GENERAL MEDICAL COUNCIL

DR JANE BARTON

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CHAPTER 22

Pain Relief

P. Crome

Introduction

Persistent or recurrent pain is probably the commonest health problem faced by older people. Pain varies in location, nature, frequency and severity and there are numerous underlying causes. Clearly, the prognosis varies too, related to the aetiology. Inadequately treated acute pain, for example after surgery, results in increased morbidity through immobility leading to deep venous thrombosis, chest infections and delayed return of normal bowel function. Additionally, chronic and recurrent pain is important because it is associated with mental and sleep disturbances, decreased functioning and mobility and increased risk of hospitalisation. There are a large number of analgesic drugs available for physicians to prescribe and treatment strategies have been developed for conditions such as arthritis and the pain of cancer. However, it is the general experience that effective management with complete remission of symptoms and without drug side-effects often proves elusive. It is certainly the view of patients that pain is poorly managed.[1] This chapter summarises present knowledge about pain and its treatment in older people.

Epidemiology

A recent community study provides important information on the prevalence, location, temporal pattern and severity of pain.

Table 22.1. Percentage prevalence of pain and persistent pain* in 741 community dwelling subjects over 65

Location	Pain	Persistent pain
Head	5.1	1.5
Face	0.4	0
Neck	11.6	4.7
Back	29.6	12
Limb joints	44.5	19.4
Chest	2.4	0.7
Abdomen	5.1	1.9
Limb except joints	17.3	10.4

*Defined as pain daily for six months or more.

Adapted from Brochet et al.[2]

In a French study of community-living older people aged over 65, over 70% of the 741 subjects surveyed complained of pain, most commonly in the limb joints and back (see Table 22.1).[2] Almost a third of the sample complained of pain each day for more than six months. The prevalence of persistent pain was higher in the older cohorts. Thus, 49% of women and 35% of men over 84 complained of persistent pain compared to 33% and 20% of women and men aged 68–74. This high prevalence of arthritis has been confirmed in the U.K. One study reported that arthritis affected 40% and 54% of men and women respectively aged 65–74 years with slightly higher rates of 44% and 66% for men and women aged 75 or more.[3] The effect of this increased prevalence of pain on self-perceived health status may be less marked. In the Tipping the Balance Study, the SF-36 domain bodily pain score was only slightly lower (more pain) in the

80–89 year old group compared to the 70–79 age group[4] indicating that the impact of pain continues to increase into extreme old age.

Types of Pain

Pain may be defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".[5] Patients use a wide range of adjectives to describe pain. These include sharp, burning, throbbing, aching and crushing. The meanings patients ascribe to these terms varies and other communication difficulties such as dysphasia or cognitive impairment may make it difficult for the physician to fully appreciate the sufferers' experiences. The use of visual aids to aid assessment of severity is used in a growing number of centres. Examples of such aids include visual analogue scales on which severity of pain is graded from "no pain" to "worse possible pain" or showing patients a series of faces ranging from a happy smiling face to one contorted with pain and asking the patient to point to the one that best shows how they feel.

Pains may be grouped into four main classes (nocioceptive, neuropathic, undetermined and psychological) which are usually managed in different ways (Table 22.2).

Pain and Old Age

The traditional view has been that older people are more stoical about pain and complain less. Studies of experimental pain produced by such stimuli as thermal radiant heat, electric shock or pressure on the Achilles Tendon have produced contradictory results; some suggest that older persons tolerance is higher whilst others show no age effect.[7–8] These studies have focussed largely and not surprisingly on superficial pain. Further criticisms

Table 22.2. Classification of pain by pathophysiological process and principal treatment modality

Type of pain	Causes	Principal treatments
Nocioceptive	Arthritis, visceral pain, ulceration, limb ischaemia	Analgesics
Neuropathic	Trigeminal neuralgia, postherpetic neuralgia, painful neuropathies, phantom limb	Antidepressants/anti-convulsants
Undetermined	Headaches, migraine	Various
Psychological	Somatisation disorder Hysterical reaction	Psychological approaches

