

Role of Intrasilicon Oil Methotrexate Injection to Prevent Development of Proliferative Vitreoretinopathy

Ahmad Zeeshan Jamil¹, Muhammad Hannan Jamil²,
Abdullah Muaz³, Hina Nazir⁴, Muhammad Nauraiz Zubair
Chawla⁵

^{1,3,4,5}Sahiwal Teaching Hospital and Sahiwal Medical College,
²Abu Umara Medical and Dental College, Lahore

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ABSTRACT

Purpose: To determine the role of intra-silicon oil methotrexate injection to prevent Proliferative Vitreoretinopathy.

Study Design: Quasi experimental Study.

Place and Duration: Ophthalmology department of Sahiwal Teaching Hospital, Sahiwal from February 2022 to August 2022.

Methods: Study included patients of either gender, older than 19 years with rhegmatogenous retinal detachment with Proliferative vitreoretinopathy (PVR) grade B or less. There were two groups and each group had fifty-one patients. All patients underwent pars plana vitrectomy and silicon oil tamponade. Group 1 was control group. Group 2 had intravitreal injections of methotrexate 500µg at the end of surgery. We repeated the injections at 1st, 2nd, and 4th week postoperatively.

Results: There were 56(54.9%) male and 46(45.1%) female patients. Postoperatively visual acuity improved in thirty cases (58.82%) in group 1 and in forty-two cases (82.35%) in group 2. Postoperatively PVR developed in 11(21.57%) patients in group 1 while in group 2 no patient had PVR. Recurrent Retinal detachment occurred in 9(19.61%) patients in group 1 and 3(5.88%) patients in group 2. Chi square test demonstrated statistically significant difference in the frequency of development of PVR and re-detachment of retina between two groups, $p < 0.05$.

Conclusion: Methotrexate is an effective adjuvant used in Pars plana Vitrectomy for rhegmatogenous retinal detachment repair. It prevents PVR resulting in better surgical and functional outcome.

Key Words: Methotrexate, Proliferative Vitreoretinopathy, Retinal Detachment, Vitrectomy.

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*Correspondence: Ahmad Zeeshan Jamil
Sahiwal Teaching Hospital and Sahiwal Medical College
Email: ahmadzeeshandr@gmail.com*

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INTRODUCTION

There is a complex and dynamic interplay between retina and vitreous. A healthy vitreous is essential for

the integrity of retina. Neurosensory retina can develop a break because of aging, trauma, infection, inflammation, genetic predisposition and surgical complication. Sick vitreous and break in the neurosensory retina allow passage of fluid into the subretinal space thus separating neurosensory retina from the retinal pigment epithelium. Rhegmatogenous retinal detachment affects about 13.3 persons per million population.¹ Incidence of rhegmatogenous retinal detachment is increasing over time.^{2,3} It has increased by more than 50% during the last ten years

and this increase is primarily in men older than 50 years.⁴

Retinal detachment is the most common retinal emergency that can lead to permanent blindness.⁵ Timely surgical intervention is essential to save vision. Although conventional scleral buckling has been the mainstay of treatment but nowadays vitrectomy is more commonly employed. Primary surgical success rate with modern techniques reaches up to 90%.⁶ Initial failure of surgery is due to failure to close all the existing breaks and inability to sufficiently relieve retinal tractions.^{7,8} Late failure is most commonly due to contraction of vitreous base, formation of new breaks and development of PVR.^{9,10}

PVR occurs in about 10% cases of retinal detachment surgery and is responsible for two third of surgical failures.⁵ Retinal tear alters homeostasis of the eye and retinal pigment epithelial cells become exposed to vitreous cavity. Inflammatory mediators step in due to breakdown of blood ocular barrier. Retinal glial cells, retinal pigment epithelial cells, fibroblasts, macrophages and cytokines result in membrane formation over and under the surface of retina.¹¹ PVR can take the form of star folds, retinal shortening, traction, rolled edges of breaks and wrinkling of retinal surface.¹²

PVR can lead to blindness even after successful primary surgical retinal repair. Various techniques have been employed to prevent development of PVR.¹³ Infusion of low molecular weight heparin and 5 fluorouracil have been tried. It assumed that these drugs might block inflammatory cascades.¹⁴ Recently methotrexate has been used in preventing development and progression of PVR in retinal detachment surgeries. Methotrexate has been used in the form of per operative infusion and postoperative repeated intra-silicon oil injections in various injection regimens.^{15,16}

Objective of the study is to evaluate the Role of intrasilicon oil methotrexate injection to prevent development of proliferative vitreoretinopathy.

METHODS

This quasi experimental study was conducted in Ophthalmology department of Sahiwal Teaching Hospital, Sahiwal from February 2022 to August 2022. The research protocol was approved by institutional review board of the institution. Informed consent was taken from all the patients. Patients of either sex aged

19 and above presenting with rhegmatogenous retinal detachment (RRD) with PVR grade B or less were included. Exclusion criteria comprised of combined rhegmatogenous and tractional retinal detachment, previous history of retinal detachment surgery in the same eye, giant retinal tear, proliferative vitreoretinopathy of grade C, retinal detachment associated with penetrating ocular trauma, pregnant and breast-feeding ladies.

