MANAGING OSTEOARTHRITIS PAIN IN THE OLDER POPULATION
Pain management requires specific considerations, say Professor Peter Passmore and Emma Cunningham

CAN WE PREVENT ACUTE PAIN BECOMING CHRONIC?
The transition from acute to chronic pain is a growing area of interest, according to Professor Margarita M Puig

SUCCESSFUL MANAGEMENT OF CHRONIC PELVIC PAIN
Dr Annica Rhodin describes how chronic pelvic pain can have multiple causes and may require a multidisciplinary approach

RESEARCH UPDATE
Dr Karen H Simpson’s review of the journals highlights chronic postsurgical pain, channel-complex autoimmunity and acceptance strategies.

YOUR QUESTIONS ANSWERED
Professor Harald Breivik discusses problematic opioid use.

CASE STUDY
A clinician presents a case of chronic pain management. Two European specialists provide their perspectives on the treatment.

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Research UPDATE

Pain specialist and joint editor Dr Karen H Simpson reviews the latest research in pain, including papers on chronic postsurgical pain, channel-complex autoimmunity and acceptance strategies

Andreea MH, Andreea DA.
Local anaesthetics and regional anaesthesia for preventing chronic pain after surgery.
Cochrane Database of Systematic Reviews 2012;10:CD007105.

Chronic postsurgical pain (CPSP) is an important source of morbidity that has been increasingly recognised over the past 10-15 years. Despite the belief amongst pain specialists that good perioperative analgesia will reduce the risk of CPSP, there are few data to support this. It has long been thought that regional anaesthesia may reduce CPSP.

The authors carried out a systematic review to compare local anaesthetics and regional anaesthesia versus conventional analgesia for the prevention of CPSP at six or 12 months after surgery.

The authors searched the Cochrane Central Register of Controlled Trials for RCTs; they also conducted a hand search in reference lists of included trials, review articles and conference abstracts – this was a rigorous search. Two authors independently assessed trial quality and extracted data, including information on adverse events. They grouped studies (all in adults) according to surgical interventions, having identified 23 RCTs. Data from 1,090 patients with outcomes at six months and 441 patients with outcomes at 12 months were presented.

Data from 250 thoracotomy patients with outcomes at six months were pooled; regional anaesthesia was superior to conventional analgesia in prevention of CPSP in this group. The authors also pooled two studies of paravertebral block for breast cancer surgery (n=89) that favoured paravertebral block. Adverse effects were not studied systematically and were reported sparsely; however, it must be remembered that although serious complications are rare, they are reported with regional techniques and can be devastating.

The authors conclude that epidural anaesthesia may reduce the risk of developing CPSP after thoracotomy in about one patient out of every four treated. Paravertebral block may reduce the risk of chronic pain after breast cancer surgery in about one out of every five women treated.

However their conclusions are weakened by performance bias, shortcomings in allocation concealment, considerable attrition and incomplete outcome data. More studies with high methodological quality, addressing various types of surgery and different age groups, including children, are needed to answer the questions about prevention of CPSP.

Klein CJ, Lennon VA, et al.
Chronic pain as a manifestation of potassium channel-complex autoimmunity.

The importance of the immune system in a variety of chronic pain conditions is an emerging field. However, translational research in this area often provides more questions than answers for the pain clinician. We know that autoantibodies targeting the voltage-gated potassium channel (VGKC)-complex cause a spectrum of neuronal hyperexcitability disorders and the authors have investigated pain as a manifestation of VGKC-complex autoimmunity.

The authors reviewed the prevalence and characteristics of pain in VGKC-complex-immunoglobulin G (IgG)-seropositive patients over 25 months of comprehensive testing. They looked at neural autoantibodies,
in most patients the antigenic VGKC-IgG significantly associates with pain, but nociceptive pathways is implicated. CASPR2-complex autoimmunity. Hyperexcitability of pain is a syndromic manifestation of VGKC-complex-IgG. Fewer than 10% of the 167 patients with CASPR2-IgG-positivity but not with LGI1-therapy. Pain was significantly associated with in 70% of patients (opioids in 30%); 13 of 16 management required multiple medications 25-fold more common in pain patients. Pain algesia or electromyographic excitability was (hyperhidrosis, quantitative heat-pain hyper-ous system function, measured by neuropathy impairment scores and nerve conduction. Evidence of neuronal hyperexcitability (hyperhidrosis, quantitative heat-pain hyperalgesia or electromyographic excitability) was 25-fold more common in pain patients. Pain management required multiple medications in 70% of patients (opioids in 30%); 13 of 16 patients reported pain relief with immuno-therapy. Pain was significantly associated with CASPR2-IgG-positivity but not with LGI1-IgG. Fewer than 10% of the 167 patients with neural autoantibodies other than VGKC-complex-IgG reported pain.

