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Yokoi, Masahiko; Yamagishi, Sho-ichi; Takeuchi, Masayoshi; Matsui, Takanori; Yoshida, Yumiko; Ohgami, Kazuhiro; Amano-Okamoto, Tamami; Ohno, Shigeaki

British Journal of Ophthalmology, 91(3): 397-398

2007-03

http://hdl.handle.net/2115/20277
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Masahiko Yokoi, Sho-ichi Yamagishi, Masayoshi Takeuchi, Takanori Matsui, Yumiko Yoshida, Kazuhiro Ohgami, Tamami Amano-Okamoto and Shigeaki Ohno

doi:10.1136/bjo.2006.100198

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Competing interests: None declared.

The present observations suggest that AGE may induce VEGF expression in an ischaemia-independent mechanism. AGE could be one of the important determinants of VEGF in diabetic retinopathy without obvious ischaemic regions.

Background
Vascular endothelial growth factor (VEGF) elicits retinal vascular hyperpermeability, thrombosis and angiogenesis, having a central role in the pathogenesis of diabetic retinopathy. Moreover, vitreous VEGF levels are increased in proliferative diabetic retinopathy, whereas the levels are decreased after treatment with panretinal photocoagulation (PRP). These observations suggest that retinal ischaemia and resultant hypoxia could mainly contribute to VEGF induction in diabetic retinopathy.

Advanced glycation end products (AGEs), senescent macroprotein derivatives formed at an accelerated rate under diabetes, also stimulate VEGF expression in cell cultures and animal models. In addition, vitreous AGE levels are positively correlated with VEGF in patients with diabetic retinopathy, suggesting that AGEs may be a stimulant of VEGF in vivo. However, as AGEs predispose the retinal vessels to thrombogenesis, whether AGEs could induce VEGF expression in an ischaemia-independent manner remains unknown.

Therefore, in this study, we determined the relationship between vitreous levels of AGEs and VEGF in patients with diabetic retinopathy who were sufficiently treated with PRP for controlling retinal ischaemia.

Figure 2 Correlation between the vitreous levels of advanced glycation end products (AGEs) and vascular endothelial growth factor (VEGF) in the sufficiently treated group with panretinal photocoagulation (S-PRP; A) and in the insufficiently treated group with no or focal photocoagulation (IS-PRP; B). Spearman’s correlation coefficient calculated by rank test.

Patients and methods
The study protocol was approved by our institutional ethics committee, and informed consent was obtained from all patients. Undiluted vitreous samples were collected during vitrectomy from patients with diabetes, having idiopathic macular hole or epiretinal membrane, served as controls. Vitreous levels of AGEs and VEGF were measured as described previously.

We classified patients with diabetes into two groups: a sufficiently treated group with PRP (S-PRP; n = 23) and an insufficiently treated group (no or focal photocoagulation; IS-PRP; n = 28), on the basis of the extent of retinal photocoagulation before vitrectomy as described previously. The data were analysed by the Mann-Whitney U test and Spearman’s correlation coefficient by rank test.

Results
Vitreous levels of AGEs and VEGF were significantly higher in patients with diabetes than in controls (mean (SD) 0.13 (0.07) vs 0.04 (0.03) U and 2.15 (2) vs 1.22 (0.23) ng/ml, respectively; p < 0.01). As fig 1A and B shows, vitreous VEGF levels were higher in IS-PRP than those in S-PRP (2.75 (2.3) vs 1.4 (1.3) ng/ml, respectively; p < 0.05), whereas there was no significant difference of vitreous levels of AGEs between IS-PRP and S-PRP (0.13 (0.07) vs 0.13 (0.06) U, respectively). A positive correlation was found between AGEs and VEGF in S-PRP (r = 0.44, p < 0.05), but not in IS-PRP (r = 0.26, p = 0.18; fig 2 A, B).

Comment
Our observations suggest that AGEs may induce VEGF expression in an ischaemia-independent mechanism. In this study, the
positive correlation between vitreous AGEs and VEGF levels disappeared when retinal ischaemia was not sufficiently controlled. Therefore, with the progress of diabetic retinopathy, retinal ischaemia and subsequent hypoxia may become a major determinant of VEGF. Our findings suggest that inhibition of AGE formation could prevent the development of early diabetic retinopathy by suppressing VEGF expression.

