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Welsh Medicines Resource Centre
Canolfan Adnoddau Moddion Cymru

Bulletin
"Independent prescribing information for NHS Wales"
March 2014

Management of chronic non-malignant pain

Chronic pain can have a significant impact on quality of life, and can lead to a cycle of distress and disability as well as other disorders such as chronic fatigue, sleep disturbance, and mood disorder (see Fig. 1). Appropriate and effective interventions are not only beneficial for an individual, but are also potentially beneficial for healthcare delivery and society.[1]

In 2008, the Welsh Government outlined proposals for specialist services for chronic conditions, including pain. There appears to be wide variation in the provision of such services nationally,[2,3] and it is likely that many patients with chronic pain will be managed by their GP. This bulletin discusses the management of **chronic non-malignant pain in adults in primary care**, including pharmacological and non-pharmacological approaches.

What is chronic pain?

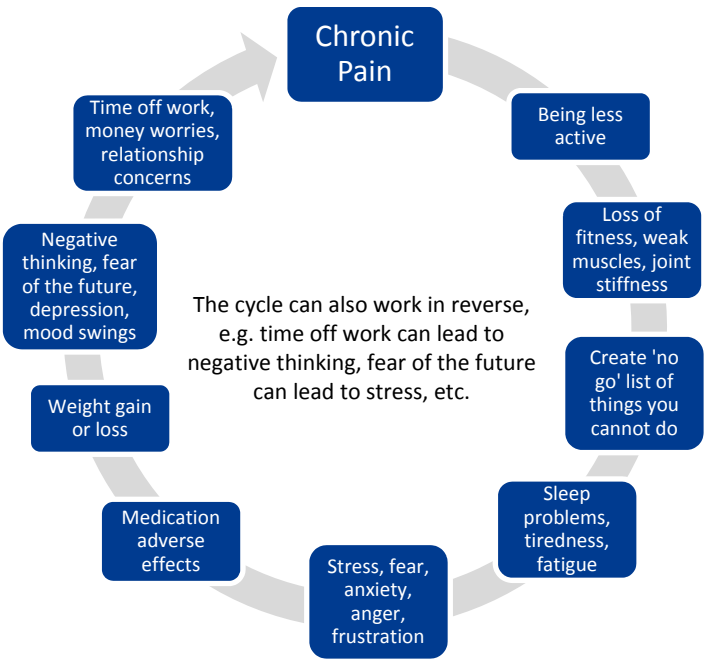
Chronic pain is a symptom that can be associated with a variety of causes, but is usually described as pain that has lasted for more than three months following the usual recovery period for an illness or injury. An individual's experience of pain may be mediated and moderated by genotype, emotional, cognitive, environmental and socioeconomic factors, and physical pathology.[4] This complex bio-psychosocial experience can be difficult to treat.[2]

Chronic pain should not be viewed simply as long-lasting acute pain, and therefore, management options will be quite different.[5] Acute pain occurs in the presence of noxious stimuli, serving as an alarm system to warn of tissue trauma. Conversely, chronic pain appears to serve no purpose and its persistence cannot always be explained as a consequence of an obvious anatomic defect or possible tissue damage. There is evidence that patients with chronic pain have abnormal regulation within the central nervous system, i.e. it has somehow become 'sensitised'.[6] Pain-causing conditions may be incurable, irreversible, or may induce changes, which set up a cycle where pain continues although the condition no longer exists.[3]

Summary

- Chronic pain can have a significant impact on a person's quality of life, leading to a cycle of distress and disability.
- Chronic pain should not be viewed as long-lasting acute pain; management options differ.
- Effective management requires biological, psychological, and social factors to be addressed simultaneously.
- Promoting self-management and coping skills is crucial to chronic pain control.
- Pharmacotherapy should be considered as only one aspect of an overall rehabilitative strategy.
- Non-pharmacological therapies and medicines with proven efficacy for chronic pain syndromes (e.g. tricyclic antidepressants or antiepileptic drugs for neuropathic pain) should always be tried before starting opioids.