It seems therefore that chronic idiopathic pain is a syndromic manifestation of VGKC-complex autoimmunity. Hyperexcitability of nociceptive pathways is implicated. CASPR2-IgG significantly associates with pain, but in most patients the antigenic VGKC-complex molecule remains to be determined.

VGKC-complex autoimmunity represents an important new direction for pain research and therapy. This work may explain why some patients with difficult pain do well with immunosuppression.


There have been many psychological therapies developed for patients with chronic pain and acceptance commitment therapy is one of the more recent. However, experimental research on acceptance strategies has revealed differing results about the superiority of these strategies compared with other emotion regulation strategies. The reviewers set out to compare acceptance and other strategies (for example, suppression, distraction and reappraisal), their search identified 30 relevant studies.

Many studies reported that acceptance strategies were superior for the outcomes of pain tolerance, negative affect and believability of thoughts. This meta-analytic approach replicated existing findings of primary studies for pain tolerance by favouring acceptance strategies. With respect to pain intensity and negative affect, meta-analysis did not show significant differences between acceptance and the other strategies. Therefore acceptance strategies were superior to other emotion regulation strategies for pain tolerance but not for pain intensity and negative affect. This work does show that acceptance strategies are at least as effective, but more work is needed.


Piriformis syndrome is an uncommon disorder that is presumed to be a compression neuropathy of the sciatic nerve at the level of the piriformis muscle within the pelvis. The diagnosis is hampered by a lack of agreed clinical criteria and a lack of definitive investigations, for example, imaging or electrophysiology. Treatment has focused on stretching, physical therapies, local injections, including botulinum toxin, and surgical management.

This excellent article fully explores piriformis syndrome and should be read by all those treating musculoskeletal problems.

Dr Karen H Simpson is a consultant in anaesthesia and pain medicine, Leeds, UK

Further key clinical papers


Meetings and events update

16-19 April 2013
Bournemouth, UK
British Pain Society Annual Scientific Meeting
Website: www.britishpainsociety.org

23-26 May 2013
Toronto, Canada
4th International Congress on Neuropathic Pain
Website: www.kenes.com/neupsig

30 May-1 June 2013
Amsterdam, The Netherlands
1st World Congress on Pelvic Pain
Website: www.pelvicpain-meeting.com

30 May-1 June 2013
Tarragona, Spain
IV International Forum on Pediatric Pain
Website: www.dolorinfamili2013.com

30 May-2 June 2013
Prague, Czech Republic
13th World Congress of the European Association for Palliative Care
Website: www.eapc-2013.org

12-15 June 2013
Madrid, Spain
2013 Annual European Congress of Rheumatology
Website: www.eular.org

17-20 June 2013
Stockholm, Sweden
9th International Symposium on Pediatric Pain
Website: www.ispp2013.org

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Managing osteoarthritis pain in the older population

Pain management in elderly people, particularly the oldest old, requires specific considerations, say Professor Peter Passmore and Emma Cunningham

Key learning points
- Challenges to pharmacological management in this patient group include treatment concordance, comorbidity, polypharmacy and age-related physiological changes affecting pharmacokinetics.
- Paracetamol is generally recommended as a first-choice analgesic in osteoarthritis pain.
- Topical NSAIDs should be considered ahead of oral formulations, and prescribing NSAIDs for older people requires careful consideration.
- There are some data relating to opioid use for non-cancer pain in older people.

The estimated prevalence of pain approaches 60% in those aged over 65 years. The consequences of pain in the older population are far reaching, with effects on quality of life, sleep and mood. Pain in older people is often inappropriately viewed as an inevitable accompaniment to ageing, which can result in lack of recognition and underdiagnosis, with subsequent undertreatment of the pain. Osteoarthritis (OA) is a common cause, accounting – with osteoporosis – for 65% of painful conditions. OA prevalence is greater in women than men, increases with age and all racial and ethnic groups are affected.

Specific issues for older people
Older people, particularly the oldest old, are a distinct but heterogeneous group when it comes to pharmacological management. Challenges include concordance with medications, comorbidity and polypharmacy. Age-related changes in physiology mean pharmacokinetic considerations are particularly pertinent, as older people are more prone to drug interactions and adverse events. Acute illness can result in rapid reduction in renal function particularly if dehydration is evident. Furthermore, there are few relevant studies of analgesia in older people, particularly in the oldest old.

