Management of Proliferative Vitreoretinopathy with Intravitreal Methotrexate using a Treat-and-Extend Protocol

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The treatment discussed represents an off-label use of methotrexate as an intravitreal pharmacotherapy.

All patients were informed and consented to the off-label use of methotrexate.

Disclosures and Affiliations

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(none relevant)

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No disclosures
Summary

Treat-and-Extend Study Results

- 50 consecutive patients with RD and grade C/B PVR were treated with postop methotrexate (MTX) injections q1-6wks
- The majority of patients received 6 or fewer injections
- The single operation success rate was 88%, with a final reattachment rate of 96%
- A significant improvement in visual acuity was observed
- The incidence of corneal toxicity was ~40%

Dosing Recommendation – based on this study

- Inject q1-2wks until retinectomy edge stable (~3-4 injections during PO month 1)
- Inject q3-6wks until SO removal (~2 injections during PO months 2-3)
Intravitreal injection (IVI) of MTX has shown promise for the prevention of recurrent RD from PVR.  

**Dr. Elliott’s Protocol** involves 8 weekly injections followed by 1-4 bi-weekly injections. In a series of 26 eyes, there was a 92% reattachment rate.

*Elliott, Stryjewski, & Kim. NEOS 2018; meeting abstract.*
An individualized "treat-and-extend" protocol may also be effective in preventing recurrent RD from PVR.
# Methods

**Retrospective consecutive case series** of patients receiving intraoperative and post-operative IVIs of MTX

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
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<tbody>
<tr>
<td>• Retinal detachment</td>
<td>• &lt;3 Months follow-up</td>
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<tr>
<td>• Grade C or severe grade B PVR</td>
<td>• &lt;3 post-operative IVIs of MTX</td>
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<tr>
<td>• Age ≥18 years</td>
<td>• ≥12 IVIs of MTX</td>
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</table>
All patients underwent 25 gauge pars plana vitrectomy (PPV) with membrane peeling and/or relaxing retinectomy (RR)

Variables at Surgeon’s Discretion

- Scleral Buckling (SB)
- Internal Limiting Membrane Peeling (ILMP)
- Degrees of RR
- Choice of Tamponade (SO, PFO, C3F8, SF6)

**Intravitreal Dose:** 400µg MTX/0.1mL, produced by a compounding pharmacy
**N = 50 eyes of 50 patients**

- Median age = 63 years (range 18-82)
- 86% Grade C PVR (vs. 14% severe Grade B)

**Risk Factors**
- Prior vitrectomy (70%; avg. 1.5; range 1-5)
- Hemorrhage (22%)
- Hypotony (18%)
- Giant retinal tear (14%)
- Severe trauma (14%)
- Endophthalmitis or uveitis (10%)

**Comorbidities**
- Full-thickness macular hole (18%)
- Retinal neovascularization (10%)
- Amblyopia (6%)
- Advanced glaucoma (4%)
- Choroidal neovascularization (4%)
Results

Total number of post-operative IVIs = 264
Results

Versus 650 IVIs required with Dean Eliott’s protocol

(60% fewer with T&E)
The majority of patients received 6 or fewer injections

Median = 5
Average = 5.3
Range = 3-11
How frequently were doses administered?

Median = 11.5
Results

Dosing was “front-loaded” with the majority of IVIs occurring during the initial “loading phase”

[Bar chart showing the distribution of IVIs across different time phases]

- Loading Phase (71%)
- Extension Phase (29%)
How many IVIs occurred during the “loading phase”?

- Median = 3
- Average = 3.6
- Range = 1-11

Results

<table>
<thead>
<tr>
<th>Loading Phase</th>
<th>Extension Phase</th>
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<tbody>
<tr>
<td>q1-2wks</td>
<td></td>
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</table>
How many IVIs occurred during the “extension phase”?  

<table>
<thead>
<tr>
<th>Loading Phase</th>
<th>Extension Phase</th>
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</thead>
<tbody>
<tr>
<td>Median = 2</td>
<td>Median = 3</td>
</tr>
<tr>
<td>Average = 1.8</td>
<td>Average = 3.6</td>
</tr>
<tr>
<td>Range = 0-5</td>
<td>Range = 1-11</td>
</tr>
</tbody>
</table>
Single Operation Success = 88%

- Comparable to Dean Eliott’s results (92%)

<table>
<thead>
<tr>
<th></th>
<th>Success</th>
<th>Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>DE Cohort</td>
<td>24</td>
<td>2</td>
</tr>
<tr>
<td>SDW Cohort</td>
<td>44</td>
<td>6</td>
</tr>
</tbody>
</table>

No significant difference by $\chi^2$, $p=0.56$
Final Reattachment = 96%

- 4 eyes (8%) required a single re-operation for recurrent RD with PVR
- 2 patients (4%) declined additional surgery
Results: Visual Acuity

There was a significant improvement in mean visual acuity (p<0.0005)

Pre-Op VA

Mean
= 2.2 logMAR
≈ 20/3170 (HM)

Post-Op VA

Mean
= 1.34 logMAR
≈ 20/438
Results: Visual Acuity

78% increase in ambulatory vision
Is there any potential toxicity associated with IVI of MTX?

38% developed some form of keratopathy during the loading phase

- Non-healing corneal epithelial defect (22%)
- Vortex-like keratopathy (20%)
- Generally keratopathy improved with lubrication, BCL, extended MTX dosing intervals
A comparable rate of **single operation success was achieved** using 60% fewer MTX injections than in the previously described treatment protocol.
A significant improvement in visual acuity was observed among eyes included in the study.
Dosing Recommendation – *based on my experience*

- Inject q1-2wks until RR edge stable (~3-4 injections during PO month 1)
- Inject q3-6wks until SO removal (~2 injections during PO months 2-3)

**Further study is needed** to clarify the optimal MTX dosing frequency to prevent recurrent RD from PVR.