C1 Esterase Inhibitor for Drug-Induced Angioedema at a Community Teaching Health System

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BACKGROUND

• Acute drug-induced angioedema is a serious emergency that can cause life-threatening symptoms and death if not treated promptly.
• Drug-induced angioedema, particularly angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARBs), is thought to be caused by excess accumulation of bradykinin due to ineffective breakdown pathways and downregulation of the kallikrein-kinin system.
• This pathophysiologic mechanism suggests that treatments aimed at preventing the accumulation of bradykinin might be effective in treating drug-induced angioedema.
• Currently, no FDA-approved medications exist to treat drug-induced angioedema.
• Small randomized studies, case reports, and a meta-analysis have evaluated off-label use of c1 esterase inhibitor (C1Ei), and other therapies with no clear delineation of their role in the treatment of drug-induced angioedema.1,2

OBJECTIVE

• To evaluate the use, clinical efficacy, and angioedema on in groups a in secondary endpoints
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• Small randomized studies, case reports, and a meta-
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• JM. Use of c1 inhibitor for angiotensin
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• Med 2015;33:479.e1
• AC, et al. Efficacy of treatment of non
• Comorbidity Index, initial patient disposition, standard of care
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• -induced angioedema is a serious emergency that can cause life-threatening symptoms and death if not treated promptly.
• Drug-induced angioedema, particularly angiotensin-converting enzyme inhibitors (ACEi) and angiotensin receptor blockers (ARBs), is thought to be caused by excess accumulation of bradykinin due to ineffective breakdown pathways and downregulation of the kallikrein-kinin system.
• This pathophysiologic mechanism suggests that treatments aimed at preventing the accumulation of bradykinin might be effective in treating drug-induced angioedema.
• Currently, no FDA-approved medications exist to treat drug-induced angioedema.
• Small randomized studies, case reports, and a meta-analysis have evaluated off-label use of c1 esterase inhibitor (C1Ei), and other therapies with no clear delineation of their role in the treatment of drug-induced angioedema.1,2

METHODS (continued)

• Study Design: IRB approved retrospective, observational study comparing patients who received C1Ei to those who did not for drug-induced angioedema from January 2018 to December 2019
• Patient Population: Inclusion criteria:
  • Adults ≥ 18 years of age
  • Primary diagnosis of drug-induced angioedema
  • Exclusion criteria:
  • Inactive patient status
  • Regularly prescribed fresh-frozen plasma
  • Recent C1Ei post initiation
• Primary Endpoints: Incidence of intubation secondary to drug-induced angioedema
• Secondary Endpoints: Duration of mechanical ventilation, intensive care unit (ICU) length of stay (LOS), hospital LOS, in-hospital mortality, angioedema-related medication therapy costs, and reported C1Ei adverse effects
• Other data points collected included: Age, gender, race, ethnicity, weight, Charlson Comorbidity Index, initial patient disposition, standard of care received (defined as equiv-pH 2.0 to 0.1 mg intravenously or 0.05 to 0.01 mg intravenously), concurrent medications, comorbid conditions, complications, and adverse effects

RESULTS

• Overall (n = 50), the mean age was 60.7 (±13.8) years, and 48 patients (96.0%) were female. The majority of patients were Caucasian (83 patients, 80.2%), had a history of angioedema (84 patients, 88.4%), had a patient-reported duration of symptoms less than three hours (16 patients, 32.0%), had an ACE as the angioedema-associated medication (82 patients, 85.6%), and were discharged home upon initial presentation (50 patients, 52.6%).

