Interdisciplinary Management of Pelvic Pain: Bridging the Gap Between Primary Care and Specialty Referral

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Disclosures

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Learning Objectives

- Describe the process of appropriate specialist referral and ongoing care by the primary care provider in the interdisciplinary management of chronic pelvic pain
- Differentiate bladder pain syndrome/interstitial cystitis from a myriad of other pelvic pain conditions including endometriosis, vulvodynia, and peripheral nerve entrapments
- Discuss evidence-based pain management strategies for the treatment of bladder pain syndrome/interstitial cystitis from the perspectives of a pain medicine specialist and a pain psychologist

Simplified diagram showing the major pain pathways from the viscera to the central nervous system.

Visceral Pain

- Diffuse and poorly localized
- Pain can refer to area innervated by same spinal segment as organ
- Vague discomfort
- Associated motor and autonomic reflexes
- Triggered by distention, contraction, ischemia, inflammation

Peripheral Visceral Innervation

- Visceral nociceptors
  - free nerve endings, large receptive fields
  - chemoreceptors sensitive to ischemia, inflammation, irritant, distention, contraction
  - stimulation ↑ and afferent firing ↑ (low-threshold mechanosensory afferents)
  - 50-90% of visceral afferents are silent until they are switched on (important role in central sensitization)
Visceral Nociceptors

• Mucosal afferents
• Muscular afferents
• Serosal and Mesenteric afferents
• Muscular-mucosal afferents


Peripheral Visceral Innervation

• Visceral afferent and efferent fibers are carried by spinal nerves
• Visceral afferents travel with autonomic nerves centrally
• Cell bodies reside in the dorsal root ganglia
• Large receptive field and low density of innervation by visceral afferents causes diffuse pain

Visceral Pain

- Visceral afferents synapse above and below the entering segment
- Dorsal horn (lamina I and V) → dorsal column pathways, spinothalamic and spinoreticular tracts
- Autonomic spinal reflex:
  - sympathetic activation results in sweating and ↑ BP
  - sympathetic inhibition or parasympathetic activation results in ↓ BP, and bradycardia

Viscerosomatic Convergence
Viscerosomatic Convergence

- Pain originating from sacral sympathetic segments experienced in sacral somatic regions
- Visceral afferents reach upper lumbar/ lower thoracic spinal cord at same levels as visceral fibers from lower lumbar discs
- Sensory convergence from visceral afferents leads to somatic symptoms and vice versa
- Trigger points can develop in peripheral somatic tissue in response to increased nociceptive visceral input

<table>
<thead>
<tr>
<th>Organ</th>
<th>Level of CNS Entry of Visceral Afferents</th>
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<tbody>
<tr>
<td>Esophagus</td>
<td>T2-T4, Nucleus tractus solitarius</td>
</tr>
<tr>
<td>Stomach, duodenum, gallbladder, bile ducts, liver, pancreas</td>
<td>T5-T11</td>
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<tr>
<td>Small intestines</td>
<td>T8-T11</td>
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<tr>
<td>Cecum and appendix</td>
<td>T10-T12</td>
</tr>
<tr>
<td>Colon to splenic flexure</td>
<td>T10-L1</td>
</tr>
<tr>
<td>Splenic flexure to rectum</td>
<td>S2-S4</td>
</tr>
<tr>
<td>Kidneys, ureters</td>
<td>T10-T12 (L1,L2)</td>
</tr>
<tr>
<td>Bladder</td>
<td>S2-S4</td>
</tr>
<tr>
<td>Uterus</td>
<td>T11-L2</td>
</tr>
<tr>
<td>Testes</td>
<td>T10</td>
</tr>
<tr>
<td>Prostate</td>
<td>S2-S4</td>
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Epigenetic and Environmental Influences

- Traumatic early life events produce long-term effects on the brain circuitry involved in visceral pain processing
- Chronic stress in adulthood predisposes to visceral pathology and pain states
- Chronic social stress in rats increases DNA methylation and histone acetylation of genes that regulate visceral pain sensation in the peripheral nervous system.
- In rats in which hypersensitivity to colonic distension had been experimentally induced, expression of the gene encoding the glucocorticoid receptor and cannabinoid CB1 receptors was reduced but expression of TRPV1 receptor increased in lumbosacral dorsal root ganglia