Figure 1. The cycle of chronic pain (adapted)[7]



NHS WALES GIG CYMRU

All Wales Therapeutics and Toxicology Centre
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Assessment of pain

Because pain is a personal experience, it is difficult to define and quantify objectively, but assessment is important to establish a baseline and to evaluate management. Several validated tools for pain assessment are available. A biopsychosocial approach should be used to assess:

- biomedical issues (e.g. adequate investigation, previous treatment, concurrent medical or surgical problems, and any 'red flags').
- levels of physical activity (e.g. ability to look after personal care, to work, and perform activities of daily living).
- psychological and social features (e.g. co-existing psychiatric problems, unresolved grief, major misconceptions, willingness to change, and 'yellow flags').

Early identification and 'Yellow Flags'

'Yellow Flags' were first developed to assist in the early management of lower back pain, but have now been adopted as prognostic indicators for pain conditions in general.[8] In particular, Yellow Flags, or psychological barriers to progress, can be used to determine which patients may require psychological support at an early stage (see Fig. 2). Patients displaying early signs of distress or inability to cope with their pain are likely to make more progress from early referral to specialist pain services. However, there is also much that GPs and their primary care colleagues can achieve while waiting for specialist input.

Many patients welcome the opportunity to discuss the impact of pain on their life and this can often be therapeutic in its own right. Knowledge of common factors that can affect the experience of pain is helpful in guiding those discussions. Previous pain experiences may play a large role in how a person copes with a new incident of pain. Acknowledging this without dwelling on it can be an important step for the clinician to understand the patient's current presentation or barriers to change.

The role of partners, carers, family, and other support is crucial in a person's rehabilitation. However, what may be seen by family members as helpful behaviour, e.g. taking over roles or encouraging rest, may be detrimental in the long term. Often, the GP is well placed to observe influencing factors; sharing this insight with specialist services enables a holistic approach to be taken to management.

Figure 2. Examples of Yellow Flags for pain

The presence of multiple biopsychosocial factors may highlight the need for a multidisciplinary approach.

Attitudes and beliefs	▪ Pain is harmful or severely disabling ▪ Expectation that passive treatment rather than active participation will help ▪ Feeling that 'no-one believes the pain is real' – may relate to previous encounters with health professionals
Emotions and behaviour	▪ Fear-avoidance (avoiding activity due to fear of pain) ▪ Low mood and social withdrawal
Other psychosocial factors	▪ Poor family relationships or history of abusive relationships ▪ Financial concerns particularly related to ill-health or ongoing pain ▪ Work-related factors e.g. conflict over sick-leave, ability to perform current job tasks ▪ Ongoing litigation related to persistent pain condition

Chronic pain management

Currently available treatments for chronic pain often do not result in complete resolution of symptoms.[4] Patients who accept the chronic nature of their pain, rather than continuing to seek relief or cure may fare better with therapeutic interventions.[9]

Therefore, management should focus on improving the function of patients, their ability to cope with their pain, and the effect it has on wider aspects of their life. How this is achieved will depend on the individual patient. For some, finding a suitable medication that provides some reduction in pain levels will be sufficient to allow them to increase their activity and trigger their own rehabilitation; others may require significant input from specialist services.

The biopsychosocial approach

A biopsychosocial approach to the management of chronic pain should move patients towards a more positive way to manage their pain in the long term. Effective management will require biological, psychological, and social factors to be addressed simultaneously in order to achieve the best outcomes. Knowledge of local services and self-help resources for patients will promote understanding and improve consultations even in the short time available in primary care. This is the model of pain management that the majority of pain services have now adopted and setting the scene early, particularly with a self-management message, will ensure that referrals to specialist services have an optimal effect.