The key to successful pain management in older people lies in the recognition of pain as a valid complaint, along with detection, assessment, management and re-evaluation. In the chronic pain of OA, because no disease-modifying therapies are available, treatment is directed at managing pain, minimising functional impairment and preserving quality of life. Non-pharmacologic treatments such as patient education, exercise, weight loss and physiotherapy can be of substantial benefit, but many older adults are reluctant to use them.

Prescribing
The ‘start low and go slow’ principle should be applied when prescribing for older people; however, where pain is concerned, this might not be possible. It is important to provide the patient with an explanation for their pain and discuss options for treatment, even for confused patients; this can involve the family and/or carers if the patient has cognitive problems. Advice on potential side-effects of medications and, where relevant, the need to persist with treatment should be given to combat treatment concordance issues.

When deciding on the need for medication, the frequency and severity of pain should be considered. In older people, oral administration is preferred, but sublingual and transdermal preparations can be very useful. Regular long-acting medications may be preferable.

Continued review of the management plan and patient side-effects is vital, particularly if NSAIDs or opioids are being prescribed.

Paracetamol
Although there are no studies of paracetamol in older people, it is recommended as a first choice analgesic for OA in consensus guidelines. However the severity of pain often means that stronger agents are needed.

Topical and oral NSAIDs
A number of studies, mainly of knee OA, have shown short-term benefits from topical NSAID gels, creams and ointments compared with placebo. There are no data on long-term effectiveness, and limited studies comparing topical with oral NSAIDs. In one study, topical diclofenac was equivalent to oral diclofenac for knee OA over three months.

The UK’s National Institute for Health and Clinical Excellence recommends that healthcare professionals should consider offering topical NSAIDs for pain relief for people with knee or hand OA in addition to core treatment (defined as access to appropriate information, activity and exercise, and interventions to effect weight loss if overweight or obese). Topical NSAIDs and/or paracetamol should be considered ahead of oral NSAIDs, COX-2 inhibitors or opioids. Topical capsaicin 0.025% w/w cream can also be considered as an adjunct to core treatment for knee or hand OA.

NSAIDs can be effective for OA pain particularly when there is substantial inflammation. However, prescribing for older people must be considered carefully, especially in terms of risk of gastric and renal toxicity, and hypertension. When NSAIDs are necessary in older people, a PPI is usually co-prescribed. It is important to be aware of possible drug interactions, particularly with ACE inhibitors and ARBs. NSAIDs should be avoided in hepatic and renal impairment. If patients are taking NSAIDs and an intercurrent illness develops, the NSAID should be discontinued until the illness resolves. NSAIDs can be administered alone or with other non-opioids or opioids and should be used in as low a dosage as possible for as short a time as possible. Patients taking NSAIDs for OA pain should be monitored for renal impairment, even if this was not present at the start of treatment.

Opioids
There are a few studies relating to opioid use in older people for non-cancer pain. In carefully selected and monitored patients, opioids may provide effective pain relief as part of a comprehensive pain management strategy.

Older people require low-dose opioids because initial regimens are not effective.
**Osteoarthritis is a major cause of chronic pain in older people**

**Tramadol**
Tramadol is a centrally acting analgesic that has weak opioid agonist activity and also inhibits monoamine uptake. It may have less effect on respiratory function than other opioids. Due to the mode of action there is a risk of serotonin syndrome with tramadol and it is important to remember the interaction with SSRIs.10,11

**Codeine phosphate**
Codeine is metabolised to morphine. The capacity to metabolise codeine varies considerably and can lead to reduced therapeutic effect or marked increase in side-effects. It is important to consider dose adjustment in cases of renal and hepatic impairment. A significant problem in older people is constipation.12

**Morphine**
Morphine has been used for management of persistent non-cancer pain, often as a comparator to newer opioids13 where similar efficacy has been demonstrated. No studies have been undertaken specifically in older people.

Morphine undergoes substantial hepatic metabolism to morphine-6-glucuronide (M6G) and morphine-3-glucuronide (M3G). Enterohepatic recirculation of M3G and M6G results in these metabolites being excreted in bile and then faeces and urine for several days after administration of the last dose. Renal impairment results in accumulation of metabolites that may cause side-effects requiring dosage adjustment or switching to an alternative opioid.13

**Oxycodone**
Studies of short duration have demonstrated efficacy of oxycodone in OA. However, in patients aged over 65 years oral oxycodone was associated with seven times more constipation than transdermal fentanyl.14

**Buprenorphine**
Buprenorphine is available for sublingual, parenteral and transdermal administration. There are now some studies of buprenorphine in older people. A recent study of a low-dose transdermal buprenorphine patch*16 in people older than 75 years, compared with two groups of younger people (≤ 50 years and 51-64 years).17 Incidence and severity of side-effects was similar in all groups with dizziness and nausea being most commonly reported.

