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"Managing Submacular Haemorrhage (SMH) by Pneumatic Displacement (PD) Only without Using Tissue Plasminogen Activator (tPA)"

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Abstract

Objective: To report results of management of submacular hemorrhage (SMH) by pneumatic displacement (PD) without use of tissue plasminogen activator (tPA).

Methods: This is a retrospective analysis from March 2007 to February 2016, of patients presenting with sudden onset dimness of vision due to SMH involving the fovea. Optical coherence tomography was done. Intravitreal injection of pure perfluoropropane 0.3 ml was done under local anesthesia. Patients were instructed to maintain prone position for 7 days for 12 hours per day. After some amount of displacement occurred, funds fluorescein angiography and indocyanin green angiography were done as required to find out cause of bleed. Patients were treated as needed depending on FFA and ICG findings. The main outcome measures were clearing of haemorrhage under the macula and improvement in vision after displacement. Patients with a follow up of less than 3 months were excluded from the study.

Results: There were 15 (51.7%) males and 14 (48.27%) females of 29. Age was 52.58 ± 20.81, (range: 11-80) years. Patients presented at a mean of 12.62 days ± 14.00(range: 1-60) days. Mean Log MAR visual acuity was 1.26 (range 0.30-1.78) before gas injection and 1.17 (range 0.30-1.78), on the day of gas injection, p=0.23. Final visual acuity improved in all cases, up to Log MAR mean 0.85 (range 0.17-1.78). The improvement in visual acuity at final visit is statistically significant, p=0.0008. SMH was displaced in all cases. Follow up were from 90 days to 10 years (average 2.68 years).

Conclusion: Pure perfluoropropane gas (0.3) injected into the vitreous cavity can displace SMH without the use of tPA in all cases. Visual acuity after gas injection improves, making this treatment an alternative to evacuation of SMH. This also helps to find out the cause for SMH after the displacement of the haemorrhage.

Keywords: Tissue plasminogen activator (tPA); Submacular haemorrhage (SMH); Perfluoropropane (C3F8); Pneumatic displacement (PD)

Introduction

One of the common manifestations of several diseases of the retina and choroid is SMH which is defined as the haemorrhage located in the potential space between the retinal pigment epithelium and the neurosensory retina arising from choroidal and retinal circulation [1]. There is severe visual impairment when the fovea and or the macula are involved. Natural history studies have demonstrated relatively poor initial visual acuities leading to variable outcomes [2]. Poor visual outcomes after subretinal haemorrhage are likely due to a combination of factors. First, there are the direct toxic or traumatic effects of the subretinal blood, and subsequent clot formation. The accumulated blood in the subretinal space is thought to involve impairment of nutrient exchange between the retinal pigment epithelium and the outer retina, mechanical damage to the photoreceptors during clot contraction, and possibly iron toxicity. Based on the EM study of rabbit eyes in his study, Glut H and Michener R [3] had proposed three separate mechanisms of retinal damage. First, the subretinal blood acts as a physical barrier to metabolic exchange between the retina and RPE. This was consistent with the findings that the earliest detectable changes occurred in the photoreceptor cells. Second, tractional forces from the blood clot represent another potential mechanism for retinal damage. Third, iron released from intraocular whole blood and haemoglobin has also been shown to have direct toxic effect on the retina. There are a number of treatment strategies for massive submacular haemorrhage, but there are no formal guidelines regarding optimal management. In this study, we tried to find out an effective method for displacement of submacular haemorrhage by pneumatic displacement of intravitreal injection of perfluoropropane gas without the use of tissue plasminogen activator.

