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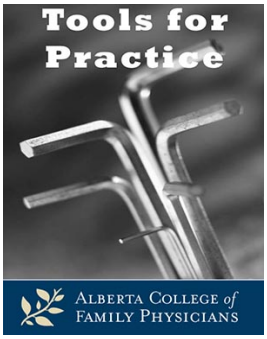

A Serendipitous Discovery and Novel Treatment for Infantile Hemangiomas

Clinical Question: Are beta-blockers effective in treating small infantile hemangiomas?

Bottom-line: One small randomized controlled trial (RCT) and numerous observational studies demonstrate that oral propranolol stops growth and induces regression of infantile hemangiomas (IH) by four weeks. Similar evidence suggests topical timolol stops IH growth and induces regression by >5% after 4-6 months for every one in 2-3 patients.

Evidence:

- Oral Propranolol:
  - RCT (40 children, aged nine weeks to five years, followed x 6.0 months).[1] Compared to placebo, propranolol 2mg/kg (divided three times per day) statistically significantly:
    - Stopped IH growth by week four for all children.
    - Reduced IH volume at all weeks (example Week 12: -48.5% vs. +17.9%).
    - No significant hypotension, hypoglycemia, or bradycardia.
  - Systematic review (40 observational studies plus above RCT,[1] 1,264 children, mean age 6.6 months, treated x 6.4 months):[2]
    - Mean response rate (any improvement) 98%.
    - Serious side effects rare: symptomatic hypotension, bradycardia, or hypoglycemia in ten.
- Topical Timolol:
  - RCT (41 children, median nine weeks old).[3] At 20-24 weeks, significantly more IHs with one drop timolol maleate 0.5% gel twice a day vs. placebo:
    - Decreased in size by >5% (vs. normal increase in size at this age) Number Needed to Treat (NNT)=3.
    - Limitations: Small numbers.
  - Prospective clinical study (124 children, ≤12 months age).[4] At four months, significantly more in timolol group than observational group reported:
    - IH stopped growing and/or became smaller, 92% vs. 34%, NNT=2.
    - No serious adverse events.
  - Numerous smaller retrospective cohort and prospective clinical studies report

similar findings.[5-9]

Context:

- Beta-blockers for IH first reported in 2008 when two infants started on propranolol for cardiac reasons experienced dramatic involution of severe hemangiomas.[10]
- Hemangiomas often develop in the first few weeks of life, reach 80% of their final size by three months and 80% complete growth by five months.[11] By five years the majority of lesions completely disappear without treatment.[12]
- Oral propranolol FDA-approved for severe IHs.[13] No beta-blocker approved by Health Canada for this.

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References:

1. Hogeling M, Adams S, Wargon O. Pediatrics. 2011; 128(2):e259-66.
2. Marqueling AL, Oza V, Frieden IJ, *et al*. Pediatr Dermatol. 2013; 30(2):182-91.
3. Chan H, McKay C, Adams S, *et al*. Pediatrics. 2013; 131(6):e1739-47.
4. Yu L, Li S, Su B, *et al*. Exp Ther Med. 2013; 6(2):388-390.
5. Pope E, Chakkittakandiyil A. Arch Dermatol. 2010; 146:564-5.
6. Ni N, Langer P, Wagner R, *et al*. Arch Ophthalmol. 2011; 129:377-9.
7. Chambers CB, Katowitz WR, Katowitz JA, *et al*. Ophthal Plast Reconstr Surg. 2012; 28(2):103-6.
8. Chakkittakandiyil A, Phillips R, Frieden IJ, *et al*. Pediatr Dermatol. 2012. Jan-Feb; 29(1):28-31.
9. Moehrle M, Léauté-Labrèze C, Schmidt V, *et al*. Pediatr Dermatol. 2013; 30:245-9.
10. Léauté-Labrèze C, Dumas de la Roque E, Hubiche T, *et al*. N Engl J Med. 2008; 358:2649-51.
11. Chang LC, Haggstrom AN, Drolet BA, *et al*. Pediatrics. 2008; 122(2):360-7.
12. Jacobs AH. Calif Med. 1957; 86(1):8-10.
13. June 2014 Approved Drug Product List. Available at: www.fda.gov/downloads/drugs/developmentapprovalprocess/ucm071120.pdf+hemangeol&client=FDAgov&proxystylesheet=FDAgov&output=xml_no_dtd&site=FDAgov&ie=UTF-8&access=p&oe=ISO-8859-1. Accessed September 4, 2014.

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