In a study of a low-dose weekly buprenorphine patch at 5-20 microgram/hour in patients with a median age of 63 years, most having radiographically graded moderate or severe OA, daytime movement-related pain and patients’ global impression of improvement at the end of the six-months double-blind treatment period were significantly greater in patients treated with buprenorphine compared with placebo.18 The primary end point for this study, the Western Ontario and McMaster Universities OA Index for Pain, was not statistically significant.19 Opioid side-effects caused 33% of the buprenorphine patients to withdraw before the end of the study period. Thus a low-dose weekly buprenorphine patch at 5-20 microgram/hour is a possible means of pain relief in about two thirds of elderly OA patients, in whom pain is opioid-sensitive, where surgery is not possible, NSAIDs and coxibs are not recommended, and paracetamol in tolerable dosages is not effective enough.

The convenience of a transdermal preparation that requires changing every seven days reduces administration time and staffing requirements in residential and nursing homes.12

**Summary**
OA pain is common and effective management reduces associated problems like mood and insomnia. Where possible, NSAIDs should be avoided in older people. Paracetamol and/or topical NSAIDs are preferred ahead of oral NSAIDs. Mild opioids are often required and older people need special considerations mainly because of impaired renal function. Buprenorphine has been shown to be efficacious in older people and has a favourable pharmacokinetic profile for use in this population. For all opioids, vigilant focus on and management of side-effects are essential.

*Peter Passmore is professor of ageing and geriatric medicine and Emma Cunningham is clinical research fellow, Queens University Belfast, UK*

*Low-dose transdermal buprenorphine (BuTrans® /Norspan®) is licensed for non-malignant moderate chronic pain when an opioid is necessary. Prescribing information can be found attached to the back cover and/or on the inside back cover.*

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**References**
Can we prevent acute pain becoming chronic?

The transition from acute to chronic pain is a growing area of interest, here paineurope joint editor Professor Margarita M Puig describes what is known about the mechanisms of chronic pain and where the evidence is leading.

Acute and chronic pain are two distinct entities defined by their duration. However, the point at which pain is considered to be chronic can vary considerably. Some consider that any pain lasting more than 30 days has become chronic, others claim that pain must persist for longer than three to six months to be considered chronic. The burden of chronic pain is substantial, with 19% of the European adult population affected with a high socioeconomic cost.1 There is insufficient relief with existing treatments in approximately 40% of patients,1 and typically poor or no response to drugs that are useful to relieve acute pain.

The transition from acute to chronic pain has been shown to involve peripheral and central pain sensitisation (changes in neuronal plasticity), enhanced descending facilitation from the rostral ventromedial medulla to the spinal cord and early glial cell activation.2 Life stressors and cognitive/affective factors have also been associated with an increased risk of chronic back pain one year after the acute injury,3 suggesting that these may exert pain-modulating effects through enhanced descending facilitation and glial cell activation.

Preventing the transition from acute to chronic pain is one of the main goals in pain medicine, but efforts have been mostly unsuccessful. Multiple studies have reported predictive factors (Box 1) for the transition to chronic pain in different syndromes.4 It is of interest that psychological aspects and fear at baseline correlate with the progression to persistent pain indicating that life stressors and cognitive/affective factors play a key role in the transition from acute to chronic pain syndromes.

Predisposing factors

The recognition that acute postoperative pain may become chronic in certain predisposed individuals is under active investigation in preclinical models5 and also in humans. Acute postoperative pain is followed by persistent pain in 10-50% of patients after in preclinical models6 and also in humans. Acute postoperative pain in certain predisposed individuals is under active investigation.

Investigations are ongoing into the predicting factors for chronic postsurgical pain.7-10 Preventive measures in surgical patients include an aggressive, multimodal, perioperative analgesic regimen that incorporates drugs that target the sensitisation process. There is increasing evidence that perioperative administration of IV ketamine and/or oral gabapentin in some types of surgeries (thoracic, upper abdominal and orthopaedic) may decrease a patient’s postoperative opioid requirement as well as the incidence of CPSP.11,12 However, optimal dosage regimens, timing or duration of administration, possible adverse effects and likely drug interactions have not been completely defined. Furthermore, the use of anti-hyperalgesic drugs to prevent the development of chronic pain after other types of injury, for example, trauma, has not been widely investigated.