Materials and Methods

This is a retrospective and interventional case series of 29 patients from, March 2007 to February 2016. The study was approved by the Institutional Ethics committee and conformed to the declaration of

Helsinki. Included were patients who had presented with sudden onset dimness of vision and was diagnosed with submacular haemorrhage involving the macula. Patients upon presentation, after detailed ophthalmological examinations were given intravitreal injection of pure perfluoropropane gas (0.3 mL) in the involved eye under topical anaesthesia. The patients were instructed to maintain a prone position for 7 days for 12 hours per day. The procedure was known as pneumatic displacement of submacular haemorrhage. They were followed up for any raised intraocular pressure along with recording of vision and for fading of submacular haemorrhage when they were subjected for coloured fundus photographs and fluorescence angiogram and if required indocyanin green angiography(HRA 2 Heidelberg Engineering). Optical coherence tomogram (spectral OCT SLO combination imaging system, Optos) was performed in every visit. The cause of bleed was ascertained and they were treated as required with laser, photodynamic therapy, intravitreal anti-vegf and surgical treatment. Patients who were not in follow up for a minimum of 3 months after the procedure were excluded from the study. The main outcome measures were clearing of haemorrhage under the macula, improvement in vision after displacement, time interval between occurrence and intervention, final visual acuity improvement, causes of the bleed, requirement of FFA and or ICG, other intervention required, final outcome and any other complications and final outcome group wise.

Technique of Pneumatic Displacement

- Subconjunctival anaesthesia is adequate for pneumatic displacement. The site of the injection is anaesthetized. Small amount of 2% xylocaine is used.
- Preparation of Gas Syringe: A step down regulator is used to avoid high pressure that may blow a hole in the Millipore filter. The filter is placed on the regulator and the syringe is filled two or three times to minimise the dilution of the gas within it. A 30 gauge sterile needle is fitted to the syringe and the predetermined amount of gas which is to be used, is injected.
- Preparing the patient: Eye is painted with povidone-iodine. A sterile drape is used to cover the eye.
- After the lid speculum is placed, 5-10% povidone iodine drops with a sterile bud to the injection site are applied.
- Anterior chamber paracentesis is done by piercing a 27 or 30 gauge needle with a syringe and aspirate two tenths of a milliliter of aqueous. The needle is placed over the iris to avoid lens touch.
- Gas injection: Patient's head is rotated away from the injection site so that the injection is directed towards the centre of the eye and also towards the centre of the earth. Insert the needle 4 mm behind the limbus in phakic eyes. The needle should go in about half way and then be retracted so that it is 7-8 mm outside the eye. This can be measured with a calliper. A smooth even injection is the carried out in order to get a single bubble. After the injection the patient's head or eye is rotated so that the bubble is away from the injection site. The needle is taken out.
- Prone position: The patient is asked to take a prone position after the injection. This pushes the submacular haemorrhage away from the macula. Intraocular pressure is checked and the eye for the patency of the central retinal artery and a single gas bubble. The patient is reinstructed about prone positioning for the next 7 days for 12 hours per day.

Results

There were 15 (51.70%) males and 14 (48.27%) females. Mean age of the patients were 52.58 ± 20.81, (range: 11-80) years. Patients presented with sudden onset dimness of vision on a mean of 12.62 ± 14.00 days (range: 1-60 days) (Table 1).

S.No.	AGE in Years	SEX	OD/OS	Days of onset to presentation on	VA at presentation (LogMAR)	VA after PD (Log MAR)	Final VA (LogMAR)
1	76	M	OS	60 Days	1.4	1.3	1.3
2	60	M	OS	08 Days	0.8	0.8	0.6
3	22	M	OD	10 Days	1.2	0.5	0.3
4	56	F	OD	2 Days	1.4	0.6	1
5	33	M	OS	30 Days	1.3	1.3	1
6	68	F	OD	10 Days post IOL	1.4	1.3	0.5
7	63	M	OD	7 Days	1	0.5	0.2
8	25	F	OS	7 Days	1.4	1.3	0.2
9	75	F	OS	3 Days post IOL	1.2	1	1
10	52	M	OD	45 Days	1.3	1.3	1
11	66	M	OD	1 Day	1	1	0.6
12	11	M	OD	7 Days	1.3	1	0.5

