Dietary Citrate and Plasma Ionized Calcium: What Should We Advise our Platelet Donors?

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Stefanie has no conflicts of interest, financial or otherwise.
Is Dietary Citrate Anion a Factor in Apheresis Platelet Donation?

- Oral hydration traditionally advised prior to blood donation
  - Non-alcoholic beverages
  - Juice or water
- Citrus juice rich in vitamin C but also citrate anion
- No separate dietary recommendations for platelet donors
- Exposure to IV citrate anion during platelet donation
- Drinking high-citrate fluids prior to platelet donation
  - Adds to the total citrate anion burden of platelet donors
  - Increased likelihood of hypocalcemic toxicity?
Clinical Utilization of IV and Oral Citrate-Containing Fluids

• ACD-A
  – Citrate-based anticoagulant
  – Most frequently used for platelet donors

• Popular juices
  – Clinically relevant amounts of citrate anion
  – *Used in regimens for suppressing urinary calcium oxalate stone formation
  – What is their effect on plasma ionized calcium?

<table>
<thead>
<tr>
<th>Fluid</th>
<th>Citrate Anion (mmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACD-A</td>
<td>113</td>
</tr>
<tr>
<td>Grapefruit Juice</td>
<td>64.7</td>
</tr>
<tr>
<td>Orange Juice</td>
<td>47.36</td>
</tr>
<tr>
<td>Pineapple Juice</td>
<td>41.57</td>
</tr>
<tr>
<td>Lemon Juice</td>
<td>47.66</td>
</tr>
<tr>
<td>Lemonade</td>
<td>38.65</td>
</tr>
<tr>
<td>Crystal Light</td>
<td>38.39</td>
</tr>
</tbody>
</table>

ACD-A and Hypocalcemic Toxicity in UMass Apheresis Platelet Donors

- ACD-A returned to platelet donors at UMass (Trima Accel®)
  - $322.65 \pm 73.16$ mL ($n=20$; range 245-492 mL)
  - 36.46 mmol of citrate anion

- Hypocalcemic toxicity in UMass platelet donors
  - ~16-20% fall in plasma $[\text{Ca}^{2+}]$
  - ~50% of donors experience symptoms

- Could ingestion of a citrate-containing beverage prior to donation worsen the fall in plasma $[\text{Ca}^{2+}]$ during donation?
QA Study Protocol

Measure plasma [Ca 2+] Administer Beverage

<table>
<thead>
<tr>
<th>Beverage</th>
<th>mmol/L Citrate</th>
<th>Volume Consumed</th>
<th>mmol of Citrate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ruby Red Grapefruit Juice</td>
<td>64.7</td>
<td>314.7 mL</td>
<td>10.6 oz</td>
</tr>
<tr>
<td>Orange Juice (Tropicana® Original Style)</td>
<td>47.4</td>
<td>429.5 mL</td>
<td>14.5 oz</td>
</tr>
</tbody>
</table>

Outcome Measure: % change in plasma [Ca^{2+}] from T_0
Measurement of Plasma $[\text{Ca}^{2+}]$ by Fingerstick Blood Sample

- iSTAT® System point-of-care blood analyzer
  - CG8+ cartridge
    - Chemistry analyzer
    - 95 µL blood sample
  - Abbott Point of Care, Inc.
    - Abbott Park, IL
- Unistick 3 Comfort Lancet
  - Owen Mumford
    - Marietta, GA
- Natelson heparinized blood collection tubes (0.2 mL)
  - Fisher Scientific
    - Pittsburgh, PA
### Antecubital (Venous) vs. Fingerstick (Capillary) \([\text{Ca}^{2+}]\)

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Antecubital</th>
<th>Fingerstick</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>W</td>
<td>3.0</td>
<td>3.5</td>
<td>1.00</td>
</tr>
<tr>
<td>Z</td>
<td>4.0</td>
<td>3.5</td>
<td>0.80</td>
</tr>
<tr>
<td>H</td>
<td>4.5</td>
<td>4.0</td>
<td>0.80</td>
</tr>
<tr>
<td>S</td>
<td>5.0</td>
<td>4.5</td>
<td>1.00</td>
</tr>
<tr>
<td>E</td>
<td>5.0</td>
<td>4.0</td>
<td>0.67</td>
</tr>
<tr>
<td>A</td>
<td>5.0</td>
<td>4.5</td>
<td>0.80</td>
</tr>
</tbody>
</table>

Mann-Whitney Rank Sum Test

- * n = 2
- ** n = 3

\([\text{Ca}^{2+}]\) (4.6-5.3 mg/dL)
Effect of Grapefruit Juice on Plasma $[\text{Ca}^{2+}]$

-14  -12  -10  -8  -6  -4  -2  0  2  4  6

$[\text{Ca}^{2+}]%$ Change from Baseline

$\text{Minutes After Ingestion}$

$*=\text{N/A}$
Effect of Orange Juice on Plasma $[\text{Ca}^{2+}]$

- minutes after ingestion

$[\text{Ca}^{2+}]$ % change from baseline

- $m$ 2.072 M$^2$
- $m$ 1.804 M$^2$
- $f$ 1.788 M$^2$
- $f$ 1.705 M$^2$
- $f$ 1.608 M$^2$
- $m$ 2.111 M$^2$

Minutes After Ingestion

* = N/A
No Consistent Effect of Gender or BSA on Response to Citrus Juice Ingestion

<table>
<thead>
<tr>
<th>Juice</th>
<th>Parameter</th>
<th>↓ Ca(^{2+})</th>
<th>No ↓ Ca(^{2+})</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grapefruit</td>
<td>BSA</td>
<td>1.807±0.218</td>
<td>1.930±0.201</td>
<td>0.800*</td>
</tr>
<tr>
<td></td>
<td>M:F</td>
<td>1:1</td>
<td>1:1</td>
<td>1.000§</td>
</tr>
<tr>
<td>Orange</td>
<td>BSA</td>
<td>1.852±0.178</td>
<td>1.840±0.328</td>
<td>0.800*</td>
</tr>
<tr>
<td></td>
<td>M:F</td>
<td>1:1</td>
<td>1:1</td>
<td>1.000§</td>
</tr>
</tbody>
</table>

*Mann-Whitney Rank Sum Test  
§Fisher Exact Test
• Popular beverages contain clinically relevant amounts of citrate anion.
• Ingestion may markedly lower plasma $[\text{Ca}^{2+}]$.
• The effect may last for 2-3 hours (or longer).
• This could add to the effect of IV citrate infusion during platelet donation, resulting in hypocalcemic toxicity.
• We conclude that it is prudent to advise platelet donors to avoid high citrate anion beverages, such as citrus juice, for at least 4 hours prior to donation.
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