Multidimensional Pain Assessment for Improved Outcomes

Patient Report of Pain

Assess Outcomes
- Pain relief
- Progress to treatment goals
- Side effects

Comprehensive Pain Assessment
- Assess PQRST
- Physical exam
- Detailed medical history
- Clarify pathophysiology (treat the treatable)
- Determine effects on QoL, function, psychosocial status

Intolerable side effects and/or failure to meet treatment goals

Monitor Treatment Adherence

Document, Assess, and Plan

Develop Treatment Plan: Review With Patient

Evaluate Treatment Goals

PQRST, palliative or precipitating factors, quality of pain, region of radiation of pain, severity, temporal nature of pain; QoL, quality of life.


Aberrant Opioid Use

- Misuse and abuse of prescription drugs is a major problem in the United States
  - In 2006, almost 14,000 prescription opioid–related deaths
- Opioid abuse is rampant even among cancer patients
- Physicians are significant contributors to the problem
  - Unanticipated medical and mental health comorbidities, including substance use disorders
  - Belief that cancer protects individuals from aberrant medication use
  - Lack of a systematic approach to dispensing and monitoring opioids for acute and chronic pain
  - Strategies that are effective for limiting abuse are not being implemented

Rational Opioid Prescribing

- Stratify patients based on risk factors related to abuse, addiction, and diversion
  - Personal history of alcohol or drug abuse
  - Family history of alcohol or drug abuse
  - Significant psychiatric disorders (impulsivity)
- Consider office-based screening tools
  - ORT, SOAPP-R
- Structure therapy based on risk stratification
  - Opioid treatment agreement
  - Pill counts, smaller prescriptions, frequent follow-up
  - Prescription monitoring programs
  - Urine drug testing

ORT, Opioid Risk Tool; SOAPP-R, Screener and Opioid Assessment for Patients with Pain—Revised.

Cancer-Related Breakthrough Pain

Characteristics

<table>
<thead>
<tr>
<th>Frequency Among Patients With BTP</th>
<th>Type of BTP Onset</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3</td>
<td>Paroxysmal</td>
</tr>
<tr>
<td>4-6</td>
<td>Gradual</td>
</tr>
<tr>
<td>7-10</td>
<td></td>
</tr>
<tr>
<td>&gt;10</td>
<td></td>
</tr>
</tbody>
</table>

- Median numbers of BTP episodes were 4\(^1\) and 6\(^2\)
- Time to peak intensity of BTP episodes ranged from 1 second to 30 minutes (mean, 3.2 min)\(^2\)

Prevalence of Cancer BTP

Breakthrough Pain

Nosology

• Original definition\(^1\)
  - A transitory increase in pain to greater than moderate intensity, which occurs on a controlled background pain of moderate intensity or less, in patients receiving chronic opioid therapy

• Additional definitions
  - A transitory increase in pain that has a negative effect on function or quality of life in patients with adequately controlled baseline pain who receive analgesic drug therapy on most days\(^2\)
  - Episodic flares of pain on a treated or untreated background pain\(^3\)

Consensus on a definition is lacking

How do you define “controlled” baseline pain?

## Cancer BTP Subtypes

### Characteristics

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Speed of Onset</th>
<th>Comments</th>
<th>Example(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incident, Predictable</td>
<td>Usually rapid</td>
<td>Shows consistent, temporal relationship with motor activity</td>
<td>Vertebral Metastasis: Movement</td>
</tr>
<tr>
<td>Incident, Unpredictable</td>
<td>Usually rapid</td>
<td>Shows consistent, temporal relationship with involuntary act</td>
<td>Rib Metastasis, Pleura: Cough</td>
</tr>
<tr>
<td>Idiopathic, Spontaneous</td>
<td>Variable</td>
<td>Unexpected and unrelated to provoking causes</td>
<td>Partial Small Bowel Obstruction, Spontaneous Colic Pain</td>
</tr>
<tr>
<td>End-of-Dose</td>
<td>Gradual</td>
<td>Presents before scheduled dose of ATC analgesic</td>
<td>Pain After Awakening or Before Nighttime Dosing</td>
</tr>
</tbody>
</table>

ATC, around-the-clock.


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## Cancer BTP Significantly Impairs Function, QoL, and Mood

### Effects on Function and QoL

![Graph showing effects on function and QoL](image)

### Effect on Mood

![Graph showing effect on mood](image)

*P<0.05 for all domains; N=78; bP<0.001; N=164 cancer pain patients.

BPI-SF: Brief Pain Inventory—Modified Short Form where 0=Does not interfere and 10=Completely interferes; QoL, quality of life; VAS, visual analog scale.

Opioid Analgesics

<table>
<thead>
<tr>
<th>Type</th>
<th>Characteristics</th>
<th>Therapeutic Setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-acting opioid (LAO)</td>
<td>• Releases drug gradually into bloodstream or long duration of action</td>
<td>• Persistent cancer pain</td>
</tr>
<tr>
<td>Short-acting opioid (SAO)</td>
<td>• Faster increase and decrease in serum levels than LAO</td>
<td>• Initial dose titration for persistent cancer pain with eventual rotation to LAO</td>
</tr>
<tr>
<td></td>
<td>• Limited duration of action precludes long periods of discomfort if side effects develop</td>
<td>• Acute exacerbations of pain not attributed to inadequate dosing of ATC opioid</td>
</tr>
<tr>
<td>Rapid-onset opioid (ROO)</td>
<td>• All outpatient formulations use fentanyl</td>
<td>• Acute exacerbations of pain not attributed to inadequate dosing of ATC opioid</td>
</tr>
<tr>
<td></td>
<td>• Pharmacokinetic profile mirrors temporal pattern of BTP</td>
<td></td>
</tr>
</tbody>
</table>

ATC, around-the-clock; NCCN, national comprehensive cancer network.

