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Effective dose of bevacizumab for the treatment of retinopathy of prematurity

A dose eficaz de bevacizumab para o tratamento da retinopatia da prematuridade

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Dear Editor,

We read, with great interest, the article entitled "Which dose of bevacizumab is more effective for the treatment of aggressive posterior retinopathy of prematurity: lower or higher dose?" by Dikci et al.[1]. In the article, the authors compared 0.625 mg vs 0.5 mg intravitreal bevacizumab injection in patients with aggressive posterior retinopathy of prematurity (ROP). They concluded that the lower dose (0.5 mg) may require additional treatment compared with the 0.625 mg dose regimen. However, we have some comments with regard to this article.

Firstly, intravitreal injection of 0.625 mg bevacizumab was reported to be 10,000 times higher than the dose necessary to block vascular endothelial growth factor A (VEGF-A) molecules in the vitreous cavity[2]. Wang et al.[3] reported that a 10-fold higher-than-required dose of bevacizumab can bind total VEGF-A in the vitreous cavity. The researchers aimed to lower the bevacizumab dose to avoid possible systemic or ocular side effects[4-6]. Recently, we demonstrated that 0.0625 mg bevacizumab has similar clinical outcomes as observed with 0.625 mg bevacizumab[6]. We also reported that retinal vascularization restarts approximately 8 days earlier in the eyes of patients treated with an ultra-low dose of bevacizumab (0.0625 mg) compared with those treated with 0.625 mg of bevacizumab. The recurrence rates were similar between the two dose regimens in our study. Therefore, we disagree with the authors because a lower dose of bevacizumab, even 0.0625 mg, works in patients with ROP.

Secondly, the retreatment indications were not clearly defined in the study. According to our clinical experience, a stable plus-like appearance after intravitreal bevacizumab injection, particularly in AP-ROP, may exist even after the completion of retinal vascularization. This usually does not resemble ROP reactivation. However, we suggest taking into account the fact that thinner calibration of retinal vessels is merely a structural appearance rather than a result of disease reactivation, even with the presence of vascular tortuosity. Therefore, we want to emphasize the avoidance of unnecessary reinjection or adjuvant laser treatment in such cases.

Thirdly, according to our clinical experience with intravitreal bevacizumab treatment in ROP, recurrence occurs in infants who have serious comorbidities such as cardiac disorders with cyanosis and those receiving blood transfusion[7]. The patient demographics in this study may have altered the retreatment indications such as the lower birth weight and gestational age of the infants treated with 0.5 mg bevacizumab. Hence, the study results should be meticulously analyzed to define treatment modalities with bevacizumab.

Lastly, did the authors exclude zone I ROP? The gestational age of the infants in their series is extremely low, particularly in the group that received 0.5 mg bevacizumab.

We hope our comments will contribute to the improvement of the treatment approach with bevacizumab in patients with ROP.

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