Adapted from AGS[6]

of this area include the absence of longitudinal studies, the large number of methods used to study pain and variability of end-points that were employed. Harkins' overall conclusion was that superficial pain is not altered in old age however deep pain appears to be less frequent and less intense in a number of acute conditions.[8] The evidence for the latter is based on the phenomenon of silent myocardial infarction[9] or silent perforated peptic ulcer[10] in which the older patient presents with atypical features such as fatigue and immobility rather than with pain. However, patient selection for these studies may have affected the results and whilst clinicians should always be aware of atypical presentation, classical presentation is still more common. Denial of pain may have other causes. Interestingly, Barsky et al. in their review of this subject do not present any evidence of age being a factor.[11] However it is doubtful whether these differences have any influence on treatment strategies which depend on the titration of analgesic dose and dosing interval against clinical symptoms.

Pain in Nursing Home and Cognitively Impaired Patients

The assessment and treatment of pain in patients in nursing homes deserves special consideration. This group of older people has the highest prevalence of pain (several studies reporting rates over 50%), the highest rates of co-morbidity, the highest levels of dependency and the highest rates of cognitive impairment due to dementia or sequelae of stroke. Assessment and management therefore pose particular problems. However, they do also have the potential advantage that they are observed 24 hours a day by nursing staff. Their general frailty may make investigation of underlying causes difficult. Important points in management include treating all co-morbid conditions as optimally as possible. For example, pain from an enlarged liver will respond to treatment for the heart failure producing hepatomegaly. Depression should be treated and patients should be encouraged to be as independent as possible. Exercise programmes should become standard.[12,13] This subject has been reviewed elsewhere by Ferrell[14] and Pamelee.[15-16] The latter author makes the point that there is good evidence that the expression of pain by cognitively impaired individuals should be regarded as valid and should not be dismissed.[15] Whenever possible clues should be sought from observations of staff and relatives, for example, groaning on moving. Within the limits imposed by the patient's condition and co-operation relevant investigations should be undertaken (simple X-rays, ultrasound). In addition to the obvious discomfort caused to the sufferer, families and friends may also be extremely distressed by the observation of such behaviour. Patients with dementia may enter a terminal phase. Such patients should be managed along the general lines established for palliative care in cancer.

The Treatment of Pain

Acute Pain

The basic principals are relatively simple. Treat the underlying cause, (e.g., antibiotics for infection, fixation for fracture) and give adequate pain relief. The nature of the painful condition, the response of the patient and the presence of co-morbidity will dictate whether to start with a mild analgesic or to go immediately to a more potent drug. In view of the uncertainty of response and the fact that drug toxicity may occur unpredictably might suggest that the general rule "start low, go slow" should remain. In order to avoid the situation that patients remain in pain, "starting low" must be followed by regular re-evaluation with, if necessary, frequent increases in drug dose.

Chronic Pain

The management of chronic pain differs from that of acute pain in that a range of additional issues may emerge and always need to be considered. The basic principle is, however, similar — accurate diagnosis and adequate analgesic drugs. However, in all cases of chronic pain, particularly those in which the cause is not adequately diagnosed or when the severity of pain and disability seems greater than the underlying disease process would suggest, the following points should always be considered:

♦ disease modification (e.g., second-line drugs for arthritis),
♦ concerns about long-term as opposed to acute side-effects of drugs,
♦ risk of addiction,
♦ life-style coping strategies (e.g., behavioural-cognitive therapy),
♦ psychiatry co-morbidity (e.g., depression),
♦ interventional treatments (e.g., nerve blocks etc.).