Psychological interventions

There is evidence that cognitive behavioural therapy, as part of a pain management programme (PMP), is effective in improving pain experience, mood, coping, negative outlook on pain, and activity levels.[10] Although this requires specialist input, some psychological interventions do not require high levels of expertise and may be possible even when time is limited in primary care; patient education, relaxation training, and activity regulation have become a well-established part of pain management, as an alternative, or as an adjunct to pharmacotherapy.[11]

Self-management is crucial for long-term pain control, yet patients often feel helpless and unable to cope with pain themselves. This may, in part, be due to multiple failed therapies over extended periods of time, which can leave them feeling depressed, hopeless, and often passive. The re-emergence of other distressing life experiences should not be overlooked and while 'raking over' past events is not required, acknowledging them and providing the patient with systems for coping with and processing the effects is a useful method for moving forward.

The Pain Toolkit (www.paintoolkit.org) is a very useful resource to set the scene with patients.

Motivational interviewing

Providing a patient with the understanding of why they consider change so difficult to achieve is often key to enabling them to move forward. A central concept of motivational interviewing (MI) is the identification, examination, and resolution of ambivalence about changing behaviour. MI is one of several patient-centred counselling methods but they usually all employ approaches such as open-ended questions, affirmation, reflective listening, and summaries to create a positive environment for change. The use of such methods in the time available at a GP consultation may be enough to get a patient thinking of change and increases the chances of them continuing the process.[12]

Relaxation and mindfulness

Stress and anxiety may worsen the experience of pain and make daily tasks harder to achieve. Relaxation techniques such as progressive muscle relaxation and visualisation can be a useful part of a patient's daily management regimen. In specialist settings, relaxation is often mentored by nurses or occupational therapists, but it is a skill that patients can adopt for themselves with a little guidance.

Mindfulness is the practice of paying close attention to present events. The aim is to reduce pain experience, anxiety, and 'catastrophising' (viewing or presenting a situation as worse than it actually is). Patients with chronic pain who practice mindfulness learn to be curious rather than resentful about their pain. One aim is to move away from the 'this is going to work' mentality that can often inhibit progress when plans do not work out.

Goal setting and pacing activity

Goal setting can be useful to help patients maintain motivation or restart activity by allowing them to work towards something positive, e.g. increasing walking distance. If the person was previously very fit and active, they may envisage the end-goal as being able to walk a considerable distance, but setting smaller, achievable targets, e.g. firstly to the end of the road and back and later around the block, allows the patient to see their progress, which then encourages them towards the next step.

Pacing is a useful self-management skill focussing on increasing activity without causing significant fluctuations in pain levels. Patients work towards maintaining even levels of activity throughout a day, week, month, etc. Initially small increases are made, with the longer-term aim of regaining more significant levels of functioning.

While simple in theory, pacing is often one of the most difficult activities for patients with chronic pain. On a 'good' day vacuuming the whole house might be physically possible. However, this might result in the patient being unable to do anything for the next few days while they recover. Breaking this down to perhaps cleaning one room every day might seem an easy solution, but the practice can be difficult. Reassurance and encouragement is required, making primary care practitioners ideally placed to provide support.

Improving functional performance

People with long-term pain can often be severely incapacitated and physically deconditioned with little reserve for recreational or 'emergency' activity. Patients may frequently rest until pain subsides; this may be for several days. In some cases, lack of activity worsens deconditioning to the point that any movement becomes painful. The result is abstention from anything that may result in pain, including the basic activities of daily living. Patients with pain of any severity should be repeatedly encouraged to maintain a level of activity, although exactly what that entails will need to be tailored to their specific circumstances.

