Research protocol

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Title:

Use of topical anaesthetics in cutaneous head and neck malignancies: a randomized controlled trial

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1. Background:

Operations on cutaneous tissues of the head and neck are some of the most frequently performed types of operation performed. They can often successfully be performed using local anaesthetic (LA). However, tissues in this anatomic area are some of most sensitive tissues in the body to nociceptive pain. As such, local anaesthetic can be a distressing experience for patients in many ways. Unfortunately, it is also the most common anatomical site for cutaneous malignancies. Advanced age and chronic sun exposure are two potent risk factors. The majority of these lesions are resected under local anaesthetic for several reasons including economic, patient-factors, theatre availability and speed. However, one of the major disadvantages of local anaesthetic such as lidocaine is pain during administration. This is exacerbated as the head and neck area is one of the most sensitive parts of the body. Several interventions have been used to reduce pain from needles and injections including ethylene chloride cryoanalgesic spray and topical anaesthetic agents including EMLA (lidocaine and prilocaine) and Ametop ointments. These have been extensively used in paediatric populations with great success to reduce pain during procedures requiring hypodermics such as cannulation. Several studies have trialled these interventions in adult populations across a variety of anatomical locations with variable results.

1.1. Hypothesis:

EMLA and ethyl chloride reduce pain associated with local anaesthetic administration

1.2. Aim

The aim of this study is to assess if ethylene chloride or EMLA are effective in reducing the pain associated with local anaesthetic administration

2. Outcome Measures

2.1. Primary outcome measure:

The primary outcome measure is patient reported pain on a numeric rating scale (NRS) (1; no pain, 10; worst pain imaginable)

2.2. Secondary outcome measures:

Patient satisfaction measured on NRS scale of 1=not bad at all, to 10=worst experience imaginable.

Analysis of risk factors associated with pain from local anaesthetic in the head and neck including size of resection and injection volume:

- Pathology – malignant versus benign
- Local anaesthetic volume
- Size of resection
- Site of resection

3. Methodological design

3.1. Study design

Randomized controlled trial

3.2. Selection:

Patients will be selected from those attending scheduled excision of cutaneous head and neck malignancies at our centre

3.3. Inclusion criteria:

- Aged at least 18 years
- Receiving surgery to cutaneous tissues of the head and neck
- Procedure performed under local anaesthetic

3.4. Exclusion criteria:

- Paediatric patients
- Surgery performed under general anaesthetic
- Mucosal operative site (e.g. oral cavity)
- Significant cognitive impairment (e.g. severe dementia)
- Known sensitivity/allergy to EMLA
- History of a pain disorder (e.g. complex regional pain syndrome).

3.5. Sample size calculation:

A formal sample size calculation will be performed after an initial pilot study of ten patients per group to calculate the effect size. Other studies on using topical anaesthetic agents in other non head and neck anatomical sites typically required less than 50 participants per group. G*Power 3.1 (Universität Düsseldorf) software will be used to calculate the necessary sample size. We will likely employ an α error probability of 0.05 and a power of 95%. A 10% margin for safety will be used to mitigate the possible risks of participant attrition

3.6. Randomization:

Computer randomization will be performed. A random number sequence will be generated using randomizer.org® with numbers allocated using stratified permuted blocks of four and these will be concealed in individual sealed envelopes with the aid of a research contributor.

Participants will be allocated in order of recruitment and in participants with more than two lesions will have the more superiorly located lesion allocated first.

3.7. Interventions

Patients will be split into 4 groups:

- EMLA
- Aqueous ointment
- Ethyl chloride spray
- no treatment.

3.8. Study procedures

Written informed consent will be obtained prior to group allocation. Following group allocation, topical agents will be administered as follows. EMLA (EMLA cream 5% 25g lidocaine, 25g prilocaine) and aqueous cream will be applied to cover the surgical site, delivered via an unmarked syringe to achieve single blinding. A Tegaderm® adhesive dressing will then be applied over this to prevent the cream from drying out, and it will be removed in the theatre before the administration of LA. The local anesthetic to be used will be 1% lidocaine with 1:200,000 adrenaline and will be injected via a 25-gauge needle attached to a 10ml syringe. A 5ml syringe will be occasionally used when it is not possible to inject via a 10ml syringe.

EC will be applied to the surgical site before LA injection. The area will be sprayed at a distance of 5-10cm for 4-8 seconds until the skin slightly blanches, and the fluid will be allowed to evaporate.

3.9. Assessing outcomes

The key focus in this study will be the assessment of pain linked to the injection of local anesthesia (LA). Following the LA administration, each participant will be prompted to evaluate the pain they undergo using a numeric rating scale (NRS; 1=no pain, 10=worst pain imaginable). Subsequent to the procedure, patients will be inquired about their overall perception of the experience (1=not bad at all, 10=worst experience imaginable).

4. Statistical analysis

The distribution pattern of variables will be assessed using the Kolmogorov-Smirnov test. The Kruskal-Wallis test and Mann Whitney test will be employed to compare groups for non-parametric data and for covariate analysis. The Chi-squared test will be applied to detect differences for categorical data. Spearman's Rho will be used to quantify the strength of the linear relationship between non-parametric continuous variables. A per protocol analysis will be conducted as it is believed that in cases where patients are unable to describe their pain by using a number, it will disproportionately affect the results by conducting a "worst case scenario" analysis. Furthermore, due to a minimal interval between intervention and measurement of pain outcomes in this study, there will be low rates of attrition. Statistical analysis will be performed using SPSS v.26 (Aramonk, US). Statistical significance will be considered at $p<0.05$.

5. Miscellaneous

5.1. Ethical considerations:

This trial will be registered with the University Hospital Waterford Research and Ethics Committee where full ethical approval will be obtained prior to study commencement. It is considered that patient risks from this study are negligible.

5.2. Funding:

No funding will be necessary for this study

5.3. Dissemination of results

Results will be prepared into a scientific manuscript for publication and presented at scientific surgical meetings