Critical Issues for Cancer BTP Assessment

**PQRST**
- **P** alliative or precipitating factors
- **Q** uality of pain
- **R** egion of pain
- **S** everity
- **T** emporal pattern of pain

• Effects on function, including avoidance of activities
• Inferred pathophysiology and origins of the cancer pain syndrome
  – Nociceptive vs neuropathic
• Current and prior analgesic strategies (opioids and others)

**Cancer Persistent Pain and BTP**  
*Nonpharmacologic Options*

- Acupuncture
- CBT
- Heat and cold
- TENS
- Stretching
- Relaxation
- Weight reduction

CBT, cognitive behavioral therapy; TENS, transcutaneous electrical nerve stimulation.


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**BTP Management**  
*End-of-Dose Failure*

- Treatment approaches
  - Rotate to a longer-acting agent
  - Increase dose of ATC analgesic
  - Shorten the baseline dosing interval
    - Patients on LAOs often require more frequent dosing than recommended in prescribing information

BTP Management
Spontaneous vs Provoked Subtypes

<table>
<thead>
<tr>
<th>BTP Subtype</th>
<th>Management Approach</th>
</tr>
</thead>
</table>
| Predictable Precipitated/Procedural | • Target the pain generator  
                                  |   • Adjust baseline regimen  
                                  |   • Proactively administer an analgesic before exacerbating activity |
| Spontaneous/Unpredictable    | • Target the pain generator  
                                  |   • Adjust baseline regimen  
                                  |   • Rescue medication: consider PK profile of analgesic and BTP temporal profile |

PK, pharmacokinetic.

BTP Pharmacologic Options

• Nonopioids
  – Antidepressants
  – Anticonvulsants
  – Bisphosphonates
  – NSAIDs
  – Benzodiazepines
  – Ketamine
  – Nitrous oxide

• Opioids

NSAID, nonsteroidal anti-inflammatory drug.
Cancer Persistent Pain and BTP
Interventional Options

Indications
- Pain that is poorly responsive to systemic analgesics or intolerable side effects of systemic analgesics
- Patients with short life expectancy that precludes safe titration of systemic analgesics

Approaches
- Neurolytic blockade
  - Lidocaine, bupivacaine, and ropivacaine commonly used
  - Longer pain relief with nerve-destroying alcohol, phenol, or glycerol
- Epidural/Intrathecal therapy
  - Intrathecal route may provide better analgesia with reduced risk
  - Morphine commonly used, but other opioids may provide better side effect profiles
- Radiofrequency lesioning
  - Continuous or pulsed electric current
  - Extend relief when nerve block is helpful but of limited duration


Opioid Analgesics
Routes of Administration

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Oral</th>
<th>Rectal</th>
<th>Intravenous</th>
<th>Intramuscular</th>
<th>Subcutaneous</th>
<th>Transbuccal</th>
<th>Sublingual</th>
<th>Intranasal</th>
</tr>
</thead>
<tbody>
<tr>
<td>First-pass metabolism</td>
<td>++</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Bioavailability</td>
<td>Variable</td>
<td>Variable</td>
<td>Maximum</td>
<td>High</td>
<td>Medium to high</td>
<td>Medium to high</td>
<td>Medium to high</td>
<td>Medium to high</td>
</tr>
<tr>
<td>Onset of action, min</td>
<td>&gt;30</td>
<td>&gt;30</td>
<td>5</td>
<td>10-15</td>
<td>10-15</td>
<td>5-15</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Invasive method</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>++</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Self-administered method</td>
<td>+</td>
<td>+</td>
<td>–</td>
<td>–</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

*Approved ROO formulations: oral transmucosal fentanyl citrate, fentanyl buccal tablet, fentanyl buccal soluble film, sublingual fentanyl, and fentanyl nasal spray.
– = negative; ++ = positive.
Prescribing ROOs
Opioid-Tolerant Patients

• Prior opioid exposure reduces the risks for respiratory depression and overdose

Opioid-Tolerant Patients

<table>
<thead>
<tr>
<th>Patients taking a minimum of the following for ≥1 week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral morphine, 60 mg daily</td>
</tr>
<tr>
<td>Transdermal fentanyl, 25 µg/h</td>
</tr>
<tr>
<td>Oral oxycodone, 30 mg daily</td>
</tr>
<tr>
<td>Oral hydromorphone, 8 mg daily</td>
</tr>
<tr>
<td>Oxymorphone, 25 mg daily</td>
</tr>
<tr>
<td>Equianalgesic daily dose of another opioid</td>
</tr>
</tbody>
</table>


Prescribing Opioids for BTP
Safe Dosing and Titration

• Titrate to predefined, realistic, and patient-specific goals
  – Ongoing clinical interviews help establish functional and QoL goals

• “Start low, go slow”
  – Recommended SAO doses for BTP are traditionally 5%-15% of daily opioid dose
  – Mixed data on the relationship between ROO and background dose
  – Neuropathic cancer pain trends towards increased ATC opioid dose
  – Older patients may require reduced fentanyl dose

In your clinical experience, do you see a relationship between ATC and BTP doses?

QoL, quality of life.