Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/15804
DOI URL: http://dx.doi.org/10.21474/IJAR01/15804

RESEARCH ARTICLE

EFFECT OF ROCK INHIBITORS ON DIABETIC MACULAR EDEMA

Reddi Bhagya Sree, Chenna Bhaskar Sai and Vejendla Bhavya Sri Sai
Postgraduate, Department of Ophthalmology, Government Regional Eye Hospital, Visakhapatnam, Andhra Pradesh, India.

Manuscript Info

Manuscript History
Received: 05 October 2022
Final Accepted: 09 November 2022
Published: December 2022

Key words:-
Ripasudil, Diabetic Macular Edema, Fovealthickness(ft)

Abstract

Aims and objectives : To study the effects of topical Ripasudil on diabetic macular edema in tertiary eye care hospital.
Materials and Methods:: Ethics approval was obtained. Written and informed consent was obtained. It is a prospective interventional study of 20 eyes (10 eyes as controls,10 eyes as tests) presenting to our opd. Inclusion criteria for patients in whom ripasudil administered are with DME of FT->300µm with no history of ocular surgery or no photocoagulation, anti VEGF treatment and prescribed ripasudileyedrops 2t/d 4 weeks and followed up for FT measurement. we enrolled 10 eyes as control for comparision with ripasudil with age and sex matched individuals with other criteria as test group. After taking detailed history BCVA, anterior segment and fundus, oct macula with spectral domain oct done. Investigations like Blood pressure, FBS, PPBS, HbA1C, serum creatinine, serum lipid profile were done.
Results: After ripasudil administration in those 10 eyes the mean FT decreased significantly from $430 \pm 60\mu m$ to $380 \pm 62\ \mu m$ ($P = 0.003$); this change was significantly different from that in the controls, in which the mean FT increased by $1 \pm 40\mu m$ ($P = 0.01$).
Conclusion: In conclusion, the current findings showed that FT were decreased significantly after 4 weeks after the initiation of ripasudil therapy, suggesting that ripasudil might be effective noninvasive alternative treatment for DME.

Introduction:-

Diabetes is a progressive systemic disease which leads to macrovascular and microvascular complications.One of microvascular complications is Diabetic retinopathy.Theover all prevalence of diabetic retinopathy in diabetic patients is 17.6% according to CURES[3]

Diabetic macular edema and Proliferative diabetic retinopathy are the leading causes of blindness in diabetic retinopathy. The global prevalence of DME is 6.8%[1] according to Yau et al (2012). One of the pathogenesis of DME is Rho coiled coil containing protein kinase (ROCK) activation which contributed to damage outer blood retinal barrier (BRB) and retinal microvasculopathy. The definitive treatment for DME is Intravitreal anti VEGF or Intravitreal steroids which are invasive. There are studies previously reported that a combination therapy of Bevacizumab and Fasudil (ROCK inhibitor) intravitreally was effective in eyes with refractory DME[2]. So now we studied the effectiveness of topical Ripasudil the drug which is currently used for treatment of glaucoma on DME by

Corresponding Author:- Reddi Bhagya Sree
Address**:-** Postgraduate, Department of Ophthalmology, Government Regional Eye Hospital, Visakhapatnam, Andhra Pradesh, India.

measuring fovealthickness(FT).One of pathogenesis of diabetic retinopathy is related to increased leukocyte adhesion, leading to endothelial damage. It has been shown that ROCK pathways promote leukocyte adhesion to microvascular structures, through increased levels of activated Intercellular Adhesion Molecule-1 (ICAM-1) . Therefore, increased levels of activity of the Rho pathway are related to the pathogenesis of diabetic macular edema and diabetic retinopathy.(7)AIMS AND OBJECTIVES : To study the effects of topical Ripasudil on diabetic macular edema in tertiary eye care hospital by comparing Foveal thickness (FT) between test and control group

Aims And Objectives:-

To study the effects of topical Ripasudil on diabetic macular edema in tertiary eye care hospital by comparing Foveal thickness (FT) between test and control group