P. CROME

The issues relating to drugs are discussed below but detailed discussion of non-pharmacological issues is outside the scope of this chapter. Many patients will benefit from multi-disciplinary assessment in pain clinics.[17]

Pharmacological Approaches

The basic principles of drug therapy are to keep drug regimens simple, to prevent side-effects, to reassess frequently, to recognise that dosage needs to be individualised and that large doses may be required. Although there is wisdom in the standard aphorism "start low and go slow" it should not be so low and so slow that the patient gets no pain relief. This is important because of the evidence that the elderly are denied analgesics when younger patients are given them.[18]

The Analgesic Ladder

There are a large number of analgesic drugs. They can be grouped into three main classes according to the severity of pain for which they are suitable to be prescribed. In practice, one can suffice with a relatively small formulary of drugs. Table 22.3 lists those drugs which are available in our hospital grouped by type of pain for which they might be used. The drugs for mild pain (aspirin, ibuprofen and paracetamol) are generally regarded as being equipotent and, in the U.K. are available for over the counter sale without prescription. Morphine is generally regarded as the drug of choice for severe pain. The use of drugs between these two poles of efficacy is more problematic in that their potential usefulness is often hampered by unacceptable side-effects.

Paracetamol (acetaminophem)

This is the safest analgesic drug being virtually devoid of side-effects at standard therapeutic doses. There is some evidence that

Table 22.3. Analgesic drugs available in North Staffordshire Hospital

For mild pain	Aspirin Paracetamol Ibuprofen
For moderate pain	Combination analgesics: Co-codamol 8/500 (codeine 8 mg, paracetamol 500 mg) Co-proxamol 32.5/325 (dextropropoxypehene 32.5 mg, paracetamol 325 mg) Non-steroidal anti-inflammatory drugs Diclofenac, indomethacin, naproxen
Opioid	Codeine Diamorphine Dihydrocodeine Morphine Pethidine
Adjuvant therapy	Amitriptyline Carbamazepine Valproate

prolonged therapeutic dosage might increase renal impairment but this is not proven. The only significant toxicity is hepatic and renal failure following acute overdosage. A number of studies have shown no clinically relevant difference in pharmacokinetics between young and elderly subjects.[19–22] Wynne et al. investigated the drug's pharmacokinetics in both healthy and frail older subjects.[23] Half-life was not prolonged in the fit elderly group but was in the frail group when compared to healthy young subjects (mean values 123, 144 and 226 minutes respectively). Clearance was reduced by approximately 50% in the frail older group compared to the young healthy subjects. Clearance for the fit elderly fell mid-way between these two groups. Thus although the pharmacokinetics of paracetamol do show some significant alterations in old age they are probably of insufficient size to warrant routine dosage reduction, except possibly in frail older

subjects. Hepatotoxicity in this group with usual dosing has not been reported.

Aspirin

Acetyl-salicylic acid or aspirin as it is usually referred to in the U.K. has anti-inflammatory and antipyretic actions as well as being a widely used analgesic. Its major role now is as an anti-platelet drug in the secondary prevention of cardio-vascular and cerebro-vascular disease (see Chapters 11 and 15). Its principal disadvantage is that it causes gastric erosions and may precipitate haemorrhage and perforation. Aspirin is rapidly absorbed undergoing hydrolysis both in the gut wall and liver. Further hydrolysis occurs in the blood by red cell esterase. Its metabolite, salicylic acid undergoes conjugation and oxidation before excretion. There have been several studies examining the influence of age on the drug's pharmacokinetics. Although statistically significant changes in some pharmacokinetic measurements have been shown after oral administration of aspirin, these are regarded as being not of sufficient magnitude to justify dosage alteration.[24-25] It is not clearly stated in the above two papers whether the elderly subjects were fit or frail. The influence of frailty on pharmacokinetics is potentially important (see Chapter 4). The influence of frailty of aspirin esterase has subsequently been investigated. Williams *et al.* found that plasma esterase activity was reduced in frail elderly subjects compared healthy elderly subjects.[26] This was investigated further by Summerbell *et al.* who concluded that the impaired aspirin metabolism in frail elderly people was the consequence of a reduction in quantity of the esterase.[27]

Enteric-coated aspirin may reduce side-effects but with in at least one brand, clear absorption profiles were not observed.[28] In practice no dosage reduction is necessary in older people. It is suitable as an alternative to paracetamol in those already taking

the drug as prophylaxis for vascular disease and in those small number of patients who can not tolerate paracetamol. It should be avoided in those with upper gastro-intestinal pathology because of the increased risk of bleeding[29] and in those who have shown other sensitivities to the drug (e.g., asthma).

