COMPOUNDED MEDICATION OPTIONS FOR WOUND CARE
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OBJECTIVES
- Learn about the process of wound healing
- What factors impair wound healing
- How can compounding pharmacists help patients with wounds
- What medications could be considered
- What base or vehicle is most appropriate to use
- How to put it all together for individual patient needs!

PROCESS OF WOUND HEALING
- Wound = barrier of skin is breached
  - Vasoconstriction (limit blood loss)
  - Fibrin and platelets (plugs or clots)

- 3 phases of wound healing
  - Inflammation
  - Proliferation
  - Wound maturation or remodeling
INFLAMMATION PHASE

- Cell migration
- Release of pro-inflammatory mediators
  - Histamine, prostaglandins, leukotrienes
- Promote vasodilation
- Remove debris
- Destroy microscopic pathogens
- Normal length is 2-4 days


CELL PROLIFERATION PHASE

- Fibroblasts and epithelial cells make and release extracellular matrix (ECM) proteins and proteoglycans
- Re-epithelialization occurs
- Formation of granulation tissue
- Scar formation ends this phase
- Weeks to months

REMODELING PHASE

- Granulation tissue replaced by more ECM proteins
- Scar formation
- Tissue becomes more pliant and soft
- Healed tissue formed during this phase
  - Functional but not as durable
  - Maximum strength determined by interconnection of collagen subunits

参考文献:

IMPAIRMENT OF WOUND HEALING

- Impaired blood circulation
  - Peripheral artery disease
  - Chronic venous insufficiency
- Diabetes
  - Vascular changes
  - Neuropathy
  - Immune system changes
- Elderly
  - Loss of collagen
- Immunocompromised
  - Including corticosteroids
  - Neuropathy
  - Spinal cord injury
  - Cancer therapy
  - Malnutrition
  - Infection
  - Smoking

参考文献:
Armstrong DG, Meyr AJ. "Wound healing and the chronic wound healing patient." UpToDate. 19.2:June 16, 2011

WHAT IS COMPOUNDING?

- Compounding is the method of preparing customized medications to help meet unique physician and patient needs.
- In Washington state, all compounded medications require a prescription

参考文献:
ADVANTAGES OF COMPOUNDED TOPICAL MEDICATIONS

- Little to no side effects (compared to oral)
- Largely avoid potential drug-drug interactions
- Dosage form specific to patient’s needs
  - Combine medications
  - Avoidance of dyes, preservatives, fillers
  - Dosage form easier to administer
  - Provide medications not commercially available
    - Unique dosage forms
    - Cost-effective therapy

WHAT DRUGS TO USE?

- Most common active ingredients:
  - Phenytoin
  - Misoprostol
  - Metronidazole
  - Lidocaine or Bupivacaine
  - Pentoxifylline
  - Nifedipine
  - Sucralfate
  - Hyaluronic acid
**PHENYTOIN**
- Anticonvulsant with classic oral side effect is gingival hyperplasia
- Stimulates fibroblast proliferation
- Enhances tissue granulation
- Inhibits collagenase activity and promotes collagen deposition
- Decreases bacterial contamination
- Reduces wound exudate production
- Powder form may cause burning when first applied
  - Phenytoin Sodium = burning!
- Phenytoin 2% cream
  - Easier to apply and less burning

**PHENYTOIN (CONT.)**
- Useful for many types of wounds:
  - Traumatic wounds
  - Burns
  - Diabetic ulcers
  - Venous stasis ulcers
  - Abscesses
  - Periodontal lesions
  - Chronic wounds

**PHENYTOIN (STUDIES)**
  - Reduction in ulcer size
  - Appearance of healthy granulated tissue
  - Reduction of wound exudate
  - Overall significantly shorter healing time
  - No adverse events or interactions
  - No detectable phenytoin serum levels
PHENYTOIN (STUDIES)

  - Decreased inflammation
  - Decreased bacterial colonies
  - Enhanced vascularization
  - Enhanced collagen deposition
  - Enhanced fibroblast proliferation

  - Half had negative cultures by day 7
  - 72.5% completely healed by week 4

  - Reviewed 14 RCT, suggest “may be” a positive effect on wound healing in a variety of wounds.

PHENYTOIN (REFERENCES)


MISOPROSTOL

- Synthetic prostaglandin (E1) that accelerates wound healing
- Replaces endogenous prostaglandins
- Used for ulcerative wounds and mouth sores (radiation burns)
- Cytoprotectant
- Reduced bacterial infections in mice following a burn injury
- Numerous case studies
- Misoprostol 0.0024% cream

MISOPROSTOL (CONT)

  - 5 mcg sprayed to wound daily x 3 weeks
  - Results: Decrease in healing time of acute wounds in rats.

