Intravitreal Triple Therapy with Vancomycin, Ceftazidime, and Moxifloxacin for Bacterial Endophthalmitis

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None
Summary

- Antibiotic resistance is prevalent and a major healthcare concern
- Intravitreal moxifloxacin (160µg) was well tolerated
- Visual acuity outcomes of eyes with endophthalmitis after cataract surgery treated with intravitreal moxifloxacin in addition to standard therapy compared favorably to those in the Endophthalmitis Vitrectomy Study treated with standard therapy alone
• Special thanks to Kenneth Taubenslag, MD for his primary role in this research
Background

• Increasing antibiotic resistance

• Acute-onset bacterial endophthalmitis
  – vancomycin for gram-positive coverage
  – either ceftazidime or an aminoglycoside for gram-negative coverage

• Endophthalmitis Vitrectomy Study (EVS)
  – All gram-positive isolates (94.2%) were susceptible to vancomycin
  – 11% of gram-negative isolates (6.5%) were resistant to both amikacin and ceftazidime
  – Gram-negative infections had worse visual outcomes

Questions

• Is vancomycin and a 3rd or 4th generation cephalosporin (ceftazidime) enough coverage for causative organisms in 2020?

• Is single coverage for gram-negative bacteria adequate?
Moxifloxacin

• *Broad-spectrum* 4\(^{\text{th}}\) generation quinolone that is active again both gram-positive and gram-negative bacteria

• Inhibits DNA gyrase and topoisomerase IV, enzymes necessary to unwind bacterial DNA for replication
• Oral administration of 400 mg moxifloxacin results in intravitreal drug levels that exceeded the mean inhibitory concentration (MIC) 90 (1.2 µg/ml) of many bacteria implicated in endophthalmitis ¹

• Intravitreal injection of moxifloxacin at a concentration of ≤ 160 µg/0.1 ml was nontoxic in rabbit eyes ²,³

Added Coverage

- Vancomycin
- Ceftazidime
- Moxifloxacin

Triple cover gram +
Double cover gram -
Synergy

- “the interaction of two or more agents to produce a combined effect greater than the sum of their separate effects”
- Combination of a penicillin and aminoglycoside significantly reduces the MIC of each antibiotic
Mechanism of Action

• Vancomycin: inhibits cell wall synthesis
  – Not effective against most gram-negative bacteria

• Ceftazidime: inhibits cell wall synthesis
  – Effective against pseudomonas aeruginosa
  – Ineffective against MRSA

• Moxifloxacin: inhibits cell replication
Purpose

• To examine visual and safety outcomes of patients with bacterial endophthalmitis treated with:
  – vancomycin 1mg
  – ceftazidime 2mg
  – moxifloxacin 160 µg

Methods

• Single-center retrospective review of all patients treated for endophthalmitis from January 2009 to August 2019

• Inclusion criteria:
  – Bacterial endophthalmitis
  – Treatment with intravitreal vancomycin, ceftazidime, and moxifloxacin: “triple therapy”

• Patients with less than 3 months follow-up were excluded

• Patients could receive topical or systemic antibiotics and steroids at discretion of treating physician
Primary Outcomes

• Percent of eyes attaining ≥ 20/200 Snellen visual acuity
• Percent of eyes attaining ≥ 20/50 Snellen visual acuity
• Adverse effects
Overall Results

• 94 eyes met inclusion criteria
• 51 of 94 eyes (54%) achieved a final visual acuity of ≥ 20/200
• 29 of 94 eyes (31%) achieved a final visual acuity of ≥ 20/50
### Table 1. Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>All patients (n=94)</th>
<th>Post-cataract (n=18)</th>
<th>Post-injection (n=18)</th>
<th>Bleb-associated (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, y</strong></td>
<td>Median (range)</td>
<td>64 (15-95)</td>
<td>67 (43-80)</td>
<td>72 (54-95)</td>
</tr>
<tr>
<td><strong>Right eye</strong></td>
<td></td>
<td>43 (46%)</td>
<td>8 (44%)</td>
<td>6 (33%)</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td></td>
<td>47 (50%)</td>
<td>11 (61%)</td>
<td>11 (61%)</td>
</tr>
<tr>
<td><strong>Black</strong></td>
<td></td>
<td>13 (14%)</td>
<td>1 (6%)</td>
<td>2 (11%)</td>
</tr>
<tr>
<td><strong>History of Diabetes</strong></td>
<td></td>
<td>22 (23%)</td>
<td>2 (11%)</td>
<td>6 (33%)</td>
</tr>
<tr>
<td><strong>History of Glaucoma</strong></td>
<td></td>
<td>23 (24%)</td>
<td>2 (11%)</td>
<td>4 (22%)</td>
</tr>
<tr>
<td><strong>History of AMD</strong></td>
<td></td>
<td>14 (15%)</td>
<td>1 (6%)</td>
<td>11 (61%)</td>
</tr>
<tr>
<td><strong>Days from procedure</strong></td>
<td>median (range)</td>
<td>—</td>
<td>5 (1-80)</td>
<td>3 (2-7)</td>
</tr>
<tr>
<td><strong>Visual acuity</strong></td>
<td>≤LP</td>
<td>32 (34%)</td>
<td>2 (11%)</td>
<td>2 (11%)</td>
</tr>
<tr>
<td></td>
<td>HM</td>
<td>32 (34%)</td>
<td>8 (44%)</td>
<td>7 (39%)</td>
</tr>
<tr>
<td></td>
<td>CF (&lt;5/200)</td>
<td>17 (18%)</td>
<td>4 (22%)</td>
<td>5 (22%)</td>
</tr>
<tr>
<td></td>
<td>≥5/200</td>
<td>13 (14%)</td>
<td>4 (22%)</td>
<td>4 (28%)</td>
</tr>
<tr>
<td><strong>Intraocular pressure</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0-5</td>
<td>1 (1%)</td>
<td>1 (6%)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>6-25</td>
<td>71 (76%)</td>
<td>16 (88%)</td>
<td>12 (66%)</td>
</tr>
<tr>
<td></td>
<td>&gt;25</td>
<td>22 (23%)</td>
<td>1 (6%)</td>
<td>4 (22%)</td>
</tr>
</tbody>
</table>
Subgroup Analysis