Box 1. Predicting factors for transition from acute to chronic pain1-4

- Cumulative trauma exposure (low back pain)
- Acute pain intensity, duration and disability
- Level of education, female sex, older age
- Early use of prescription opioids (acute low back pain)
- Negative beliefs on chronic pain severity and disability
- High baseline fear, anxiety and depression
- Repeated environmental stress

References
Discussion Forum

Pain expert Professor Harald Breivik offers his views on pain management scenarios presented by clinicians

Clinical scenario

In my pain clinic, we have tried to help a 23-year-old man with haemophilia B who, under the care of his GP and various haematologists, developed a severe case of problematic opioid use for the management of frequent episodes of severe pain from spontaneous bleeding into weight-bearing joints and often also into muscles. Eventually, all the healthcare providers he encountered blamed the patient for misuse/abuse of his pain medication and he was treated as an addicted person.

We have tried to adjust his opioid medication by using depot-opioids as well as fast-onset opioids for breakthrough pain when he has a new bleed, with added co-analgesic drugs such as a tricyclic antidepressant, gabapentin, pregabalin, carbamazepine, clonidine and more.

Q. No medication seems to relieve his pain or improve function and quality of life. How can we help this patient now?

According to Dr Annica Rhodin and co-authors, substituting the patient’s opioids with methadone may help a majority of such patients. Methadone differs from other opioids in several ways: its receptor binding profile is different; it is an NMDA-receptor antagonist (like ketamine, but less potent). In addition, the pharmacokinetics of methadone are unusual, with a short onset-time and a long, and varying, half-life (24-72 hours).

However, there are worrisome reports of increasing numbers of fatal complications during methadone treatment for pain as well as for maintenance treatment of heroin-addicted patients. Methadone substitution of other opioids in treatment for chronic non-cancer pain is therefore not a straightforward therapy.

Fatal complications of methadone treatment are possible from three different mechanisms:

- Overdose leading to respiratory arrest. This can happen in the start-up phase if the equipotent dose of methadone is underestimated (see below).
- Interaction with other drugs that inhibit CYP450 2B6 and other enzymes that metabolise methadone in the liver may cause accumulation of methadone and respiratory arrest (Box 1).

Box 1. Drugs that inhibit metabolism of methadone

- Antibiotics/antifungals: ciprofloxacin, ofloxacin, erythromycin, clarithromycin, telithromycin, fluconazole, ketoconazole
- Antiviral drugs: indinavir, ritonavir
- Cardiac or BP medication: verapamil, diltiazem
- Anxiolytics/antidepressants: fluoxetine, fluvoxamine
- Tricyclic antidepressants
- Cancer drugs: imatinib
- Antiemetics: aprepitant
- Anti-parkinsonism drugs: orphenadrine

Box 2. Drugs that can induce prolonged QT and thus add to risk of QT-prolongation by methadone alone

- Antiarrhythmic drugs: class I₄ (disopyramide), I₃ (flecainide) and class III (amiodarone)
- Neuroleptics (such as chlorpromazine, haloperidol, droperidol)
- Tricyclic antidepressants
- Antihistamines
- Antibiotics (such as erythromycin, clarithromycin, telithromycin)
- Antiemetics: ondansetron
- Interaction with other drugs that also increase the risk of QT-prolongation can cause ventricular arrhythmias (namely torsade de pointes) and sudden cardiac arrest (Box 2).

I suspect that the latter two points are the most dangerous because so few healthcare providers are aware of the many possibilities of interactions with other drugs. A well-documented interaction occurs when UTI is treated with ciprofloxacin in a patient taking methadone: the interaction causes inhibition of methadone metabolism, accumulation of methadone and severe slowing of respiratory rate, or respiratory arrest if not treated in time.

Cardiac arrhythmias are more problematic: ECGs are needed in the start-up phase and always if another drug with possible QT-prolongation is indicated. Pain specialists responsible for methadone treatment must know about all these important interactions. Patients and their GPs should also be informed in writing, in order to eliminate the risk of such dangerous surprise interactions. Prescribers of methadone and pharmacists should take particular care to enquire about any new medications (including natural products and over-the-counter medications) periodically, and especially when an otherwise stable patient suddenly experiences drug craving, withdrawal (some drugs can induce more rapid liver metabolism of methadone) or intoxication.

Harald Breivik is emeritus professor of anaesthesiology, Universitetet i Oslo, Norway. He is also editor-in-chief of the Scandinavian Journal of Pain

References


YOUR QUESTIONS ...

