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ORIGINAL ARTICLE

Efficacy of dorzolamide to reduce retinal thickness after photocoagulation, in diabetic macular edema[☆]



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KEYWORDS

Dorzolamide;
Diabetic macular
oedema;
Photocoagulation;
Diabetic retinopathy

Abstract

Background: Focal photocoagulation interrupts vascular leakage in diabetic macular oedema, and allows the retinal pigment epithelium to withdraw fluid that thickens the retina; this mechanism could be enhanced by dorzolamide, a topical carbonic anhydrase inhibitor.

Objective: To determine the efficacy of dorzolamide compared to placebo, in reducing retinal thickness after focal photocoagulation in eyes with diabetic macular oedema.

Material and methods: Experimental, comparative, prospective, longitudinal, double blind study in diabetics with focal macular oedema treated with photocoagulation. Treated eyes were randomly assigned three weeks after the procedure to receive dorzolamide (group 1) or placebo (group 2), three times daily for three weeks. Means of visual acuity, centre point thickness and macular volume were compared 3 and 6 weeks after photocoagulation within groups (Wilcoxon t) and between groups (Mann-Whitney-U).

Results: Sixty-nine eyes from patients aged 58.3 ± 8.3 years; 37 were assigned to group 1 and 42 to group 2. Mean centre point thickness changed from $178.4 \pm 34 \mu\text{m}$ to $170 \pm 29.1 \mu\text{m}$ in group 1 ($p = 0.04$), and from $179.2 \pm 22.4 \mu\text{m}$ to $178.6 \pm 20.8 \mu\text{m}$ in group 2 ($p = 0.07$); mean macular volume changed from $7.63 \pm 0.52 \text{ mm}^3$ to $7.50 \pm 0.50 \text{ mm}^3$ in group 1 ($p = 0.002$) and from $7.82 \pm 0.43 \text{ mm}^3$ to $7.76 \pm 0.42 \text{ mm}^3$ in group 2 ($p = 0.013$).

Conclusions: The efficacy of dorzolamide was higher than that of placebo in reducing retinal thickness after focal photocoagulation in diabetics with macular oedema.

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PALABRAS CLAVE

Dorzolamida;
Edema macular
diabético;
Fotocoagulación;
Retinopatía diabética

Eficacia de la dorzolamida para reducir el grosor retiniano después de fotocoagulación en el edema macular diabético

Resumen

Antecedentes: La fotocoagulación focal interrumpe la fuga vascular en el edema macular diabético, con lo cual el epitelio pigmentario retiniano puede retirar el líquido que engrosa la retina; este mecanismo podría facilitarse con dorzolamida, un inhibidor tópico de la anhidrasa carbónica.

Objetivo: Determinar la eficacia de dorzolamida comparada contra placebo, para reducir el grosor retiniano después de la fotocoagulación focal, en el edema macular diabético.

Material y métodos: Estudio experimental, comparativo, prospectivo, longitudinal, doble ciego, en diabéticos con edema macular focal tratados con fotocoagulación, aleatorizados 3 semanas después del procedimiento para recibir dorzolamida (grupo 1) o placebo (grupo 2). Se compararon los promedios de agudeza visual, grosor del punto central y volumen macular 3 y 6 semanas después de la fotocoagulación en cada grupo (t de Wilcoxon) y entre grupos (U de Mann-Whitney).

Resultados: Setenta y nueve ojos de pacientes con una edad \pm desviación estándar de 58.3 ± 8.3 años; se asignaron 37 al grupo 1 y 42 al grupo 2. El grosor del punto central cambió de $178.4 \pm 34 \mu\text{m}$ a $170 \pm 29.1 \mu\text{m}$ en el grupo 1 ($p = 0.04$), y de $179.2 \pm 22.4 \mu\text{m}$ a $178.6 \pm 20.8 \mu\text{m}$ en el 2 ($p = 0.7$); el volumen macular cambió de $7.63 \pm 0.52 \text{ mm}^3$ a $7.50 \pm 0.50 \text{ mm}^3$ en el grupo 1 ($p = 0.002$) y de $7.82 \pm 0.43 \text{ mm}^3$ a $7.76 \pm 0.42 \text{ mm}^3$ en el grupo 2 ($p = 0.013$).

Conclusiones: La dorzolamida aplicada durante 3 semanas fue más eficaz que el placebo para reducir el grosor retiniano después de la fotocoagulación focal en diabéticos con edema macular.

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Background

Macular oedema is the most frequent cause of vision loss in diabetic retinopathy; when clinically significant, it involves risk of moderate vision loss (doubling of visual angle, loss of 3 lines on an eye chart)¹, present in 6.8% of diabetic patients².

In macular oedema, the thickness of the retina in the macula increases due to leakage of intravascular fluid coming from microaneurysms (focal leakage) or dilated capillaries next to a microvascular occlusion area (diffuse oedema). The thickening of the macula distorts photoreceptors, which causes vision loss³.

One treatment for macular oedema is photocoagulation, which reduces the incidence of moderate vision loss from 33 to 13% in a 3-year period¹. In focal oedema, photocoagulation, the treatment of choice⁴, seals the leaking microaneurysms, and intraretinal fluid may retract towards adjacent capillaries and the choroid.

Under normal conditions, the retinal pigment epithelium transports water from the vitreous humour to the choroid, maintaining normal retinal thickness⁵. When the leakage of a microaneurysm exceeds the transport capacity of the pigment epithelium, the macula thickens; once the leakage ceases, the pigment epithelium progressively withdraws intraretinal fluid, which decreases the thickness of the macula.

The pigment epithelium of the retina withdraws the fluid through a Na/K⁺ ATPase located in the basolateral membrane, the activity of which is facilitated when the concentration of H₂CO₃ in the subretinal space increases. High levels of CO₂ in the subretinal space reduce adhesion among

the pigment epithelium and the neurosensory retina, and allows for the accumulation of intraretinal and subretinal fluid⁶; this condition is more common when there are high concentrations of carbonic anhydrases, as in the case of diabetes⁷.

Carbonic anhydrase inhibitors have been used orally for more than 50 years to reduce the formation of aqueous humour and to lower intraocular pressure, but they cause systemic adverse reactions; dorzolamide is a topical inhibitor of carbonic anhydrases, efficient as an ocular hypotensor, and usually well tolerated⁸, reaching peak concentrations of 24.0 $\mu\text{g/g}$ in the cornea, 7.8 $\mu\text{g/ml}$ in aqueous humour and 27.0 $\mu\text{g/g}$ in the ciliary body. In the retina, it reaches a maximum concentration of 5.29 $\mu\text{g/g}$, which would explain its effect on intraretinal fluid⁹.

Dorzolamide has been efficient in treating macular oedema present in diseases such as retinitis pigmentosa¹⁰, choroïderemia¹¹ and retinoschisis¹². The mechanism proposed for this response is the inhibition of carbonic anhydrases of the pigment epithelium, which favours the activity of Na/K⁺ ATPase and increases the transport of fluid towards the choroid.

The increase in the transport of fluid through the retinal pigment epithelium may facilitate the resolution of retinal thickening in eyes with diabetic macular oedema, once the capillary leak site is closed; this intervention would shorten the time of resolution of the thickening and probably limit visual dysfunction.

A study was carried out to determine the efficacy of dorzolamide, as compared to placebo, to reduce retinal thickness after focal photocoagulation, in eyes with diabetic macular oedema.

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