Outcome of submacular haemorrhage (SMH) displacement and drainage following injection of intravitreal tissue plasminogen activator (tPA)

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*Authors report no financial interest in any product mentioned in this poster.

Background

- Intraretinal injection of vascular endothelial growth factor inhibitors (anti-VEGF) is the standard of care for patients with neovascular age-related macular degeneration (nAMD).
- However, anti-VEGF injections alone are not effective in restoring or improving visual acuity (VA) when a large submacular haemorrhage is present.
- t-PA is an efficient fibrinolytic agent which activates plasminogen into plasmin, thus speeding the lysis of submacular blood clots.
- SMH is uncommon but a sight-threatening complication of nAMD. The mechanisms of damage caused by SMH includes iron toxicity from the blood, mechanical barrier of the clot, clot retraction and shearing of photoreceptors.

Purpose

To evaluate the results in patients with SMH due to nAMD treated with intravitreal injection of tPA and anti-VEGF medications followed by pneumatic displacement or submacular drainage:

1. The primary outcome of interest was final best-corrected Snellen VA.
2. Secondary outcomes were the displacement of SMH and complications.

Methods

- Retrospective case series of twelve eyes of 12 patients who presented with loss of vision due to SMH between June 2014 and April 2015.
- The off-label use of tPA was explained when consenting the patients for treatment.
- Patients received intravitreal injection of tPA (25 to 100 μg/0.1ml) combined with either Ranibizumab (0.5mg/0.05ml), Aflibercept (2 mg/0.05) or Bevacizumab (1.25mg/0.05ml) and followed 24 hours later by either:
  - Observation alone (i.e. no pneumatic displacement) (n=2),
  - Intravitreal injection of 0.4ml of 100% perfluoropropane/C3F8 (n=6) combined with 24-hour forward head posturing or
  - Pars plana vitrectomy (PPV) and drainage of SMH and sulphur hexafluoride/SF6 (n=4)
- Patient age ranged between 79.4 and 94.7 years, sex ratio M:F=5:7
- Follow-up period between 6 weeks to 6 months.

Results

- Seven patients (58.3%) experienced improvement in visual acuity: in 5 patients (41.6%) of 2 or more Snellen’s lines.
- No visual improvement was associated with duration of > 6 weeks, extensive SMH i.e. more than SDD, retinal elevation of ≥1500 microns and the presence of previous disciform scarring.
- Submacular drainage lead to significant visual improvement in 3 patients (75%).
- Partial or complete displacement and absorption of SMH occurred in all patients within 2 to 6 weeks.
- Complications: 1 patient who had extensive SMH (8%) developed retinal detachment associated with extensive proliferative vitreoretinopathy at 1 month following PPV and drainage.

Discussions and Conclusions

- No consensus exists as to the single best approach to use in cases of SMH. However, left untreated, SMHs will most likely result in significant permanent loss of central vision.
- Our results are consistent with larger studies which revealed:
  1. VA improvement rates of 47-73%;
  2. Complication rates of 7-16%;
  3. Complete displacement in 57-85%.
- Our cases showed that prompt treatment with tPA combined with anti-VEGF and either pneumatic displacement or submacular drainage leads to visual improvement in the majority of patients with SMH due to nAMD.
- Selection of the technique to use in patient should be dependent on the extent and duration of SMH. Based on our experience and literature review, we propose the following protocol for tPA management:
  - 1 DD → inject anti-VEGF and tPA without gas displacement
  - 1-2DD → inject anti-VEGF and tPA with gas displacement
  - >2DD → inject tPA then PPV with SMH drainage and anti-VEGF
- Pneumatic displacement should be avoided in subretinal haemorrhage situated superior to the fovea e.g. in patient with macularneumus or extramacular CNVM as it may lead to displacement of the blood into the subfoveal space.
- Awareness should be increased among non-retinal specialists regarding the availability and relative safety and effectiveness of this treatment in those group of patients who otherwise end up with severe loss of central vision.
- Once the SMH resolved, the underlying disease must be continued to be managed with anti-VEGF medications to prevent recurrence of SMH and to help preserve vision.
- The current study was limited by the small number of patients and the retrospective study design. A prospective, randomized study is needed in order to investigate how the pneumatic gas displacement compares with vitrectomy and drainage of SMH, in terms of safety and efficacy.

Summary of cases

<table>
<thead>
<tr>
<th>tPA dose</th>
<th>VA Pre-Treatment</th>
<th>VA Post-Treatment</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 µg</td>
<td>6/36</td>
<td>6/19+2</td>
<td>90 left 10 days &gt;5 DDx5 DD; &gt;1500 μm; massive SMH &amp; vitreous Hx</td>
</tr>
<tr>
<td>100 µg</td>
<td>6/19</td>
<td>6/24</td>
<td>HM PL tPA (50 µg) + PPV + endolaser + Ranibizumab + SF6</td>
</tr>
<tr>
<td>100 µg</td>
<td>6/19</td>
<td>6/12</td>
<td>100 µg tPA, followed by PPV, drainage of SMH, Aflibercept and SF6 20%; only eye</td>
</tr>
</tbody>
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References