Enteric Nervous System

- Division of ANS
- GI motility, secretion, visceral sensation
- Myenteric and Submucous plexuses (sympathetic, parasympathetic, and enteric neurons)
- Can function autonomously
- Enteric neuronal plasticity contributes to visceral hypersensitivity
Superior Hypogastric Plexus

- Anterior to L5 vertebral body and sacrum at bifurcation of common iliac vessels
- Union of aortic plexus, L3/L4 splanchnic nerves
- Divides into hypogastric nerves (a.k.a. Middle Hypogastric Plexus)

Superior Hypogastric Plexus

- Sensory fibers transmit nociceptive impulses from uterus, cervix, fallopian tubes, bladder, rectum
- Visceral afferents with cell bodies in DRG of T10 to L2
- Parasympathetic nerves from S2-S4
Within bilateral presacral tissues on either side of rectum, ventral to S2,S3,S4 spinal segments
The hypogastric nerves send branches to the internal iliac arteries and the IHP
Also contribution from lowest lumbar splanchnic nerves, pelvic splanchnic nerves
Branches to ovarian/testicular plexus, ureteric plexus, sigmoid colon
Visceral afferents from bladder, penis, vagina, rectum, anus, perineum, and lower pelvis
Inferior Hypogastric Plexus

- Supplied by sacral splanchnics from S1 to S4 sympathetic ganglia (mostly postganglionic sympathetic fibers)
- Supplied by Nervi Erigentes (Pelvic Splanchnic Nerves): preganglionic parasympathetic fibers with cell bodies in S2, S3, and S4 (synapse with cell bodies of postganglionic parasympathetic neurons or viscera walls)
- Cell bodies of preganglionic sympathetic fibers originate from T9 to L2
Ganglion Impar

- Solitary retroperitoneal structure at the sacrococcygeal junction
- End of the 2 sympathetic chains
- Treats visceral pain in the perineal area
- Treats sympathetically mediated pain in the perineum, rectum, genitalia
Case

- A 43 year-old female with a PMH of migraines, depression, and GERD presents to your office to establish care. She also has a long-standing history of pelvic pain, which has significantly worsened over the past year.
Chronic Pelvic Pain

- Nonmalignant pain perceived in the structures related to the pelvis that has been present for > 6 months or has a non-acute pain mechanism of shorter duration
- Disorders of urological, gynecological, gastrointestinal, musculoskeletal and nervous system
- Indication for 15-40% of laparoscopies and 12% of hysterectomies in the U.S


Terms

- Pelvic Pain- pain arising from the visceral or somatic system encompassing structures supplied by the nervous tissue from T10 and below
- Pelvic Pain Syndrome- recurrent or persistent pain associated with symptoms suggesting involvement of the musculoskeletal, gynecological, urological, or gastrointestinal systems and the absence of inflammation or other specific pathology
- Pelvic floor- fascial and muscular layers that span the bony outlet of the pelvis
**Case**

- She describes a sharp, shooting right groin pain radiating to her genitals and a dull, constant aching pain most notable in the suprapubic region
- Alleviating Factors: Rest, symptoms partially relieved by urination
- Exacerbating Factors: exercise, long car rides

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**Differential Diagnosis**

Case

- PSH: C-section 20 years ago, Exploratory laparoscopy with lysis of adhesions 5 years ago
- Medications: ibuprofen 200mg prn, sumatriptan 50mg prn, fluoxetine 20mg qd, famotidine 20mg BID, tramadol 50mg prn
- Social History: She is currently separated and going through a divorce. She has not been able to work over the last year due to pain, and had a previous history of suicidal ideations at age 18 due to a major life event

Case

- The patient is asking for a refill of her tramadol and referral to specialists as she has just moved to the area
- How would you proceed?
**Sacral and Coccygeal Plexus**

