Clinical Guideline

HNEkidshealth
Children, Young People & Families

NSW GOVERNMENT Health
Hunter New England
Local Health District

Atenolol for Treatment of Haemangioma

Sites where Clinical Guideline applies	All HNELHD sites that provide care to paediatric patients
This Clinical Guideline applies to:	
1. Adults	No
2. Children up to 16 years	Yes
3. Neonates – less than 29 days	Yes
Target audience	Clinicians treating infants and children with haemangioma
Description	Outlines the assessment, treatment and ongoing management of infantile haemangiomas with oral atenolol

Go to Guideline

Keywords	Haemangioma, atenolol
Document registration number	HNELHD CG 20_44
Replaces existing document?	No

Related Legislation, Australian Standard, NSW Ministry of Health Policy Directive or Guideline, National Safety and Quality Health Service Standard (NSQHSS) and/or other, HNE Health Document, Professional Guideline, Code of Practice or Ethics:

- NSW Health Policy Directive PD2017_013 Infection Prevention and Control Policy
- NSW Health Policy Directive PD2017_032 Clinical Procedure Safety
- NSW Health Policy Directive PD2013_043 Medication Handling in NSW Public Health Facilities
- NSW Health Policy Directive PD2016_033 Approval Process of Medicines for Use in NSW Public Hospitals
- HNELHD DPG 20_06 Atenolol for infantile haemangiomas

Position responsible for Clinical Guideline Governance and authorised by	Paul Craven, Executive Director – Children, Young People and Families Services
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This document contains advice on therapeutics	Yes, Approval gained from HNE Quality Use of Medicines Committee on 11 August 2020
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GLOSSARY

Acronym or Term	Definition
ENT	Ear, nose and throat specialty
PHACE	PHACE stands for Posterior fossa brain malformations, Hemangioma, Arterial lesions, Cardiac abnormalities, and Eye abnormalities It is a syndrome involving facial haemangiomas, cardiovascular and intracranial anomalies.

PURPOSE AND RISKS

Infantile haemangiomas are the most common soft tissue tumours of infancy[1]. More than 60% occur on the face, head and neck and can impede breathing, feeding, vision and can lead to disfigurement. Oral beta-blockers have been shown to be effective in treating infantile haemangiomas. While propranolol has traditionally been the preferred agent, atenolol has been shown to be as effective as propranolol[2] and to have less adverse events, in particular hypoglycaemia, bronchospasm, hypotension and bradycardia[3]. This guideline intends to standardise the use of atenolol in this setting.

Risks:

- Although some studies show that atenolol has a better adverse event profile than propranolol, there is still risk of adverse events including bradycardia, cardiac conduction abnormalities (heart block), hypotension, hypoglycaemia and bronchospasm

These risks are minimised by:

- Initiating treatment as inpatient in “at-risk” patients
- Ensuring full assessment by paediatrician and/or dermatologist before initiating treatment
- Providing comprehensive education for families

Risk Category: Clinical Care & Patient Safety

While not requiring mandatory compliance, staff must have sound reasons for not implementing standards or practices set out within guidelines issued by HNE Health, or for measuring consistent variance in practice.

STAFF PREPARATION

It is mandatory for staff to follow relevant: “Five moments of hand hygiene”, infection control, moving safely/safe manual handling, documentation practices and to use HAIDET for patient/carer communication: **H**and hygiene **A**cknowledge, **I**ntroduce, **D**uration, **E**xplanation, **T**hank you or closing comment.

INTRODUCTION

Infantile haemangiomas are the most common soft tissue tumours of infancy[1]. They typically present in the weeks following birth, though some patients may have precursor lesions present at birth. The clinical course of infantile haemangiomas typically includes three phases:

1. Proliferation – this is most rapid between weeks 5 and 8 and most infantile haemangiomas have reached 80% of their final size by approximately 3 months, they may then undergo a slow growth phase up to 1 year of age;
2. Plateau – the infantile haemangiomas stabilises and stops growing; and
3. Spontaneous involution – the infantile haemangiomas regress with the median age of complete regression being 3 years[4]. In some patients, involution may be incomplete, leaving residual fibrofatty changes, telangiectasia, erythema or atrophy.

