Buffered Local Anesthesia

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Local Anesthetic Drawbacks

- Patient concerns
  - "needle pinch in mouth" → single stick or multiple
  - anxiety, pain, & burning on injection
- Clinical concerns
  - local anesthesia onset
  - pH of local anesthesia in carpule
  - pH of tissue bed
  - identification of landmarks for injections
  - post injection tissue reactions
  - implications of vasoconstrictor

Local Anesthesia → pH

- Vasoconstrictor in local anesthetic
  - pH is similar to pH of lemon juice → 3.5
  - low pH needed to preserve epinephrine
- Injections into oral mucosa
  - painful → burning or stinging
  - post treatment soreness in tissue bed not uncommon
  - acidic local anesthetic → activates acid sensing ion channels in soft tissue
    - ASIC (acid sensing ion channels)
    - noiceceptive channels → pain

Local Anesthetics Chemistry

- Local anesthesia equilibrium → 2 molecules
  - cation charged molecule → RNH+
  - uncharged base molecule → RN
  - RN + H+ $\rightleftharpoons$ RNH+
  - amount of charged & uncharged molecule depends on Henderson – Hasselbalch equation , pH , and pKa
- Lidocaine at pH of 3.5
  - 99.996% molecules → RNH+
  - 0.004% molecules → RN

Local Anesthesia Diffusion

- lipid soluble (RN) diffuses across membrane into nerve
  - greater the RN concentration outside the nerve → more RN to diffuse across the membrane
- in axoplasm → RN reacts with H+ to form RNH+
  - RN + H+ ⟷ RNH+
  - RNH+ binds to Na channels to block nerve transmission

Local Anesthesia Diffusion

- body must buffer local anesthesia to be effective
  - pH of local = 3.5
  - body buffers to physiologic range of 7.35 to 7.4
  - now have more uncharged RN base to diffuse across membrane
- physiologic buffering time determines
  - onset of local anesthesia

Buffered Local Anesthesia

- Buffered local anesthesia common in medicine
  - less pain on injection → especially skin
  - used in eye surgery, ENT, & dermatology
- Add sodium bicarbonate to local anesthesia
  - NaHCO3
  - added just before inject local anesthesia
  - ratios of LA to bicarb
    - 3:1, 5:1, 6:1, 10:1, & 30:1
  - ratios of 5:1 to 10:1 seem most effective

J Derm Surg Oncol. 1990; 16: 842 Ear Nose Throat J. 1992;71:405
South Med J 1994;87:225

Dental Buffered Local

- Potential Benefits
  - Decreased pain on injection
  - Decreased onset time in normal tissues
  - More effective local anesthesia in infected tissues
  - Possible more profound local anesthesia in normal tissue
  - Potential to decrease patient's anxiety to injection
    - less pain on injection
    - some claim " pain free injections" start to finish
  - Potential for less down chair time → faster onset = faster start times

Buffered Dental Anesthetics

- Lidocaine is most studied
  - 2 commercially available buffering systems for lidocaine
    - Onpharma
    - Anutra
- Add $NaHCO_3$ to lidocaine
  - trying to raise pH in carpule to ~ 7.4
  - get a 6000 fold increase in amount of RN base
  - should result in more rapid onset of local, less pain on injection, and less post injection discomfort

pH & RN concentrations

pH	Lidocaine pKa = 7.9	Articaine pKa = 7.8	Mepivacaine pKa = 7.6	Bupivacaine pKa = 8.1
7.4	24.03%	28.47%	38.69%	16.63%
3.5 Epinephrine	0.004%	0.005%	0.008%	0.003%
6.5	3.83%	4.77%	7.36%	2.45%

- As pH & pKa approach physiologic pH of 7.4
  - get more RN to diffuse across nerve membrane
  - mepivacaine would have fastest onset buffered or not buffered

Malamed. Local Anesthesia

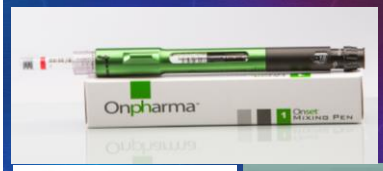
Carbon Dioxide

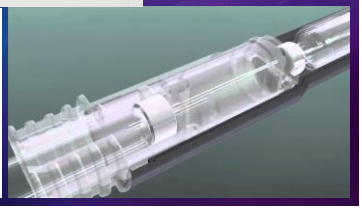
- $NaHCO_3$ + Acidic local → H_2O + CO_2
- CO_2 will diffuse through tissues when injected
  - has independent direct anesthetic effect on nerve
  - causes ion trapping in axoplasm → carbon dioxide diffuses into the axoplasm
    - CO_2 + H_2O ⟷ H_2CO_3 (carbonic acid) which causes free base NH to ionize to RNH+
    - RNH+ binds to Na channels inside the nerve & are now trapped inside the nerve

Catchlove. J Pharmacol Exp Ther. 1972;181:298
Condouris. Nature. 1964;204:57

Buffering Systems

Onpharma Buffering System





Onpharma Buffering System

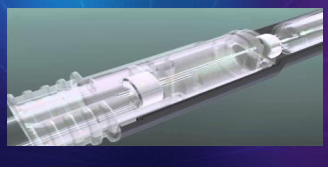
- Components
  - non sterile mixing pen → disposable 1.7 ml sodium bicarb (8.4%) cartridge & volume dial to dispense bicarb
  - sterile cartridge connector → attaches to mixing pen
    - has 2 needles → one adds bicarb to local carpule while other discards same amount of local into connector reservoir
  - add local anesthetic carpule to other end of cartridge connector

