فعالية حقن عامل مضاد النمو الوعائي (بيفاسيزوماب) داخل الزجاجيّة قبل قطع زجاجيّة العين لتدبير اعتلال الشبكيّة السكريّ المنميّ المختلط

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الملخص

خلفية البحث وهدفه: تحديد فعالية حقن عامل مضاد النمو الوعائي (بيفاسيزوماب) داخل الزجاجيّة قبل قطع زجاجيّة العين وفائدته لتدبير اعتلال الشبكيّة السكريّ المنمي المختلط.

مواد البحث وطرائقه: دراسة راجعة أجريت على (29) عين مصابة باعتلال شبكيّة سكريّ منمي مختلط وقد قسّم المرضى إلى مجموعتين: مجموعة A وتشمل 19 عيناً أجري لهم قطع زجاجيّة العين بعد حقن البيفاسيزوماب داخل زجاجيّة العين قبل الجراحة. والمجموعة B وتشمل 10 عيون أجريت لها الجراحة من دون الحقن قبل الجراحة. لقد حُقن البيفاسيزوماب قبل الجراحة بـ 4–8 أيام. ما قيّم بشكل أساسي هو حدة الإبصار، وحدوث شقوق شبكيّة في أثناء الجراحة، والنزف في أثناء الجراحة، وزمن الجراحة، والدّكة النهائية.

النتائج: تحسنت حدة الإبصار بشكل ملحوظ بعد شهر من الجراحة في المجموعة A (84.2%) من الأعين ونسبة (80%) من أعين المجموعة B ، ولم يكن الاختلاف بين المجموعتين مهمًا. شقوق الشبكيّة في أثناء الجراحة حصلت في 3 حالات من المجموعة A (15.7%) وفي 4 أخرى في المجموعة B (40%). وحدث النزف في أثناء الجراحة في المجموعتين ولكنه أقل إزعاجًا في المجموعة A. وسطي زمن الجراحة في المجموعة A كان 91 دقيقة، وفي المجموعة B وصل إلى 120 دقيقة. استخدم زيت السيليكون كدكة في 13 عين من أعين المجموعة A (68.4%) و6 أعين (31.5%) كان الهواء هو الدكة، في حين دكت أعين المجموعة B العشرة كلّها بزيت السليكون.

الاستنتاج: إن حقن مضاد عامل نمو بطانة الأوعية قبل قطع زجاجيّة العين في مرضى اعتلال الشبكيّة السكريّ المنمي المختلط يسهل الجراحة ويسرّعها، ويعطي حدة إبصار أفضل نسبيًا، ويقلل من حدوث شقوق الشبكيّة في أثناء الجراحة ومن استخدام زيت السليكون بوصفه دكة.

نحن بحاجة إلى دراسة أخرى بعينة أكبر لتقييم إضافي لفعالية حقن مضاد عامل نمو بطانة الأوعية للوصول إلى استنتاجات محكمة.

كلمات مفتاحيّة: اعتلال الشبكيّة السكريّ المنمي المختلط – انفصال اللطخة الشّدّي – قطع الزجاجيّة – بيفاسيزوماب – شق شبكيّة – سليكون.

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The Efficacy of Antivascular Endothelial Growth Factor (Bivacizumab) Pretreatment before Vitrectomy for Patients with Complicated Proliferative Diabetic Retinopathy

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Abstract

Background/aims: To evaluate the efficacy of antivascular endothelial growth factor (anti-VEGF) agents pretreatment before vitrectomy for patients with complicated proliferative diabetic retinopathy (PDR)

Methods: A retrospective research was done on (29) Proliferative Diabetic Retinopathy (PDR) eyes who were divided into two groups, group A (n=19) Pars Plana Vitrectomy (PPV) with preoperative Intra Vitreous Bevacizumab (IVB) and PPV group B (n=10). Bevacizumab was injected 4-8 days before PPV. Main outcome measures were visual acuity, incidence of iatrogenic retinal breaks, intraoperative bleeding ,surgery time and final tamponed.

