THE UNIVERSITY of York

(Pharmacist letter version 1 4/5/2007)

Insert Trust /site logo
DEPT OF HEALTH SCIENCES
University of York
Area 4, Seebohm Rowntree Building
York YO10 5DQ
Insert date

Name and address of pharmacist

Dear Name of pharmacist

Re: A NHS HTA Programme funded trial of two treatments of verrucae

We are writing to inform you about a research study which is currently being undertaken in your PCT. This study is being funded by the NHS Health Technology Assessment Programme under their call for Medicines for Children (http://www.hta.nhsweb.nhs.uk/calls/M4CUpdate.htm) and is a joint research project between the Podiatry Department at (insert name) and the York Trials Unit at the University of York. The aim of the study is to compare the clinical effectiveness of cryotherapy using liquid nitrogen versus patient daily self-treatment with an over the counter preparation of 50% salicylic acid (Verrugon) for the treatment of verruca.

This study aims to recruit 266 participants and we are writing to ask for your assistance with this study in two ways. First, we would like to ask you to put a poster advertising for trial participants in your pharmacy. Second, we would like you to inform suitable potential participants (ie individuals aged 12 to 24 years with a verruca) that the trial is being conducted, and if the patient agrees give them the contact details of the recruiting site (insert name and contact details of recruiting site). Participation in the trial will not involve any commitments on your part other than putting up a poster and passing on recruiting site contact details to potential participants.

As this study is being funded under a call for medicines for children, we currently wish to recruit participants aged between 12 to 24 years inclusively. Patients will however, be ineligible if they are currently in a trial evaluating other treatments for their verruca, are unable to give informed consent, have impaired healing eg due to diabetes, peripheral vascular disease, are immunosuppressed, are on renal dialysis, have cold intolerance or have any of the following conditions; blood dyscrasias of unknown origin, cryoglobulinaemia, cryofibrinogenaemia, collagen and auto-immune disease.

We have enclosed further details of the study with this letter, but if you require any additional information or would like to discuss the study further, please contact either (Name of Podiatrist/Health care professional) on (insert telephone number and email address) or (Name of trial coordinator and contact details).

Yours sincerely

Name of PI	Professor David Torgerson	Sarah Cockayne
Title	Director of York Trials Unit	Trial coordinator

Please contact Sarah Cockayne, telephone number 01904 321736 or email esc5@york.ac.uk if you are able to put up a poster in your pharmacy. Alternatively please complete the form below and return it to Sarah Cockayne, in the pre-paid envelope provided.

Please send me a poster to put in our pharmacy:

Name of Pharmacist: _____

Address of Pharmacy _____

_____

_____

_____

_____

Telephone Number: _____

Email address: _____

Title: Cryotherapy versus salicylic acid for the treatment of verrucae: A randomised controlled trial.

Background

Verrucae are a common, infectious and sometimes painful problem. Using incidence figures from the 4th National Morbidity Survey (1991-92)[i] an unpublished economic decision model assessing the effectiveness and cost-effectiveness of salicylic acid and cryotherapy has estimated that almost 2 million people see their GP per year about cutaneous warts at a cost of at least £40 million per annum. Although most verrucae will spontaneously disappear without treatment many patients seek treatment to remove a verruca due to it being painful or because they are being prevented from doing sports.

A recent systematic review conducted by the Cochrane Skin Group assessed the effects of different local treatments of cutaneous, non-genital warts in healthy people[ii]. This review highlighted the uncertainty with respect to the optimal treatment of verrucae. There was however, some evidence from six trials to suggest that treatment with salicylic acid was more effective than placebo/no treatment, odds ratio 3.91 (95% confidence interval 2.40 to 6.36). Freezing warts using cryotherapy is widespread. Many patients experience unpleasant side effects such as pain and blistering during cryotherapy treatment, yet the same review found no evidence to suggest that it is more effective than treatment with topical agents such as salicylic acid. Only two trials were identified which compared salicylic acid and/or lactic acid with cryotherapy, but there was no difference in the efficacy between the treatments (OR 1.15, 95% CI 0.72 to 1.82). However, both trials were reported as low quality, due to unclear allocation concealment, inadequate blinding procedures, small sample sizes and inappropriate follow-up and analysis. There is a need therefore, for a high quality randomised controlled trial to ascertain which is the best approach for the treatment of verrucae.

Primary objective

To compare the clinical effectiveness of cryotherapy versus salicylic acid for the treatment of verrucae in terms of the complete clearance of all verrucae as observed on digital photographs taken at baseline and 12 weeks and assessed by an independent health care professional (eg podiatrist, GP, Practice nurse). Blinded health care professional assessment will be used if for some reason the digital photograph is not interpretable. 'Clearance' of verrucae will be defined as being the restoration of normal skin upon close inspection, as assessed by the health care professional.