Detailed history of all the patients regarding duration of symptoms of decreased vision, floater and flashes was taken. History of risk factors for retinal detachment was noted. Presenting visual acuity and intraocular pressure were noted. Anterior and posterior segment examination was performed by slit lamp. Indirect ophthalmoscope was also used to examine posterior segment. Extent of retinal detachment with location of retinal breaks was documented. Severity and extent of PVR was also noted. Patients were divided into two groups with the help of lottery method. Group 1 was control group and group 2 was study group who received methotrexate injections. Single surgeon performed standard 23-gauge pars plana vitrectomy (PPV) in all patients. Silicon oil was injected to give postoperative tamponade. Group 2 patients received 500 µg methotrexate intravitreal injection. Patients were given steroid and antibiotic drops eight times in a day for the first week postoperatively. Subsequently eye drops regimen was changed to four times a day for the next three weeks. Patients were instructed to adopt posture according to the location of retinal breaks. In group 2 patients additional intrasilicon oil methotrexate injections were given at postoperative week 1, 2 and 4. All patients were followed up at week 1, 2, 4, 8 and 12. At each visit visual acuity and intraocular pressure were measured. Detailed slit lamp examination was performed. Retinal examination was performed with the help of 90 D and wide field contact lens. Retina was examined for evidence of development of PVR and recurrence of retinal detachment. Study outcomes were prevention of development of PVR and attached retina at the end of three months.

All information was collected with the help of self-designed proforma. SPSS version 23 was used for statistical analysis. Qualitative variables like gender, preoperative and post-operative visual acuity, PVR development and recurrent retinal detachment were presented as frequency and percentage. Quantitative variable like age was presented as mean and standard deviation. Chi square test was used to calculate

Table 1: Characteristics of Retinal Detachment.

Extent	Characteristics of Retinal Detachment				
	Break Location		Risk Factors		
Four quadrants	56(54.9%)	All quadrants	22(21.6%)	Cataract surgery	43(42.2%)
Three quadrants	15(14.7%)	Superior	42(41.2%)	Myopia	17(16.7%)
		Lateral & Inferior	13(12.7%)	PVD	16(15.7%)
		Inferior	10(9.8%)	Trauma	9(8.8%)
Two quadrants	2(2%)	Lateral	5(4.9%)	YAG Capsulotomy	5(4.9%)
		Superior & Lateral	4(3.9%)	RD in other eye	5(4.9%)
One quadrant	29(28.4%)	Superior & Inferior	4(3.9%)	Lattice Degeneration	5(4.9%)
		Macular	2(2%)	Family History of RD	2(2%)
Duration of Retinal Detachment		Baseline PVR Grade		Macular Involvement	
Less than one week	20(19.6%)	No PVR	22(21.6%)	Macula detached	90(88.2%)
One week to one month	33(32.2%)	Grade A	16(15.7%)	Macula attached	12(11.8%)
More than one month	49(48%)	Grade B	64(62.7%)		

Table 2: Baseline and Final Visual Acuity at 3 Month Followup.

Visual acuity	Baseline VA		Final VA	
	Control	Methotrexate	Control	Methotrexate
6/18 to 6/6	4(7.84%)	5(9.80%)	11(21.57%)	11(21.57%)
6/60 to 6/24	3(5.89%)	0(0%)	23(45.09%)	27(52.94%)
FC to HM	31(60.78%)	28(54.90%)	9(17.65%)	9(17.65%)
Less than HM	13(25.49%)	18(35.29%)	8(15.69%)	4(7.84%)

difference in the development of PVR and recurrence of retinal detachment between two groups. $P \leq 0.05$ was taken statistically significant.

RESULTS

There were 56(54.9%) male and 46(45.1%) female patients. In that study 47(46.1%) right and 55(53.9%) left eyes were included. Characteristics of Retinal detachment are shown in table1. After PPV, PVR development was noted in 11(21.57%) eyes in control group while none of the eyes in methotrexate group showed PVR development. There was statistically significant difference between two groups with respect to development of PVR $p=0.000$. Recurrent retinal detachment occurred in 10(19.61%) eyes in control group and 3(5.88%) eyes in methotrexate group. Chi-Square showed statistically significant difference between two groups regarding recurrent retinal detachment $p=0.038$. New breaks without PVR were noted in 1(1.96%) eye in control group and 3(5.9%) eyes in methotrexate group. New breaks with PVR occurred in 9(17.64%) eyes in control group while in methotrexate group there was not a single eye with new break with PVR.

Baseline and final visual acuity at 3 months follow up is shown in Table 2. The Chi-square test was used to calculate difference in visual acuity preoperatively and postoperatively.

In the control group 30(58.82%) eyes showed improvement in visual acuity but this improvement was not statistically significant ($p=0.21$). In methotrexate group 42(82.35%) eyes showed improvement in visual acuity, this improvement was statistically significant ($p=0.000$).