More than 60% of infantile haemangiomas occur on the face, head and neck and can impede breathing, feeding, vision and can lead to disfigurement[5]

Oral atenolol has been shown to be an effective treatment for infantile haemangiomas and is an alternative to oral propranolol. Atenolol is a hydrophilic, selective, β_1-adrenoceptor blocker and some studies suggest it has less adverse events, in particular hypoglycaemia, bronchospasm, hypotension and bradycardia, than propranolol, a non-selective, β-adrenoceptor blocker[3]. This guideline intends to standardise the use of atenolol in this setting.

Infantile Haemangiomas – Requiring treatment with atenolol

PRIOR TO TREATMENT FOR ALL PATIENTS

Before starting atenolol treatment
- Education to be provided by medical officer or pharmacist about atenolol treatment
- Informed consent to be recorded in patient notes or in DMR
- Medical examination to be conducted
- Haemangioma to be photographed and measured and uploaded to DMR

Initiation of atenolol – Dose
- Start dose 0.5 – 1 mg/kg/day
- Lower starting doses, If tolerated may increase to 1 mg/kg/day after a fortnight

Education
- Parent handout regarding atenolol given and explained to parent and/or carer

SCREENING ASSESSMENT - If yes to any of these, start treatment as an inpatient
- Age <2 month or premature birth
- Increased risk of hypoglycaemia: *premature on corticosteroids*
- Increased risk of bradycardia and/or hypotension: *known CVD, abnormal echo/ECG.*

Contradiction to atenolol
- PHACE
- Multiple Haemangiomas
- Cardiogenic or hypovolemic stock
- Patients with history of anaphylactic reactions Diabetes mellitus

TREATMENT AS IN INPATIENT

Baseline observations
- Weight, height/length
- BP, HR, RR, SaO2, BSL

Administer atenolol

Ongoing Observation
- 30 mins – BP, HR, RR, SaO2, BSL
- 60 mins – BP, HR, RR, SaO2
- 90 mins – BP, HR, RR, SaO2, BSL
- 2 hrs + 3 hrs – BP, HR, RR, SaO2
- 4 hrs – BP, HR, RR, SaO2, BSL

TREATMENT AS AN OUTPATIENT

Baseline observations
- Weight, height/length
- BP, HR, RR, SaO2, BSL

Administer atenolol

Ongoing Observations
- 30 mins – BP, HR, RR, SaO2, BSL
- 60 mins – BP, HR, RR, SaO2
- 90 mins – BP, HR, RR, SaO2
- 2 hrs – BP, HR, RR, SaO2, BSL

Any clinical concerns or observations outside the flags or BSL <3.4 mmol/L

YES → **STOP TREATMENT**
Assessment by treating team and MET call if warranted.

NO

DISCHARGE
Child can be discharged after 4hours if:
- Observations are in the white zone (or back to baseline with review)
- Education Has been provided
- Patient handout and scripts provided

ONGOING MANAGEMENT
Follow up
- Appointment fortnightly – monthly (Treating doctor's discretion)
- Observations: Weight, BP, HR, RR , SaO2, BSL
- Photograph and measure haemangioma

Duration of therapy
- 6-12 months depending on severity, response to treatment and age of child
- Adjust dose with increases in the infant's weight at follow-up appointments

INDICATIONS FOR TREATMENT

Infants and children will be assessed by a paediatrician and/or dermatologist. Indications for treatment of infantile haemangiomas include:

- Life-threatening locations such as causing airway obstruction or cardiac failure
- Local complications such as ulceration, vision impairment and feeding difficulty
- Cosmetic concerns especially at lip, nose and ear sites
- Functional risks such as potential anatomical distortion and scarring

The presence or a history of the following need to be excluded or further investigated before initiating treatment with atenolol:

- Risk of hypoglycaemia i.e. oral corticosteroid therapy, poor feeding, failure to thrive
- Bronchospasm or any ENT concerns related to the position of the haemangioma
- Cardiovascular disease, including cardiac arrhythmias, bradycardia, coarctation of the aorta or family history of cardiac disease
- CNS vascular anomalies i.e., suspected PHACE syndrome (a syndrome involving facial haemangiomas, cardiovascular and intracranial anomalies) as these patients have a higher risk of stroke when treated with β-blockers
- Large cervicofacial haemangiomas or multiple haemangiomas
- Other systemic disease
- Systemic lupus erythematosus in mother

If oral atenolol is contraindicated there are alternatives and consultation with the dermatology team is recommended.