Do you have a question on pain management?
Submit your questions on www.paineurope.com
Successful management of chronic pelvic pain

Chronic pelvic pain is a syndrome that can have multiple causes, explains pain specialist Dr Annica Rhodin, and may require a multidisciplinary approach

Key learning points

- Chronic pelvic pain is a common, multifactorial complaint that affects both women and men, causing disability and frustration for patients.
- The exact aetiology remains unknown, although several theories have been proposed.
- Assessment should be undertaken with care and compassion, taking into account the sensitive nature of the area.
- Management involves ruling out treatable pathology concomitant with strategies to control pain.
- Novel treatment approaches have been investigated for specific clinical scenarios.

Chronic pelvic pain (CPP) is a common complaint, of multifactorial aetiology, leading to disability and suffering. As such it is often a source of frustration to both physicians and patients.

A diagnosis of CPP implies intermittent or constant pain in the lower abdomen, the anatomic pelvis or lumbosacral region for at least six months. IASP has provided a more specific definition for CPP without obvious pathology (CPPWOP) as ‘chronic or recurrent pelvic pain that apparently has a gynaecological origin but for which no definitive lesion or cause is found.’ This definition should be extended to include pain of urological origin.

This debilitating condition affects both men and women. The prevalence in the general US population is 15% in women aged 18-50. In the UK, an annual prevalence in primary care of 38/1000 was found in women aged 15-73, a rate comparable to that of asthma (37/1000) and back pain (41/1000). CPP syndrome in men has an estimated prevalence of 10-16%.

Comorbidity with chronic headache, irritable bowel syndrome, non-specific rheumatoid disease and fibromyalgia is common, as well as with factors of stress, fatigue, anxiety and depression.

Aetiology

CPP is considered a syndrome of multiple causes with several postulated pathogenetic mechanisms. The involvement of the peripheral and central nervous system is pivotal and may result in a complex pain syndrome affecting the whole pelvis and, as a consequence, multiple-organ symptomatology.

The initial trigger may be relatively benign, such as a urinary tract or GI infection, minor trauma, endometriosis or postoperative adhesions. However, a predisposed patient may develop a range of significant sensory and efferent functional abnormalities indicating involvement of a sensitised peripheral and central nervous system. The ultimate consequence may evolve into a severe chronic pain disorder with physical, psychosocial and sexual dysfunction.

One proposed theory is abnormal permeation of bladder or bowel epithelium due to lack of glycosaminoglycan production. Other current theories include atypical bacterial infection, nonlinear colonisation, and altered immune or host-cell responses resulting in central sensitisation with visceral hyperalgesia in a vulnerable individual.

Voiding dysfunction, bladder sphincter and anorectal dyssynergy and abnormal intra-prostatic pressure in men can contribute to pelvic floor myalgia. Myofascial pain syndromes in the perineal region and lower abdomen can add to persistence of the pain condition.

The same mechanisms can be applied to women with endometriosis, adhesions or pelvic inflammatory diseases including pelvic congestion.

Magnetic resonance studies of the brain in men with CPP show significant reduction in relative grey matter volume in the anterior cingulate cortex of the dominant hemisphere compared with healthy controls. Women with endometriosis-associated CPP display decreased grey matter volume in brain regions involved in pain perception, including the left thalamus, left cingulate gyrus, right putamen and right insula. These areas are core structures of emotional pain processing, supporting the central pathological mechanisms of CPP syndrome.

Phenotypes

CPP is divided into specific pelvic organ pain or non-pelvic pain syndromes. The symptoms may arise from the bladder, prostate, scrotum, internal or external gynaecological organs, anorectum, regional nerves, muscular pelvic floor, lower abdominal or lumbosacral regions, or evolve as a more generalised pain syndrome.

Prostatitis and interstitial cystitis or painful bladder syndrome have common symptomatology consisting of urgency, voiding problems, and frequency during the day or night.

Pain localised to a specific pelvic organ should lead to investigation of that organ.

The papers by Fall et al and Potts et al have more details about the different pain syndromes.

Differential diagnosis

The primary end point of differential diagnosis is to exclude evidence of end-organ disease from the genitourinary, GI, neurologic and musculoskeletal areas, as well as systemic diseases.

It is important to start by considering the organ system in which the symptoms appear to be primarily perceived. Organ-specific conditions, such as urethritis, cystitis and prostatitis, should be...
TREATMENT

The more severe CPP cases are best managed using a multidisciplinary approach. Management requires good integration of all pelvic organ systems and including musculoskeletal, neurologic and psychological mechanisms.

