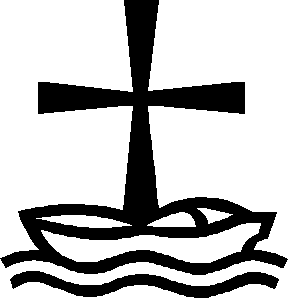
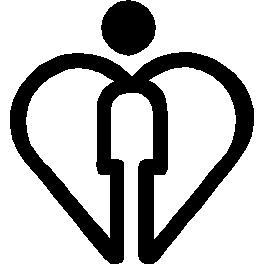
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 **HOSPITAL AUTHORITY**

# UNITED CHRISTIAN HOSPITAL

Department of Paediatrics &

## Adolescent Medicine

**Randomized Control Trial: Can topical Timolol reduce the use of Propranolol for the treatment of infantile haemangioma?**

PARTICIPANT INFORMATION SHEET

Introduction

As the most common vascular tumour of infancy, infantile haemangiomata are a major source of concern and stress for parents around the world, affecting around 3-5% of all infants worldwide. They often proliferate rapidly shortly after birth and then subsequently spontaneously involute gradually. A small proportion of patients may develop ulceration and haemorrhage that can result in disfigurement, tissue necrosis and even life-threatening complications.

Aim

To investigate the effect of topical Timolol in prevention of complications and need for further interventions for clinically significant infantile haemangiomata.

Background

More and more options have been introduced for treatment of haemangiomata nowadays, and topical timolol eye drops - a drug previously used for glaucoma patients - has been widely used across the world for eligible patients in view of its safety profile and potential benefits. However its role in the management of infantile haemangiomata is still not well defined. Previous studies suggest that a consensus on preparation, dose and duration is needed, yet the exact indications and benefits for Timolol usage for this condition is still not known and has not been studied thoroughly.

We aim to investigate the effect of topical Timolol in prevention of complications and need for further interventions for clinically significant infantile haemangiomata. We expect topical Timolol to reduce the need for systemic beta blocker or laser treatment for infantile haemangiomata.

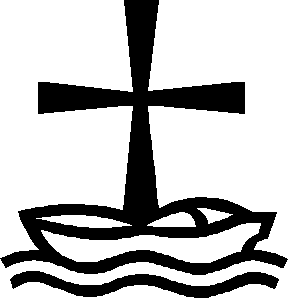
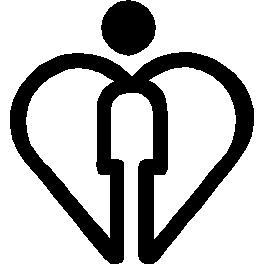
Methods

All patients with superficial haemangiomata that fit our inclusion criteria and are in at risk areas of the body in our hospital will be recruited for the study, where patients can choose whether to reject or accept the recruitment. Recruited patients will be randomized to either the Timolol group or the no Timolol group. Timolol will be prescribed at 1 drop (0.25mg) per 1cm in length/width of lesion twice daily for 6-12 months.

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***Intervention group (Timolol group)***

Topical Timolol will be initiated on agreement to recruitment in the study. Local application of 0.5% Timolol maleate at 1 drop (0.25mg) per 1cm in length or width of lesion for 6-12 months will be prescribed for all patients. Parents are taught how to apply and gently rub the applied Timolol onto the haemangiomata in a circular motion for 1 to 3 minutes. No occlusion of the lesion is necessary. Follow up will be arranged at 1 month, 3 months, 6 months and 12 months after initiation of drug. Parents are educated on the diagnosis, the pathophysiology and the normal course of the lesion, detailed explanation on possible options of management and their risks and benefits, importance in avoiding ulceration or complications of the lesion, education on skin care and methods to reduce such risks, and information on contact methods and first-line management of the patient should such untoward events occur.

***Non-intervention group (No-Timolol group)***

All treatment and follow up interval are same as intervention group. Our current practice of haemangioma treatment includes regular follow up and vigilant observation of the patient at 1 month, 3 months, 6 months and 12 months after the first consultation. As with the intervention group, parents are educated on the diagnosis, the pathophysiology and the normal course of the lesion, detailed explanation on possible options of management and their risks and benefits, importance in avoiding ulceration or complications of the lesion, education on skin care and methods to reduce such risks, and information on contact methods and first-line management of the patient should such untoward events occur.