- Visual acuity survival curves were superior for patients with post-cataract endophthalmitis compared to post-injection ($P < 0.005$) or bleb-associated ($P < 0.005$).
• 17 of 18 (94%) eyes with post-cataract endophthalmitis obtained ≥ 20/200 visual acuity (78% of patients achieved ≥ 20/200 in EVS)\(^1\)
• 14 of 18 (77%) obtained ≥ 20/50 visual acuity (59% of patients achieved ≥ 20/50 in EVS)\(^1\)

Safety of Moxifloxacin

• No cases of macular infarction
• No higher rates of retinal detachment
• No cases of excessive inflammation
Conclusions

• Intravitreal moxifloxacin (160µg) appeared to be well tolerated

• Visual acuity outcomes of post-cataract endophthalmitis group treated with triple therapy compared favorably to EVS

• Addition of moxifloxacin to standard treatment with vancomycin and ceftazidime for acute bacterial endophthalmitis may be advantageous
Thanks for your Attention!
### Table 4. Cumulative Final Visual Acuity by Treatment Type

<table>
<thead>
<tr>
<th>Snellen Equivalent</th>
<th>Visual Acuity Score (No. of Letters)</th>
<th>Vitrectomy (n=201)</th>
<th>Tap/Biopsy (n=193)</th>
<th>P</th>
<th>IV Antibiotics (n=193)</th>
<th>No IV Antibiotics (n=201)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>20/25 or better</td>
<td>≥80</td>
<td>60 (29.9)</td>
<td>67 (34.7)</td>
<td></td>
<td>62 (32.1)</td>
<td>65 (32.3)</td>
<td></td>
</tr>
<tr>
<td>20/40 or better</td>
<td>≥70</td>
<td>108 (53.7)</td>
<td>101 (52.3)</td>
<td>.78</td>
<td>99 (51.3)</td>
<td>110 (54.7)</td>
<td>.50</td>
</tr>
<tr>
<td>20/50 or better</td>
<td>≥65</td>
<td>127 (63.2)</td>
<td>114 (59.1)</td>
<td></td>
<td>114 (59.1)</td>
<td>127 (63.2)</td>
<td></td>
</tr>
<tr>
<td>20/100 or better</td>
<td>≥50</td>
<td>154 (76.6)</td>
<td>139 (72.0)</td>
<td>.30</td>
<td>140 (72.5)</td>
<td>153 (76.1)</td>
<td>.42</td>
</tr>
<tr>
<td>20/200 or better</td>
<td>≥35</td>
<td>165 (82.1)</td>
<td>150 (77.7)</td>
<td></td>
<td>154 (79.8)</td>
<td>161 (80.1)</td>
<td></td>
</tr>
<tr>
<td>10/200 or better</td>
<td>≥20</td>
<td>175 (87.1)</td>
<td>159 (83.4)</td>
<td></td>
<td>163 (84.5)</td>
<td>171 (85.1)</td>
<td></td>
</tr>
<tr>
<td>5/200 or better</td>
<td>≥5</td>
<td>185 (92.0)</td>
<td>164 (85.0)</td>
<td>.03</td>
<td>168 (87.1)</td>
<td>181 (90.1)</td>
<td>.35</td>
</tr>
<tr>
<td>LP or better</td>
<td>≥LP</td>
<td>193 (96.0)</td>
<td>183 (94.8)</td>
<td></td>
<td>182 (94.3)</td>
<td>194 (96.5)</td>
<td></td>
</tr>
</tbody>
</table>

*IV indicates intravenous; LP, light perception.*