Results: At six month after surgery, visual acuity in group A: IVB PPV (84.2%) and group B: PPV (80%) improved significantly and the difference between the two groups was not significant. Iatrogenic retinal breaks were reported in 3 cases (15.7%) in group A and 4 cases (40%) in IVB group. Intraoperative bleeding was encountered in all cases in two groups but it was less annoying in group A. median surgery time was in group A 91 minute, and in group B 120 minute. In group A13 eye (68.4%) was tamponed with Silicon oil while 6 eyes(31.5%) tamponed with air, and in group B all 10 eyes (100%) was tamponed with silicon oil.

Conclusion: The pretreatment of anti-VEGF agents before vitrectomy for patients with complicated PDR facilitates much faster surgery and better visual rehabilitation, reduces iatrogenic retinal breaks, and silicon oil tamponad. Moreover, studies with larger sample sizes are required to further evaluation the efficacy of anti-VEGF agents and reach a firmer conclusion.

Key words: Diabetic Proliferative Retinopathy (PDR), Tractional Macular Detachment (TMD), Bevacizumab, Vitrectomy, Retinal Break, Silicon.

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Introduction:

Despite all the important progress in the understanding and management of diabetes over the recent years, diabetic retinopathy (DR) remains one of the leading causes of legally blind in the working-age population worldwide.[1] The prevalence of DR in diabetic patients was reported as high as 54% after 10–19 years of evolution.[2] Proliferative diabetic retinopathy (PDR) is the severest stage of DR, the formation of retinal neovascularization (RNV) in the vitreous–retinal interface usually lead to serum leakage, hemorrhage and fibrovascular proliferation. All these will further induce macular edema, vitreous hemorrhage (VH) and even tractional retinal detachment (TRD), these complications may severely damage patient's visual function and need surgical intervention. Pars plana vitrectomy (PPV) is widely regarded as the milestone for the management for severe complications of PDR like TRD and non-resolvingVH.[3]PPV is generally indicated when the TRD is macula-involving or macula-threatening, and the postoperative functional result may not be as good as the anatomical outcome.[4] [5] [6] The surgical technique includes removal of the fibrovascular membranes and relief of vitreoretinal traction. Particular attention is focused on minimizing intraoperative bleeding and avoiding iatrogenic retinal breaks.[7] [8]

However, serious events including intraocular hemorrhage during surgery may prevent the successful conclusions of diabetic vitrectomy. Angiogenesis is the fundamental mechanism of PDR.[9] Studies have recently confirmed that vascular endothelial growth factor (VEGF) is the pivotal driver of the increase of vascular permeability that results in diabetic macular edema, of the neovascularization that can lead to VH and TRD.[1]Current clinical studies suggested that the regression of Retinal Neo Vascularization (RNV) could be induced by the inhibition of VEGF receptors. Therefore, easier diabetic PPV and fibrovascular membrane dissection could be achieved with less risk of intraoperative bleeding.

To minimise the surgical complications and maximize the surgical outcomes, intravitreal injection of anti-VEGF agents before diabetic PPV has been widely regarded as a necessary adjunctive therapy.[12-14]

While other authors insisted that anti-VEGF agents have no significant effect on facilitation of the surgery or the postoperative course.[15–17]

Patients and methods

Twenty nine Diabetic Retinopathy (PDR) eyes were divided into two groups, group A (n=19) Pars Plana Vitrectomy (PPV) with preoperative Intra Vitreous Bevacizumab (IVB) and only PPV group (n=10).

Patients were offered study participation if they had: (1) PDR and macula-involving TRD (defined as the presence of retinal elevation within two disc diameters of the centre of macula associated with epiretinal fibrovascular membranes on dilated biomicroscopic fundus examination); (2) macular TRD of recent onset.

All patients underwent an initial screening visit which included a detailed ophthalmic evaluation with BCVA measurement using a standard refraction protocol, applanation tonometry, biomicroscopy of the anterior segment, dilated biomicroscopic fundus examination and binocular ophthalmoscopy as well as OCT.