Onpharma Buffering System

- Mixing Pen Volume Dial (Black Dial)
  - lidocaine IAN block → dial set at 18 (0.18 ml)
  - lidocaine infiltrations → set at 9 (0.09 ml)
  - all other local anesthetics → set at 9 (0.09 ml)
    - IAN Blocks & Infiltrations
    - Bupivacaine → Onpharma does not recommend buffering

Onpharma Buffering System

- Cartridge Connector → sterile component
  - change cartridge connector each time you replace sodium bicarbonate cartridge
    - sodium bicarb cartridge → 5 day shelf life
  - company says cartridge will buffer → 16 to 20 carpules of local anesthesia
    - my calculations → 9 to 18 carpules



1.7 / 0 .18 = 9 carpules
1.7 / 0.09 = 18 carpules

Company communication

Onpharma Buffering System

- Don't premix the solution
  - buffer local anesthetic as needed
  - actual mixing takes 1 to 2 seconds in cartridge connector
- Consistent final pH 7.35 to 7.5

- pH of 3.9
  - 1 molecule of RN → 10,000 molecules LA
  - no diffusion across nerve membrane
- pH of 7.4
  - 1 molecule of RN for every 4 molecules RNH+
  - 2500 times more active form of LA

Onpharma Company Data

Anutra Buffering System

Anutra Buffering System

- 3 Components to system
  - Dispensing Unit → non sterile unit containing buffering cassette and medications
    - 50 ml multi dose vial 2% lidocaine 1:100,000 Epi
    - 10 ml prefilled syringe 8.4% sodium bicarbonate
  - Anutra cassette → sterile unit to dispense lidocaine + sodium bicarbonate buffered solution
  - Anutra syringe → sterile, single use syringe
    - 5 ml capacity

Anutra Cassette

- Holds lidocaine and bicarb
- 0.2 micron hydrophobic filter to prevent contamination
- Can buffer up to 50 ml lidocaine

Anutra Buffering System

- Need to prime unit once a day
  - draw up 1 ml of buffered local in syringe & discard
- Anutra cassette
  - 7 day self life
    - after 7 days replace cassette, bicarb, and LA
  - using a 10:1 ratio of local anesthesia to bicarbonate
    - adding 0.10 ml of bicarbonate
    - get total volume of 1 ml of buffered 2% lidocaine with 1:100,00 Epi
  - at end of 1 week, if used all 50 ml of local → still bicarb left in bicarb syringe

Anutra Buffering System

- Anutra Syringe → size similar to typical dental syringe
- Company Claims → buffered local can act as topical agent
  - CO_2 dissolved in buffered solution = "CO_2 bubble"
  - acts as immediate analgesic – anesthetic agent
  - add 1 to 2 drops on dry mucosa as a topical
  - inject after 5 to 10 seconds

Buffering by Hand

- Common buffering ratio is 10:1
- Use TB syringes
  - 1st syringe → discard 0.18 ml of lidocaine from dental carpule
  - 2nd syringe → draw up 0.18 ml 8.4% sodium bicarbonate from multi dose vial
    - inject this into the lidocaine dental carpule
    - use immediately

Local Anesthesia Buffering Data

- Inferior Alveolar Nerve Blocks
  - Onset time for pulpal anesthesia
    - Buffered LA → 71% patients onset in 2 minutes
    - Average Buffered Onset → 1.51 minutes
    - Non buffered LA → 12% patients onset in 2 min.
    - Averaged Non Buffered Onset → 6.37 minutes
  - Pain on injection
    - Buffered LA → 44% pain free injection
    - Non Buffered LA → 6% pain free injection

Malamed. Compendium Cont Ed. 2013; 34(2)

Local Anesthesia Buffering Data

Local Anesthetic	pH Carpule	Hand Buffered pH	Onpharma Buffered pH
2% lidocaine 1:100,000 Epi	4.27	6.96	7.10
4% articaine 1:100,000 Epi	3.62	6.87	6.97
4% prilocaine 1:200,000 Epi	3.60	6.80	6.92
4% prilocaine plain	6.31	6.91	7.05
3% mepivacaine	6.37	7.02	7.01

- Hand buffering is an effective technique
- Plain LA → less of response to buffering
- Use buffered agents soon after mixing
  - avoids precipitates

Goodchild. Compendium Cont Ed. 2016;37(5)

Systematic Review of Buffering

- Injection Pain
  - Skin Injections → buffering will decrease injection pain
  - Mucosal or Penile Blocks → review shows little to no effect on injection pain
- International Endodontic Journal
  - The effect of adjusting the pH of local anaesthetics in dentistry: a systematic review and meta-analysis
    - 2018 doi:10.1111/iej.12899

Systematic Review of Buffering

- Onset time for local anesthesia
  - Infiltrations of LA in normal tissue → onset time was not decreased
    - buffering capacity of body will increase pH of local anesthetic rapidly enough to make additional buffering clinically ineffective
  - Inferior alveolar nerve blocks → onset time was decreased by → 1.26 minutes
  - Infiltrations in inflamed tissues → onset time was decreased by → 1.37 minutes

International Endodontic Journal 2018

Summary of Buffering

- Articles will support the position you want
- Onset time
  - decreased in infected tissues and IAN blocks
- Decreased pain on injection
  - subjective or objective ???
- Decreased patient pain & anxiety over needle
  - subjective or objective ????
- Costs of buffering
- Less wasted time → More production ???
- No apparent harm to patient → simple to use

Thank you