REFERENCES


Table 1. Baseline Characteristics Before and After Propensity Score Matching

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Non-C1EI Group (n=44)</th>
<th>C1EI Group (n=22)</th>
<th>p value</th>
<th>Non-C1EI Group (n=44)</th>
<th>C1EI Group (n=22)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>54 (50, 58)</td>
<td>56 (50, 60)</td>
<td>0.125</td>
<td>54 (50, 58)</td>
<td>56 (50, 60)</td>
<td>0.125</td>
</tr>
<tr>
<td>Sex, female</td>
<td>40 (90.9)</td>
<td>20 (90.9)</td>
<td>&gt;0.999</td>
<td>40 (90.9)</td>
<td>20 (90.9)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>History of angioedema, n (%)</td>
<td>44 (100)</td>
<td>22 (100)</td>
<td>&gt;0.999</td>
<td>44 (100)</td>
<td>22 (100)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Prior C1Ei therapy, n (%)</td>
<td>2 (4.5)</td>
<td>2 (9.1)</td>
<td>0.630</td>
<td>2 (4.5)</td>
<td>2 (9.1)</td>
<td>0.630</td>
</tr>
<tr>
<td>Standard of care, n (%)</td>
<td>42 (95.5)</td>
<td>20 (90.9)</td>
<td>0.125</td>
<td>42 (95.5)</td>
<td>20 (90.9)</td>
<td>0.125</td>
</tr>
<tr>
<td>Weight, kg, median (IQR)</td>
<td>40 (35, 43)</td>
<td>40 (35, 43)</td>
<td>&gt;0.999</td>
<td>40 (35, 43)</td>
<td>40 (35, 43)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Age, years, mean (SD)</td>
<td>54.9 (13.8)</td>
<td>56.4 (13.8)</td>
<td>0.018</td>
<td>54.9 (13.8)</td>
<td>56.4 (13.8)</td>
<td>0.018</td>
</tr>
<tr>
<td>Comorbidity Index</td>
<td>1 (0, 2)</td>
<td>1 (0, 2.2)</td>
<td>0.314</td>
<td>1 (0, 2)</td>
<td>1 (0, 2.2)</td>
<td>0.314</td>
</tr>
<tr>
<td>Propensity score</td>
<td>0.999 (0.999)</td>
<td>0.999 (0.999)</td>
<td>&gt;0.999</td>
<td>0.999 (0.999)</td>
<td>0.999 (0.999)</td>
<td>&gt;0.999</td>
</tr>
</tbody>
</table>

Table 2. Study Endpoints Before and After Propensity Score Matching

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Non-C1EI Group (n=44)</th>
<th>C1EI Group (n=22)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Length of mechanical ventilation, hours</td>
<td>7 (7, 10)</td>
<td>6 (5, 10)</td>
<td>0.125</td>
</tr>
<tr>
<td>Intubation time, hours</td>
<td>10 (8, 12)</td>
<td>8 (6, 10)</td>
<td>0.125</td>
</tr>
<tr>
<td>Mortality</td>
<td>1 (2.3)</td>
<td>1 (4.5)</td>
<td>0.727</td>
</tr>
<tr>
<td>associated medications, n (%)</td>
<td>44 (100)</td>
<td>22 (100)</td>
<td>&gt;0.999</td>
</tr>
<tr>
<td>Rehospitalization, n (%)</td>
<td>3 (13.6)</td>
<td>1 (4.5)</td>
<td>0.314</td>
</tr>
<tr>
<td>Rehospitalization rate, %</td>
<td>13.6 (13.6)</td>
<td>4.5 (4.5)</td>
<td>&gt;0.999</td>
</tr>
</tbody>
</table>

CONCLUSION

• This retrospective, observational study suggests that C1Ei may not prevent drug-induced angioedema-related intubation, while also incuring a larger angioedema-related medication therapy cost.
• Larger, multicenter, randomized controlled trials are needed to further validate the results of this study.

DISCUSSION

• Any baseline characteristics differences between C1EI and non-C1EI groups were resolved with propensity score matching (Table 1).
• While there was a statistically significant difference in incidence of intubation, duration of mechanical ventilation, and hospital LOS in the unmatched population, there was no statistically significant difference between the C1EI and non-C1EI groups after propensity score matching (Table 2).
• C1EI LOS was longer in the C1EI group compared to the non-C1EI group both before and after propensity score matching (Table 2).
• No in-hospital mortality was observed and no C1EI adverse effects were reported.