The Role of Aflibercept (Eylea) Intravitreal Injection in Treatment of Resistant or CNV Complicated CSR (Central Serous Retinopathy)

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KEYWORDS

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ABSTRACT

Purpose to evaluate the benefit and side effects of intravitreal Aflibercept (Eylea) injection in the treatment of cases that are resistant to previous treatment choices or complicated with CNV due to central serous retinopathy [CSR]

Methods

It is retrospective study on 72 patients with diagnosed to have CSR and follow up for 12-18 months we can consider that there is complete resolution if subretinal fluid disappeare for 3 months from last intravitreal injection of Eylea

We planned this research to demonstrate the efficiency of aflibercept intravitreal injection in the treatment of cases that resistant to treatment or complicated with CNV secondary to CSR.

1. Introduction

Theirare many types of retinopathy one of the most common types is (CSR) central serous retinopathy in theses cases our patients usually complain of many visual problems such as micropsia or macropsia, the visual, acuity is diminished, contrast vision is affected and also there is central scotoma, dyschromatopsia and metamorphopsia (1)

Central serous retinopathy (CSR) is an idiopathic inflammatory chorio retinopathy characterized by multiple recurrent, usually limited, multifocal retinal detachments in the posterior pole due to choroidal hydrops resulting from choroidopathy (2)

It is usually self-limiting over time, and when needed, laser photocoagulation PDT can be used if corticosteroids either local or systemic cannot be given or do not provide benefit (17)

In some recently published small-scale clinical research, aflibercept, a VEGF inactivator, has been shown to have a therapeutic effect on CSR cases, especially on chronic, persistent patients (3)

The pathogenesis in theses cases started by choroidal vessels congestion which is followed by increasing their permeability and accumulation of subretinal serous fluid (SRF) this process lead to damage in pigmented epithelium of the retina and subsequently increase thickness of choroid (2)

According to the fate of this pathogenesis CSR can be classified into two types, if the subretinal fluid absorbed within four months it is acute form and if the fluid remains for more than four months it becomes chronic which if prolonged more become more aggressive and associated with more complications as (CNV) choroidal neovascularization (4)

This condition is reported in about 3.5-7% of cases

Spontaneous resolution will occur within 4 months, if not occur we will use different methods of treatment one of the most recent methods is intrevitreal injection of aflibercept

(Eylea) wihch is anti –VEGF substance as it has strong effect on permeability of choroidal blood vessels(4)

Another methods of treatment may be used as photocoagulation by argon laser or oral administration of corticosteroid and photodynamic therapy (5)

Although photodynamic therapy is considered an effective method in treatment of CSR but it needs laser equipments and associated with many complications (6)

So we will study the outcome of cases treated with aflibercept and those treated with other modalities in decreasing permeability of choroidal blood vessels

2. Methodology

We took72 cases with chronic central serous retinopathy in the form of retrospective study we choose this sample from our ophthalmology department all patients are undergoing to proper medical history taking as all cases were complaining for more than four months and then complete fundus examination

A written consent is taken from each patient as all of them are more than 18 years

We make injection at 1 to 3 months interval and repeat it till SRF completely resolved and then we can repeat the process according to the requirements of the patients when SRF reappear again

All cases enrolled in this study undergo to proper occular examination by measuring intra occular pressure, pupillary dilatation and fundus examination,fundus autofluresence image and angiography are done and central macular thickness is measured using optical coherence tomography

Intervention

At first we give the patients propracaine eye drops in the eye affected then disinfect the field by betadine 5%solution then we use lid speculum and then we use a needle 27 gauge, pars plana should marked which is 3 mm from limbus in pseudophakic patients and 3.5mm in in phakic patients then we inject aflibercept in the vitreous then remove the needle and cover the site then use antibiotic eye drops and the patient continue on it for one weak. we must repeat the procdure till complete disappearance of CNV.

Complications in some cases are observed as pain it is present in about 14%of cases there is vitrous reflux in about 19% of cases and subconjunctival hemorrhage in 21% of cases so the complications are minimal and tolerable. Their is no reported systemic side effects and their is no reactivation in the follow up period but repeated injections at short intervals to maintain our results give discomfort to our patient beside financial problem

3. Result and Discussion

The patients enrolled in this study are 72 their age ranged from(23-62) at the beginning of this study with mean of 46.6±10.5 years and follow up duration (12-18) months.