DISCUSSION

This study entails the role of intrasilicon oil methotrexate injections after pars plana vitrectomy in the prevention of PVR. Results of the current study demonstrated improved functional and anatomical success after pars plana vitrectomy for retinal detachment repair with adjunctive use of methotrexate injections. PVR developed in 11(21.56%) eyes in control group and no eyes in methotrexate group. Recurrent retinal detachment occurred in 10(19.61%) eyes in control group and 3(5.88%) eyes in methotrexate group.

Methotrexate is a folate analogue, and it competitively inhibits enzymes used to form deoxyribonucleic acid and ribonucleic acid. It results in inhibition of metaplasia of retinal pigment epithelial cells and formation of contractile fibro cellular membranes. Rationally Methotrexate should prevent the formation of PVR and result in better anatomical and functional outcome after retinal detachment surgery.

In the current study intrasilicon oil injections of 500 microgram methotrexate were used. Those injections were given per operatively and afterward at 1 week, 2 week and 4 weeks postoperatively. Falayarjani and co-authors injected intrasilicon oil methotrexate in a dose of 250 microgram at the end of retinal detachment surgery. Retinal re-detachment occurred in 4.5% cases in methotrexate group and 22.7% cases in the control group.¹⁷ Results of our study are comparable to the results of their study.

Nourina and co-authors injected 250 microgram intra silicon oil methotrexate injections at the time of surgery and then at 3 and 6 weeks postoperatively. There were no adverse effects noted and all cases showed attached retina at the conclusion of the study.¹⁸

Baha and colleagues used methotrexate infusion during vitrectomy. In their study retinal reattachment rate was 82% in study and 86% in control group. They reported functional improvement in patients of high risk of PVR when methotrexate infusion was used. In contrast to the results of our study, they did not find any extra advantage of use of methotrexate infusion in terms of anatomical success.¹²

Sadaqa's study demonstrated that none of the eyes that received intra operative methotrexate infusion during pars plana vitrectomy developed PVR and recurrent RD. Postoperatively visual acuity improved in 72.41% cases.¹⁹ In our study 83.25% cases in methotrexate group showed improvement in visual acuity.

In another study that included eyes with open globe injuries, re-detachments and advanced PVR, use of per operative methotrexate infusion showed promising results. In that study retinal attachment rate was 80% at the end of study. Mean preoperative visual acuity was 1.35 logMAR that improved to 1.01 logMAR postoperatively.¹⁶ Results of our study have supported that methotrexate group showed an improvement in the attachment of the retina and a better visual acuity.

In a study that was focused to evaluate the results of repeated intrasilicon oil injections of methotrexate in cases of advanced PVR, retinal attachment was seen in 86% cases in study group compared to 22.2% cases in control group. Mean number of methotrexate injections was six.²⁰

Retinal attachment rate in our study is better than the attachment rates of other studies. Possible reason may be that we chose cases with low grade PVR and

used repeated intrasilicon oil methotrexate injections in higher doses. The process of PVR formation and progression may continue as long as 90 days after retinal detachment repair.¹² Half-life of intravitreal methotrexate is 3 to 5 days. Repeated methotrexate injections are required to suppress development of PVR.

The present study did not include cases of complex retinal detachments associated with penetrating ocular trauma, recurrent retinal detachments and retinal detachments with advanced proliferative vitreoretinopathy. These limitations are acknowledged in the current research. Additionally, short follow up of the study is another limitation. Moreover, we did not assess the potential detrimental effects of methotrexate on retina, which signifies a major shortcoming of our study.

In future we suggest studies with larger sample size and longer follow up period to see the optimum dose and timing of methotrexate injections in the prevention of PVR.

CONCLUSION

Majority of cases of failed retinal detachment surgery are due to development of PVR. Methotrexate is an effective adjuvant used in pars planavitrectomy for rhegmatogenous retinal detachment repair. It prevents proliferative vitreoretinopathy and leads to better surgical and functional outcome.

Conflict of Interest: Authors declared no conflict of interest.

Ethical Approval: The study was approved by the Institutional review board/Ethical review board (No.54/DME/SLMC/SWL).

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Authors' Designation and Contribution

Ahmad Zeeshan Jamil; Professor: *Concepts, Design, Literature Search, Data Acquisition, Data Analysis, Statistical Analysis, Manuscript Preparation, Manuscript Editing, Manuscript Review.*

Muhammad Hannan Jamil; Assistant Professor: *Concepts, Design, Literature Search, Data Acquisition, Data Analysis, Statistical Analysis, Manuscript Preparation, Manuscript Editing, Manuscript Review.*

Abdullah Muaz; Resident: *Concepts, Design, Literature Search, Data Acquisition, Data Analysis, Statistical Analysis, Manuscript Preparation, Manuscript Editing, Manuscript Review.*

Hina Nazir; Resident: *Concepts, Design, Literature Search, Data Acquisition, Data Analysis, Statistical Analysis, Manuscript*

Preparation, Manuscript Editing, Manuscript Review.

Muhammad Nauraiz Zubair Chawla; Resident: *Concepts, Design, Literature Search, Data Acquisition, Data Analysis, Statistical Analysis, Manuscript Preparation, Manuscript Editing, Manuscript Review.*