INITIAL INVESTIGATIONS

The initial assessment and investigations are to be instigated by the treating clinician (paediatrician or dermatologist). These may include:

- Cardiovascular examination (including femoral pulses)
- Electrocardiogram
- Full blood count, electrolytes, renal function, liver function tests, thyroid function tests, blood glucose level

Depending on the results of the initial assessment, other investigations may be required, and consideration given to consultation with appropriate specialists:

- For haemangiomas in a beard distribution: consider ENT referral and indirect laryngoscopy
- For segmental head and neck haemangiomas at risk of PHACES syndrome: consider echocardiogram, MRI/MRA of head and neck, laryngoscopy & bronchoscopy, ophthalmology assessment
- For segmental lumbar region haemangiomas at risk of LUMBAR syndrome: consider ultrasound or MRI of the spine, US of abdomen and pelvis, neurology assessment, urology assessment
- For multiple haemangiomas: consider abdominal and brain ultrasound, echocardiogram, CXR, head CT/MRI

- Echocardiogram is indicated if there are concerns as a result of the physical examination or history

These investigations will be coordinated by the treating clinician in consultation with appropriate specialists.

Clinical photos should be taken, with documented parental consent, of all lesions, including front and side-on views. They should be attached to the patient's medical record.
NB. If clinical photography is not available at the local hospital, please ask the patient's parent or carer to keep a photographic record

ATENOLOL DOSING

Atenolol is a selective β_1-adrenoceptor blocker. The terminal half-life of atenolol is 6–8 hours. It can be administered as a once daily dose. Risks and benefits of atenolol should be discussed with the family and, before commencing, informed consent is to be gained and documented appropriately in the patient's medical notes. The Atenolol Information Sheet should form the basis of this discussion with the family. Following the initial medical assessment, the patient may commence therapy either as an inpatient or in an outpatient setting, depending on the individual patient risk factors.

BENEFITS

- Relatively low-risk medication (compared with other treatment modalities)
- Non-surgical approach

RISKS

- New treatment option, off-label use of a medication
- Bradycardia
- Bronchoconstriction
- Hypotension
- Hypoglycaemia (especially if reduced feeding secondary to illness)

If any of the following is present, atenolol treatment is to be commenced as an inpatient:

- Age < 2 months or premature birth
- Increased risk of hypoglycaemia, i.e. oral corticosteroids, poor feeding, failure to thrive
- Increased risk of bradycardia and/or hypotension i.e., known cardiovascular disease, abnormal echo/ECG

DOSING

Infantile haemangioma(s)

- Patients should commence atenolol at a dose between 0.5 and 1 mg/kg/day as a single daily dose
- When starting on lower doses, if tolerated, the dose of atenolol may be increased to 1 mg/kg/day as a single daily dose after a fortnight or month of therapy (at the time of this increase the patient should receive the same level of monitoring as for the initial dose)
- Atenolol liquid 5mg/mL is available on the Pharmaceutical Benefits Scheme

- Assessment of atenolol adverse effects and efficacy should be made at monthly follow-up appointments in outpatient clinic, the dose should be adjusted with the increasing weight of the patient

In selected patients, higher doses may be used at the discretion of the physician, based on clinical indication. For details on prescribing see the atenolol drug prescribing guideline.

COMPLICATIONS

Complications to be aware of include:

- Bradycardia
- Cardiac conduction abnormalities (heart block)
- Hypoglycaemia (BSL <3.4 mmol/L)
- Hypotension
- Bronchospasm (uncommon but may occur)
- Gastrointestinal upset including gastro-oesophageal reflux, diarrhoea or constipation
- Sleep and mood disturbances have been reported

ALERT

Hyperkalaemia has been reported in a case involving an infant with a large haemangioma with a very rapid response to therapy with propranolol who possibly suffered tumour lysis syndrome[6].

