

PHACES Medical Treatment

Dr. Elena Pope, MSc, FRCPC
The Hospital for Sick Children
Professor, University of Toronto

Hemangioma: Therapeutic indications

Definitive

- Functionally impairment
- Large, deforming hemangiomas

Relative

- Potential for cosmetic deformity
- Superficial hemangiomas
- Ulcerated hemangiomas

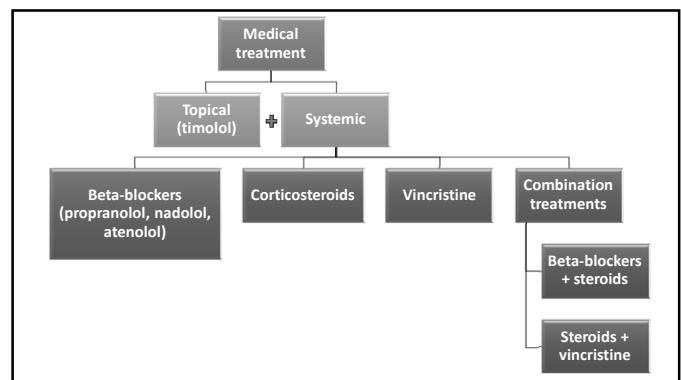
PHACES: Therapeutic indications

Definitive

- Functionally impairment
- Large, deforming hemangiomas

Relative

- Potential for cosmetic deformity
- Ulcerated hemangiomas



Topical
(timolol)

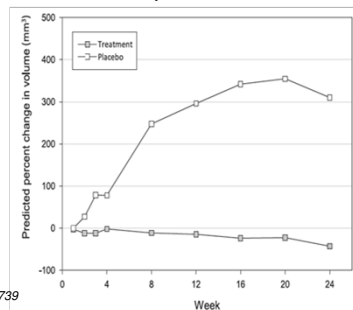
Topical Timolol Treatment

- Indications
 - *Superficial lesions*
 - *Non-complicated*
 - *Small surface area*
 - *Residual changes after systemic treatment*
- Timolol 0.5% gel forming solution

Chan et al. *Pediatrics* 2013; 131; e1739
Pope et al. *Arch Dermatol* 2010
Chakraborty et al. *Ped Dermatol* 2012

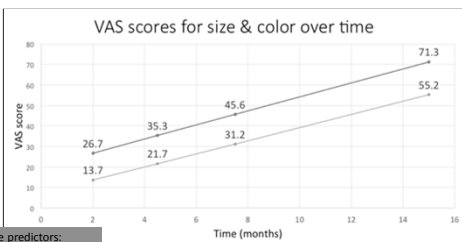
Randomized Trial Timolol 0.5% vs Placebo

- 41 patients
- Treated for 24 weeks
- % change volume of the IH



Chan et al. *Pediatrics* 2013; 131; e1739

Timolol Large Retrospective Study (N=731)



Best response predictors:
 - Thin hemangiomas (<1 mm)
 - 0.5% gel concentration
 - Proliferative lesions

Pediatrics 2016; 138(3):e20160355

Timolol safety

- Potential side effects: bradycardia, hypotension, hypothermia, apnea
 - Risk factors: prematurity and low birth weight
- Systemic absorption
 - 93% of patients had systemic absorption
 - 13% had high levels
 - Predictor for high levels: thickness of hemangioma
 - None of the patients had symptoms

Frommelt et al. *Pediatr Dermatol* 2016; 33(4): 363
 Drolet et al. *ISSVA* 2018

Timolol and PHACES syndrome

- Case reports
 - 3 month-old treated for 12 mos with complete resolution
 - 18 month-old, failed multiple systemic therapies- 50% decrease in the size after 1 week
 - 20 drops of timolol/d = 5 mg/d timolol~ 40 mg/d of propranolol

BJD 2011; 164: 878-99
JEADV 2017; 31: 346-48

Topical Timolol: When to Use?