Treatment modalities can be divided into disease specific and the treatment of pain as such.

For painful bladder and prostatitis the use of antibiotics should only be instituted after two localisation cultures positively identify the same organism.

Alpha-blockers and antiandrogens may be tried, as well as pentoxyphylline or dimethylsulfoxide bladder instillations (where available) as plausible effective organ-based therapy.

Endometriosis should be treated with oral contraceptives, danazol, progesterone and GnRH-agonists as appropriate.

At the same time it is important to also treat the pain as such. Nonpharmacological therapies include cognitive behavioural therapy and stress management, such as physiotherapy, acupuncture and TENS. Biofeedback\(^6\) and trigger point\(^4\) treatment are indicated for myofascial pain in the pelvic and lower abdominal areas. Treatment for myofascial pain implies techniques of needling; either acupuncture or injection of a local anaesthetic into the the trigger points of the affected muscles. Biofeedback is performed by attaching electromyography apparatus to the muscles of the patient and instructing him or her to relax and contract in order to gain and perceive control of the tension of the muscle.

Pharmacological approaches include paracetamol/NSAIDs, tricyclics or SNRIs, gabapentin/pregabalin, and opioids for severe cases. When using strong opioids for a chronic disorder it is important to carry out a risk evaluation for problematic use or addiction and to carefully evaluate response not only regarding pain relief but also on restored function and quality of life.

Nerve blocks on the pudendal nerve have been described as well as lidocaine instillation in the bladder or the uterus.

Sacral neuromodulation has been used for interstitial cystitis/ bladd pain. The percentage of patients who responded to test stimulation was reported between 51 and 77\%.\(^12\)

Surgery is an option in severe organ disease, such as in endometriosis, enterocolitis or bladder ulceration. Unfortunately excision of diseased organs does not always cure the pain, and chronic pain may persist even after successful surgery.

As with all chronic pain conditions emphasis should be placed on recovering and preserving function rather than attempts to cure or eliminate all pain. Specific goals should be set regarding an individual patient’s ability to work, attend school, care for children, perform leisure activities and exercise in a reasonable way instead of aiming at complete pain relief.

Dr Annica Rhodin is a pain specialist from Akademiska Sjukhuset, Uppsala, Sweden.

REFERENCES

Managing musculoskeletal pain in an elderly woman

A case of severe pain in multiple areas, in a 76-year-old woman with several co-morbidities is presented by Dr Chris Edwards

Background
Chronic pain can occur due to a number of musculoskeletal conditions. These conditions are common, with over nine million people in the UK affected by arthritis alone. An estimated 40% of adults experience an episode of spinal pain arising from the back or neck in any one year. The establishment of long-term pain in these individuals is often complicated by associated depression.

Case Assessment
A 76-year-old woman presented to her rheumatologist. She complained of severe pain in multiple areas, including her lower back, shoulders, neck and knees. She described the pain as very severe and explained that it was aggravated by physical activity. There was some early morning stiffness but this did not last longer than 10-15 minutes. In the past, she had had pain in these areas and was diagnosed with osteoarthritis on the basis of X-ray findings. Both hips were replaced several years before. She had a past history of indigestion, as well as AF that had started following an inferior MI. Recent blood tests showed a mild iron-deficiency anaemia, for which no cause could be found and reduced creatinine clearance. The ESR was normal.

The low back pain made it difficult to perform the examination because lying down was very uncomfortable. The examination revealed:
- Reduced movement of the shoulders and knees, associated with severe pain
- Severe crepitus and grinding on active movement of the knees, consistent with bone-on-bone contact between the femur and tibia.

Repeat X-rays of the knees, shoulders and lumbar spine confirmed osteoarthritic changes. In the knees there was clear bone-on-bone contact, as suspected from the examination.

The most severe pain originated from the knees. Ideally, this would have been resolved by bilateral knee arthroplasty. However, it was felt that the surgical risk from the other medical problems was too great and the patient was also against this. The rheumatologist felt that NSAIDs should be avoided due to the cardiac history, anaemia and poor renal function. Initially, a combination of paracetamol 500mg and codeine 30mg was given three times per day. The rheumatologist also performed local injections of corticosteroid and lidocaine into both knee joints.

The patient returned one month later. The analgesics had produced some benefit but the pain was still intense. As a result, the patient’s GP had doubled the dose to paracetamol 1g and codeine 60mg three times per day. Unfortunately, this had resulted in constipation. The patient had also suffered with some indigestion and nausea. The steroid joint injections had been very effective for a few weeks but had now worn off. A further examination confirmed that the pain was coming from the same joints as before.