13	75	F	OS I	1 Days post IOL	0.6	1.3	1
14	70	M	OD	20 Days	0.6	0.5	0.5
15	57	M	OD	8 Days	1.2	1.3	1
16	80	M	OD	1Days post IOL	1.3	1.2	0.8
17	67	M	OD	15 Days	1.2	1	1
18	49	M	OD	30 Days post IOL	1	1	0.6
19	56	F	OD	3 Days	1.3	1	1
20	75	F	OD	10 Days	1.3	1.3	1
21	23	M	OD	3 Days	1.3	1.3	0.2
22	46	F	OD	2 Days	0.6	0.6	1
23	14	M	OS	10 Days	1.3	1.3	0.6
24	42	F	OS	7 Days	1.3	1.3	0.6
25	65	F	OD	3 Days	0.8	1.4	0.5
26	35	F	OS	10 Days	1.3	0.5	0.6
27	28	F	OD	8 Days	0.3	1.4	0.3
28	59	F	OS	15 Days	0.6	0.3	0.2
29	57	F	OS	30 Days post IOL	0.6	0.6	0.2

Table 1: Demographic profile along with visual acuity in LogMAR.

Age groups above 50-80 years were more upto 19 (65%) patients (Figure 1).

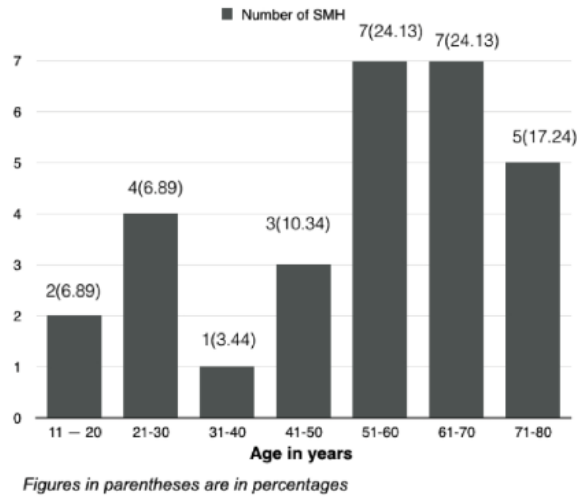

Figure 1: Number of SMH in different ages.

Visual acuity ranged from LogMAR mean 1.26 ± 0.47 (range: 0.30-1.78) before gas injection. On the day after gas injection, visual acuity ranged from LogMAR mean 1.17 ± 0.52 (range: 0.30-1.78).Improvement in visual acuity at first postoperative day compared to visual acuity at presentation is not significant. p=0.23 (p>0.05). Final visual acuity improved in all cases, upto Log MAR mean 0.85 ± 0.56 (range: 0.17-1.78). The improvement in visual acuity at the final visit is statistically significant, p=0.0008 (p<0.05).

SMH was displaced in all cases after displacement allowing for the examinations necessary to find out the cause for bleed. FA and or ICG were done in 20 cases. 2 cases of trauma, 2 cases of IPCV,2 cases of vitreous bleed,1 case of CNVM, 1 case of retinal detachment with macular hole and 1 case who was lost to follow ups did not had a FA and/or ICG.FFA and/or ICG was done at an average of 31.07 days after pneumatic displacement.

In this series, SMH was due to IPCV in 11cases (37.84%), CNVM in 11cases (37.84%), macroaneurysm in 2 cases (6.80%) and trauma in 3 cases (10.34%) and in 2 cases (6.80%) no cause could be found out.

2 (6.80%) cases had breakthrough vitreous haemorrhage for which, in 1 (3.44%) vitrectomy had to be done and the other had resolved vitreous haemorrhage during follow-up without any intervention. 1 (3.44%) case of vitreous haem had CNVM and other had idiopathic submacular haemorrhage. 1 (3.44%) patient of CNVM had to undergo repeat gas injection.

The cause of CNVM was: ARMD in 9 (81.81%), Myopia and trauma in 1 (9.09%) each eyes.