Physiotherapy

The main aim of physiotherapy is functional restoration, focusing on assisting the patient to improve exercise tolerance and stamina, while simultaneously addressing concerns about activity-related pain and its meaning. It is important that patients understand that pain is not always a sign of increasing or ongoing damage. Patients will vary in their ability and goals for physical improvement. To optimise participation, it is essential to understand the level of function that the patient feels is achievable. For some, being able to stand to make a cup of tea might be the priority, for others it may be getting back to the gym. Exercise programmes should be regular and look to gradually increase in duration and intensity to limit any consequential increases in pain. Tailoring exercise to the patient's daily routine may result in better adherence. Many patients, particularly those who are well-motivated, will not necessarily require referral but will be able to adopt a programme with graded increases themselves. Specialist chronic pain physiotherapists commonly have additional training, enabling them to provide a level of psychological support to the patient.

Pharmacotherapy

Analgesic medicines have been the mainstay of pain treatment for decades. The cost of NHS Wales GP prescribing of analgesics was £50.5 million in 2013, showing a 34% increase over five years.[13]

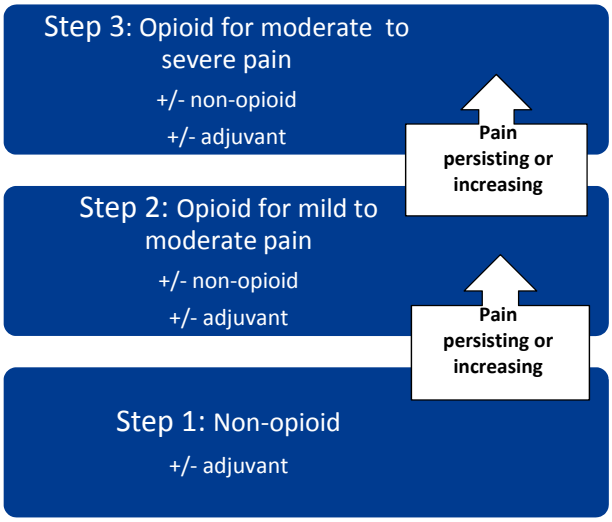
Chronic pain is complex; individual response rates to pain medication vary greatly and failure rates are high. Data from systematic reviews of pain medication show that fewer than half of patients achieved at least a 50% reduction in pain intensity; failure rates were highest in patients with chronic pain.[14,15] There is evidence to suggest that individuals who do respond to pain medication in terms of reduction in pain also experience improvements in associated problems such as fatigue, depression, sleep disturbance, and general measures of function and quality of life, including ability to work. However, it is difficult to determine which patients will respond before trying different medicines. An implication of high failure rates is that populations with pain need access to a range of medication to have a better chance of success. Importantly, pharmacotherapy should be considered as only one aspect of an overall rehabilitative strategy.

Choice of medication

The order in which analgesics are tried should be based on efficacy and safety, adjusted for individual characteristics. An individual may need a combination of analgesics as pain may have several different aetiologies.[14]

The World Health Organization (WHO) analgesic ladder (see Fig. 3) was initially developed as a framework to help clinicians establish treatment plans for cancer pain. There have been proposals for modification of the analgesic ladder to address other types of pain, such as chronic non-malignant pain.[16] However, even in its original form, it provides an analgesic strategy for non-specialists.[17]

Figure 3. WHO analgesic ladder (adapted)[18]



Careful assessment and diagnosis is fundamental in deciding appropriate pharmacotherapy. The choice of individual agent will be influenced by factors such as severity and type of pain, previous drug efficacy or adverse effects, co-morbidities, risk of drug misuse, and clinician experience. Regular review of analgesia is essential to assess tolerability and efficacy, particularly after initiating or changing treatment. Treatments that are ineffective should be changed or stopped. The analgesic ladder should be used pragmatically and if a particular medicine is not tolerated or is ineffective, then it may be worth considering a different agent from the same class before moving to the next step.[17]

Paracetamol

Paracetamol is often the first step in the pharmacological management of pain, although its exact mechanism of action is not known. Serious adverse effects of paracetamol are considered rare, however, doses greater than the maximum daily dose (i.e. 4g per day) can lead to fatal liver toxicity, and, less frequently, renal damage.[19]

Non-steroidal anti-inflammatory drugs

NSAIDs limit prostaglandin production, resulting in anti-inflammatory and analgesic actions. They are appropriate for the treatment of pain associated with inflammatory conditions and are of modest benefit in non-specific low back pain.[20,21]

Pharmacotherapy should be considered as only one aspect of an overall rehabilitative strategy.

