(s)
North West – Greater Manchester East Research Ethics Committee, 14/05/2018, ref: 234851

Study design
Randomised; Interventional; Design type: Treatment, Surgery

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Head and neck cancer

Interventions
Randomisation lists shall be produced by a statistician at the NWSTC prior to the recruitment of the first patient. Patients shall be randomised using a 1:1 ratio. Lists shall be produced based on the principle of randomly permuted blocks with random block sizes of 2 and 4. Patients will only be stratified according to the hospital in which they receive their treatment.

Participants will be randomised to either receive fibrin sealant during their surgery or have their surgery as normal without it:
Arm A: Neck dissection with ARTISS fibrin sealant and standard wound closure. Application of ARTISS fibrin sealant to the surgical wound in addition to “Standard of care”. “Standard of care” will include the establishment of a dry surgical field after performing the neck dissection using electrocautery &/or surgical ties &/or clips. The wound should then be irrigated with 100ml of Normal Saline and dried. Up to 2ml of ARTISS will be sprayed into the wound adhering to the manufacturer’s instructions and surgical protocol steps
Arm B: Neck dissection with standard wound closure. Arm B is the control arm and constitutes “standard of care” alone. This will include the establishment of a dry surgical field after performing the neck dissection using electrocautery and/or surgical ties and/or clips. Patients will have a surgical drain placed and the wound closed in the usual manner.

Patients will be followed up for 6 weeks after the date of their surgery. This will include their hospital in-patient stay and two scheduled out-patient clinic appointments. Any unscheduled hospital visits within the 6 week period will also be included.

Intervention Type
Procedure/Surgery

Primary outcome(s)

As this research is a 'pilot study' no formal primary outcome measure has been specified. The outcomes measures for this study can be divided into those that will inform the pilot study and those that will inform the future 'full' clinical trial.

1. Proportion of eligible patients recruited to the study, calculated as the screened to randomisation rate at 12 months at the end of the DEFeND study
2. Reasons for failure to screen potentially eligible patients. Qualitative data recorded as free text for every patient who was potentially eligible but was not screened recorded at screening
3. Recruitment rate measured as the number of patients randomised each month throughout the study for 12 months
4. Reasons for failure to randomise. Qualitative data recorded as free text for every patient who was recruited but not randomised recorded at baseline
5. Reasons for failure to reveal allocation at a specific time point during surgery. Qualitative data recorded as free text for every patient who was randomised but did not have their allocation revealed at the correct timepoint during surgery. This is recorded on the day of surgery
6. Fidelity of the blinding process (both patients and outcome assessors) as detected by blinding indices. This is assessed by asking the patient and research team members what the allocation for that particular patient when they exit the study at follow-up 2 (day 28 – 42) or premature discontinuation
7. Accuracy of data recording, summarised by the number of key data items with missing /incomplete data entries recorded per patient when they exit the study at follow-up 2 (day 28 – 42) or premature discontinuation
8. Number of patients lost to follow-up recorded at 12 months at the end of the DEFeND study
9. Protocol adherence, measured by the number of major/minor protocol deviations observed per patient when they exit the study at follow-up 2 (day 28 – 42) or premature discontinuation
10. The minimal clinically important difference (MCID) in clinical endpoints, determined by questioning recruited patients and recruiting clinicians. Qualitative data recorded as free text for every patient when they exit the study at follow-up 2 (day 28 – 42) or premature discontinuation

Key secondary outcome(s))

1. Surgical complications recorded using the Clavien-Dindo classification of surgical complications recorded every day of in-patient stay, follow-ups 1 and 2, any unscheduled follow-up and at premature discontinuation
2. Wound drainage volume (ml) recorded 2 – 3 times daily during inpatient stay while surgical drain is in situ
3. Time (hours) for wound drainage volume to reach a rate of <30ml/24hrs (<1.25ml/hr) from the end of surgery. Recorded during inpatient stay
4. Time (hours) to drain removal (as dictated by drainage volume) from end of surgery. Recorded during inpatient stay
5. Total wound drainage volume (ml) from the time of drain activation to drain removal. Recorded during inpatient stay
6. Time (hours) to be declared medically fit for hospital discharge and time (hours) to actual hospital discharge. Recorded during inpatient stay
7. Incremental cost-effectiveness ratio, calculated per patient when they exit the study at follow-up 2 (day 28 – 42) or premature discontinuation
8. Neck Dissection Impairment Index (NDII). This is a procedure specific validated patient reported outcome measure. Recorded at baseline and when they exit the study at follow-up 2 (day 28 – 42) or premature discontinuation

9. Daily patient reported pain score using Visual Analogue Scale (VAS) recorded at baseline, every day of in-patient stay, follow-ups 1 and 2, any unscheduled follow-up and at premature discontinuation

Completion date
09/10/2019

Eligibility

Key inclusion criteria
1. Patients due to undergo lateral neck dissection
2. Neck dissection to include a minimum of 3 levels
3. Patients who have capacity to consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Total final enrolment
51

Key exclusion criteria
1. Known allergy to Aprotinin (an ingredient of Fibrin Sealants known to cause allergic reactions)
2. Pregnancy or breastfeeding
3. Age less than 18 years
4. Bilateral neck dissection
5. Previous exposure to Fibrin Sealant within the last 6 months
6. The patient has a cancer that requires complex reconstructive surgery
7. Allergy to dairy products

Date of first enrolment
06/08/2018

Date of final enrolment
30/08/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Aintree University Hospital
Longmoor Ln
Liverpool
United Kingdom
L9 7AL

Study participating centre
Queen Victoria Hospital
Holtye Rd
East Grinstead
United Kingdom
RH19 3DZ

Sponsor information

Organisation
University of Liverpool

ROR
https://ror.org/04xs57h96

Funder(s)

Funder type
Government

Funder Name
NIHR Trainees Co-ordinating Centre (TCC); Grant Codes: DRF-2017-10-117

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication (including PhD thesis).

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		20/10/2023	30/10/2023	Yes	No
Protocol article	protocol	26/05/2020	23/11/2020	Yes	No
Participant information sheet	version V2.1	14/05/2018	16/05/2018	No	Yes
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Protocol file	version V1.0	12/02/2018	16/05/2018	No	No