The prostaglandin analogue misoprostol, histamine$_2$-receptor antagonists and proton-pump antagonists have been shown to reduce gastro-intestinal toxicity from aspirin and other non-steroidal anti-inflammatory drugs in a variety of clinical and experimental situations. However, it is yet clear whether one or other of these classes of drugs should be co-prescribed routinely to elderly patients when they are receiving long-term analgesic treatment with aspirin. This is the subject of a Cochrane Collaboration review.[30]

Ibuprofen and the Non-steroidal Anti-inflammatory Drugs

Ibuprofen is a non-steroidal inflammatory drug that is believed to act by inhibiting the enzyme cyclo-oxygenase and reducing the production of prostaglandins. The principal side-effect is upper gastro-intestinal erosion leading to haemorrhage and perforation. There is good evidence that ibuprofen is the least damaging in this respect and it may be the most effective of the simple analgesics for acute pain.[31] There are a wide range of other often over-looked side-effects including salt and water retention, hypertension and renal failure. The other drugs of this class are more potent, but also produce more side-effects. They have their major role in the treatment of arthritis and discussed in more detail in Chapter 21.

Combination Analgesics

The use of analgesic combinations containing two drugs acting through different pharmacological mechanisms offers theoretical

advantages of greater pain relief without the disadvantage of side-effects. A large number of combinations of simple analgesics such as aspirin and paracetamol with low dose or low potency narcotic drugs are available both as over the counter and prescription only medication. de Craen *et al.* concluded in their systematic review of codeine-paracetamol combinations, used principally in the post-operative situation, that the analgesic advantage of the combination over paracetamol alone was small.[32] Side-effects were higher with the combination following multiple dosing (pooled rate ratio 2.5, 95% CI 1.5–4.2) but not statistically significant after single doses. There is no information about the effect of age on this interaction. Codeine combinations can lead to constipation whilst those containing dextropropoxyphene are a commonly involved in deliberate self-harm. Overdoses of co-proxamol (paracetamol and dextropropoxyphene) are particularly difficult to manage. Not only is there the problem of early toxicity from the opioid component but also a delayed risk of paracetamol hepatoxicity. This combination is extremely popular and well tolerated as an analgesic despite there being a lack of good evidence of superior efficacy compared to paracetamol alone. There is little information about the use of the drug in older patients but its elimination half-life is significantly prolonged in older people. The half-life of its major metabolite nor-dextropropoxyphene is prolonged even more and in many patients had not reached steady-state plasma concentrations even after several days treatment.[33]

Opioid or Narcotic Analgesics[34]

These exert their analgesic effects through central nervous system opioid receptors. Most of the commonly used drugs (morphine, codeine, dextropropoxyphene) are agonists exerting their principal therapeutic action through the μ_1 opioid receptor. Other generally less potent opioids have partial agonist or agonist-antagonist

Table 22.4. Adverse effects of opioid drugs

Respiratory system	Respiratory depression (reduced respiratory rate, tidal volume) Hypoxia and hypercapnoea Cough suppression
Cardiovascular system	Hypotension Bradycardia (vagal effect)
Gastro-intestinal system	Reduced oesophageal pressure — incresed reflux Delayed gastric emptying and gastro-intestinal motility *Constipation Abdominal pain
Central nervous system	Tolerance *Drowsiness Coma Seizures Movement disorders *Nausea and vomiting Pupillary constriction *Confusion Hallucinations
Urinary system	Retention of urine

*Common

activity (e.g., buprenorphine, pentazocine). These latter drugs tend not to be so useful in older people because of their dysphoric side-effects. The range of recognised side-effects of opioids is quite considerable and these are listed in Table 22.4.

