THE NORTHERN HOSPITAL

LOCAL ANAESTHETIC AGENTS TOXICITY

The Crater, Petersburg, July 1864.

"It was the saddest affair I have ever witnessed in the war…"

Ulysses S Grant

"July 21st, Thursday, in front of Petersburg. The mine which General Burnside is making causes a good deal of talk and is generally much laughed at. It is an affair of his own entirely and has nothing to do with the regular siege". (Union soldier)

For a month, a regiment of Pennsylvania coal miners worked to dig a 500 foot tunnel beneath Confederate lines and pack it with four tons of gunpowder.

Burnside's idea was to blow a hole in the Petersburg defenses, then rush through to take the town. Above ground, not far from the tunnel, the unsuspecting Confederate commander was General William Mahone, a veteran of almost every major battle fought by the army of Northern Virginia.

At dawn on July 30, Union sappers lit the fuse. A great crater was torn in the earth 30 feet deep, 70 feet wide, 250 feet long.

The stunned Confederates fell back.

Then the plan began to fall apart.

A precious hour went by before the Union assault force got started, and when it did three divisions stormed down into the great hole, rather than around it. Their commander General James H. Ledlie, did not even watch the battle, huddling instead in a bombproof shelter with a bottle of rum. Once inside the crater, the Union soldiers found there was no way up the sheer 30 foot wall of the pit, and no one had thought to provide ladders. General Mahone ordered his men back to the rim to pour fire down upon them. Scores of black troops were killed when they tried to surrender at the crater, bayoneted or clubbed by Confederates shouting, "Take the white man, Kill, the nigger!"

"It was the saddest affair I have ever witnessed in the war. Such opportunity for carrying fortifications I have never seen and do not expect again to have".
(Ulysses S Grant).

General Ledlie was dismissed from the service. Burnside was granted extended leave and never recalled to duty.

"July 30, 1864:

The work and expectations of almost two months have been blasted. The first temporary success had elated everyone so much that we already had imagined ourselves in Petersburg. But 15 minutes changed it all and plunged everyone into a feeling of despair almost of ever accomplishing anything. Few officers can be found this evening who have not drowned their sorrows in the flowing bowl".
(Washington Roebling)

Ken Burns', "The Civil War", 1990.

By July 1864, Ulysses S. Grant had stalled at the interminable siege of Petersburg, unable to dislodge Robert E. Lee. Out West William Tecumseh Sherman was similarly stalled outside of Atlanta. Lincoln was up for re-election. The Democratic nomination, of all people, was none other than General George B. McClellan. He was campaigning on a platform of negotiating with the Confederates to end the war. Lincoln had to have a victory on the battlefield or he would lose the election and with it, the war. "Both Grant

and Sherman", George Templeton Strong predicted from New York, "are on the eve of disaster".

But outside of Petersburg, General Ambrose Burnside, had come up with an audacious plan that he believed would provide the critical breakthrough at Petersburg. A mine would be dug under the Confederate lines, then 320 kegs of gunpowder, totalling four tons would be detonated, creating a vast breach through which Union troops could storm into the Rebel city. The plan seemed good enough, the only problem, however was its execution. Instead of charging around the massive crater, Union field commanders led their troops straight into it. Once within the crater, to their horror, they found they could not scale the shear wall in front of them. Confederate troops, now recovered from their momentary stunned state rushed to the edge of the crater and poured a hellish fire into the floundering Union troops below. To the Confederates it became known as the great "Turkey Shoot". The Union lost a staggering 4000 men. Ulysses S. Grant was deeply shocked, pronouncing it "the saddest affair I have ever witnessed in the war". General Burnside was relieved of command permanently. General Ledlie was dismissed from the army.

One of our best strategies for the delivery of anaesthesia in the Emergency Department is the technique of the Bier's block. But we need be mindful of the lessons learnt of the Crater of Petersburg. Whilst the plan may be sound enough in theory, the utmost care must be observed in its execution!

General Ambrose Burnside, July 1864.

LOCAL ANAESTHETIC AGENTS TOXICITY

Introduction

Toxicity caused by **local anaesthetic agents** is usually the result of therapeutic errors.

These errors include those relating to dosing, route of administration and technique.

Toxicity is predominantly **neurologica**l and **cardiac** and can **be life-threatening**.

Initial symptoms are usually neurological unless there has been a large intravenous bolus where cardiac arrhythmia or arrest may be the first manifestation of toxicity.

Treatment is supportive, but there is also some evidence for the role of **lipid emulsion therapy** in the management of life-threatening cases.

See also separate documents on:

- **Lipid Emulsion Therapy (in Drugs folder)**
- **Methaemoglobinemia (in Toxicology folder)**
- **Sodium Bicarbonate (in Toxicology folder)**

Preparations

Local anesthetics in current use in Australia include:

- Amethocaine
- Benzocaine
- Bupivacaine
- Levobupivacaine
- Lignocaine
- Mepivacaine
- Prilocaine
- Ropivacaine.

