Thrombotic Microangiopathy Secondary to Intravenous Abuse of Oral Opana ER: Etiology, Diagnosis and Treatment

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Critical Care Fellow 2014-present
Hematology 2012-2014
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Off-Label Use Disclosure(s)

I do not intend to discuss an off-label use of a product during this activity.
Financial Disclosure(s)

I **have not had** any relevant financial relations during the past 12 months to disclose.
Goals and Objectives:

• to make physicians and health care providers aware of IV abused Opana TMA
• to learn when to suspect TMA secondary to IV abused Opana
• to standardize terminology
• to learn patient approach
• to learn how to interpret supportive tests
• to learn rationale for guidance in treatment (or withholding)
History

• August 2012:
  • a nephrologist reports to the TN DOH three cases of unexplained thrombotic thrombocytopenic purpura (TTP).

• January 2013:
  • CDC reports an illness associated with IV abuse of oral Opana ER (oxymorphone) that resembled TTP.*

With Opana ER,
Your patients may not have to face chronic pain alone

OXymORPhONE
(Trade Names: Opana®, Opana ER®; Street Names: Blue Heaven, Blues, Mrs. O, New Blues, Octagons, Oranges, Orgasna IR, OM, Pink, Pink Heaven, Pink Lady, Pink O, Stop Signs, and The O Bomb)

April 2013
DEA/OD/ODE

OPANA® ER is an opioid agonist indicated for the relief of moderate to severe pain in patients requiring continuous around-the-clock opioid treatment for an extended period of time.

IMPORTANT SAFETY INFORMATION

WARNING: ABUSE POTENTIAL, LIFE-THREATENING RESPIRATORY DEPRESSION, ACCIDENTAL EXPOSURE, AND INTERACTION WITH ALCOHOL

Abuse Potential
OPANA® ER contains oxymorphone, an opioid agonist and Schedule II controlled substance with an abuse liability similar to other opioid agonists. Labeled or

Source: Opana.com
History

- CDC performed case controlled series.
- Total of 15 cases
- No fatalities during acute episode
- 14/15 patients reported injecting Opana ER
  - 1 subcu
- Median time from injection of Opana ER to hospital presentation was 1 day with a range of 0–2 days.

History

• No guidance on diagnosis or treatment
Case reports spike

Resurgence of intravenous Opana as a cause of secondary thrombotic thrombocytopenic purpura.
Rane M¹, Aggarwal A², Banas E², Sharma A².

Thrombotic Microangiopathy Associated with Intravenous Injection of Opana ER®: University Medical Center Case Series.
Marcus R. Winkler¹, Thomas C. Watkins¹ and Christopher T. Clark¹

Opana-ER used the wrong way: intravenous abuse leading to microangiopathic hemolysis and a TTP-like syndrome.
Amjad A¹, Parikh RA

A NARROW ESCAPE FROM THE DEADLY DOSE OF Opana
D. Chaudhary ¹, ² A. Mori ¹
Drug Forums “light up”
Thrombotic Thrombocytopenic Purpura

• A pro-thrombotic state in the microvasculature caused by severe ADAMTS13 deficiency.*


• Fever, Anemia, Renal Failure, Thrombocytopenia, Altered Mental Status

• The so-called “pentad”


Thrombotic Thrombocytopenic Purpura

- An autoimmune disease
- AutoAb to ADAMTS-13
  - Undetectable (<5%)
- MAHA or TMA
- Thrombocytopenia
• Prior to therapeutic plasma exchange, mortality ~90%
• Treatments now include therapeutic plasma exchange, steroids, anti-platelets and Rituximab
TTP – Therapeutic Plasma Exchange

• Mainstay of treatment for TTP
• Believed to remove anti-ADAMTS13 autoantibody
• Replaces deficient ADAMTS13
• Role in drug-induced thrombotic microangiopathy is less clear
• Only ticlopidine-associated microangiopathy shown benefit from TPE
  • +autoantibodies to ADAMTS13