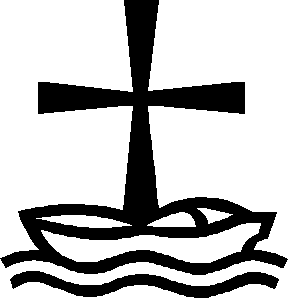
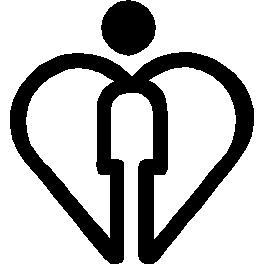
The follow up interval and frequency will be the same as those who opt not to enroll in this study. Patients do not need to come back for any extra visits. All patients will be arranged to receive follow-up visits at 1 month, 3 months, 6 months and 12 months after the first consultation. Systemic Propranolol or laser treatment will be arranged should such a need arises. The assessment for study purpose will be done after their scheduled follow up in the skin clinic.

Patients will be followed up regularly, with the patient's name and study code recorded. The lesion will then be photographed to document its colour, superficial and deep components and margin regularity by way of password-protected devices available only to the investigators. A colorimeter will be used to measure the amount of pigment in the vascular lesion. The width, length, depth and blanchability of the haemangioma will be measured and documented in the patient's CMS. The data will then be analysed qualitative and quantitatively. Patients will be observed for 6 to 12 months, and Propranolol will be given should the haemangioma develop into mixed type or develops complications, while laser treatment will be given if the lesion develops ulceration or a significant increase in size of 20%.

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Target number of patients recruit in the study: 64 (32 in intervention group; 32 in non-intervention group).

Duration of study: 6-12 months

Expected treatment benefit

Topical Timolol is expected to reduce the need for systemic beta blocker or laser treatment for infantile haemangiomata.

Termination of the study

Haemangioma requires intervention by meeting any one of the following criteria:

1. Rapid increase of at least 20% in size
2. Becomes mixed haemangioma by developing deep component
3. Develops ulceration
4. Impairs vital function (e.g. breathing, vision)
5. Risk of permanent disfigurement

Alternative treatment modalities

1. Conservative management
2. Systemic Propranolol
3. Laser treatment

Fees and subsidies

Participation in this study is entirely voluntary. Parents and legal guardians are not required to pay additional fees and will not receive subsidies for participation in this study.

Compensation and treatment

In rare cases where patients develop complications or side effects from the medication as a result of participation in this study, treatment and intervention will be arranged as soon as possible. However there will be no compensation in case such events occur.

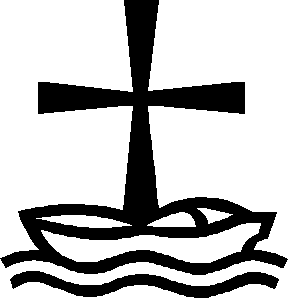
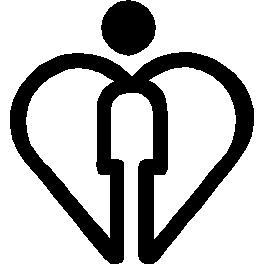
New information

All parents will be kept updated with any new information available.

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Voluntary participation and opting out

Participation in this study is entirely voluntary. The decision of parents or legal guardians will always be respected. Parents or legal guardians may choose to opt out of the study any time during the study without any penalty or negative impact. Frequency and quality of follow up and care will not be affected by this decision. Unless parents or legal guardians have specific requests, study data obtained prior to withdrawal from the study will be retained for study purposes. Parents or legal guardians will be provided adequate time to make this decision.

Data collection and privacy

All patient data and identity documents are strictly confidential. All data collected in this study are solely for study purpose and will be kept confidential in a secured cabinet or stored in password protected and encrypted Hospital Authority servers. This policy will be subjected to audit. The Research Ethics committee and regulatory authorities will be granted direct access to the study data for verification. The identity of patients, parents and legal guardians will be kept private.

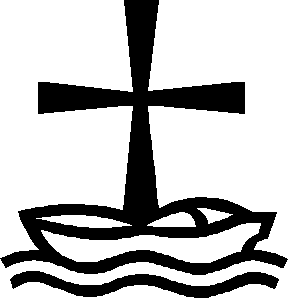
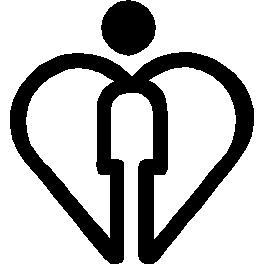
To improve confidentiality, we will not put your names in data collection sheets or questionnaires, and data will be stored in coded form with a study number. Informed consent forms will be kept separate from documents containing your personal data and will only be accessible by investigators under authorization. All patient data will be kept in computers that only investigators can access, and can be retrieved and destroyed upon request. All data will be kept for 5 years and destroyed afterwards.