INPATIENT MANAGEMENT

Baseline clinical photos of the infantile haemangioma(s) should be taken with signed parental consent and images attached to the patient's healthcare record.

Baseline examination and investigations including:

- Weight and height/length
- BP, HR, RR, oxygen saturation and temperature
- Conscious state and pain score
- BSL
- ECG

Atenolol is to be commenced at recommended starting dose and ongoing observations undertaken as follows:

- Baseline observations and investigations as above
- 30 minutes after administration – BP, HR, RR, oxygen saturation + BSL
- 60 minutes after administration – BP, HR, RR, oxygen saturation
- 90 minutes after administration – BP, HR, RR, oxygen saturation + BSL
- 2 hours after administration – BP, HR, RR, oxygen saturation
- 3 hours after administration – BP, HR, RR, oxygen saturation
- 4 hours after administration – BP, HR, RR, oxygen saturation + BSL

Discharge can be considered at a minimum of 4 hours if the patient remains stable. Before discharge, family education and follow-up appointments are to be provided as per below.

ALERT

If any patient who is on atenolol therapy is admitted and requires fasting or restricted oral intake, then BSL will need to be monitored closely and support provided.

OUTPATIENT MANAGMENT

Baseline clinical photos of the infantile haemangioma(s) should be taken with signed parental consent and images attached to the patient's healthcare record.
Baseline examinations and investigations including:

- Weight and height/length
- BP, HR, RR and oxygen saturations and temperature
- BSL

Atenolol is to be commenced at recommended starting dose and ongoing observations undertaken as follows:

- Baseline observations and investigations as above
- 30 minutes after administration – BP, HR, RR, oxygen saturation + BSL
- 60 minutes after administration – BP, HR, RR, oxygen saturation
- 90 minutes after administration – BP, HR, RR, oxygen saturation
- 2 hours after administration – BP, HR, RR, oxygen saturation + BSL

Discharge can be considered at 2 hours if the patient remains stable. Before discharge, family education and follow-up appointments are to be provided as per below.

FAMILY EDUCATION ON DISCHARGE

Families require education by a pharmacist or medical officer regarding the administration of atenolol at home and monitoring and reporting of adverse effects.

Family education should include the following:

- To safely store atenolol
- To always give atenolol after the first feed or meal in the morning
- To avoid prolonged fasting
- If a dose it missed and it is less than 6 hours since the missed dose, the dose can be given with a feed or meal, if it is more than 6 hours since the missed dose, skip the dose and resume the following day as normal
- To not give the dose if their child is wheezing, unwell, vomiting or not feeding normally and to seek medical advice as they would do for any unwell child
- To be aware of the signs and symptoms of hypoglycaemia and hypotension
- To seek medical attention from their closest hospital if they are worried or see signs of hypoglycaemia unresolved by feeding

- To keep routine immunisations up to date while on atenolol therapy
- To ensure regular follow-up

As part of the education, the follow-up appointments should be provided.

FOLLOW-UP

The first follow-up may be in one fortnight, when the dose may be increased. This appointment needs to be the same as the initial treatment appointment (either as inpatient or outpatient) as they will require the same degree of monitoring with the subsequent dose increase. Refer to Inpatient Management or Outpatient Management above for details.

During these appointments, the haemangioma(s) should be measured and photographed with parental consent to evaluate treatment efficacy and monitor clinical response. The clinical photos should be attached to the patient's healthcare record.

Assessment and monitoring of weight, height/length, BP, HR, RR, oxygen saturation, temperature and BSLs should be performed during follow-up appointments.

Further follow-up appointments should occur at monthly intervals with the treating clinician (may increase when stable). If the dose is increased due to an increase in weight, future clinic appointments will not require additional monitoring as the recommended dosage schedule is weight-based i.e., mg/kg.