ADAMTS13

• ADAMTS-13: vW factor cleaving protease
• Deficiency results in high levels of very large vW multimers
• Activates coagulation in microvasculature
ADAMTS13 assay*

• measured using a quantitative assay
• Standard practice at our institution for patients with a suspected diagnosis of TTP
• Rapid in-house result turnaround time
• ADAMTS13 activity of <5% is consistent with classical TTP

Our experience

• CDC report sparks interest
• Hindsight of patient presentations
• Increased numbers of patients with unexplained TMA
• Patients directly inquired about dissolving and injecting Opana-ER
• Cases identified
Case Series

- 15 patients, 18 cases
- 2 rural communities in NC
- Admitted or consulted for suspicion of TTP
- Classic MAHA evident on all peripheral blood film fields
  - Marked schistocytes, thrombocytopenia, reticulocytosis
Case Series

• Age range: 22-52 years
• 7 men, 8 women
• IV abuse oral Opana-ER 0-5 days prior
• 23 year old pregnant woman, TPE x 1
Case Series Results

- Platelets: 9,000 – 128,000 (mean 65,000/cmm)
- Initial platelet recovery: 2-12 days (mean 6 days)
- 3 patients left AMA
Case Series Results

• Infection vs Uninfected
  • 10 with documented infections
  • Staph most common organism (MSSA, MRSA)
  • Endocarditis, sepsis, bacteremia, UTI, pneumonia, septic arthritis, septic emboli
## Case Series Results

<table>
<thead>
<tr>
<th></th>
<th>+ Infection</th>
<th>- Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADAMTS 13%</td>
<td>12-79% (mean 44%)</td>
<td>56-119% (mean 81%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>12-119% (mean 63%)</td>
</tr>
</tbody>
</table>

Levels did not correlate with serum creatinine or LDH
Case Series Results

- HIV: negative 13/15 patients
- LDH elevated 14/15 patients
  - Did not correlate with severity of illness
Case Series Results

• Results similar to CDC report
• Recovery time varied
• Symptoms improved:
  • Withholding offending agent
  • Provision of supportive care
  • Treatment of underlying infections
How is this different from TTP

- NO evidence of ADAMTS13 deficiency
- NO evidence of detectable autoAb to ADAMTS13
- Recovered without therapeutic plasma exchange
How is this different from TTP

• Platelet counts typically higher than TTP
• ADAMTS13% normal or mildly decreased
  • >5%
Real life clinical presentations – So what did we do?

• Withheld offending agent
• ADAMTS13 assay
  • Results available less than 24 hrs in house
• Initiated supportive therapy
## TPE compared to CDC

<table>
<thead>
<tr>
<th></th>
<th>CDC</th>
<th>WFUBMC</th>
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</thead>
<tbody>
<tr>
<td>Therapeutic plasma exchange</td>
<td>12/15</td>
<td>1/18</td>
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</table>

All patients recovered from the TMA/MAHA

- Individually considered but did not utilize TPE
What we were not able to determine

• Concomitant Hep C infection correlation
• Number of tablets used
• Methods of preparation
• Long term data
What makes this information important?

- Similar patient profiles
- 10 total patients
- ADAMTS13% not tested
- Examined costs
  - Fees, blood bank, etc

Winkler et.al

• Total inpatient fees: $1,025,382
• Individual fees: $29,021 - $149,270 per admission

Winkler et.al – TPE – 9 patients

<table>
<thead>
<tr>
<th></th>
<th>Initial Admission</th>
<th>Readmission</th>
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<tbody>
<tr>
<td>TPE procedures</td>
<td>77</td>
<td>36</td>
</tr>
<tr>
<td>Plasma volume</td>
<td>272,757</td>
<td>60,895</td>
</tr>
<tr>
<td>pRBC</td>
<td></td>
<td>47</td>
</tr>
<tr>
<td>Platelets</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Plasma cryoprecipitate</td>
<td></td>
<td>120</td>
</tr>
</tbody>
</table>

