Infantile hemangiomas (IHs) affect approximately 5% to 10% of white children. Most IHs undergo spontaneous involution, with only a small proportion requiring systemic intervention. For these, propranolol, a nonselective β-blocker, has emerged as an alternative systemic treatment to corticosteroids. The proposed therapeutic effects of propranolol on IHs are vasoconstriction; decreased expression of vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) genes through downregulation of the RAF/mitogen–activated protein kinase pathway; and apoptosis of capillary endothelial cells.

Superficial IHs, particularly facial IHs, are associated with substantial parental distress, and we currently have a limited therapeutic repertoire. Timolol, a nonselective β-blocker similar to propranolol, is available in a topical gel formulation for treatment of glaucoma. We describe herein a series of 6 patients with superficial head and neck IHs treated with timolol maleate, 0.5%, gel.

**Methods.** A retrospective medical chart review analysis was performed of 6 patients with uncomplicated IHs in the head and neck area who were treated with timolol maleate, 0.5%, gel after informed consent. Timolol maleate, 0.5%, gel was applied topically twice daily to the IHs. Two investigators independently analyzed the response to treatment by comparing digital photographs at baseline vs at 4 weeks, 8 weeks, and final visits using a global score (−4 to +4) representing the difference in the size and/or extent and color of IHs (−2 [much worse], −1 [worse], 0 [same], +1 [better], and +2 [much better]) and a visual analog scale (VAS) (a 100-mm scale where −100 indicates that the hemangioma is twice as big; 0, no change; 100, normal skin).
Figure 2. Change in mean combined visual analog scale score (VAS) (range, 0-100 mm) over the course of treatment with timolol maleate, 0.5%, gel.

Results. The Table lists patient characteristics and response data. Clinically, 3 patients had IHs still in the proliferative phase; 2 had IHs that were stable; and 1 had IHs in regression. The difference in appearance of IHs at the various stages of treatment is shown in Figure 1. The mean change in VAS over time is presented in Figure 2. None of the patients experienced any local or systemic adverse events.

Comment. This proof of concept study shows that timolol maleate, 0.5%, gel, a nonselective β-blocker in topical formulation, is effective and safe for the treatment of IHs. Patients with superficial IHs and those treated for longer periods showed better response to timolol. Early intervention during the rapid proliferative phase (age 1-6 months) may result in better and faster resolution of IHs. This preliminary work suggests that topical timolol maleate, 0.5%, gel is an alternative to systemic propranolol for treatment of superficial IHs. Further prospective studies are required to substantiate the safety and efficacy of timolol maleate, 0.5%, gel in the treatment of IHs.

Elena Pope, MD, FRCPC
Ajith Chakkittakandiyil, MD

Accepted for Publication: November 15, 2009.

Author Affiliations: Pope. Section of Dermatology (Dr Pope), Hospital for Sick Children (Dr Chakkittakandiyil), Toronto, Ontario, Canada.

Correspondence: Dr Pope, Section of Dermatology, 555 University Ave, Toronto, ON M5G 1X8, Canada (elena.pope@sickkids.ca).

Author Contributions: Both authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Pope. Acquisition of data: Pope and Chakkittakandiyil. Analysis and interpretation of data: Pope and Chakkittakandiyil. Drafting of the manuscript: Pope and Chakkittakandiyil. Critical revision of the manuscript for important intellectual content: Pope. Statistical analysis: Pope.

Administrative, technical, or material support: Chakkittakandiyil. Study supervision: Pope.

Financial Disclosure: None reported.


Anetoderma of Prematurity: An Iatrogenic Consequence of Neonatal Intensive Care

Anetoderma of prematurity was described by Pri- zant et al1 in very-low-birth-weight infants in neonatal intensive care units (NICUs). This recent description probably reflects improvement in care of premature neonates who were previously unable to survive. The mechanism for the development of anetoderma is unknown, but the role of monitoring leads has been suspected. To further delineate this clinical condition, we have studied 11 additional cases.

Methods. All cases of anetoderma of prematurity seen in a single NICU (University Hospital, Dijon, France) from 1999 to 2006 were retrospectively studied. Anetoderma was diagnosed clinically.

Results. Gestational age and birth weight ranged from 25 to 30 weeks and from 725 to 1250 g, respectively. All neonates had pulmonary diseases and required assisted ventilation. Ten developed bronchopulmonary dysplasia and received oral steroid treatment. Three had severe digestive tract complications (necrotizing enterocolitis or ileal perforation). Nine were treated with indomethacin for patent ductus arteriosus, and 4 of these needed surgical closure. The median duration of hospitalization in the NICU was 125.0 days vs 99.5 days in 30 control neonates matched for gestational age (P= .001).

Twin pregnancies occurred in 5 cases, but no co-twins were affected with anetoderma. In these twin pairs, the affected twin had the lower birth weight in 2 instances, and the higher in 3 instances. The incidence and severity of pulmonary or digestive tract diseases were similar in twins without anetoderma.

Localized, rounded flat, atrophic skin patches 5 to 20 mm in diameter were first noted between age 6 weeks and 5 months (Figure 1B and Figure 2A). Five infants had previously been examined for ecchymoses without atrophy or necrosis (Figure 1A) at the sites where monitoring leads had been applied. On follow-up, all ecchymoses turned into atrophic patches within a few days. Previous placement of monitoring leads at the site of atrophic patches was noted in 8 cases. All lesions were centrally located: in the subclavicular areas on the chest in 8 cases (Figure 1) and in paraumbilical areas on the abdomen in 6 (Figure 2).