Since narcotic analgesics are one of the principal drugs of addiction, there is obvious concern that by giving these drugs to patients they will become dependent. However there is little evidence that therapeutic administration of narcotic drugs produces addiction. For example, Porter and Jick[35] reported that only four of 11,882 patients who were prescribed a narcotic

analgesics during their hospital stay developed evidence of addiction. However, dependency is a real, albeit uncommon occurrence and it is wise to exercise some precautions in prescribing. Special care needs to be taken over decision to prescribe opioids to patients with pre-existing psychiatric disease, alcoholism or those with a personality disorders.

Morphine

Morphine is by far the most commonly used opioid and may be prescribed both orally and parenterally. It is metabolised in the liver to glucuronides, morphine-6-glucuronide, being the major active metabolite. The excretion of this metabolite is dependent on renal function which is relatively reduced in older people. Baillie et al. reported that morphine clearance was reduced by a third following intravenous administration. The areas under the plasma concentration time curve were greater following both morphine slow-release and elixir preparations.[36] Sear et al. found that the area under the plasma concentration time curve for morphine-6-glucuronide was similar in elderly and middle aged patients undergoing surgery although the clearance of the parent compound was reduced.[37] If clearance was reduced one might expect less of the glucuronide to be formed. The observation that the area under the plasma concentration time curve was not in fact reduced suggests that clearance of the metabolite is also reduced. The greater pharmacodynamic effect reported below may therefore be due to relative accumulation of morphine-6-glucuronide.

The evidence suggests that older people require a smaller initial dose of the drug but subsequent doses should be guided by response. Bellville et al. reviewed 712 patients who received either morphine or pentazocine commented that age had an effect independent of operation site, height and weight and hospital.[38] In another study, Kaiko found that for a given dose

of morphine both the duration of pain relief and the quantity of pain relief were approximately 50% more in patients aged 70–89 than those aged 18–29.[39] Studies on the pharmacokinetics of the drug mentioned above are compatible with these observations.

Morphine has the advantage of being available in a number of formulations including oral solutions and various sustained release preparations. The conversion dose for oral to parenteral morphine is three to one. It may also be used in more sophisticated ways for example by patient controlled infusion. Thus Egbert et al. reported a clinical trial of patient controlled intravenous morphine compared to standard intra-muscular morphine in a group of frail elderly surgical patients.[40] They found that, not only was pain better controlled when given by the self-administered route, but that post-operative confusion and pulmonary complications were reduced. Morphine is also commonly given by sub-cutaneous infusion via a syringe driver to patients who cannot swallow and who are terminally ill.

Pethidine

Pethidine (meperidine in U.S.A.) is converted to an active metabolite nor-pethidine which acts predominately on the μ-receptors. Accumulation can occur with dysphoric neuropsychiatric symptoms and seizures. It has a short duration of action that makes it unsuitable as an analgesic for anything other than pain of brief duration. It is therefore now used to a much lesser degree in the management of chronic pain and should be avoided in older people.

Prescribing Guidelines

The usual method of prescribing morphine for chronic pain is to start with standard oral morphine (tablet or liquid) in a dose of 5–10 mg every four hours. This dose should be halved in frail

older people. In addition further doses should be given if breakthrough pain occurs. Patients should then be switched to a twice daily sustained-release preparation (e.g., MST) with additional doses of 1/6 the total daily dose for breakthrough pain. At the same time laxatives (e.g., senna and lactulose or codanthramer) should be started to avoid constipation. Nausea and vomiting should be treated with regular metoclopramide or haloperidol.