Key learning points
- Musculoskeletal conditions are common and a major cause of chronic pain; more than nine million people in the UK are affected by arthritis alone.
- Successful treatment of pain can lead to increased physical activity with consequent improvement of muscle tone around the affected joints.
- In older patients with multiple comorbidities, fewer therapeutic approaches or surgical interventions tend to be indicated.
- Where opioid therapy is unsuccessful, possible strategies include opioid rotation and/or changing route of administration.

In view of the widespread pain, the GP had rechecked the ESR and sent a protein electrophoresis test to rule out polymyalgia rheumatica and myeloma. Both tests were normal. As the pain was severe and widespread, the GP also asked about symptoms of depression, but none appeared to be present.

The rheumatologist was concerned about the possible risks associated with the analgesic treatment options. The decision was to add a small dose of meloxicam (7.5mg per day) to the paracetamol and codeine. Physiotherapy was also arranged to attempt to increase mobility and muscle strength around the painful joints. The physiotherapy resulted in a little benefit, as did a course of acupuncture performed by the physiotherapist.

One month later, the rheumatologist was called by the GP because the patient’s creatinine had increased significantly. The GP had therefore stopped the meloxicam and the renal function was now returning to the pre-treatment level. The patient was still complaining of pain from multiple joints. A further joint injection to the right knee produced only short-term benefit once again. The GP and rheumatologist agreed to discontinue codeine and to start tramadol 50mg three times per day. This produced some benefit but the patient was troubled with breakthrough pain a few hours before the next dose of tramadol was due. Paracetamol 1g four times per day was continued.
Discussion
As a result of inadequate pain control, the rheumatologist suggested an opioid patch. The patch was continued with regular paracetamol. The GP was concerned that opioids might lead to confusion and falls at night and monitored for this, however, this did not occur. The patient continued to have some pain but found the new regimen provided an acceptable level of control. As a result, the patient was able to increase physical activity a little, which appeared to increase muscle tone around the affected joints.

Case review: Italy

Professor Maurizio Cutolo
Full professor of rheumatology, and director, Research Laboratories and Academic Unit of Clinical Rheumatology, Department of Internal Medicine, University of Genova, Italy

This case report presents a condition of highly symptomatic and particularly diffuse osteoarthritis (OA), of a severity that is fortunately quite rare in the clinical experience of rheumatologists.

The therapeutic management of the patient has clearly been deficient in the previous 30-40 years, resulting in the present severe and progressive clinical status of this patient. As consequence of several stratified co-morbidities, and in view of the age of the patient, few therapeutic approaches and/or surgical interventions are available without severe contraindications and associated adverse effects.

Case review: The Netherlands

Dr Jan H Vranken
Anaesthesiologist and coordinator, pain relief unit, Medical Center Alkmaar, Alkmaar, The Netherlands

In 1986, the WHO published a three-step analgesic ladder which, depending on individual pain intensity, progresses from non-opioid analgesics to weak opioids to strong opioids. However, there is a debate as to whether the second step of the WHO analgesic ladder comprising opioid analgesics such as tramadol, codeine, dihydrocodeine, and dextropropoxyphene is still needed for the treatment of chronic pain. Additionally, codeine is a weak opioid and its usefulness in pain management is further limited due to side-effects, especially constipation. With this in view, a direct move to the third step of the ladder can be feasible and may reduce pain scores – but also requires careful management of side-effects.

In this patient, a switch to transdermal administration of opioids was made resulting in an improved pain management. Although oral remains the preferred route of administration, alternative routes (sublingual, transdermal) are available and provide clinicians with the means to treat patients who cannot take oral medications because of head, neck, mouth or bowel lesions. In addition, transdermal opioids have been increasingly used for the treatment of chronic pain because of perceived advantages to their side-effect profile.

When patients experience either insufficient analgesia or problematic side-effects following opioid administration, it may be worthwhile trying another opioid. Sequential trials of different opioids – opioid rotation – can help identify the most favourable drug. Variability in analgesic or adverse effect response to different opioids is relatively common and is probably due to incomplete cross-tolerance. Indications for opioid rotation include poorly controlled pain with unacceptable adverse effects, refractory pain and difficult pain syndromes. Alternatively, switching to transdermal, rectal, nasal, parenteral or neuraxial administration may improve analgesia with less accumulation of metabolites and consequent toxicity.

References
Kan du se att den här kvinnan har cancer?
Kan du se att hon får en opioid mot svår smärta?
Kan du se att hon har fått förstoppling och att laxantia inte räcker?

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