All pars plana vitrectomy (PPVs) were performed by one surgeon. All were standard 23-gauge, 3-port PPVs. After core vitrectomy, the posterior hyaloid was opened and carefully removed as completely as possible. Preretinal fibrovascular tissue and tractional membranes were removed using a combination of segmentation and delamination techniques, primarily with the vitrectome and if it is not easy with bimanual dissection and retinal scissors. The surgical endpoint was relief of traction on the macula and on neovascular fronds that allowed the entire retina to flatten. Hemostasis was maintained by endodiathermy and by prudent elevation of the intraocular pressure. Care was taken not to compromise the intraocular perfusion by high intraocular pressure or low systemic blood pressure. Thorough PRP was administered at 360° extending anterior to the equator in all eyes, regardless of whether the eye had prior PRP. Intraocular retinal tamponade was tailored according to the appearance of the retina after the membranes were removed. If the retina appeared flat, without memory of the removed membrane air was used. Silicone oil was injected if retinectomy was performed or if multiple inadvertent retinal breaks occurred. Cryotherapy was not used, and no supplemental PRP was given in the 6-month postoperative period.

19 eyes for 12 patients operated for complicated proliferative diabetic retinopathy after the injection bevacizumab 1.23mg intra vitreous 4 – 8 days before surgery. And other group of control of 10 eyes for 10 patients with the same degree of diabetic retinopathy also operated but without injection of bevacizumab. Seven male and five women in group A and six male and four women for group. Nine patients of group A and seven were treated by insulin.

Results

The initial Visual Acuity (VA) for the two groups ranged between light perception and counting fingers

at five meters. At one month post PPV the VA improved in the two groups 89% (17/19) group A and 90% (9/10) group B one month post operation, and continued to improve with median 2/10 for group A 84.2% (16/19) and group B 80% (8/10) at six months.(figure 1&2)

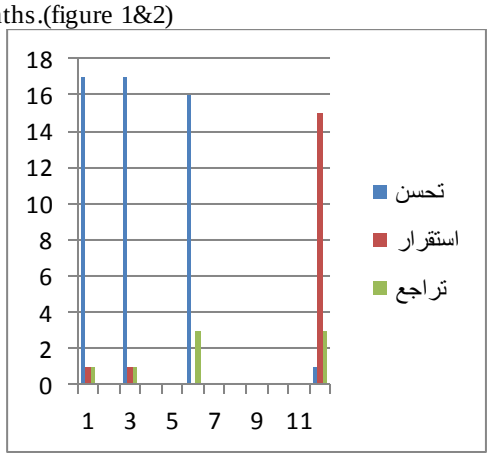

Figure (1):(Visual Acuity group A)

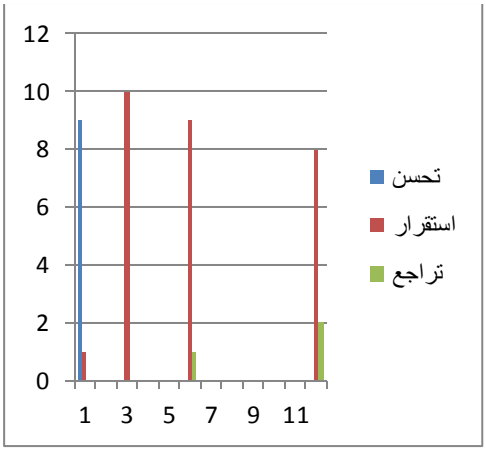

Figure (2): (Visual Acuity group B).

In the bevacizumab group A there was more facility in dissection of membranes witch became less vascularized and less adhesive to the retina with only three cases of inadvertent retina breaks and though less bleeding and less operating time (medium time 91 minute), while in group B there was some difficulty in dissection with more percentage of retinal breaks(fives of ten) , more hemorrhage and more surgery time (medium time 120). (figure 3 & 4).