Toxicology

Local anaesthetic agents bind **reversibly** to the **fast sodium channels** and so inhibit the propagation of action potentials.

Toxic effects are manifested predominantly as neurological and cardiac symptoms.

Bupivacaine has the most cardiac toxicity due to its prolonged binding to myocardial tissue.

Some agents may also induce **methaemoglobinemia**, in particular:

- Benzocaine.
- Lignocaine
- Prilocaine.

Pharmacokinetics

Absorption

- Amide anaesthetics are administered by the topical, parenteral, epidural or intra-thecal routes.

  Oral administration is subject to extensive first pass metabolism and so toxicity is rare via this route.

- Toxic effects are related to peak blood levels of the agent

  Peak blood levels will be influenced by:

  - ♥ Route of administration
  - ♥ Rate of administration
  - ♥ Total dose
  - ♥ Location of administration
  - ♥ Presence (or absence) of tourniquets
  - ♥ Local blood flow

Some preparations contain adrenaline which slow the rate of absorption from subcutaneous and muscular sites of administration and so prolong the action of the agent

Distribution

- The amide local anaesthetics have small volumes of distribution

Metabolism and excretion

- The amide local anaesthetics are extensively metabolized in the liver.
- Elimination half lives are around 2 hours for most agents, but somewhat longer for bupivacaine.

Risk Assessment

1. Early neurological symptoms are an important clue to toxicity

3. Maximum doses are listed below, but toxicity may occur with lower doses depending on how the agent is administered, such as direct intravenous or intra-arterial.

   Slightly higher doses are safe when given with adrenaline as subcutaneous or muscular infiltration.

Local anaesthetic	Maximum dose (mg/kg)
Bupivacaine	2.5 mg/kg
Lignocaine	5 mg/kg
Mepivacaine	5 mg/kg
Prilocaine	7 mg/kg
Ropivacaine.	3 mg/kg

4. Methemaglobinemia is not dose related. It is an idiosyncratic reaction.

5. Bupivicaine is especially cardiotoxic, due to prolonged binding to myocardial tissue.

6. Ingestion does not usually result in toxicity, because of extensive first past metabolism.

   Ingestions of lignocaine containing topical preparations of < 6mg/kg by children are safe, but larger doses than this may cause toxicity.

Clinical Features

Initial symptoms are usually neurological unless there has been a large intravenous bolus where cardiac arrhythmia or arrest may be the first manifestation of toxicity.

Onset of symptoms is usually rapid.

1. Early neurological symptoms include:
    - Dizziness
    - Anxiety/ agitation / confusion
    - Peri-oral parasthesia or numbness.
    - Tinnitus

More severe toxicity will produce cardiac and more serious neurological symptoms:

2. CNS:
    - Seizures
    - Coma
3. CVS:
    - Bradycardia
    - Hypotension
    - Arrhythmias, which may be lethal VT/ VF or asystole.
4. Respiratory:
    - Respiratory depression/ apnea
5. Methaemoglobinaemia:
    - It manifests as cyanosis and the signs of hypoxia
    - See also separate guidelines on Methaemoglobinaemia

Investigations

1. ABG co-oximetry:

- If methaemoglobinaemia is suspected.

2. ECG:

   - Serial ECGs for evidence of sodium channel blockade:
     - ♥ Prolongation of the PR interval
     - ♥ Prolongation of the QRS interval
     - ♥ Large terminal R wave in aVR.

Management

1. Immediate attention to ABC according to standard protocols.

   - IV access

2. Seizures:

   - These should be treated with IV benzodiazepines

3. Hypotension:

   - Treat with IV fluids
   - Inotropes may be used as necessary

4. Specific antidotes:

   Sodium bicarbonate:

   Ventricular arrhythmias:

   - These should be treated with **sodium bicarbonate** as for other class I fast sodium channel blocking induced ventricular arrhythmias

     Give 100 mmols IV, and repeat every 1- 2 minutes as required until restoration of a perfusing rhythm is achieved.

   Lipid emulsion therapy:

   - This can be used for cardiovascular collapse and arrhythmias refractory to standard measures and sodium bicarbonate.

     It is currently unclear whether this treatment should be considered as “first line” and ongoing trials are currently in progress to help determine this.

See also separate document on Lipid emulsion therapy (in Drugs folder)

Methylene blue:

- This is used to treat symptomatic methaemoglobinemia.

See also separate document on methaemoglobinemia (in Toxicology folder).

Disposition

The development of any neurological symptoms during or shortly after administration of a local anaesthetic agent indicates early toxicity and the patient should be closely and monitored in a resuscitation area.

"……Few officers can be found this evening who have not drowned their sorrows in the flowing bowl".

Washington Roebling

References:

1. Local anaesthetic agents in: L Murray et al. Toxicology Handbook 3rd ed 2015.

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