No complications noted from TPE

Winkler et.al - Impacts identified

- Financial - > $1 million
- Availability of staffing and equipment
- Blood supply:
  - Local supplier could not meet demand for cryoprecipitate-reduced units for TPE
  - Had to be acquired and shipped

How is this learned?
MATERIALS NEEDED:
1. Opium ER tablets (5mg, 15mg, 20mg, 30mg, 40mg)
2. Insulin Syringe (1cc)
3. Cotton Ball
4. Large Metal Spoon (I used a soup ladle)
5. Shovel
6. Electric Heat Source (An electric stove or a clothing iron is suitable)
7. 70% Isopropyl Alcohol
8. Water (Distilled if available)
9. Hose Clamp

TECHNIQUE:
1. Take your pill and remove the coating. I suggest using a nail file to do so and not use a wet paper towel like you would on an Oxycodone pill because remember that TIMERx! It will gel up upon contact with moisture.
2. Decide upon your dose. Please bear in mind that amphetamine is a very potent narcotic; injectable solutions come in formulations of 1mg/ml. I had a 40mg ER tablet and I used a little less than a quarter of it. Remember that it is almost impossible to lose some product if the process so I used a 10mg chunk and probably yielded 5mg - 8mg. This is a large dose even for an opioid tolerant individual.
3. Grind up your chunk using a hose clamp into a fine and fluffy powder and add it to your abuser.
4. Place roughly 1 tablespoon of 70% Isopropyl alcohol into the glass and stir it. Allow this mixture to sit for a couple of minutes - stirring occasionally.
5. Take a large cotton and drop it into the solution and filter it out with a syringe. You may use an infant oral syringe (like the ones preferred for sucking) or a 3cc syringe to suck up more liquid. I unfortunately only had a 1cc insulin syringe so I used that to draw up the amphetamine/alcohol solution.
6. Squirt the extracted liquid into your metal spoon - it should be free of any visible materials at this point (a speck or two won’t hurt).
7. Place the spoon onto your electric heat source. I used an electric clothing iron and simply placed the spoon on the flipped-over iron as it was on the highest setting.
8. Allow the solution to simmer and evaporate. You can speed up the process by blowing on the alcohol as it simmers. The solution should not be as a rolling ball. Just a consistent simmer and try to breathe in the evaporated fumes as it can give you quite a headache.
9. When the alcohol has been completely evaporated, you will be left with a yellowish residue at the bottom of the spoon. This is your extracted amphetamine. Fill up your syringe with as much (hot) water as possible (preferably 1cc) and squirt it into the spoon and mix it quickly and drop a medium sized cotton to absorb the liquid. You will see a portion of the product gel up. You can add the remaining gel or mix it again for a second shot although I don’t really know how effective it will be.
10. Inject your amphetamine solution, sit back and pop in Drugstore Cowboy and feel the connection between yourself and Bob (Matt Dillon’s character in the movie).

I hope the above technique works for you and you can soon join the ranks of esteemed IV amphetamine users everywhere. Remember to exercise extreme caution with these bad boys and never underestimate the power they hold. Always remember that you can ALWAYS do more but you can’t always do less and I’d rather wake up from a enjoyable than a state of confusion with a shot of naron running through my veins.

Love, Peace & Chicken Grease.
Recommendations

• Aggressively question all patients presenting with TMA, MAHA or suspected diagnoses of TTP for IV opana abuse

• Consideration of supportive care in lieu of TPE

• Caveat – always err on the side of caution if TTP suspected
Recommendations

• DO NOT refer to as “Opana-TTP” or “TTP-like illness”

• Best described as:
  Intravenously abused oral Opana ER-induced thrombotic microangiopathy

• In reality: Opana-induced TMA
Questions?

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