- Iliohypogastric Nerve
  - T12-L1
  - Converge on dorsal horn structures shared with ipsilateral ovary and distal fallopian tube
  - Cutaneous branch-anterior abdominal wall
  - Motor branch-innervates TrA and internal oblique
  - Sensory branch-groin and pubic symphysis

Ilioinguinal Nerve

- T12-L1
- Converge on dorsal horn structures shared with proximal fallopian tubes and uterine fundus
- Enters inguinal canal 2cm medial to ASIS
- Sensory to groin, mons, labia, inner thigh
- Entrapment by suture at lateral edges of Pfannenstiel’s incision
- Trauma during needle bladder suspension

Genitofemoral Nerve

- L1-L2
- Converge on dorsal horn structures shared with proximal fallopian tube and uterine fundus
- Genital branch-skin of mons pubis and labia majora
- Femoral branch-skin of the femoral triangle
- Right genitofemoral neuralgia due to postappendectomy perineural fibrosis at exit through psoas


Pudendal Nerve

- Dorsal nerve of the penis/clitoris
- Perineal branch: motor to external anal sphincter and perineal muscles, sensory to vaginal tissues and vestibule, motor to external urethral sphincter
- Inferior rectal branch: motor to external anal sphincter, sensory to perineal skin
- Converges on dorsal horn structures shared with cervix, uterosacral, vulvovaginal region

Pudendal Neuralgia

- Prolonged 2nd stage of labor, 3rd degree tear through perineal body, high neonatal birth weight
- Sacrospinous vaginal vault suspension, laser to vulva/perineum
- Vaginal laceration repairs, episiotomies
- Straddle injuries, motorcycle or bicycle riding, repeated squatting, constipation

Apte, G., et al., Chronic female pelvic pain--part 1: clinical pathoanatomy and examination of the pelvic region

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<table>
<thead>
<tr>
<th>Table 1. Sites of entrapment.</th>
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<tbody>
<tr>
<td>Infrapiriform foramen (E1)</td>
<td>15</td>
<td>10</td>
</tr>
<tr>
<td>Ischial spine (E2)</td>
<td>101</td>
<td>70</td>
</tr>
<tr>
<td>Alcock's canal (E3)</td>
<td>36</td>
<td>25</td>
</tr>
<tr>
<td>Falciform process</td>
<td>58</td>
<td>40</td>
</tr>
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</table>

Piriformis Syndrome

- Symptoms: Pain in the buttock, hip, and leg
- Mean age (38 years-old)
- Etiology: gluteal trauma, anatomic variants, myofascial trigger points
- Conservative Treatment: PT, lifestyle modifications, NSAIDs


Lateral Femoral Cutaneous Nerve

- L2-L3
- Converge on dorsal horn structures shared with uterine fundus and lower uterus
- Meralgia paresthetica- pain and numbness in upper outer thigh
  - Post-surgical abdominal scars, iliac bone graft harvest, ascites, abdominal/pelvic mass

Case

- Physical Exam: Decreased sensation to cold over the right inguinal ligament and a portion of the upper inner thigh, no tactile allodynia over laparoscopic scars of pfannenstiel incision, deep aching pain with palpation of the suprapubic region, tenderness to intravaginal palpation of pelvic floor muscles with minimal contraction strength
- Next steps from the pain specialist's perspective?

Endometriosis

- Affects 5-10% of women of reproductive age
- Growth of endometrial glands and stroma outside the uterus
- Severe pelvic pain
- Reduced fertility
- Histologic diagnosis

Endometriosis

- Retrograde menstrual flow (site in the pelvis)
- Coelomic (peritoneal) metaplastic change of undifferentiated tissue outside uterine cavity
- Adult stem cells, which play a role in endometrial self-renewal, may contribute to the pathogenesis of ectopic sites of endometrial growth
- Lymphatic or vascular factors (endometrial tissue in brain, lung, skin, and eye)

Genetic Factors

Environmental Factors


Endometriosis

- Dysmenorrhea
- Dyspareunia
- Heavy menstrual bleeding
- Non-menstrual pelvic pain
- Pain at ovulation
- Dyschezia
- Dysuria
- Chronic fatigue