Materials And Methods:-

Ethics committee approval was obtained ,written and informed consent taken from patients. It is a prospective interventional study of 20 eyes (10 eyes as controls,10 eyes as tests) presenting to our opd. INCLUSION CRITERIA – patients who are diagnosed with diabetes and are with DME of FT->300µm with no history of ocular surgery or no photocoagulation, anti VEGF treatment, these patients were prescribed ripasudileyedrops 2t/d 4 weeks and followed up for FT measurement after 4 weeks . we enrolled 10 eyes as control for comparision with ripasudil with age and sex matched individuals. EXCLUSION CRITERIA – patients who didn't give consent,patients with no DME, with any h/o ocular surgery,photocoagulation, intra vitreal anti VEGF.

After taking detailed history BCVA, Anterior segment and fundus examinationWith 78D was done ,oct macula with cirrus spectral domain oct done. Investigations like FBS, PPBS, HbA1C were done.

Statistical Analysis:Data analysis done with SPSS soft ware, all values are expressed as mean ± standard deviation ,the p value was for parameters were assessed ,the BCVA is expressed in LOG MAR values ,iop in mm hg, Foveal thickness(FT) in microns. p value < 0.05 is considered significant.

Results:-

Table 1:-

Sub group	Ripasudil group	Control group
Patients eyes	10	10
Age(Mean + SD)	55.2+/- 8.8	59.8+/-9.4
Gender(Male:Female)	7:3	7:3
HbA1c	7.56+/- 0.51	7.79+/-0.49

Table 2:-

	Ripasudil group			Control group		
	Before drug	After drug	P value	Before 4 weeks	After 4 weeks	P value
Log MAR VA	0.362+/- 0.213	0.274+/- 0.22	0.23(not significant)	0.284+/- 0.247	0.41+/- 0.41	0.16(not significant)
IOP	14.8+/- 2.3	12.9+/- 2.6	0.001(significant)	13.8+/- 1.2	14.2+/- 1.3	0.37(not significant)
FT	439.1+/- 50	376.3+/- 58.9	0.01(significant)	380.6+/- 61.0	445.1+/- 52.8	0.02(significant)

The mean FT in ripasudil group has decreased from to 439.1 ± 50 to 376.3 ± 58.9 with p value (0.01) and FT increased in control group from 380.6 ± 61.0 to 445.1 ± 52.8 with p value (0.02) which showed significant statistical difference. There is no significant difference in visual acuity.BCVA in ripasudil group improved from logMAR 0.362±0.213 to 0.274±0.22 with p value (0.23) which is not significant and in control group LogMAR VA 0.284±0.247 to 0.41±0.41 with p value (0.16) which is not significant.IOP in ripasudil group decreased from 14.8±2.3 to 12.9±2.6 with p value (0.001) which is statistically significant.IOP in control group from 13.8±1.2 to 14.2 ± 1.3 with p value(0.37) which is not significant

Discussion:-

The definitive treatment for DME is intra vitreal anti VEGF or intra vitreal steroids like dexamethasone which are invasive and are having risk facors of cataract, glaucoma and endophthalmitis in anti VEGF treatment.

Some studies have shown that combination of intra vitrealfasudil and avastin is beneficial in refractory DME[4].

So we have considered that ripasudil might have the potential to reduce FT in patients with DME.

There is a retrospective study which showed improvements in foveal thickness in patientswho are having glaucoma along with DME[5]

In current study there is significant decrease in FT, significant decrease in IOP and no significance in visual acuity improvement as seen in Minami Y et al (study done in Japan 2019).

In the current study, the degree of reduction in the FT was smaller than those reported previously with anti-VEGF therapy according to Mitchell P, et al. (6)

The limitations of the study is small sample size ,so more studies are required in future for significance

Conclusion:-

The current findings showed that Foveal thickness decreased significantly at 4 weeks after initiation of ripasudil therapy suggesting that ripasudil has the potential to improve FT in patients with DME.