METRONIDAZOLE

- Eliminates anaerobic bacteria
- Useful in wounds with foul odor, redness of surrounding tissue or necrosis of wound
- Other antibiotics used topically in wound care:
  - Gentamicin
  - Ciprofloxacin
PAIN CONTROL

> Factors that contribute to pain:
  > Ischemia, infection, breakdown of surrounding skin
  > Topical local anesthetics
  > Lidocaine (Intermediate duration – TID dosing)
  > Bupivicaine (Longer duration of action – BID dosing)

> Topical opioids
  > Morphine
  > Methadone

PENTOXIFYLLINE

> Phosphodiesterase inhibiting drug = reduced blood viscosity
  > Enhances vascular permeability
  > Improved rate of healing at 10% with calcium channel blocker.
  > May be acting as penetration enhancer
  > May improve circulation

CALCIUM CHANNEL BLOCKERS

> Blocks calcium influx into smooth muscles, decreasing vascular tone and increasing blood flow
  > Hasten wound healing—increased blood flow
  > Reduce scar formation—reduce production of collagen & proteoglycans
  > No adverse effects
CALCIUM CHANNEL BLOCKER (CONT)

- Nifedipine 2.8% Lipoderm BID
  - Causes smooth muscle relaxation, therefore, increased blood flow and vascularization
- Successfully treat anal fissures
- Diabetic foot ulcers
- Limbs post surgery

SUCRALFATE

- Inhibits inflammatory cytokine release and stimulates angiogenesis
- Sucralfate 7% ointment—second-degree burns
  - Faster epithelialization vs. silver sulfadiazine
  - Faster development of granulation tissue
- Sucralfate enema 10% BID—radiation-induced proctitis
  - Significantly reduce bleeding
- No side effects
- No increase in serum aluminum

HYALURONIC ACID

- Produced in high quantities during proliferation phase of wound healing
- Provides structural support to wound
- Speed wound healing in chronic venous leg ulcers and animal models
- Topical cream may protect newly formed granulation tissue from oxidative damage
WHAT BASE TO USE?

- **Creams**
  - Moisturizing
  - Protection of wound bed
  - Ease of removal in dressing changes

- **Pluronic gels, Carbomol gel, Versabase gel**
  - Protection of wound bed
  - Pluronic can be poured into the wound
  - Ease of removal in dressing changes
  - No oil – can be used at radiation site

- **Polyox bandage**
  - Powder base that gels when exposed to moisture
  - Adheres to oral tissue or wounds with high drainage (breast cancer wounds)

- **Ointment**
  - Protect surrounding tissue, esp. when exposed to moisture such as urine, feces, or other body fluids

FAVORITE FORMULAS

<table>
<thead>
<tr>
<th>Wound Type</th>
<th>Medication</th>
<th>Base Choices – pick the best base</th>
</tr>
</thead>
<tbody>
<tr>
<td>No odor -- No pain</td>
<td>Phenytoin 5%, Misoprostol 0.0024%</td>
<td>Emollient Cream or Pluronic Gel</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Very hydrating</td>
</tr>
<tr>
<td>2nd – No pain</td>
<td>Phenytoin 5%, Misoprostol 0.0024%</td>
<td>Protective Barrier Ointment</td>
</tr>
<tr>
<td></td>
<td>Metronidazole 2%</td>
<td>Zinc oxide/Aquaphor 1:1</td>
</tr>
<tr>
<td>No odor – Pain</td>
<td>Phenytoin 5%, Misoprostol 0.0024%</td>
<td>Good for areas with fistulas and drainage</td>
</tr>
<tr>
<td></td>
<td>Lidocaine 4%</td>
<td></td>
</tr>
<tr>
<td>2nd – Pain</td>
<td>Phenytoin 5%, Misoprostol 0.0024%</td>
<td>Polyox Bandage</td>
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<tr>
<td></td>
<td>Lidocaine 4%</td>
<td>Good for high draining wounds</td>
</tr>
<tr>
<td></td>
<td>Metronidazole 2%</td>
<td>Good for oral protection and healing</td>
</tr>
</tbody>
</table>

If local circulation is poor add nifedipine 0.2% - 10%

FAVORITE FORMULAS (CONT)

- **Decubitis ulcer**
  - Ketoprofen 2%, Lidocaine 2%, Misoprostol 0.0024%, Phenytoin 2%, Aloe vera 1.2% emollient cream
  - Metronidazole 2%, Lidocaine HCl 2%, Misoprostol 0.0024% cream
  - Phenytoin 5% paste
  - Phenytoin 5%, Misoprostol 0.0024% Gel

- **Odorous weeping wound**
  - Metronidazole 20%, Lidocaine 1% Poly Ox bandage
FAVORITE FORMULAS (CONT.)

- **Treatment of wounds without infection:**
  - Phenytoin 5% / Misoprostol 0.0024% Topical Gel
  - Phenytoin 2% / Misoprostol 0.0024% / Lidocaine 2% / Bupivacaine HCl 0.2% / Diphenhydramine HCl 1% / Aloe Vera 0.2% Polyox Bandage
  - Ketoprofen 2% / Lidocaine 2% / Misoprostol 0.0024% / Phenytoin 2% / Aloe Vera 0.2% Topical Cream

- **Treatment of infected wounds:**
  - Misoprostol 0.0024% / Phenytoin 5% / Metronidazole 2% Topical Gel
  - Misoprostol 0.0024% / Phenytoin 5% / Gentamicin 0.2% Topical Gel

- **Treatment of wounds with pain:**
  - Morphine sulfate 1mg/mL Topical Gel

QUESTIONS?

Just keep swimming! Just keep swimming!

Thank you!