Expanding Uses of Propranolol in Dermatology

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Propranolol as a dermatologic therapeutic tool was first described in 2008. Since then, propranolol has had a pivotal role in the dermatology arena for a myriad of cutaneous disorders. This article highlights the timeline of the incorporation of propranolol as a treatment option for a number of vascular lesions.


Since the serendipitous discovery of expedited involution of infantile hemangiomas (IHs) with propranolol in 2008, current research has proliferated to discern the mechanism of action of beta-blockers in the care of IHs. Propranolol is a nonselective beta-blocker with a structure similar to catecholamines and thus competes for β-adrenergic receptors. Blocking β₁-receptors is cardioselective, leading to decreased heart rate and myocardial contractility, while blocking β₂-receptors leads to inhibition of smooth muscle relaxation and decreased glycogenolysis. The endothelial cells of IH express β₂-adrenergic receptors; the mechanistic role of propranolol in these lesions is surmised to be due to vasoconstriction, decreased angiogenesis through inhibition of vascular endothelial growth factor, and subsequent endothelial cell apoptosis.

After this breakthrough finding, a subsequent novel development was made when an ophthalmologist demonstrated that timolol, a topical beta-blocker, could be utilized to expedite IH involution and prevent ocular complications such as amblyopia secondary to the mass effect of the lesion. Guo and Ni prescribed the commercially available ophthalmologic solution of timolol maleate 0.5% for twice-daily use for 5 weeks. Remarkable reduction in the periorbital IH without rebound phenomenon was observed. A recent multicenter retrospective cohort of more than 700 patients with IH were treated with topical timolol with a 70% success rate, corresponding to 10% improvement from baseline; this study highlights the efficacy of timolol while confirming the safety of the medication.

Systemic beta-blockers for IH have been used predominately for critical sites such as the nasal tip, lip, ear, perineum, and periocular area; ulcerated lesions or those that may be prone to leave a fibrofatty tissue residue after involution also have been targeted. Contraindications for use include premature infants younger than 5 weeks, infants weighing less than 2 kg, history of asthma or bronchospasm, heart rate less than 80 beats per minute, blood pressure less than 50/30 mm Hg, or hypersensitivity to the medication. Current guidelines for propranolol initiation vary; some dermatologists consult cardiology prior to initiation, while others perform routine vitals and an indication-driven electrocardiogram as needed based on family history of cardiac disease, maternal history of connective tissue disease, congenital heart block, or abnormal vital signs.

Given the demonstrated long-term safety of propranolol and the acceptable side-effect profile, the use of beta-blockers for IH has become increasingly...
mainstream. Three randomized controlled trials (RCTs) have evaluated the efficacy and minimal adverse effects of propranolol for IH. The first RCT evaluated 40 patients who received either placebo or propranolol 2 mg/kg daily (divided into 3 doses) for 6 months; IH growth stopped by week 4 in the treatment group and the largest volume difference in IH was seen at week 12.6 Léauté-Labrèze et al7 demonstrated that propranolol could be given earlier to patients and at higher doses; the treatment group included 7 patients at 3 mg/kg daily of propranolol for 15 days, followed by 15 additional days of 4 mg/kg daily of propranolol. A statistically significant (P=.004) decrease in IH volume, quantified by use of ultrasonography, was exhibited by the propranolol group.7 Lastly, the largest RCT (N=456) established the efficacy of propranolol 3 mg/kg daily for 6 months with a 60% successful treatment rate compared to 4% for patients receiving placebo.8

Given the efficacy of propranolol for IH, other investigators have experimented with nonselective beta-blockers for other dermatologic conditions. In addition to second-line use for flushing, hyperhidrosis, and adrenergic urticaria, the future of beta-blockers for the management of vascular lesions can serve as adjunctive or monotherapy for certain patient populations. The relatively low adverse risk profile of propranolol makes it a versatile tool to use both systemically and topically. Although the authors of the study assessing the β2-adrenergic expression in vascular lesions admitted that the positivity of the receptors does not necessarily correlate with therapeutic management, it is an interesting subject area with much potential in the future.11 This review serves to illuminate the expanding role of beta-blockers in dermatology.

REFERENCES