63 patients give complete resolution (87.5%) . BCVA was v0.22±0.21 (0 –0.7) log MAR at starting 0.12±0.2 (0-0.5) log MAR at 12 months ($P > 0.001$). in follow up period no one of patients showed (CNV) choroidal neovascularization. 9 patients (12.5%) failed to reach complete resolution after intravitreal injection of aflibercept

In our cases we excluded other eye problems as diabetic retinopathy, macular affection due to age problems, retinal vein occlusion ,history of PDT and any systemic disease need steroid treatment for long time

About 36% of patients give stabilization of vision after one injection and 52% give that after 2 injections

Table 1 Characteristics of patients injected with intravitreal aflibercept and their response

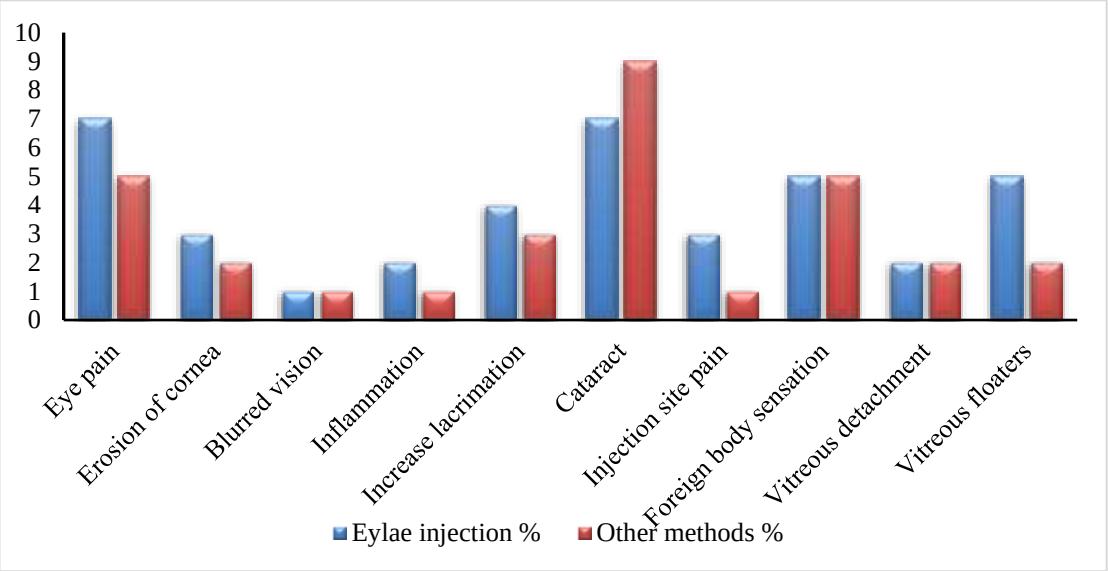
	Total number= 72	Complete resolution =63	Un resolved cases=9	P value
Age of patients	46.6±10.5	46.6±6.4	45.8.5	0.632
Gender male /female	40/32	35/28	5/4	0.893
Central macular thickness µm	338±55	247±51	336±57	0.513
Choroidal vascular index	67.3±2.5	63.8±2.9	66.4±7.3	0.765
Hyperper meability of choroidal blood vessels%	3664.5	17)68.7(	33)82(	0.632
% of RPE tract	8 12.9	4 13.1	7)12.8(	0.765
Diameter of CNV	2866±740	2632±540	2767±575	0.732

CNV = choroidal neovascularization

RPE =retinal pigment epithelium

Table3. Adverse reaction of Eylea injection against other methods of treatment (13)

Adverse reactions	Eylae injection %	Other methods %
Eye pain	7	5
Erosion of cornea	3	2
Blurred vision	1	1
Inflammation	2	1
Increase lacrimation	4	3
Cataract	7	9
Injection site pain	3	1
Foreign body sensation	5	5
Vitreous detachment	2	2
Vitreous floaters	5	2



Discussion

Naturally present glycoprotein called VEGF (vascular endothelial growth factor its role is mainly a growth factor that acts on endothelial cells as it increase vascular permeability and promote new vascular formations

(angiogenesis)

So using anti-VEGF as Eylea is one of the most effective methods in treatment of CNV as it is FDA approved as it is highly purified to decrease the incidence of eye toxicity and has long duration of action and its binding affinity is high(16)

In this study we study the effect of intravitreal injection of aflibercept (Eylea) in cases of CSR and CNV as it is one of the new generations of anti –VEGF it is very effective treatment that produce fluid absorption (6)

As injection of aflibercept lead to complete resolution in about 88% of cases

As central serous retinopathy is serous detachment of sensory retina which is associated with leakage from the choriocapillaries through the retinal pigment epithelium most cases resolves spontaneously, about 85% within 4-6 months with improvement of visual acuity(7)

Some lesions become chronic or show recurrence in about 15-20% of cases and become chronic cases which may be complicated by RPE atrophy or tear and subretinal fibrosis(8-9)

One of the most common complications is CNV, its cause and pathogenesis still unknown there is suggestion that chronic inflammation lead to decrease in VEGF intraocular level and angiogenesis which give great response to anti VEGF drugs (13)

