Comparison between different techniques for treatment of sub macular haemorrhage due to Age Related Macular Degeneration

Ahmed Abdelwahab Saad (✉ ahmed.saad@nhs.net)

James Cook University Hospital <https://orcid.org/0000-0002-5159-8001>

Daniela Vaideanu-Collins

James Cook University Hospital

Lyudmila Kishikova

South Tees Hospitals NHS Foundation Trust

Marco Isac

South Tees Hospitals NHS Foundation Trust

Dina Hamada

Zagazig University

Wael M. El-Haig

Zagazig University

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Abstract

Background To compare the outcome of vitrectomy, subretinal tissue plasminogen activator (TPA), and gas with and without subretinal air versus Intravitreal TPA and gas in the treatment of sub macular haemorrhage (SMH) due to Neovascular age related macular degeneration

Methods We analysed the notes of 29 cases presented with SMH in the period between 01/2016 and 09/2018 in James Cook University Hospital. Presenting visual acuity (BCVA), size and location of SMH, Procedure done, final BCVA at 6 months and any surgical complications were recorded. 11 Cases (Group 1) received intravitreal TPA (50ug in 0.1 ML), 0.3 ml of pure SF6. 18 cases (Group 2) received 23 G Pars Plana vitrectomy, Subretinal TPA injection (25ug in 0.1 ml), and 20% SF6 gas filling. Group 2 was further divided into 2A (10 patients) who received only subretinal TPA and group 2B (8 patients) who received additional 0.1 ml subretinal air.

Results The mean BCVA at presentation was 0.0068 in group 1 and 0.0067 in group 2 ($p=0.8734$). The mean postoperative BCVA at six months was 0.31 in group 1 and 0.58 in group 2 ($p=0.0015$). Subgroup analysis of group 2 didn't show statistically significant difference in outcome when adding subretinal air to the vitrectomy procedure ($p=0.7009$).

Conclusion Vitrectomy, gas and subretinal TPA has more successful displacement rate and better visual outcome than Intravitreal TPA & Gas alone in treating SMH involving the fovea in AMD. Additional subretinal air doesn't seem to improve the outcome in cases having vitrectomy.

Background

Age related macular degeneration is the leading cause of blindness in the western world¹. Rarely it may present with large subretinal haemorrhage involving the fovea (SMH)². Sub foveal large haemorrhages carries poor prognosis³. A few surgical techniques were described to treat SMH^{4,5,6,7,8,9,10,11,12,13}. In this study we analysed the outcome of two commonly used methods; Intravitreal gas and TPA versus PPV, Subretinal TPA and gas. Recently some authors reported using additional subretinal air injection (subretinal pneumatic displacement) could be useful to ensure SMH displacement^{12,13}. This study will analyse if additional subretinal air improves the outcome of patients undergoing vitrectomy.

Methods

A retrospective analysis of the notes of all patients presenting to a UK tertiary hospital with large sub macular haemorrhages due to neovascular AMD between 01/2016 and 09/2018. SMH due to trauma or choroidal polyps were excluded. On presentation all cases are typically fully assessed by full history and ophthalmic examination including OCT scan and fundus photos. The haemorrhage size and site are noted and recorded. All cases who presented within 2 weeks of the bleeding were offered treatment. The standard treatment in the unit is 23 pars plana vitrectomy, Subretinal injection of TPA (25 ug in 0.1 ml)

using 41G flexible subretinal cannula guided by the highest point in OCT (supplementary video 1) then filling the eye with 20% SF6. Additional subretinal air was done in some patients (Supplementary video 2). Some patients decline having full vitrectomy, so they were offered Intravitreal injection of TPA (50 ug in 0.1 ml), 0.3 of pure SF6. Avastin was used as the presenting BCVA was poor (NICE guidelines recommend Lucentis or Eylea only if BCVA is more than 4/60 (0.066). Follow up after 4 weeks with an OCT scan. If vision improves and haemorrhage is displaced, a loading dose of 3 Lucentis 4 weeks apart is prescribed. All patients were reviewed 4 weeklies with full assessment and OCT scan. The final BCVA at 6 months is recorded and compared.

