Assessment of outcomes of calciphylaxis treated with intralesional sodium thiosulfate

Colleen K. Gabel, BS¹; Emily D. Nguyen, BS¹; Allison S. Dobry, MD²; Anna Cristina Garza-Mayers MD, PhD³; Lauren Ko, MD, MEd³; Radhika Shah, MD, PharmD⁴; Jessica St. John, MD, MBA, MPH⁵; Lauren Strazzula, MD⁶; Olesya Baker PhD⁷; Sagar U. Nigwekar, MD, MMSc¹; Daniela Kroshinsky, MD, MPH¹

¹Massachusetts General Hospital, ²University of California, Irvine School of Medicine, ³Harvard Medical School, ⁴Robert Wood Johnson Medical School, ⁵University of Massachusetts Medical School, ⁶South Shore Skin Center, ⁷Center for Clinical Investigation, Brigham and Women’s Hospital
Disclosures

• I have no conflicts of interest to disclose
• Sagar U. Nigwekar has received grant support from Hope Pharmaceuticals
Outline

- Background
- Methods
- Results
- Conclusions
Background - Calciphylaxis

Pathogenesis: calcium deposition within vessels, associated endothelial dysfunction, thrombosis, and ischemia

Diagnosis: clinical exam, skin biopsy, imaging

Treatment: Intravenous sodium thiosulfate (IV STS) mainstay of therapy within a multimodal approach\(^1,2,3\)

---

Intravenous sodium thiosulfate

- No published randomized controlled trials assessing efficacy
- Proposed mechanisms
  - Antioxidant, vasodilator, calcium chelator, inhibitor of calcification
- Adverse effects:
  - Nausea, hypotension, prolonged QTc, hypocalcemia, volume overload, metabolic acidosis, fracture risk
- Intralesional STS (IL STS) has emerged as a potentially effective local alternative, however, has not been well-studied.
Study questions

• What is the impact of IL STS on clinical outcomes?
  • Clinical improvement
  • Resolution of local disease activity

• Is there any difference in outcomes of lesions treated with IL STS alone vs. both IL and IV STS?
Study design – a retrospective study

Diagnosed with calciphylaxis between 1/2006 – 12/2018 (n=149)

Treated with IL STS (n=39)

Included in study (n=33)

Excluded 6 patients due to:
- Inadequate documentation (2)
- Immediate loss-to-follow-up (3)
- Did not tolerate administration of any IL STS (1)

Individual lesions (n=104)

Excluded 1 lesion (patient enrolled in IV STS trial and was blinded)

IL STS alone (n=29)

IL STS + IV STS (n=74)
IL STS injection procedure

• Informed consent obtained
• Area cleaned with isopropyl alcohol
• STS (250mg/mL) in isolation or combined with 2% lidocaine without epinephrine based on lesion tenderness
• Injections placed in deep dermis and subcutaneous fat at active purpuric borders
• Volume adjusted based on size and number of lesions: 0.05-15mL
• Frequency: determined by clinical necessity and patient availability
• Patients medically managed and optimal wound care provided per standard
Patient demographics fit calciphylaxis profile

<table>
<thead>
<tr>
<th>Patient characteristics</th>
<th>Total (n=33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, mean (SD)</td>
<td>65.8 (13.5)</td>
</tr>
<tr>
<td>Female sex, n (%)</td>
<td>17 (51.5)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>29 (87.9)</td>
</tr>
<tr>
<td>Unknown</td>
<td>3 (9.1)</td>
</tr>
<tr>
<td>African American</td>
<td>1 (3.0)</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino/a</td>
<td>3 (9.1)</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>31.7 (7.4)</td>
</tr>
<tr>
<td>Lesion location, n (%)</td>
<td></td>
</tr>
<tr>
<td>Peripheral</td>
<td>88 (84.6)</td>
</tr>
<tr>
<td>Central</td>
<td>17 (16.3)</td>
</tr>
</tbody>
</table>

Lab values, mean (SD)
- Calcium (corrected) 9.6 (0.9)
- Phosphorus 4.4 (1.8)
- PTH, median (IQR) 178.0 (286.0)

Risk factors, n (%)
- Warfarin 23 (69.7)
- Diabetes mellitus 20 (60.6)
- Atrial fibrillation 19 (57.6)
- ESRD 18 (54.5)
- Vitamin D 10 (30.3)
- Hyperparathyroidism 9 (27.3)
- Autoimmune disease 6 (18.2)
- Corticosteroids 6 (18.2)
- Thromboembolic events 6 (18.2)

Treatment, n (%)
- IV STS* 74 (71.2)
- Sevelamer 20 (60.6)
- Bedside debridement 14 (42.4)
- Cinacalcet 13 (39.4)
- OR debridement 7 (21.2)
- Pentoxifylline 4 (12.1)
- Hyperbaric oxygen therapy 2 (6.1)
- Vitamin K replacement 1 (3.0)
- Topical STS* 2 (1.9)

*counted individual lesions

There was no significant difference between any of these characteristics in patients who received IL STS alone vs. both IL and IV STS.
IL STS injection cadence

<table>
<thead>
<tr>
<th>Injection cadence, n (%)</th>
<th>Lesions (n=104)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Once</td>
<td>36 (34.6)</td>
</tr>
<tr>
<td>Every 1-4 days</td>
<td>21 (21.2)</td>
</tr>
<tr>
<td>Every 1-2 weeks</td>
<td>39 (37.5)</td>
</tr>
<tr>
<td>Every 3 weeks</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>Monthly</td>
<td>2 (1.9)</td>
</tr>
<tr>
<td>Less frequently than monthly</td>
<td>3 (2.9)</td>
</tr>
</tbody>
</table>

43.2% treated as inpatient
IL STS may be locally effective

- Clinical improvement: 93.3% of lesions
  - Median time to improvement: 14 days (95% CI 8-21 days)
- Resolution of local disease activity: 85.6% of lesions
  - Median time to resolution: 41 days (95% CI 32-49 days)
- Pain improvement: 80% overall
- No difference in these outcomes between IL STS alone and IL + IV STS
  - Clinical improvement p=0.29
  - Resolution of local disease activity p=0.59
Clinical photos – IL STS

IL STS:

* = injection dates

Onset
6 weeks later
8 weeks later
1 week later
2 weeks later
4 weeks later

IV STS:

Week 1
Week 10

* = injection dates
Adverse effects

• Seven injections out of a total of 327 (2.1%) discontinued due to pain
  • Consistent with limited prior literature
Study limitations

• Retrospective design
  • Challenging to isolate effect of IL STS alone

• Single institution

• Subjectivity of assessment
  • Outcomes based off chart review assessment rather than prospective rating
  • Documentation limitations in assessing pain improvement

• Did not assess outcomes of IV STS alone
  • Ongoing study
Conclusions

• IL STS is a **potentially effective, well tolerated local treatment option** for calciphylaxis as part of a larger multimodal approach

• There were **no major differences in outcomes** in lesions treated with IL STS alone or both IL and IV STS

• IL STS may provide a **treatment option** for patients for whom IV STS is not an appropriate option
Future directions

• A prospective trial needed
  • Standardize lesion number, size, and depth
  • Standardize pain assessment
Thank you!