Masahiko Yokoi
Department of Ophthalmology and Visual Sciences, Hokkaido University Graduate School of Medicine, Hokkaido, Japan

Sho-ichi Yamagishi
Department of Internal Medicine, Division of Cardiovascular Medicine, Kurume University School of Medicine, Kurume, Japan

Masayoshi Takeuchi
Department of Biochemistry, Faculty of Pharmaceutical Sciences, Hokkaido University, Kanazawa, Japan

Takanori Matsui, Yumiko Yoshida
Department of Internal Medicine, Division of Cardiovascular Medicine, Kurume University School of Medicine, Kurume, Japan

Kazuhiro Ohgami
Department of Ophthalmology and Visual Sciences, Hokkaido University Graduate School of Medicine, Hokkaido, Japan

Tamami Amano-Okamoto
Department of Ophthalmology, Nippon Telegraph and Telephone East Corporation Sapporo Hospital, Sapporo, Japan

Shigeaki Ohno
Department of Ophthalmology and Visual Sciences, Hokkaido University Graduate School of Medicine, Hokkaido, Japan

Correspondence to: Dr Masahiko Yokoi, Department of Ophthalmology, Teine-Kenjinkai Hospital, Maeda 1–12, Teine-ku, Sapporo 066-8555, Japan; zoyokoi.tdr@keijinkai.or.jp
doi: 10.1136/bjo.2006.100198

Accepted 20 July 2006

Funding: This work was supported in part by Grants of the Specific Research Fund of Hokkaido University, Japan (MT).

Technology, Japan (SY), and the Specific Research Fund of the Ministry of Education, Culture, Sports, Science and Technology, Japan (MT).

References


Postoperative subconjunctival 5-fluorouracil in the management of recurring pterygium

The treatment of choice for pterygium is surgical excision. Recurrence is the most common undesirable treatment outcome. Surgery and other modalities of treatment including β-irradiation, topical thiotepa, intraoperative and postoperative use of mitomycin C, 5-fluorouracil (5-FU) and daunorubicin, have been described to reduce recurrence. Multiple surgery is itself a risk factor for recurrence. We present a case in which the fourth surgery for recurrent pterygium resulted in further recurrence, which was thwarted by multiple intraleisional injections of 5-FU.

Case report

A 34-year-old Afro-Caribbean woman was referred to us in October 2004 for the management of recurrent pterygium in the right eye. She had two previous surgeries, the first in 2002 with conjunctival autograft and the second in 2003 leaving behind bare sclera. A third attempt at removal in 2004 was aborted owing to excessive intraoperative bleeding.

Her unaided visual acuity was 6/9 right eye and 6/6 left eye. The right eye showed a highly vascularised, fleshy nasal pterygium measuring 11 × 8 mm. It had encroached 2.5 mm into the cornea (fig 1A). The recurrent pterygium in the right eye was excised for the third time in March 2005. On this occasion, mitomycin C (0.04%) was applied intraoperatively to the scleral bed for 5 min and a double-layered amniotic membrane was grafted to cover the conjunctival defect. A recurrence at the original site was noted 2 months later (fig 1B), and in an attempt to arrest progression, topical 0.02% mitomycin C was given four times daily for 7 days (three cycles with an interval of 10 days between cycles). The recurrent pterygium, however, progressed to encroach on to the cornea (fig 1C). At this point, subconjunctival injections of 5-FU into the advancing lesion, under topical anaesthesia, was started. A 26-gauge needle was used to deposit the injection in the core of the fibrovascular tissue away from the cornea. Over 5 months, she received 10 injections of 5-FU (5 mg in 0.2 ml/injection) given 1–2 weeks apart until the recurrent pterygium became less vascular and atrophic. No complications were noted. Now, 8 months after the last injection, there is no progression (fig 1D).

Comment

Pterygium recurrence is thought to be due to fibroblast proliferation and migration and hence use of 5FU, which inhibits fibroblastic activity, is believed to reduce recurrence rates. 5-FU is toxic only to proliferating cells and is considered to be safer than other agents. Postoperative use of 5-FU to halt the progression of recurrence has been described before, but involved a maximum of four injections with a maximum dose of 3 mg. Our patient received 10 injections totalling 50 mg of 5-FU with no complications.

In cases with a high risk of recurrence, such as the one described, intraleional subconjunctival injection of 5-FU even at large doses seems to be safe, effective and well tolerated by the eye. Such an intervention should be considered as an option in the management of difficult cases of recurrent pterygium.