WHAT'S NEW IN ANESTHESIA/ ANALGESIA?

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PLAN?

• Introduce new products
• Introduce new ways to use established products

ANALGESICS

CLASSIC 3-NEURON CHAIN MODEL OF NOCICEPTIVE PROCESSING (SOMATIC)
CENTRAL SENSITIZATION / WIND-UP

- Dorsal horn of the spinal cord
- Extreme or repeated activation
- Mediated by glutamate
- Results in:
  - Decreased threshold
  - Expansion of receptive field
  - Increased spontaneous firing
  - Hyperalgesia/hyperesthesia
  - Spontaneous pain

PERCEPTION

- Must reach cortex to be perceived as pain
- If patient is unconscious or anesthetized, they won’t “feel” pain but the entire pathway may be activated
- When consciousness returns, pain pathway will be in full activation
  - With less descending modulation

LOCAL ANESTHETICS

- Mechanism of action
  - Sodium channels propagate action potential
  - Local anesthetics block sodium channels
- Routes of administration
  - Perineural
  - IV
  - Dermal
- Species Differences
  - Sensitivity to toxicity
LOCAL ANESTHETIC UPDATES: LIDOCAINE PATCHES

- Lidocaine Patches
  - Little to no systemic absorption (dogs/cats)
  - CAN be cut to size/area wanted
  - Should be replaced daily
  - Potential uses
    - IVDD, bone pain, inflammatory

LOCAL ANESTHETIC UPDATES: LIDOCAINE CRI IN DOGS

- IV lidocaine in DOGS
- Systemic analgesia
- Antiinflammatory
- GI Prokinetic

Dose of IV lidocaine in dogs:
- Loading: 1.0 mg/kg
- CRI: 25 mcg/kg/min

LOCAL ANESTHETIC UPDATE: NOCITA

- Long-acting local anesthetic
  - Extended-release liposome technology
  - Multivesicular liposomes
  - 72 hr duration
  - Labeled for dogs following CCL surgery
  - Usage
    - 1.3 mg/kg (0.4 mL/kg)
    - Infiltration injection into the tissue layers
    - At the time of incisional closure
  - Very effective
  - Expensive
  - Short shelf life once opened

LOCAL ANESTHETIC UPDATE: NOCITA

- Off-label use
  - Amputations
  - Orthopedics (besides CCL)
  - Soft tissue procedures
  - Cats
  - Caution!
    - Infected wounds
    - Patients with immune disturbances

NMDA ANTAGONISTS

DISSOCIATIVE ANESTHETICS

- NMDA (N-methyl-D-aspartate) antagonists
  - NMDA receptors are excitatory receptors

- Dissociative anesthetic
  - Ketamine (part of the combination Telazol)
  - Ketamine (as an anesthetic dose)
  - Amantadine (as an anesthetic dose)
  - Analgesic role in anesthetic doses
  - Ketamine
    - Approved for use in cats and dogs
  - Telazol (part of the combination Telazol)
    - ketamine approved for use in cats and dogs
**NMDA RECEPTOR ANTAGONISTS**

- **Dorsal horn of spinal cord**
  - Opioid receptors
  - Alpha-2 receptors
  - NMDA receptors

- **Central sensitization**
  - Wind-up pain

**NMDA ANTAGONISTS**

- **Mechanism of action**
  - Antagonize activation of NMDA receptor with glutamate at dorsal horn of spinal cord
  - With extended inactivation can interrupt central sensitization
  - >24 hr (days? weeks?)
  - Ketamine, amantadine

- **Chronic pain/ wounds/ burns**
- **Amputations**

**DISSOCIATIVES: WHAT'S NEW?**

- At least 24 hr CRI needed to "break" wind-up cycle (in humans)
  - Unclear how long dogs/cats
  - Induction dose unlikely enough

- **Injectable ketamine CRI**
  - At least 24 hr is recommended to alter/ prevent windup

- **Oral amantadine**
  - At least 2-3 week trial
  - Can use with NMDA glutamatergic agents

**Ketamine: side effects**

- Anesthetic doses
  - Single kg induction dose
  - Increased CV work
  - Life-threatening behavioral effects

- Analgesic doses—few side effects
  - 5-10 mg/kg PO (animal)

**Amantadine side effects**

- Not reported
  - 3 mg/kg PO (animal)

**CALCIUM CHANNEL BLOCKERS**
CALCIUM CHANNEL BLOCKERS

**GABAPENTIN**

- **Mechanism of action**
  - Binds α₂δ-subunit-voltage gated calcium channels
  - Upregulated in pain states
  - May (?) interacts with NMDA receptors, protein kinase C, inflammatory cytokines

- **Side effects**
  - Somnolence
  - Decreases with time
  - Humans
  - Rapid withdrawal associated with seizure risk