Eyes with duration of presentation less than 3-7 days had a significantly better prognosis of achieving favourable visual outcome compared to eyes with duration of presentation more than 7 days (p=0.674) though the test of significance is non-significant by ANOVA. This means that the difference which is shown in the data is only due to chance variation (Figure 2).

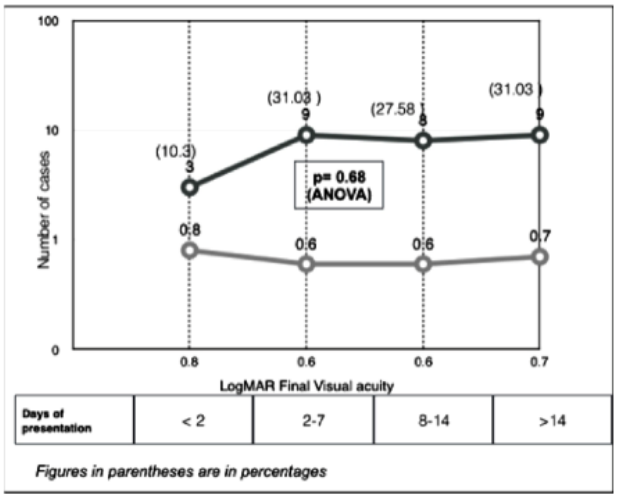

Figure 2: Days of presentation from onset of symptoms to final visual acuity.

The final visual acuity in IPCV was always better than the final visual acuity in CNVM. Independent t-test, however shows the preoperative and immediate post-injection p=0.056 and p=0.116 in IPCV and CNVM group respectively, which is not significant. But, PD for SMH and treatment causes a significant visual improvement p=0.001 (Figure 3).

Follow up were up to 90 days to 10 years ± 2.68 years.

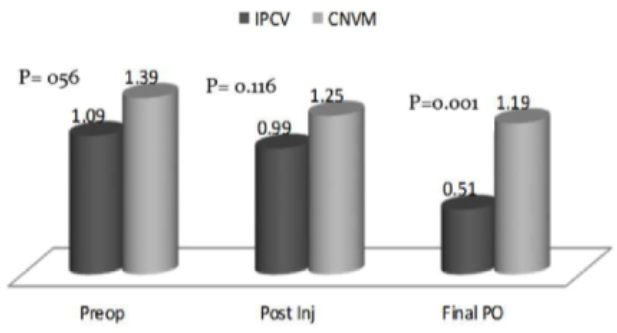

Figure 3: Visual acuities in LogMAR in the IPCV and ARMD groups.

Discussion

Given the generally poor natural history for SMH, many investigators have attempted to find effective surgical options. There have been several treatment strategies and a wide variation of PD success reported, since Heriot [4]. However, there are no consensus or treatment guidelines regarding optimal management. Lincoff's [5] work has illustrated the forces influencing SMH mobility in the subretinal space that has allowed a better understanding of its biophysical principals.

Nevertheless, with the advances in vitreoretinal surgery, their continues to evolve novel management strategies for SMH.

This study was born in a move to find out a definite protocol to effectively manage cases of SMH. We present in this study an effective way of management of SMH by PD without tPA in 29 cases which had different causes for their bleed. In all cases the bleed was significantly massive causing profound visual impairment. Gas injected into the vitreous cavity can displace SRH without the use of tPA in some cases. Visual acuity after gas injection may be improved, making this treatment an alternative to evacuation of SRH with vitrectomy [6]. However, Ohji M et al. [6] had only 5 cases (4 with ARMD and 1 with macroaneurysm) in their series. Recently, Gene et al. [7] had discussed about considering vitrectomy and subretinal tPA for surgical management of massive SMH but their discussion mainly highlights SMH due to CNVM as is also in the study by Ryan et al. [8]. PD without tPA is a safe and simple procedure which is effective [6,9,10] has been shown in earlier also but in small case series.

E.g. Gopalakrishnan et al. [9] had 20 cases and Rishi et al. [10] 7 cases, undergoing PD without tPA.