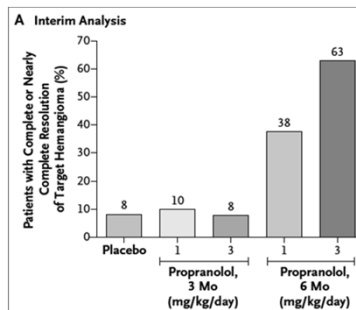
	INDICATED <ul style="list-style-type: none"> • Superficial (< 1 mm depth) • Proliferative (< 6 months) • Small surface area (< 2 drops/application)
	CONSIDER <ul style="list-style-type: none"> • Mucosal lesions • Ulcerated lesions
	CONTRAINDICATED <ul style="list-style-type: none"> • Systemic treatment • At risk patients • Under occlusion

Oral Beta-blockers

- Propranolol (2-3 mg/kg/d BID/TID) ★
- Atenolol (1mg/kg/d OD) ★
- Nadolol (2 mg/kg/d BID) ★
- Acebutolol (8-10 mg/kg/d BID)
- Captopril (0.5-1mg/kg OD)

NEJM 2015; 272:735-46 *JAAD* 2014; 70:1045-49
BJD 2013; 168:222-24 *Int J Otorhinolaryngol* 2010; 74:959-61
JAAD 2016; 74: 499-505

Propranolol



3 mg/kg > 1mg/kg
6 mos > 3 mos

- Most of the cases were very mild
- Most of the world uses 2 mg/kg
- Most patients are treated beyond 6 months

NEJM 2015; 272:735-46

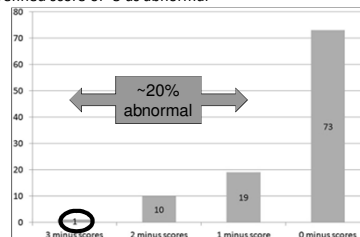
Adverse effects

- Common:
 - Cold hands and feet
 - Sleeping disturbances
- Rare
 - Agitation/somnolence
- Extremely rare
 - Bronchospasm
 - Hypotension/Bradycardia
 - Hypoglycemia

NEJM 2015; 272:735-46

Developmental Problems: What do we know?

- Dutch cohort study
- 104 patients
- Van Weichen Scheme (VWS)- screening developmental tool
- Defined score of ≤ -3 as abnormal



When to wean?

- No Clear Guidelines!
- Treat at least until proliferation is over
- Treat until no functional impairment
- Treat until minimal residua
- Wean over few months
 - 25% of IH have rebound (N=977)
 - 83% require some treatment
 - 62% require systemic medication
 - Risk factors: females, deep hemangiomas

Pediatrics 2016; 137(4): 1-11

Propranolol in PHACES patients

- 32 patients with PHACES
- **1- transient hemiparesis**
- **3- ulcerations**
- 7 had a high risk of stroke (severe, long segment non-visualization of major cerebral artery without collaterals)

Pediatr Dermatol 2013; 30: 71-89

Oral Propranolol and PHACES: When to Use?



INDICATED

- Functional impairment
- Disfiguring lesions



CONSIDER

- Ulcerations
- Potential for cosmetic deformity



Relatively CONTRAINDICATED

- High risk for stroke
- Peripheral vascular disease

Systemic

Other modalities

- **Corticosteroids**
 - Effective
 - +++ side effects
 - Mostly used in combination with beta-blockers (unresponsive lesions, concerns about adverse events, need for fast improvement)
- **Vincristine**
 - Rarely used
 - Non-responsive lesions
 - Adverse events from beta-blockers/steroids

Clin Transl Oncol 2007; 9(4): 262-3

Summary

- Most patients with PHACES require some medical intervention
- ALL require careful consideration of risks and benefits
 - What do we treat?
 - What are we trying to achieve?
 - What are the potential risks?
- May need to delay treatment until risk assessments are completed
- Occasionally combination therapies may be warranted