Secondary objectives

To compare the cost effectiveness of cryotherapy versus salicylic acid for the treatment of plantar warts in terms of the complete clearance of all verrucae. To assess the acceptability of the two approaches and to investigate self-reported time to clearance of verruca and recurrence/clearance of verrucae at six months.

Design

The proposed study is a pragmatic, multicentre, randomised controlled trial (RCT) with equal randomisation. Patients with a verruca will be allocated equally between the two treatment groups, namely: 50% salicylic acid paste and cryotherapy using liquid nitrogen.

Eligibility

Inclusion criteria:

Patients will be included if

- The patient has a verruca that in the opinion of the health care professional is suitable for treatment with either salicylic acid or cryotherapy.
- And the patient is aged 12 years and over but under 25 years of age.

Exclusion Criteria:

Patients will be excluded if any of the following criteria apply:

- Are currently in a trial evaluating other treatments for their verruca
- Have impaired healing eg due to diabetes, peripheral vascular disease or any other condition which means the patient has impaired healing
- Patients that are immunosuppressed eg have agammaglobulinaemia, or are currently taking immunosuppressant drugs such as corticosteroids
- Are unable to give informed consent
- Are currently on renal dialysis
- Have cold intolerance eg Raynaud's syndrome or cold urticaria
- Have any of the following conditions - blood dyscrasias of unknown origin, cryoglobulinaemia, cryofibrinogenaemia, collagen and auto-immune disease

Treatment details

Participants will be randomised equally between the two arms: daily self-treatment by the patient with 50% salicylic acid; cryotherapy using liquid nitrogen delivered by the health care professional (for example podiatrist, practice nurse, General Practitioner).

1. **Daily self-treatment by the patient with 50% salicylic acid paste - Verrugon as per the manufacturer's instructions.**

    - At the first appointment the health care professional will instruct the patient and/or their parent or guardian if appropriate, on its use. Thereafter, it will be applied daily for a maximum of 8 weeks as per the manufacturer's instructions as follows:
    - The self-adhesive ring should be fixed with the hole over the verruca.
    - Squeeze a little Verrugon ointment into the hole and directly onto the verruca.
    - Remove backing paper from plaster.
    - Cover ring completely with plaster. Seal into position.
    - Repeat treatment daily after gently pumicing or filing off the dead part of the verruca.

2. **Treatment with cryotherapy using liquid nitrogen delivered by the health care professional.**

Callus surrounding the verrucae will first be debrided. The tissue surrounding the verruca will be prepared according to normal practice. The area will then be sprayed with liquid nitrogen to cover the verruca area totally. The health care professional should freeze the tissue until they are satisfied that the tissue has been frozen adequately (this will be about 10 seconds). 75% silver nitrate should **NOT** to be applied to site. If the health care professional believes the area surrounding the verruca

should be padded after treatment, this will be done according to normal practice. The patient will be advised to keep the area dry for 24 hours and that the area maybe uncomfortable as the treatment removes infected skin by causing a blister. If the area is very painful the patient will be recommended to use the type of painkiller they would use for a headache, and as per the instructions on the packet. The health care professional will then re book for the next treatment 14 days later. On the patient's return the sequence should be repeated up to a maximum of four treatments.

Primary outcome

The primary outcome will be complete clearance of all verrucae as observed on digital photographs taken at baseline and 12 weeks and assessed by an independent health care professional. Blind health care professional assessment will also be assessed and will be used if for some reason the digital photograph is not interpretable. 'Clearance' of verrucae will be defined as being the restoration of normal skin upon close inspection, as assessed by the health care professional.

Secondary outcomes

Secondary outcomes are self-reported clearance of verrucae at six months, and self-reported time to clearance of verrucae. In addition to this side effects of treatment, pain intensity after treatment, use of painkillers, restrictions to lifestyle due to having the verruca and treatment details will be recorded and assessed by patient postal questionnaire.

Sample size

In this study we have decided to power the trial to show a 15% difference in effectiveness. We therefore, will recruit sufficient patients to give us 80% power (5% two sided significance) to show a difference in cure rates of 70% versus 85% at 12 weeks after treatment. This will require 120 patients in each group after allowing for a 10% drop-out rate we will require 133 in each treatment group (i.e. 266 in total).

The study has the necessary ethics, research and development and Medicines and HealthCare products Regulatory Agency approvals.