Atypical Pain

A number of pharmacological agents have been used in the treatment of atypical and neuropathic pains. Many of these diseases have their peak frequencies in later life but there is a paucity of information about the influence of age as an independent factor in determining treatment choice and response.

Antidepressants

Patients with chronic pain may become depressed and it is often difficult to disentangle somatic complaints may be part of depressive symptomatology. Differentiation of cause and effect may be difficult. Antidepressants such as amitriptyline may be useful in chronic pain even when there is little evidence of depression. Support for this view comes from an open study of different treatment approaches to post-herpetic neuralgia. The antidepressants amitriptyline and nortriptyline were reported as useful in 60% of these patients who as a group were not depressed as judged by the Beck Depressive Inventory.[41] On the other hand carbamazepine and other anti-convulsants were not helpful. Antidepressants have been shown to be more effective than carbamazepine in central post-stroke pain.[42] This beneficial effect can be achieved at doses lower than would be given for the treatment of depression.

A meta-analysis of 39 placebo-controlled studies confirmed the efficacy of antidepressants. They calculated that the average chronic pain patient had less pain than three quarters of the patients who had been treated with placebo.[43] The benefits of antidepressants in neuropathic pain have also been demonstrated in a systematic review.[44] Some of these drugs (principally the tricyclic antidepressants) are dangerous in overdose and the risk of suicide must always be assessed before they are prescribed.

Carbamazepine

This has a long-standing role in the treatment of trigeminal neuralgia but is now being used in other neuropathic condition.[45] Carbamazepine response may fluctuate but this is not related with plasma drug concentrations.[46] The relationship between the underlying cause of this condition which may be due to vascular compression[47] and the modes of action of drugs which ameliorate it are not clear. Phenytoin and baclofen may be effective if carbamazpine fails. The mode of action of carbamazepine in trigeminal neuralgia is not certain. Meta-analysis of the effects of carbamazepine and other anticonvulsants has found benefit from these drugs in a number of painful conditions.[48]

Pain Clinics

The management of chronic persistent pain is probably best undertaken by a multi-disciplinary pain clinic employing a variety of non-pharmacological approaches. The effectiveness of such an approach in older people has been reported by Helme et al.[17] They found that of their cohort 72% had less pain, 53% reported being more active and in 65% mood was improved. Only 4% reported no improvement at all. These clinics use many other techniques. Behavioural-cognitive therapy is based on a detailed understanding of the psycho-social context in which the

individual's pain is experienced. Then a range of specific strategies are devised, for example, stressor situations can be managed by, for example, avoidance, thus controlling pain and improving quality of life.[49] Physical treatments include heat, cold, massage, aromatherapy and TENS. Again there is a paucity of randomised controlled data about the efficacy of these modes of therapy in old people.

Conclusions

Pain, both acute and chronic is a common problem in older people. As in so many field of geriatric medicine there is paucity of information about the differences in approach that are required to produce optimal benefit. Indeed in one recent review of treating acute pain in hospital, the only comment made about older people related to co-existing illnesses and differences in drug handling.[31] The key practice points are to ask about pain specifically for most patients have more pain then they report, to give adequate doses of effective drugs at regular intervals. Frail older people should be started on reduced doses of opioids but otherwise healthy older people should receive standard doses.

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DC McNALLY:	And I take it that decision that there is nothing we consciousness do for her would be made by who?
MRS GIFFIN:	Er well Doctor (inaudible) I presume.
DC McNALLY:	Dr Barton.
MRS GIFFIN:	Well she being the one that's there every day.
DC McNALLY:	Yeah.
MRS GIFFIN:	And er if she queried that she would have gone to Dr Lord and spoken to her but I don't know."

That concludes the evidence relating to Nurse Giffin.

THE CHAIRMAN: Thank you very much indeed, Mr Fitzgerald. We will rise now and reconvene tomorrow morning at 9.30.

<u>(The Panel adjourned until 9.30 a.m. on Friday 26 June 2009)</u>