**Endometriosis**

- Medications: NSAIDs, combined OCP, GNRH agonists, progestins
- Surgery:
  - Laparoscopic surgical removal of endometriosis
  - Laparoscopic uterine nerve ablation in addition to surgical removal does not improve pain relief
- Superior hypogastric plexus block


**Pelvic Congestion Syndrome**

- Enlarged venous complexes of reproductive tissue (impaired circulation and drainage)
- Etiology: Anatomic dysfunction, Orgasmic dysfunction, Psychosomatic, Hormonal dysfunction, Iatrogenic
- Dull ache exacerbated by ↑ venous pressure
- Deep dyspareunia (78%)
- Postcoital aching (65%)
- Dysmenorrhea (89%) up to one week before menses

Pelvic Congestion Syndrome

- Pelvic venography-gold standard for diagnosis
- Treatment
  - Medroxyprogesterone acetate
  - PT with manual lymph drainage techniques
  - Ovarian vein ligation
  - Uterine suspension (retroverted uterus)
  - Ovarian and pelvic vein embolization

Vulvodynia

- Chronic pain or discomfort involving the vulva for more than 3 months and for which no obvious etiology can be found
- “itching, burning, stinging, irritation, stabbing, rawness”
- Lifetime prevalence: 8% up to age 70
- PVD: most common cause of sexual pain in women < age 30
- Typically affects women ages 20-40


Vulvodynia

- Initial trigger of inflammation/injury leading to altered pain processing
- Possibly from stretch injury of the nerve to the levator ani or the pudendal nerve during prolonged 2nd-stage labor or pelvic floor descent, episiotomy, straddle injury
- Hormonal changes, cysts, surgical side effect, steroids, antivirals
- Women with a history of anxiety/depression are 4 times more likely to develop PVD
Vulvodynia

- Biofeedback (decreased pelvic floor hypertonicity)
- Manual or electrotherapeutic input to thoraco-lumbar and sacral areas
- Lidocaine gel or estrogen cream (perimenopausal/postmenopausal)
- TCAs, gabapentin, pregabalin, lamotrigine, carbamazepine
- Supportive psychotherapy, CBT, sexological counseling
- Vestibuloplasty, vestibulectomy, perineoplasty

Urologic Pelvic Pain

- Interstitial Cystitis
- Painful Bladder Syndrome
- Bladder Pain Syndrome
NIDDK Criteria (1990)

- (1) Bladder pain or urinary urgency
- (2) Glomerulations or Hunner's ulcer during cystoscopy/hydrodistension
- (3) None of the exclusions listed below:
  - Awake cystometric capacity > 350 mL, Absence of intense urge to void with bladder filling during cystometry, Involuntary bladder contractions on cystometry, Urinary frequency < 8 voids per day, Absence of nocturia, Symptoms < 9 months, Age < 18 years, Cystitis (bacterial, chemical, infectious, radiation) or prostatitis, vulvitis (herpes) or vaginitis, Bladder/uterine/cervical/vaginal/urethral cancer, Bladder or ureteral calculi, Urethral diverticulum, Bladder tumors


An unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptom(s) of more than 6 weeks duration, in the absence of infection or other identifiable causes

Epidemiology

- Prevalence: 2.7-6.53% of women, 2.9-4.2% of men
- F>M
- Age at presentation: 42 years-old
- Activity avoidance (shopping, travel, exercise, sexual relationships)
- Associated with fibromyalgia, chronic fatigue syndrome, irritable bowel syndrome, temporomandibular disorder, migraine, chronic pelvic pain, vulvodynia, low back pain, allergies, asthma, depression and anxiety
- Risk factors: caffeine, anorectal disease, smoking

Clinical Presentation

Initial UTI → Persistent Symptoms

- Dysuria
- Frequency
- Pain
- ↓ QOL
- ↑ Pain
- ↑ Sleep dysfunction
- ↑ Catastrophizing
- ↑ Anxiety
- ↑ Stress
- ↑ Social functioning difficulties
Associated Psychosocial Conditions

- Depression
- Sexual dysfunction
- Sexual abuse
- Emotional abuse/neglect
- Physical abuse/neglect