Results

29 patient case notes were analysed. The age in group 1 ranged between 71 and 91 with a mean of 78 ± 6 . The age in group 2 ranged between 65 and 90 with a mean of 78 ± 6 (Figure 1). Visual acuity at presentation ranged between hand movement (HM) (0.005) and counting fingers (CF) (0.01). The mean BCVA at presentation was 0.0068 ± 0.0025 in group 1 and 0.0067 ± 0.0024 in group 2 (No statistically significant difference $p = 0.8734$).

The size and location of bleeding was analysed and compared. Haemorrhage size was measured by disc diameter (Figure 3) while haemorrhage location was noted if Intravitreal, Intraretinal, subretinal, sub RPE or a combination of the above (Figure 4).

Successful displacement is defined as absence of bleeding under the fovea and an area within half disc diameter around it. Successful displacement of the SMH was obtained in 9 out of 11 in group 1 (82%) and in all cases of group 2 (100%). (Figure 5 and 6).

The mean postoperative BCVA at six months was 0.31 ± 0.18 in group 1 and 0.58 ± 0.21 in group 2. T test was used to compare the two means and group 2 (Vitrectomy group) did better with statistically significant difference ($p = 0.0015$) (Figure 7).

To find if additional subretinal air improves the outcome, subgroup analysis of group 2 was done. Successful displacement of SMH was achieved in all cases in both subgroups. Although the mean preoperative BCVA was slightly better in Group 2A (Figure 8), the mean postoperative BCVA was slightly better in group 2B (Figure 9), Neither of the differences were statistically significant ($p = 0.7009$).

A few complications were reported in both groups. Visually significant cataract was reported in 2 cases in group 1 and 1 case in group 2. Medically controlled high IOP was reported in 3 cases in group 2 and 1 case in group 1. 2 cases of retinal detachment (1 in each group) were managed with vitrectomy, cryo and gas with successful reattachment.

Discussion

AMD complicated by SMH is a serious sight threatening condition due to permanent irreversible damage to photoreceptor layer with only 11% of eyes found to have best corrected visual acuity better than 1.0 on Log MAR chart after two years of observation in the submacular surgery trial^{1,2}.

Hattenbach et al. emphasized the importance of early treatment in his study, which showed that eyes with SMH duration of less than or equal to 14 days who had early treatment had the best visual outcome while no or poor visual prognosis is expected if the first clinical presentation was delayed for 21 days or more^{3,4}. In this study all cases who presented within 2 weeks of the bleeding were treated.

Three different possible mechanisms have been described to explain the photoreceptor damage occurs subsequent to large SMH. Firstly, is displacement of the neuroretina from RPE with subsequent deprivation of the photoreceptors from metabolic exchanges between the retina and choriocapillaries, secondly photoreceptor damage by shearing mechanism of retracting fibrin in the blood clot and thirdly is iron toxicity⁵.

Preventing this irreversible damage has been achieved in the last few years by different surgical interventions techniques share the same target of displacement of the SMH away from the fovea⁶ either by 1) intravitreal injection of tPA and gas, 2) pars plana vitrectomy + subretinal tPA + gas tamponade⁷ with or without subretinal air injection. 3) macular translocation surgeries⁸ including transplantation of RPE or choroidal patch⁹. All the previous procedures included intravitreal injection of Anti- VEGF.

Sandhu SS et al in his retrospective case series review concluded that PPV with subretinal tPA and air tamponade followed by Ranibizumab intravitreal injection has stabilized/ improved vision in nAMD patients with SMH who failed to get haemorrhage displaced in the first attempt by intravitreal injection of tPA and gas. However, he highlighted few recurrences of the SMH and suggested that it's relevant to the altered pharmacodynamics of intravitreal anti- VEGF in vitrectomised eyes and advised of doing minimal vitrectomy with posterior vitreous detachment technique in cases with vitreomacular traction on OCT prior to the surgery¹⁰. In this retrospective series, group 2 cases were offered full vitrectomy. Further follow up and analysis may be required to determine if they need more frequent AntiVegf injections than non vitrectomised cases.