All NSAIDs are associated with gastro-intestinal (GI) toxicity; the lowest risk appears to be with ibuprofen. Selective COX-2 inhibitors are associated with a lower risk of serious upper GI adverse-effects than non-selective NSAIDs. Vascular risks are increased to varying degrees by different NSAIDs; naproxen (1g daily) is associated with a lower thrombotic risk.[20] There may be variations in response and tolerance to different NSAIDs; about 60% of individuals will respond to any given NSAID, but those who do not may well respond to another. A full analgesic effect will normally be obtained within a week.[20]

Topical NSAIDs have been found to be more effective than placebo in reducing chronic musculoskeletal pain. GI adverse events do not differ from placebo and are less frequent than with oral NSAIDs.[22] Topical NSAIDs may be considered in the treatment of pain from chronic musculoskeletal conditions, particularly in patients who cannot tolerate oral NSAIDs.[17]

Anti-epilepsy drugs (AEDs) for pain

Gabapentin and pregabalin have an established adjuvant role and have been endorsed by NICE as first-line medicines for the treatment of neuropathic pain.[23] There is little evidence for the efficacy of other AEDs for chronic pain, but carbamazepine is recommended by NICE for trigeminal neuralgia.[23] Studies show that AEDs produced side effects in most people taking them, leading to cessation in around 25% of cases. However, serious events were not significantly increased.[24] Prescriptions for these medicines have increased greatly over the last five years and concerns are now being expressed regarding abuse and a growing 'black market'.[25]

Antidepressants for pain

Antidepressants can also be termed adjuvant analgesics. Their analgesic effect is independent of their antidepressant effects and may involve several mechanisms. Although it is not licensed for the treatment of neuropathic pain, the tricyclic antidepressant (TCA) amitriptyline has been used first-line for many years and is recommended by NICE.[23,26] The starting dose should be low and increased gradually every seven days or so according to response. A trial of a TCA should last for 6-8 weeks, with at least 1-2 weeks at the maximum tolerable dose.[27] Duloxetine, a serotonin and noradrenaline reuptake inhibitor (SNRI) is also recommended by NICE as a first-line treatment of neuropathic pain.[23]

Opioid analgesics

Opioid analgesics can be effective in the management of somatic, visceral, and neuropathic pain. They can produce useful analgesia in the short and medium term but evidence for sustained analgesia in the longer term is lacking, and improvements in quality of life are unlikely to be achieved unless opioids are prescribed as part of a broader approach to improve patient function.[28]

Opioid analgesics are traditionally classified as 'weak' or 'strong'. Weak opioids include codeine and dihydrocodeine. They have defined upper dose limits in the BNF and are usually included at Step 2 of the WHO analgesic ladder for mild to moderate pain. However, the term 'weak opioid' should not encourage a lack of caution in prescribing. Although the discussion that follows is most pertinent to strong opioid prescribing, it should also be borne in mind when prescribing weak opioids, particularly at higher doses. Tramadol is often included at Step 2 of the WHO analgesic ladder, but it is classified as a strong opioid by the BNF.[20]

Deciding whether to start opioid therapy

In most situations, for most pains, and for most patients, opioids should **not** be considered as first-line treatment. The risks of long-term opioid therapy are not fully understood, but are thought to include endocrine impairment (leading to hypogonadism, diminished libido, and adrenal insufficiency in both sexes), opioid-induced hyperalgesia (where patients feel more pain due to opioid-induced changes in neurophysiology), and immunosuppression.