Your confidentiality is of utmost importance. Under the laws of Hong Kong (in particular the Personal Data (Privacy) Ordinance, Cap 486), you enjoy or may enjoy rights for the protection of the confidentiality of your personal data, such as those regarding the collection, custody, retention, management, control, use (including analysis or comparison), transfer in or out of Hong Kong, non-disclosure, erasure and/or in any way dealing with or disposing of any of your personal data in or for this study. For any query, you should consult the Privacy Commissioner for Personal Data or his officer (Tel no.: 2827 2827) as to the proper monitoring or supervision of your personal data protection so that your full awareness and understanding of the significance of compliance with the law governing privacy data is assured.

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Potential side effects

Timolol is a safe medication. It is a non-selective beta blocker otherwise used for glaucoma patients. All studies currently done for Timolol have shown minimal side effects, with skin pruritus being the only side effect reported in a handful of patients. Timolol does not penetrate deeply and does not show systemic effects unlike other beta blockers like oral Propranolol. We will regularly follow up for any side effects, and arrange more aggressive treatment should there be such a need.

In rare cases where patients develop complications or side effects from the medication as a result of participation in this study, please contact our study team via the provided the phone number provided. Treatment and intervention will be arranged as soon as possible. However there will be no compensation in case such events occur. Parents and legal guardians are free to decide whether to continue participation or opt out of the study.

By signing this form, I hereby grant direct access to the Research Ethics Committee and regulatory authorities to the participant’s study data for data verification.

Enquiries

For enquiries, please kindly contact our study nurse Ms Tong at 3949 6571.

Should you have questions related to your rights as a research subject, please contact the Research Ethics Committee (Kowloon Central/Kowloon East) at 3506 8888.

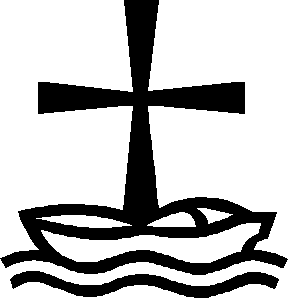
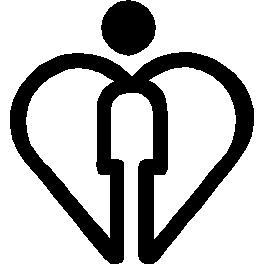
Upon signing this form, you will receive an information booklet for this study as well as a copy of this consent form for your future reference.

Informed Consent Form

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I , (Parent/Legal guardian’s name) , understand the aim of this study and consent my son / my daughter (Patient’s name) to enroll into this study.

I have read and understood all information provided and fully understand the risks and benefits of this study. I was given the opportunity to ask questions, and he/she has clearly and thoroughly answered all of them. With regard to this study, I have received adequate information.

Should I or the participant develop untoward side effects from participation in this study, investigators will provide appropriate care or referral for the condition. I understand that I am not giving up any of my personal rights by signing this form.

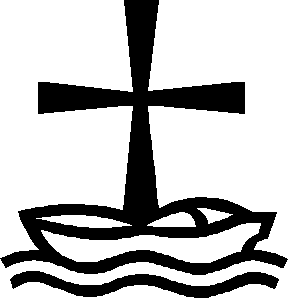
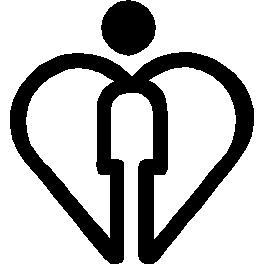
I hereby sign this form and verify that all information I have provided is accurate. I understand that I have the right to withdraw the participant from the study at any time for any reasons, without any penalty or negative impact. Frequency and quality of follow up and care will not be affected by this decision.

I understand that my identity and that of the participant will be handled confidentially. I understand that the Research Ethics committee and regulatory authorities will be given direct access to the study data for verification.

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Parent/Legal guardian’s signature: \_\_\_\_\_\_

Doctor’s name: \_\_\_\_\_\_\_\_\_\_\_\_\_

Doctor’s signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Impartial Witness’s name: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Impartial Witness’s signature: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

Should the parent or legal guardian be unable to read or write, a third party impartial witness is necessary for the signature of this consent form

Date of signatory: \_\_\_\_\_

Study code: \_\_\_\_\_