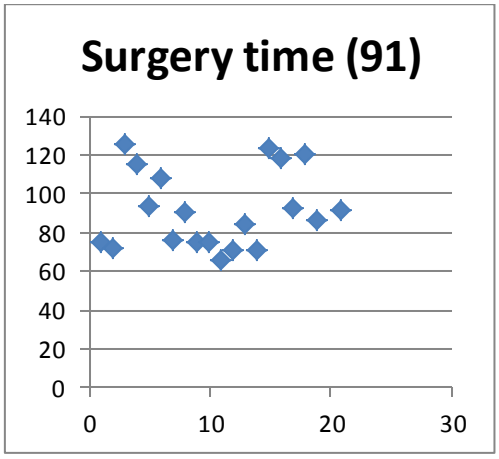

Figure (3): (group A).

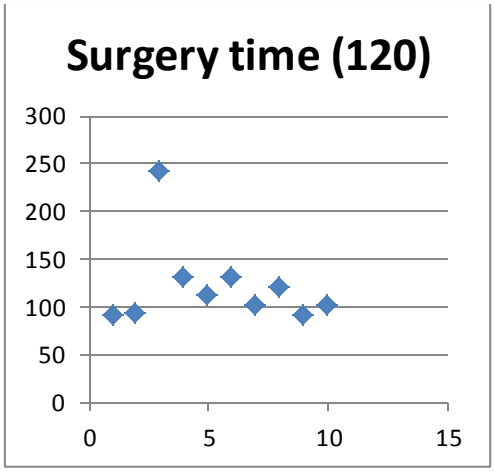

Figure (4): (group B)

All eyes of group B were tamponed by silicon oil 1000sc, while six eyes in group A were tamponed by the air. There was post vitrectomy hemorrhage in seven eyes of group A (five of them were tamponed by air) while the group B this was less frequent and less annoying (one eye only).

There were three cases of cystoid macular edema, three cases of regressed proliferation and two cases of elevated intra ocular pressure in group A. and approximately the same percentage in group B, two cases of cystoid macular edema, three cases of regressed proliferations and two cases of elevated intra ocular pressure.

Discussion:

Recently, intravitreal bevacizumab has become popular as a preoperative coadjuvant in cases of severe PDR.(18,19). The natural course of PDR is characterised by a proliferation of new vessels, proliferation of fibrous tissue accompanying new

vessels, formation of adhesions between the fibrovascular proliferations and the posterior vitreous surface; and contraction of the posterior vitreous surface and associated proliferation with accompanying hemorrhages.

Our study found that the pretreatment of anti-VEGF agents before vitrectomy for complicated PDR might facilitate much easier surgery regarding less intraoperative bleeding, less endodiathermy, shorter duration of surgery, We used the total surgical time, even though the duration of elevated intraoperative IOP, less iatrogenic retinal breaks and lower frequency of using silicone oil tamponed. Additionally, Our results show a significant improvement in VA in both the bevacizumab and non-bevacizumab groups. This, as others have suggested, is most likely due to improved vitrectomy techniques. Although the improvement in VA was not significantly greater in the IVB group, the IVB eyes had a possible trend towards better VA.

We did not notice the formation or aggravation of TRD associated with progressive fibrosis of fibrovascular membrane following the pretreatment of anti-VEGF agents, so we suggest that anti-VEGF pretreatment before vitrectomy for complicated PDR is relatively safe and may not induce development or progression of TRD

Silicone endotamponade is always used in the cases of intraoperative complications like severe bleeding, iatrogenic retinal breaks or retinotomy. It supports the retina after reattachment, decreases the chance of postoperative VH, provides the longest term tamponade and has additional benefit of non-critical posturing, indicating that anti-VEGF pretreatment could significantly reduce the frequency of silicone oil application during vitrectomy for complicated PDR, which partly implied anti-VEGF pretreatment might facilitate easier diabetic vitrectomy and less intraoperative complications.

Intraoperative bleeding was encountered in all cases in two groups but it was less annoying in group A

Conclusion

The pretreatment of anti-VEGF agents before vitrectomy for patients with complicated PDR facilitates much faster surgery and better visual rehabilitation, reduces iatronic retinal breaks, and silicon oil tamponad.

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