The aflibercept and other anti-VEGF agents are used in treatment of retinal vascular diseases and CNV they can do that by restoration of function of Bruch`s membrane by strong blocking of VEGF receptors and decreasing microvascular permeability(10)

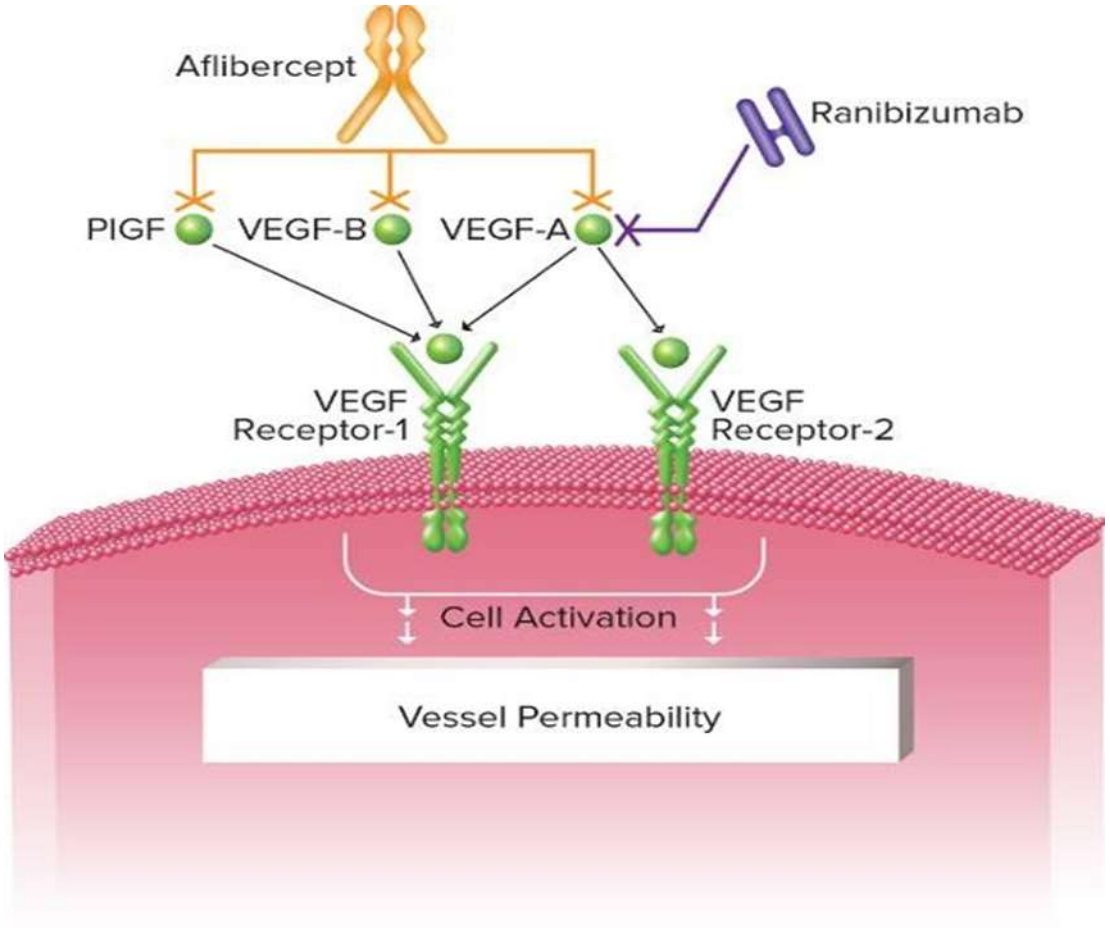


Fig 1 the role of Eylea in treatment of CNV

VEGF-A is glycoprotein that play a role in new vascular formation (angiogenesis) which lead to macular edema and

then retinal vein occlusion (11)

Aflibercept (Eylea) can block these receptors and treat CNV through its intravitreal injection we observed that there is reduction in (CRT) central retinal thickness and correction of

visual activity (BCVA)(14)

The patients enrolled in this study received injection 2 mg of

Eylea at three months interval and examined regularly for complete absorption of fluid if become free for more than

three months we can consider that as initial responder

On regular examination if recurrence occur, re injection again with Eylea.

Cases not responding to treatment by aflibercept injections we can switch the patients to PDT as combined therapy give great response and decrease the rate of recurrence (15)

4. Conclusion and future scope

From this study we can conclude that there is reduction in SRF after interavitreal injection of aflibercept with marked improvement of chronic and recurrent cases of CSR. in our

cases. In this sample show marked improvement in BCVA.

On the other hand resistant cases show no or minimal improvement need further combination therapy with PDT or corticosteroid. follow up of cases for about 18 months show marked decrease in recurrence rate with Eylea more than other treatment modalities so further comparative studies should be done.

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