In our case series, we have found displacement of SMH with perfluoropropane (0.3 ml) without the use of tPA to be very effective in all our cases. We found this series to be one of the largest reported till now in the category of only PD of SMH. The same surgeon did the procedure in all cases, thereby minimizing the surgeon bias.

Patients usually present with sudden onset profound dimness of vision in the affected eye. After, PD there is significant visual improvement (p=0.0008) as is shown in this study depending on the etiology of SMH which can be found out after the displacement at an average of around 1 month after the PD. FFA, ICG and OCT helps to find out the cause and the treatment of the cause can be initiated subsequently.

Figure 4 shows the funds photographs of the four representative cases at presentation, after PD and at 4 weeks of improvement.

Balughatta et al. [11] had reported similar procedure in 3 cases of traumatic SMH. There is case series reported in CNV [8] and IPCV [12] separately. In this study, the various causes for SMH were IPCV in 11 cases (37.84%), CNVM in 11 cases (37.84%), macroaneurysm in 2 cases(6.80%) and trauma in 3 cases (10.34%) and in 2 cases(6.80%) no cause could be found out. 1(3.44%) patient of idiopathic SMH where Valsalva mechanism was suspected had sub foveal haemorrhage even after displacement for around 1 month and thereby had disruption of IS-OS junction in OCT causing poor visual recovery.

This study comprises of several causes for SMH. ARMD was the main cause for CNVM. And so, the comparative arm of the two major groups in CNVM and IPCV shows that the visual acuity is always better in the IPCV arm including the initial presenting and final visual acuity. This is in agreement with the earlier reports. It is feasible that with a longer duration of followup, the visual prognosis of IPCV might gradually become worse [13]. In this study, however we find a significant visual improvement finally in the IPCV group.

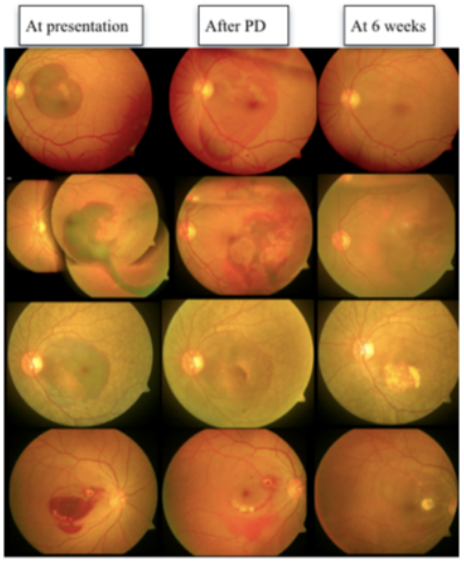

Figure 4: Four representative cases where fundus picture is shown at presentation, after pneumatic displacement (PD) and at 6 weeks.

It is seen in this study that SMH if reported within a week of symptoms after PD can have a better visual prognosis though there was no significance probably for less cases in each group or may be no significant effect of days of presentation on final LogMAR VA. The final visual prognosis revolves around the cause for SMH.

The patients were followed up for an average period of 2.68 years. Minimum period of follow-up was 90 days and 1 patient is being followed up till the reporting of the series since 2010.One patient was followed up for a period of 7 years.

Limitation of the study was its retrospective nature. But, the strength is that it is the largest reported series with varied etiologies found out for sub macular hemorrhage.

Why tPA was not used in this study was due to its non-availability readily, expensive and thinking about the complications of its use, though many reports are present suggesting its use to be safer [14,15].

This study also shows that when the patient presents within the first week of their symptoms, irrespective of the etiology, PD gives a better visual prognosis than late presentation. PD in this series was done in the next day of the presentation as an emergency procedure.

Conclusion

Pure perfluoropropane gas (0.3 ml) injected into the vitreous cavity can displace submacular hemorrhage without the use of tissue plasminogen activator in all cases. Visual acuity after gas injection improves, making this treatment an alternative to evacuation of SMH. This also helps to find out the cause for SMH after the displacement of the haemorrhage.

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