Non-pharmacological therapies and medicines with proven efficacy for chronic pain syndromes should always be tried before starting opioids.

Consider seeking advice from a pain specialist before prescribing, particularly when there is doubt as to whether opioids are appropriate.[28] The benefits must be balanced against the burdens of long-term use, as therapy for chronic pain may need to be continued for months or years.[28]

The use of opioids may shift the patient's sense of control towards an external agent, i.e. medication, for the relief of pain, leading to the neglect of other treatment goals such as increased function and a return to normal activities. An agreed treatment plan is very important and should be reviewed as part of the monitoring process.

Initiating opioid therapy

The patient should be assessed thoroughly prior to initiation of an opioid. This should include a history of their mental health, particularly depression, substance misuse, and post traumatic stress symptoms, since they may complicate pain management if left untreated.[28]

Where possible, modified-release opioids administered at regular intervals should be used, because immediate-release preparations are more associated with tolerance and problem drug use. A closely monitored trial of opioid therapy is recommended before long-term use.[28] Treatment should start with a low dose, titrated upwards according to analgesia and adverse effects. Patients should be warned that it may take several days to determine effectiveness. The doses of opioid used for chronic non-malignant pain in clinical trials usually equate to less than 180mg morphine equivalent in 24 hours. If patients do not achieve useful relief of pain at doses of 120-180mg morphine equivalent in 24 hours they should be referred to a specialist.[28]

The All Wales Medicines Strategy Group will continue to include 'morphine as a percentage of strong opioid prescribing' as a prescribing indicator for 2014-15, to encourage the use of **morphine** as the first-line strong opioid. The efficacy and safety of morphine is established in clinical practice and the familiarity of most clinicians with its use is an additional consideration for patient safety.[29] Due to evidence of increased abuse and misuse (with diversion of legitimate prescription medication being one supply route), and an increase in related harm and deaths, **tramadol** use is set to be a national prescribing indicator for 2014-15.[30]

Patients should be advised to avoid driving at the start of opioid therapy and following dose changes. Patients are permitted by law to drive in the UK if they are taking no more than the prescribed dose and feel fit to drive. However, it is their responsibility to inform the DVLA that they are taking opioid medication.[28]

Reviewing opioid therapy

During long-term opioid treatment, reviews should be conducted at least monthly for the first six months and perhaps less often (but at least twice a year) thereafter, depending on the complexity of the case.

Eighty percent of patients taking opioids will experience at least one adverse effect; patients should be advised about this before starting therapy.[28] The most common adverse effects are constipation, nausea, somnolence, itching, dizziness, and vomiting. Tolerance to some adverse effects should develop after a few days but others, such as pruritus and constipation, tend to persist.

Addiction to opioid medication

The likelihood of addiction to prescribed opioids occurring is influenced by a number of social, psychological, and health-related factors including personal or family history of substance or alcohol abuse, poor social support, and co-morbid psychiatric disturbances. The presence of risk factors should not be a reason for denying a patient opioid therapy, but should help to determine the degree of monitoring and support needed to prescribe opioids safely.[28]

Patients should be given prescriptions from one prescriber only and if concerns about addiction arise, the number of doses prescribed should be reduced. Some behaviours that may indicate problem medication use include: earlier prescription seeking or claims of lost medication; intoxication; frequent missed appointments; and use of other scheduled drugs. Any concerns about problem medication use should prompt referral to specialist pain and addiction services.[28]

Resources

- British Pain Society www.britishpainsociety.org
- All Wales Medicines Strategy Group. www.awmsg.org
  All Wales Audit: Towards appropriate NSAID prescribing 2010-2012 and Tramadol Educational Resource Materials.
- Cardiff University Pain Community Centre www.paincommunitycentre.org
  A library of pain resources and details of a diploma course in pain management for primary care practitioners.

Summaries of Product Characteristics (SPCs) should be consulted for full prescribing information.

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