Case

- How do we consider this patient’s psychosocial history in the ongoing management of her pain conditions?
Adverse Childhood Experiences

- Adverse Childhood Experience (ACE) Study
  - CDC/Kaiser Permanente collaboration
  - Co-PIs: Robert Anda, MD, Vincent Felitti, MD
  - Examining relationship between ACEs and health/behavioral outcomes later in life
  - Data gathered from 17K individuals between 1995-97

Adverse Childhood Experiences

- Physical/emotional neglect
- Recurrent emotional abuse
- Recurrent physical abuse
- Sexual abuse (contact)
- Household substance abuse
- Incarceration of household member
- Chronic mental illness
- Mother treated violently
- One or no parents
Adverse Childhood Experiences

- Higher ACE scores increase risk for developing
  - Medical/psychiatric disease
  - CD/SA issues
  - Health-related QOL issues
  - Partner violence
  - Sexual activity
  - Suicidality

Adverse Childhood Experiences

- Abuse and Somatic Disorders
- 23 studies, 4640 subjects
- Significant association between sexual abuse and a lifetime diagnosis of:
  - Functional GI disorders
  - Non-specific chronic pain
  - Psychogenic seizures
  - Chronic pelvic pain

Abuse, Pain, and Depression

- n = 273 females evaluated for CPP
- Assessed:
  - History of physical abuse
  - History of sexual abuse
  - Pain severity
  - Pain disability
  - Depression


Abuse, Pain, and Depression

- Logistic regression analyses:
  - Abuse categories not associated with pain severity
  - Sexual abuse predictive of pain-related disability
  - Physical & sexual abuse associated with higher levels of depression

Abuse, Pain, and Depression

- Conclusion:
  - Pelvic pain is always a sign of an underlying abuse history
  - Depression in a person with pelvic pain is more related to the abuse history
Evolution of Depression

**LIFE**

Family Friends Work School
Sports Leisure Self-care Music
Vacations Hobbies Dining
Entertainment Socializing
Cooking Cleaning Errands
Evolution of Depression

**LIFE**
- Family Friends Work School
- Sports Leisures Self-care Music
- Vacation Plains Dining
- Entertainment Socializing
- Cooking Cleaning Errands

**Evolution of Depression**

**LIFE**
- Decreased activity levels
- Sexual dysfunction
- Failed treatments
- Pain
- Sleep disturbances
- Increased number of doctor office visits
- Friends Work
- Pain
- Socializing
- Cooking Errands

**Evolution of Depression**
Psychological Factors and Pain

- Untreated/undertreated psychiatric distress adversely affects treatment outcome

- Necessitates an interdisciplinary approach to care


Interdisciplinary Pain Management

<table>
<thead>
<tr>
<th></th>
<th>Acute</th>
<th>Chronic</th>
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<tbody>
<tr>
<td>Meaning</td>
<td>Hurt ≠ Harm</td>
<td>Hurt ≠ Harm</td>
</tr>
<tr>
<td>Etiology</td>
<td>Clear, singular</td>
<td>Vague, multifactorial</td>
</tr>
<tr>
<td>Treatment</td>
<td>Unimodal</td>
<td>Interdisciplinary</td>
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- Pain management similar to approach used with other chronic health conditions
- Education focuses on QOL, improving functionality
Interdisciplinary Management

LIFE
- Decreased activity levels
- Sexual dysfunction
- Work
- Care of music
- Vacation
- Interpersonal problems
- Sleep disturbances
- Cooking
- Errands

Interdisciplinary Management

LIFE
- Family
- Friends
- Work
- School
- Sports
- Leisure
- Self-care
- Music
- Vacations
- Hobbies
- Dining
- Entertainment
- Socializing
- Cooking
- Cleaning
- Errands
- Pain
Summary: Role of Psychology in Pain Etiology

- Some pain conditions are primarily due to psychogenic factors but virtually all can be influenced by psychological factors.
- Employing an interdisciplinary approach can maximize outcomes.