Figures-

Figure 1 FT pre and post ripasudil with age (Age in X- axis and FT in Y -axis)
Figure 2 controls at presentation and after 4 weeks (age in x-axis and ft in y- axis)
Figure 3 ripasudil group (iop pre and postdrug)
Figure 4 control group (iop before and after 4 weeks)
Figure 5 BCVA in ripasudil group with LogMAR values
Figure 6 BCVA in LogMAR values in control group

Figure 1:- FT pre and post ripasudil with age (Age in X- axis and FT in Y -axis).

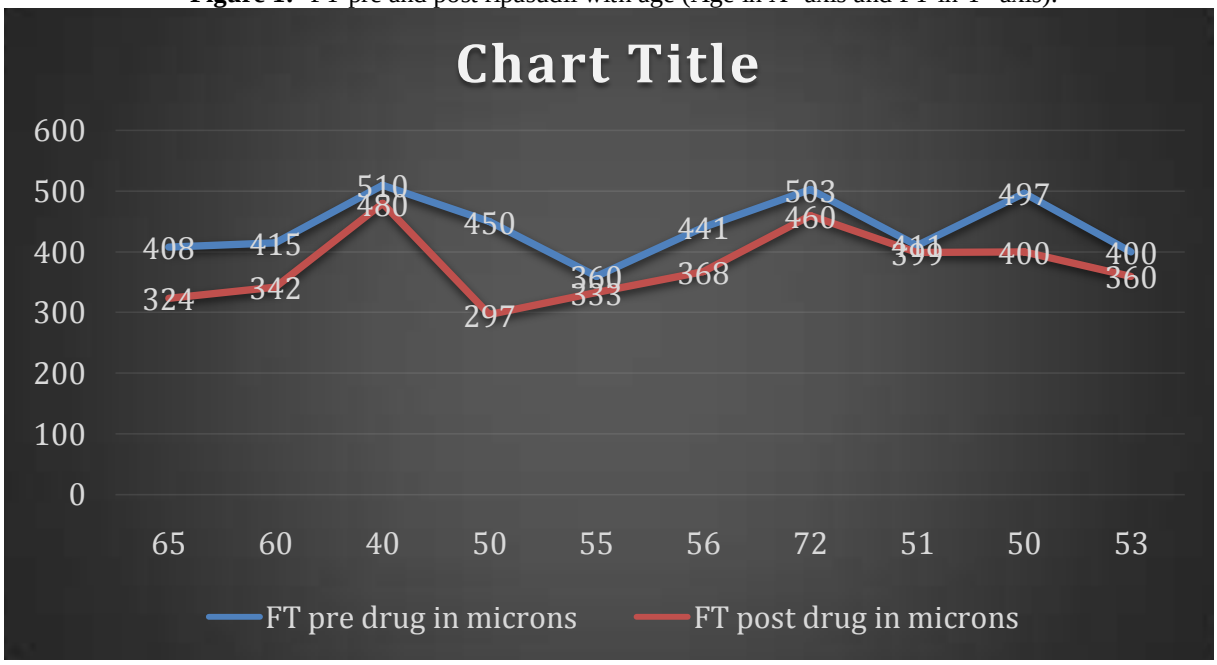


Figure 2:- controls at presentation and after 4 weeks (age in x-axis and ft in y- axis).

