Ranolazine: a novel strategy for preventing postoperative atrial fibrillation

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Objectives

1. Describe pathophysiology of postoperative atrial fibrillation
2. Examine traditional treatment options to prevent postoperative atrial fibrillation
3. Evaluate the role of ranolazine for prevention of postoperative atrial fibrillation

Disclosure

• I do not have a vested interest in or affiliation with any corporate organization offering financial support or grant monies for this continuing education activity, or any affiliation with an organization whose philosophy could potentially bias my presentation

Postoperative atrial fibrillation

How To Vote via Texting

1. Standard texting rates only (worst case US $0.20)
2. We have no access to your phone number
3. Capitalization doesn’t matter, but spaces and spelling do

TIPS

EXAMPLE

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coronary artery bypass grafting (CABG)</td>
<td>16% to 50%</td>
</tr>
<tr>
<td>Valve-replacement</td>
<td>30% to 50%</td>
</tr>
<tr>
<td>CABG and valve-replacement</td>
<td>40% to 70%</td>
</tr>
<tr>
<td>Major non-cardiac thoracic</td>
<td>&lt;1% to 40%</td>
</tr>
</tbody>
</table>

Atrial fibrillation pathophysiology

- Ectopic focus
- Pulmonary veins
- Transient triggers
- Single-circuit reentry
- Pulmonary veins
- Functional changes
- Multiple-circuit reentry
- Atria
- Structural changes

Postoperative atrial fibrillation

Background and pathophysiology
Preventative strategies
Ranolazine

Beta-blockers

- 33 studies with 4698 total research subjects
- Primarily oral therapy started postoperatively
- Reduction in postoperative atrial fibrillation
  - 16.3% vs 31.7% (OR 0.33; 95% CI, 0.26–0.43)
  - Reduction in length of stay
  - 0.74 days (95% CI 0.00–1.48)

Amiodarone

- 33 studies with 5402 total research subjects
- Perioperative oral and intravenous dosage forms
- Reduction in postoperative atrial fibrillation
  - 19.4% vs 33.3% (OR 0.43; 95% CI, 0.34–0.54)
- Trend toward reduction in stroke and CVA
  - OR 0.6 (95% CI 0.35–1.02)
- Reduction in length of stay
  - 0.95 days (95% CI 0.52–1.37)
- Considerations in high risk patient populations
Postoperative atrial fibrillation

Ranolazine for POAF after CABG

Ranolazine

- Antianginal and anti-ischemic properties
  - Inhibits late phase of inward sodium current
  - Reduced calcium influx via Na+/Ca²⁺ exchanger
  - Decreased myocardial oxygen demand
- 500–1000 mg PO twice daily
- Blood pressure and heart rate neutral
- QTc prolongation ≤ 1%

Results

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Amiodarone (n=211)</th>
<th>Ranolazine (n=182)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>POAF, n (%)</td>
<td>56 (26.5%)</td>
<td>32 (17.5%)</td>
<td>0.035</td>
</tr>
<tr>
<td>30-day readmission, n (%)</td>
<td>22 (10.4%)</td>
<td>19 (10.4%)</td>
<td>1</td>
</tr>
<tr>
<td>30-day mortality, n (%)</td>
<td>2 (0.94%)</td>
<td>2 (1.09%)</td>
<td>0.88</td>
</tr>
<tr>
<td>Length of stay, days ± SD</td>
<td>4.38 ± 5.5</td>
<td>4.12 ± 6.1</td>
<td>0.66</td>
</tr>
<tr>
<td>Discharge with beta-blocker, n (%)</td>
<td>199 (94.3%)</td>
<td>178 (97.8%)</td>
<td>0.1</td>
</tr>
</tbody>
</table>

Ranolazine antiarrhythmic properties

Results

- Amiodarone (OR 1.7, 95% CI 1.01–2.91, p = 0.045)
- Age (OR 2.2 per 10 years, 95% CI 1.63–2.95, p <0.001)
- Chronic lung disease (OR 1.86, 95% CI 1.00–3.43, p = 0.049)
- Ranolazine compared to amiodarone
  - Reduced incidence of POAF
  - No difference in adverse events
Conclusions

1. Complex and incompletely understood pathophysiology for postoperative atrial fibrillation
2. Postoperative atrial fibrillation develops despite best practices
3. Ranolazine may be a novel strategy for prevention of postoperative atrial fibrillation

References

- Green AD. Cardiac ion channels. Circ Arrhythm Electrophysiol. 2009; 2:185-194

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