- **Species Differences**
  - Administered in many species
  - Little adverse effects
  - Unknown dosing ideals

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TRPV1 RECEPTOR AGONISTS

- **Mechanism of Action**
  - Calcium channels
  - Activated by
    - Heat
    - H⁺
    - Capsaicin
    - Resiniferatoxin (RTX)
  - More on c-fibers (?)
  - “Burning, itching, stinging” sensation
  - Activate then desensitize nerve

- **Side effects**
  - First must “activate” then desensitize receptor
  - Tingling up to pain
  - Some treatments require anesthesia

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ANESTHETICS
NEUROSTEROIDS: ALFAXALONE

• GABA is the primary inhibitory neurotransmitter
• Binds to specific site on GABA receptor
  – GABA enhancer/agonist
• Structurally similar to steroids
  – Does not bind to sex hormone, glucocorticoid or mineralocorticoid receptors

ALFAXALONE: DOSE AND SAFETY

DOGS

||< 6 mg/kg IV
| ≥ 10 weeks age
| C-sections
| Safety at 10 x dose

CATS

||< 6 mg/kg IV
| ≥ 4 weeks age
| C-sections
| Safety with 5x dose

NEUROSTEROIDS & VETERINARY MEDICINE

• Saffan
  – alfaxalone and alfadolone (3:1)
  – Clinical trials and marketed in UK
  – Hard to dissolve in water-based solutions
  • Solubilized in Cremophor
  • Reports from 1974 & 1980
  • Allergic reactions (69% of cats!)
    – Ear swelling to anaphylaxis
    • Many dogs died from anaphylaxis

ALFAXALONE

ALFAXALONE: NEUROSTEROID STRUCTURE

PROGESTERONE

ALFAXALONE

ALFAXAN® ALFAXALONE

• Alfaxalone only
  – Difficult to dissolve in water-based solution
• Cyclodextrin ring
  – Water soluble delivery
• Approved in USA
  – Scheduled IV uncontrolled drug (SIV)
  – Labeled for dogs and cats, IV use
• Clear solution
  – 6 hr once opened

ALFAXAN® ALFAXALONE
ALFAXALONE: PHYSIOLOGIC EFFECTS

- CV
  - CV depression similar or better than propofol
- Respiratory
  - Depression to apnea
- Analgesia
  - No analgesia
- Metabolism
  - Liver metabolism

ALFAXALONE: MISCELLANEOUS

- Induction and recovery not as smooth as propofol
  - Particularly as a solo agent
- Head bob, uncoordinated gait
- Does not cause tissue reaction if administered outside of vein or SQ
  - Product literature and Heit 2004
- Can use as a CRI (constant rate infusion)
- More expensive than propofol in USA

ALFAXALONE: WHAT'S NEW?

- Off-label Use
  - IM administration for sedation
  - Not labeled for in USA, but is in Australia
  - Volatile anesthetic sparing factor
  - Dose
    - Dogs: ~1 mg/kg (with opioid or midazolam)
    - Cats: ~1-2 mg/kg (with opioid or midazolam)
- Indication
  - e.g. Fractious animal with CV disease
  - e.g. Feline atrial defibrillation/defibrillator

ALFAXALONE: WHAT'S NEW?

- Off-label, published, use in other species
  - Ferrets
  - Rabbits
  - Turtles
  - Reptiles
  - Fish by immersion

QUESTIONS ON ALFAXALONE?

ETOMIDATE
ETOMIDATE

- Ultrashort non-barbiturate (imidazole compound)
  - Introduced in human anesthesia 1972
  - Not approved for use in veterinary species
- Not scheduled in USA
- Propylene glycol vehicle (35%)
  - Long shelf life
  - Pain on injection
  - Can cause hemolysis with CRI

CV
- NO CV EFFECTS
- HR, RSP, CO

CNS Effects
- GABA enhancer
- Respiratory
- Muscarinic depression
- Metabolism
  - Liver metabolism (+ propylene glycol)
  - Decreases adrenal gland hormones

ETOMIDATE: ENDOCRINE EFFECTS

- Decreased adrenocortical activity
  - lasts 2 - 6 hr
- Inhibits 11-B hydroxylase
  - cholesterol to cortisol
- Decreased adrenal stress response
- Multiple doses / CRI
  - Hypoadrenocorticism
  - +/- death (dogs and humans)

ETOMIDATE: MISCELLANEOUS

- Poor muscle relaxation
  - Plausible rigidity, myoclonus, vocalization, opisthotonus
  - Administer with muscle relaxant (e.g. benzodiazepine)
- Emesis
- Expensive (2015) (~ $5/ml)
  - 4kg cat ~ $12.00
  - 40kg dog ~ $100.00

WHAT'S NEW: ETOMIDATE?

- Available
- Non scheduled
- Fills particular patient needs

QUESTIONS?