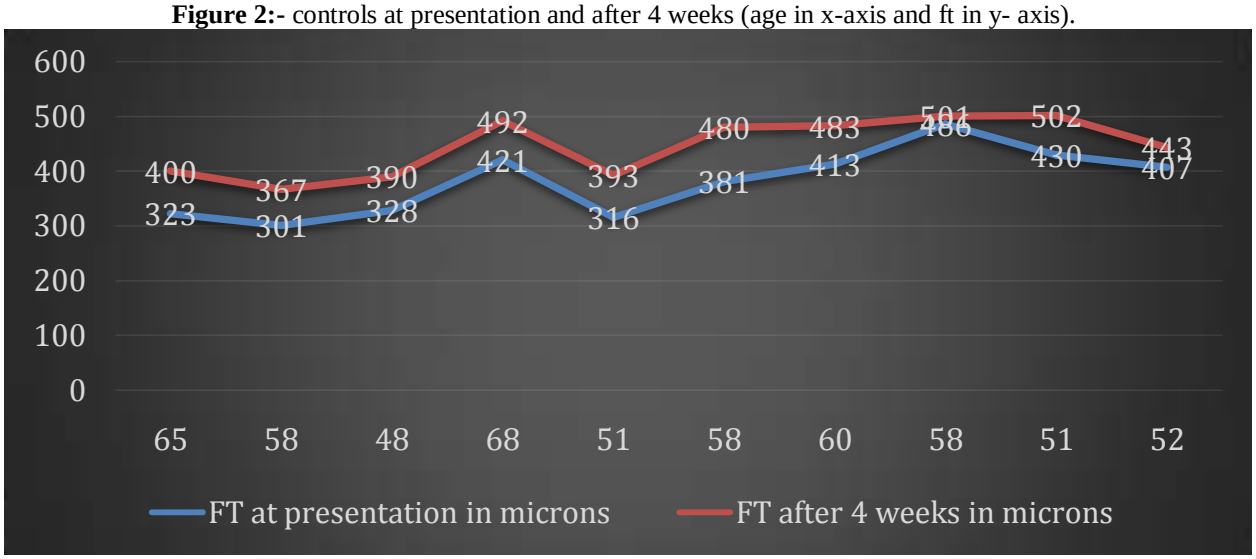


Figure 3:- Ripasudil group (iop pre and postdrug).

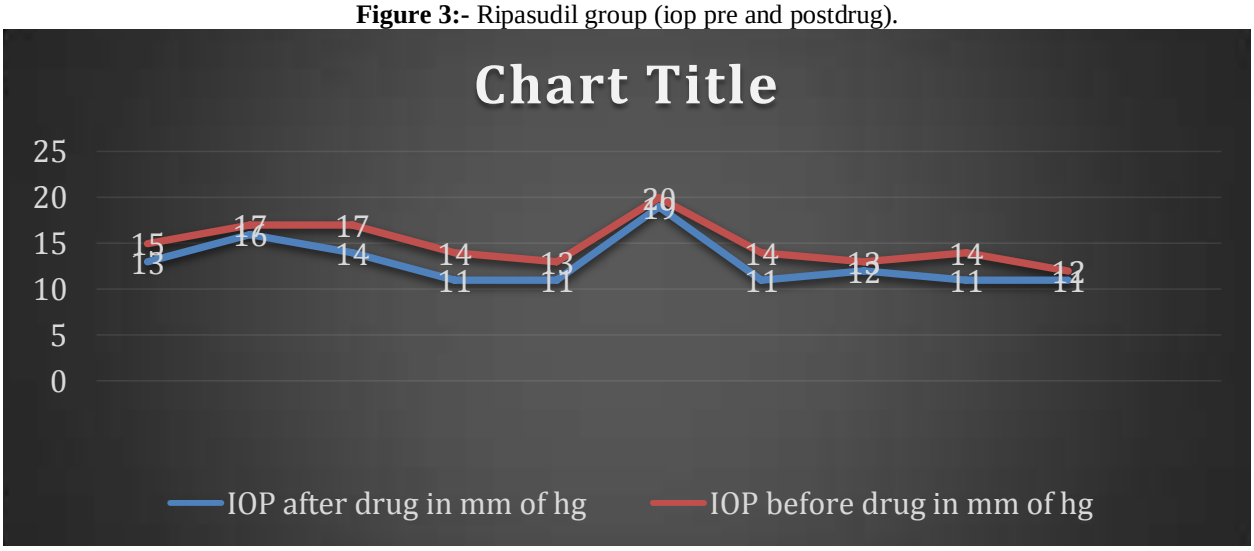


Figure 4:- Control group (iop before and after 4 weeks).

