VHL patients may have multiple causes of pain, it is important to use a regiment that treats multiple causes, not just one. This is a summary of different drug classes and considerations, for example regarding kidney health, that may be especially important for VHL patients.

<table>
<thead>
<tr>
<th>Class of drug</th>
<th>Example</th>
<th>Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioids</td>
<td>Hydrocodone, fentanyl</td>
<td>Require good liver and kidney function; can cause dependence (addiction)</td>
</tr>
<tr>
<td>NSAIDs</td>
<td>Ibuprofen (Advil, Motrin)</td>
<td>Can cause kidney injury</td>
</tr>
<tr>
<td>Anticonvulsants</td>
<td>Gabapentin</td>
<td>Must decrease dose in patients with kidney problems</td>
</tr>
<tr>
<td>Acetaminophen</td>
<td>(Tylenol)</td>
<td>Unclear how much is “safe” for a patient in liver failure</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>Duloxetine (Cymbalta)</td>
<td>Often an off-label treatment for pain</td>
</tr>
<tr>
<td>Muscle Relaxants</td>
<td>Baclofen, cyclobenzaprine (Flexeril)</td>
<td>Can be especially helpful post-surgery</td>
</tr>
</tbody>
</table>

Non-pharmacological therapies such as physical therapy, aqua therapy, acupuncture, and others may also be good options. Talk with your care team to see what portfolio of therapies might be best for you.
Von Hippel-Lindau Syndrome and Chronic Pain

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Goals

• Understand how Von Hippel-Lindau Syndrome causes chronic pain
• Understand treatments for chronic pain

Chronic Pain

• Chronic pain is defined as pain that lasts >3 months or past the time of normal tissue healing
• Chronic pain may be the result of underlying medical condition, injury, inflammation, medical treatment, etc.
• Chronic pain often has multiple generators

How does Von Hippel-Lindau Syndrome cause chronic pain?

• Von Hippel-Lindau Syndrome leads to the formation of tumors or cysts throughout the body
• Locations can include eyes, brain, spinal cord, kidneys, pancreas, uterus
How does Von Hippel-Lindau Syndrome cause chronic pain?

- Nociceptive pain
  - Pain caused by release of inflammatory substances from tissue damage
- Neuropathic pain
  - Pain caused by nerve damage

Interventions can also lead to chronic pain
- Surgery
- Radiation therapy

Treatments for Chronic Pain

- Multiple pain generators usually mean that chronic pain is better treated with medications from different classes
- What are examples of these medications?

Opioid therapy
- Codeine
- Fentanyl
- Hydrocodone
- Hydromorphone
- Meperidine
- Methadone
- Morphine
- Oxycodone
- Tramadol
Treatments for Chronic Pain

- **NSAIDs**
  - Celecoxib (Celebrex)
  - Diclofenac (Voltaren)
  - Etodolac (Lodine)
  - Ibuprofen (Motrin, Advil)
  - Indomethacin
  - Ketorolac (Toradol)
  - Meloxicam (Mobic)
  - Naproxen (Aleve)
- **Acetaminophen**

- **Anticonvulsants**
  - Gabapentin (Neurontin)
  - Pregabalin (Lyrica)
  - Carbamazepine

- **Antidepressants**
  - Duloxetine (Cymbalta)
  - Tricyclic Antidepressants (TCA)
    - Amitriptyline
    - Nortriptyline
    - Desipramine

Treatments for Chronic Pain

- **Skeletal Muscle Relaxants**
  - Baclofen
  - Cyclobenzaprine (Flexeril)
  - Methocarbamol (Robaxin)
  - Tizanidine (Xanaflex)
  - Metaxalone (Skelaxin)

- **Nonpharmacologic therapies**
  - Physical therapy or aquatic therapy
  - Pain psychology
    - Biofeedback
    - Cognitive behavioral therapy
  - Acupuncture
  - Pain interventions
    - Nerve blocks
    - Neurolysis
    - Trigger point injections
    - Intrathecal pumps
Opioids

• Widely used family of medications to treat acute and chronic pain
• Highly versatile
  – Short acting or long acting
• May be in combination medications
  – Norco/Vicodin, Percocet all have acetaminophen

Opioids

• Multiple routes of administration
  – Oral
  – Intravenous
  – Intrathecal
  – Epidural
  – Rectal
  – Sublingual
  – Intranasal
  – Buccal
  – Transdermal

Opioids

• Adverse effects
  – Constipation
  – Nausea
  – Pruritus
  – Sedation
  – Respiratory depression
  – Tolerance
  – Dependence

Opioids

• Some opioids depend on good liver and kidney function to work appropriately
• ALL opioids have the potential to cause tolerance and dependence
• ALL opioids can be abused
Opioids
• Minimization of opioids is always ideal to prevent complications
• May achieve this by adding non-opioid treatments
• Caution when using combination opioids (with acetaminophen)

Antidepressants
• Wide variety of medications which have properties of neuropathic pain medication
• These treatments are often off-label

Antidepressants
• Tricyclic antidepressants
  – Examples
    • Amitriptyline
    • Nortriptyline
    • Doxepin
  – Readily available and very effective off-label treatment for neuropathic pain

Antidepressants
– Side effects
  • Dry mouth
  • Blurry vision
  • Drowsiness
  • Tachycardia
  • Urinary retention
  • Orthostatic hypotension
  • Constipation
  • Weight gain
– Avoid in significant cardiovascular disease, glaucoma, symptomatic prostatic hypertrophy, GI dysfunction
Antidepressants

• Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)
  – Duloxetine (Cymbalta)
    • FDA approved for diabetic neuropathy, fibromyalgia, osteoarthritis, chronic back pain
    • Side effects: dizziness, nausea/vomiting, abdominal pain
    • Avoid in severe kidney or liver disease

Anticonvulsants

• Gabapentin
  – Very easy to obtain
  – Most effective if taken three times a day
  – Side effects: somnolence, dizziness, weight gain
  – Must decrease dose in patients with kidney problems

• Pregabalin
  – Similar in mechanism to gabapentin
  – Renal impairment: must decrease dose

NSAIDs

• Highly versatile medications
  – Analgesia
  – Antipyretic
  – Anti-inflammatory
**NSAIDs**
- Short-acting
  - Ibuprofen, ketorolac
- Long-acting
  - Naproxen, meloxicam

**NSAIDs**
- Can cause GI upset
- Can cause kidney injury
- Can increase bleeding risk
- Can increase risk of heart disease in a patient who pre-existing heart disease

**Acetaminophen**
- Analgesic
- Antipyretic
- Mechanism of action not clearly understood
- May be taken safely if total intake is 3 grams a day
  - This includes opioid combination drugs!
- Limit alcohol intake!

**Acetaminophen**
- Unclear how much is “safe” for a patient in liver failure
- Beware combination analgesics (hydrocone-acetaminophen or oxycodone-acetaminophen)

Skeletal Muscle Relaxants

• Highly diverse group of medications with very different mechanisms of action
• Examples
  – Cyclobenzaprine, methocarbamol, tizanidine, baclofen, carisoprodol

Summary

• Chronic pain in a patient with Von Hippel-Lindau Syndrome should be approached using multimodal pharmacotherapy and a multidisciplinary approach
  – In other words, treated with medications from different classes as well as non-medication therapies!

Questions?