Etiology

- Epithelial dysfunction
- Subclinical infection
- Mast cell and vascular abnormalities
- Neurogenic inflammation
- Autoimmune
- Central sensitization
- Altered integrity of the glycosaminoglycan (GAG) layer

“Pain management should be considered throughout the course of therapy with goal of maximizing function and minimizing pain and side effects.”


### Treatment

1. Patient education and support, Self-care/Behavioral modification
2. Appropriate PT, amitriptyline, cimetidine, hydroxyzine, PPS, intravesical instillations
3. Cystoscopy and hydrodistention, Tx of Hunner’s lesions
4. Intradetrusor onabotulinumtoxinA, Neuromodulation
5. Cyclosporine A
6. Surgery, substitution cystoplasty


Intravesical Dimethyl Sulfoxide

- FDA-approved for IC in 1997
- anti-inflammatory, analgesic, smooth muscle relaxing, and mast cell inhibiting effects
- bladder catheterization with instillation of 50 mL DMSO weekly for 6-8 weeks, followed by 50 mL every 2 weeks for 3 to 12 months
- pain and significant exacerbation of symptoms (10%)
- garlic-odor, headache side effects


Pentosan Polysulfate Sodium

- FDA approved (1996) for IC treatment
- 100mg TID with water 1 hr. before or 2hrs. after meals
- Filtered by the kidneys and appears in the urine to reconstitute the deficient glycosaminoglycan (GAG) layer over the urothelium
- Only 3-6% of active drug reaches the bladder
- Full effect may not be seen for 6-9 months
- Contraindicated with allergy to LMWHs and heparin or HIT

Cimetidine

- Mast cell degranulation postulated to initiate inflammation
- H₂ antagonist
- 2nd line agent
- 300mg BID for or 200mg TID

Thilagarajah R, Witherow RO, Walker MM. Oral cimetidine gives effective symptom relief in painful bladder disease: a prospective, randomized, double-blind placebo-controlled trial. BJU international 2001;87:207-12

Amitriptyline

- 50 subjects with IC randomized to amitriptyline or placebo
- 4 months with a self-titration protocol, escalate drug dosage by 25 mg increments weekly to a maximum of 100 mg
- Greater improvement in O’Leary-Sant Interstitial Cystitis Symptom Index than placebo
- 42% of patients in the amitriptyline group experienced greater than 30 percent decrease in symptom score, suggesting that benefits are modest

multicenter, randomized, double-blind, placebo controlled trial (N=271)
6-week titration from 10 - 75 mg daily
Evaluated after 12 weeks of treatment
No difference in GRA (moderate or marked improvement)
Subgroup reaching 50 mg daily (N=207): GRA in the amitriptyline group (66%) compared to placebo (47%) (p=0.01)

Gabapentin

- Prospective study of 38 patients with BPS, administered etodolac (600mg), gabapentin (300-900mg), and amitriptyline (5-75mg) at bedtime over 6 months
- 70% improvement in VAS scores, and 60-70% improvement in ICSI and ICPI scores

Lee JW, Han DY, Jeong HJ. Bladder pain syndrome treated with triple therapy with gabapentin, amitriptyline, and a nonsteroidal anti-inflammatory drug. International neurology journal 2010;14:256-60
Nerve Stimulation

Sacral Neuromodulation
- FDA-approved for urinary urge incontinence, refractory voiding dysfunction, urgency-frequency syndrome, and idiopathic non-obstructive urinary retention
- Implanted lead that lies along a sacral nerve root (usually at S3 level)

Posterior Tibial Nerve Stimulation
- Needle inserted 5 cm cephalad to medial malleolus at the site of the posterior tibial nerve
- Usually weekly, 30 minute sessions for 10-12 weeks


Spinal Cord Stimulation
- Not studied in large trials
- Potential efficacy in case series

Conclusions

- A wide range of disorders encompass pelvic pain
- The definition of BPS/IC has evolved to describe a chronic pain condition with a variety of associated lower urinary tract symptoms, and unpleasant sensations perceived to be related to the urinary bladder
- It is important to understand the psychosocial factors associated with chronic urologic pelvic pain syndromes, the interdisciplinary approach to management, and the role of pain management throughout the course of treatment