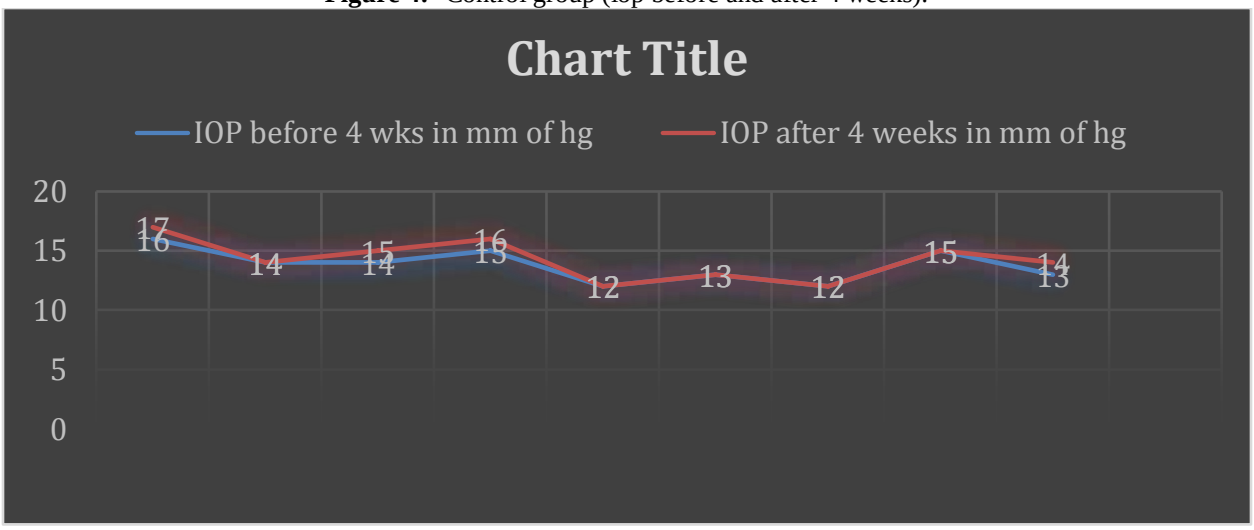


Figure 5:- BCVA in ripasudil group with LogMAR values.