If complications such as bradycardia, hypotension, bronchospasm or hypoglycaemia arise, the family should seek immediate medical treatment. The treating team should be contacted as soon as possible, and the atenolol should be withheld while this consultation is undertaken.

If the treatment is NOT being tolerated, the clinician should assess the patient and liaise with an experienced dermatologist or paediatrician.

CEASING TREATMENT

Atenolol therapy should be ceased after consultation with prescribing clinician, or if adverse effects occur. Atenolol can be ceased without tapering though continued assessment of the child's response following cessation needs to occur. Assessment of the clinical scenario and residual effects of the haemangioma will indicate the level of ongoing monitoring required. GP follow-up may be all that is required after treatment has ceased.

TOPICAL TIMOLOL

Topical beta-blockers have been shown to be an effective treatment for superficial infantile haemangiomas[7]. Their use can be considered as a treatment option for infantile haemangiomas not warranting treatment with oral beta-blockers, to prevent a rebound flare when tapering off oral beta-blockers or in conjunction with oral beta-blockers in some patients. One drop of timolol maleate 0.5% gel forming eye drops is applied twice a day to the infantile haemangioma.

IMPLEMENTATION

1. Awareness of this Clinical Guideline will be promoted through the CE Newsletter.
2. The Clinical Guideline will be communicated via email to CYPF directorate and facility managers and is to be tabled at the relevant Clinical Quality Committees for distribution to relevant clinicians.
3. The new and revised Clinical Practice Guidelines, Policy Directives and PCPs are posted on the Policy, Procedure and Guideline (PPG) Directory.

MONITORING AND AUDIT

1. Clinical incident investigations of atenolol will include a review of clinical practice. The clinical guideline will be amended in line with the recommendations.
2. Data derived from monitoring and evaluation should inform the review of the clinical guideline either as required or as scheduled.
3. The person or leadership team who has approved the clinical guideline is responsible for ensuring timely and effective review of the guideline.
4. Evaluation will include a review of the most current evidence as well as a consideration of the experience of HNE Health staff in the implementation of the clinical guideline.
5. Annual file and IIMS review will be undertaken by the relevant treating team to ensure compliance with the guideline. Results of the audits are to be presented to the local Clinical Quality and Patient Care Committee.

CONSULTATION WITH KEY STAKEHOLDERS

Dr John Relic, Dermatologist
General paediatrics
Nursing stakeholders (H1, NICU)
Michelle Jenkins, Senior Pharmacist JHCH

APPENDICES

Appendix 1: Clinical Audit

REFERENCES

1. Smithson SL, Rademaker M, Adams S, et al. Consensus statement for the treatment of infantile haemangiomas with propranolol. Australas J Dermatol 2017;58:155-9.
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6. McSwiney, E., Murray, D. & Murphy, M. Propranolol therapy for cutaneous infantile haemangiomas initiated safely as a day-case procedure. Eur J Pediatr 2014:173, 63–68.

7. Ovadia SA, Landy DC, Cohen ER, et al. Local administration of β-blockers for infantile hemangiomas: a systematic review and meta-analysis. Ann Plast Surg 2015; 74:256.

FEEDBACK

Any feedback on this document should be sent to the Contact Officer listed on the front page.

APPENDIX 1 - CLINICAL AUDIT TOOL

Only create a new and separate audit tool where necessary. Clinical Audits should be amalgamated and embedded within a Clinical Audit Program

(**National Standard 1:** 1.7.2 The use of agreed clinical guidelines by the clinical workforce is monitored)

Criterion no.	Criterion	Exceptions	Definition of terms and/or general guidance	Data source	Frequency	Position Responsible
1	To minimise the risk of clinical deterioration of the patient with the aim to monitor and respond to any identified reactions associated with administering atenolol	None	• Identify patients using atenolol and assess compliance with the steps within this guideline including: - dosage - observations	IMS+ data-ongoing Retrospective chart audits x10	12 monthly	Dermatology Team

Go to: http://intranet.hne.health.nsw.gov.au/__data/assets/word_doc/0014/133142/Clinical_Audit_Tool.docx