Commentary: Propranolol for infantile hemangiomas — The intralesional route

Following the serendipitous discovery of the effect of systemic propranolol on infantile capillary hemangioma by Léauté-Labrèze *et al.* in 2008,[1] this drug has rapidly become the first-line choice for the management of these lesions. It has been administered orally, topically and intralesionally.[2,3] By far, the greatest number of reported studies describe experience with the oral route of administration, and that is followed by experiences with the other two.[2-4] The oral route is reported to be safe with appropriate pretreatment assessment and in-treatment monitoring of patients receiving the drug.[5] However, as expected with oral administration, systemic adverse effects may not be completely eliminated. Reported adverse effects range from sleep disturbances and peripheral hypothermia to more serious ones like conduction blocks, hypotension, bronchospasm, and hypoglycemia with seizures.[5] In the event of occurrence of any of these, dose reduction or discontinuation of the drug may be necessitated. This has prompted use of alternative routes of administration that could result in a better drug safety profile, higher localized drug concentration within the lesion, and less systemic risk for the recipients. Intralesional administration of propranolol is one such route.[4]

In this issue of the journal, Mehta *et al.* have explored the outcomes of this route of administration compared to those with oral propranolol in a prospective, randomized pilot study involving twenty patients divided into two groups of ten each.[6] Oral propranolol was administered to the first group (Group 1) as per body weight in an escalating dose over five days and was continued till six months with a taper and stop over the next six days. Intralesional propranolol was given in a dosage of 0.2 ml per cm of the longest linear dimension of the lesion with a maximum dose of 1 ml with all patients receiving three injections (at baseline, between 4–6 weeks and 8–12 weeks) in the other group (Group 2). The final follow-up was at six months. The percentage decrease in cross-sectional area was the main outcome measure and this was graded on a measurement scale modified from that reported previously in the literature.[4] Other efficacy parameters studied were the change in color, appearance, improvement in ptosis, and change in corneal astigmatism. For the changes in color and appearance, the authors used representative images to design scales for subjective assessment. These were ratified by independent observers prior to the study but were not validated otherwise. There are no good, reliable objective scoring systems currently available to specifically assess periorbital and eyelid capillary hemangiomas. Scoring systems for activity and severity of infantile hemangiomas have been described in the dermatology literature[7] and may serve as a reference to develop similar instruments for assessment of periocular lesions as the authors have preliminarily attempted to do. If developed, these will subsequently need to be validated by further studies.

Mehta *et al.* report that the change in the cross-sectional area of the treated hemangiomas were statistically comparable for both oral and intralesional propranolol groups. However, it is notable that 100% of the patients in Group 1 had a response rated as good or higher on the scale used by the authors, whereas Group 2 had only 80% of patients who measured up to the same criteria. Interestingly, the baseline mean cross-sectional area of the lesions for Group 1 patients was close to double that for Group 2 patients, although this did not reach a statistically significant level. This could well be due to the small sample size of each group and the clinical implications of this should not be lost. The patients in Group 1 started treatment with lesions that were larger and yet achieved a response that was rated better than what the lesions in Group 2 did. Appearance-wise, 70% of Group 1 lesions were rated as elevated at baseline and at 6 months follow up, 60% had a flat appearance. In contrast, 90% of Group 2 lesions were elevated at baseline and only 20% had a flat appearance. Additionally, overall improvement in color was also better in Group 1 patients. Here it would seem pertinent to review reports that have stated that intralesional propranolol does not offer any significant benefit over topical application,[3] and that it may not be effective at all for infantile hemangiomas even after repeated administration.[8] The short duration of follow-up in the authors' study also precludes the possible detection of a rebound growth of the treated lesion that has been reported by others with longer follow-up periods.[3]

To put things in perspective, Mehta *et al.*'s study does show that intralesional propranolol may be a promising modality of management for periorbital and eyelid infantile capillary hemangiomas. However, the results of this study have to be carefully interpreted in the background of the small sample size and the short follow-up duration. A larger sample of patients undergoing this treatment with a longer follow-up is the need of the hour to drive home the fact conclusively that this intervention is actually significantly better than the other routes by which propranolol is administered for these lesions.

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