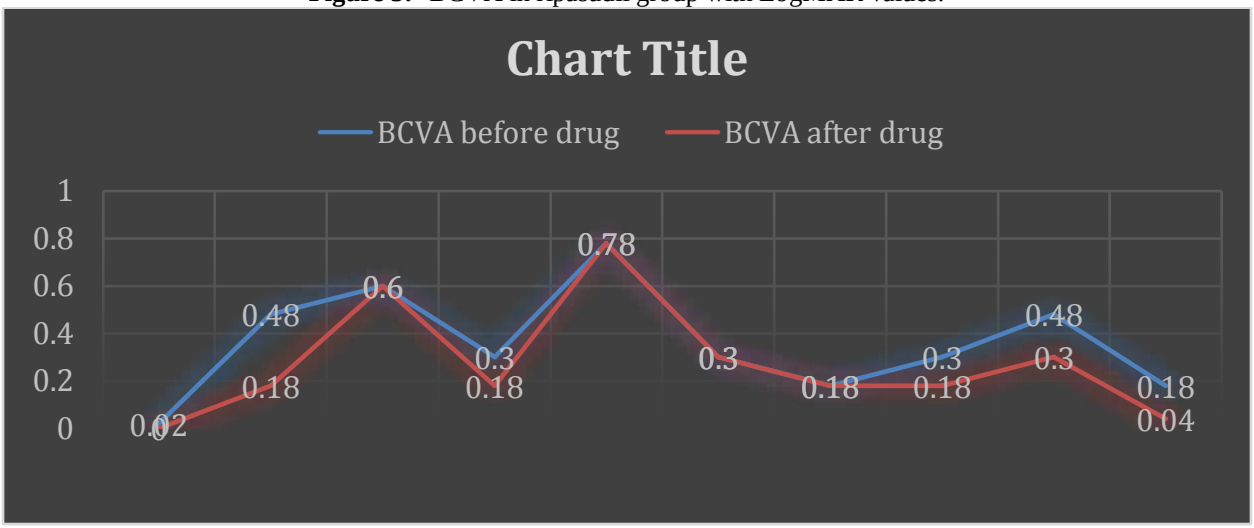
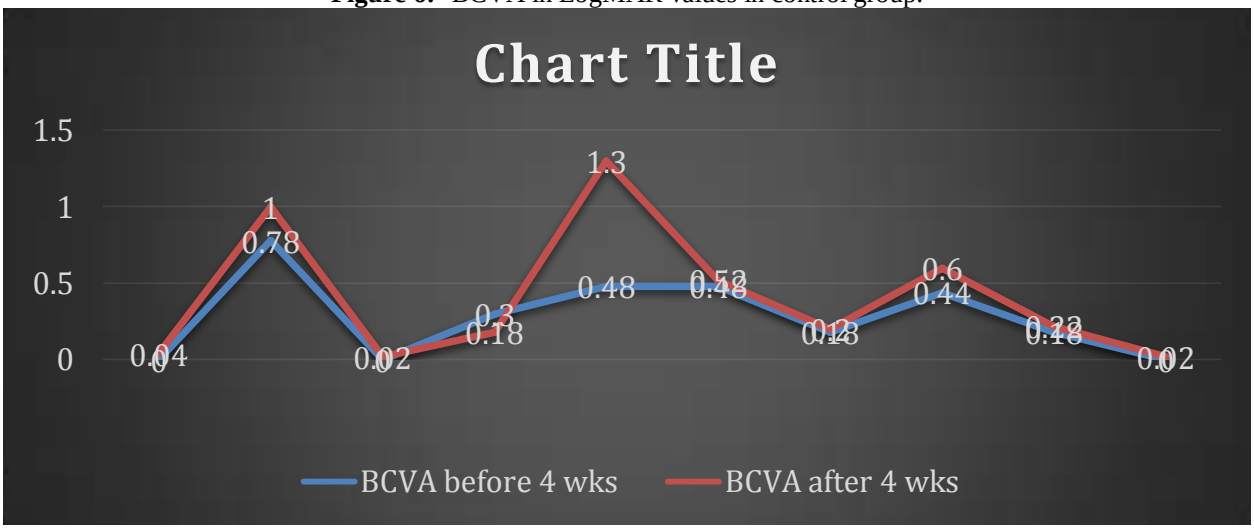


Figure 6:- BCVA in LogMAR values in control group.



References:-

1. Yau JW, et al. Global prevalence and major risk factors of diabetic retinopathy. Diabetes Care. 2012;**35**:556–564. doi: 10.2337/dc11-1909

2. Nourinia R, Ahmadieh H, Shahheidari MH, Zandi S, Nakao S, Hafezi-Moghadam A. Intravitreal fasudil combined with bevacizumab for treatment of refractory diabetic macular edema; a pilot study. J Ophthalmic Vis Res. 2013 Oct;8(4):337-40. PMID: 24653821; PMCID: PMC3957040.

3.Rema M, Premkumar S, Anitha B, Deepa R, Pradeepa R, Mohan V. Prevalence of diabetic retinopathy in urban India: the Chennai Urban Rural Epidemiology Study (CURES) eye study, I. Invest Ophthalmol Vis Sci. 2005 Jul;46(7):2328-33. doi: 10.1167/iovs.05-0019. PMID: 15980218.

4.Nourinia R, et al. Intravitreal fasudil combined with bevacizumab for treatment of refractory diabetic macular edema; a pilot study. J Ophthalmic Vis Res. 2013;**8**:337–340.

5.Minami Y, Song YS, Ishibazawa A, Omae T, Ro-Mase T, Ishiko S, Yoshida A. Effect of ripasudil on diabetic macular edema. Sci Rep. 2019 Mar 6;9(1):3703. doi: 10.1038/s41598-019-40194-5. PMID: 30842496; PMCID: PMC6403390.

6.Mitchell P, et al. The RESTORE study: Ranibizumab monotherapy or combined with laser versus laser monotherapy for diabetic macular edema. Ophthalmology. 2011;**118**:615–625. doi: 10.1016/j.ophtha.2011.01.031.