In this retrospective case series study group 2 we used 20% sulphur hexafluoride as a tamponade and added subretinal air as pneumatic subretinal displacement of the SMH in the subgroup 2A. Waizel M. et al in his retrospective analysis of 85 pseudophakic patients had undergone PPV +subretinal tPA and air or gas tamponade with 64.1% complete displacement of SMH away from fovea, highlighted that patients who had air as a tamponade achieved final visual acuity better than others who had gas tamponade either SF6 or C2F6 despite of similar anatomical outcome in the two groups¹¹. The displacement rate is 100% in our series probably due to early intervention in all cases.

Another promising method of displacing the SMH during vitrectomy is to inject subretinal air after the injection of the subretinal tPA. This has been described in the literatures justified by the physics principle of the higher air pressure achieved in the small subretinal space compared to the pneumatic displacement in the vitreous cavity; this leads to a higher flotation force of the air mixed with the RBCs altering its buoyancy with subsequent swift displacement of the SMH¹². Kadonsono K et al in their prospective interventional study of 13 eyes presented with massive SMH due to nAMD, they used specially designed 47 gauge canula and a prone position of the patient overnight after surgery and achieved 100% displacement of the SMH¹³, While Martel and Mahmoud used different 41 gauge cannula with post-operative recommendations of patient's upright position¹². In our study group 2B achieved 100% displacement of the SMH however the final VA 6 months post-operatively was slightly better than group 2A with no statistically significant difference. The number of cases in each subgroup was probably too small to elicit a statistically significant difference.

Conclusion

Vitrectomy, gas and subretinal TPA has better visual outcome than Intravitreal TPA /Gas alone in treating SMH involving the fovea in AMD. Also, vitrectomy, gas and subretinal TPA is more efficient than Intravitreal TPA and gas in displacing SMH away from the fovea. Additional subretinal pneumatic displacement (subretinal air) doesn't seem to improve the results of vitrectomy, gas & TPA.

List Of Abbreviations

SMH: Submacular Haemorrhage

TPA: Tissue Plasminogen Activator

BCVA: Best Corrected Visual acuity

AMD: Age related macular degeneration

nAMD: Neovascular age related macular degeneration

PPV: Pars plana vitrectomy

RPE: Retinal pigment epithelium

VEGF: Vascular endothelial growth factor

RBCs: Red blood cells

OCT: Optical coherence tomography

HM: Hand Movement

CF: Counting fingers

VA: Visual acuity

SF6: Sulphur hexafluoride

DD: Disc Diameter

Declarations

Ethics approval and consent to participate

Not applicable as this study is a retrospective review of outcome of different techniques (Review of notes). All patients were consented to the procedures done

Consent for publication

Not applicable for a retrospective review of data. No patient identifiable data to be published.

Availability of data and material

Master table of all the detailed results was uploaded as supplementary file. 2 videos of the surgical procedures were uploaded as supplementary files. Any further data required (e.g. imaging) could be requested from the corresponding author (Ahmed.saad@nhs.net)

Competing interests

None

Funding

None

Authors' contributions

Ahmed Saad and Daniela Vaideanu-Collins did the surgeries

Marco Isac and Lydmila Kishikova collected the data and results

Dina Hamada did the statistical analysis

Ahmed Saad wrote the manuscript

Prof El-Haig suggested the research analysis and revised the manuscript

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Figures

Figure 1

Age of patients at presentations.

Figure 2

Comparison between Mean BCVA at presentation (Group 1 versus Group 2).

Figure 3

Size of Haemorrhage at presentation (Disc diameter) (DD).

Figure 4

location of haemorrhage at presentation.

Figure 5

Successful displacement of SMH.

Figure 6

OCT of large Sub macular Haemorrhage due to AMD (Before and after Vitrectomy / Subretinal TPA and gas).

Figure 7

Comparison between Mean Post op BCVA in group 1 and 2.

Figure 8

Comparison between Mean BCVA at presentation (Subgroup 2a versus subgroup 2b).

Figure 9

Comparison between Mean Post op BCVA in Subgroup group 2A and 2B

Supplementary Files

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