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Analgesics

ROBERT G. TWYCROSS
M.A., D.M., F.R.C.P.

Sir Michael Sobell House, The Churchill Hospital, Headington, Oxford

Introduction

There is no internationally agreed classification of analgesics. The terms mild and strong are not always helpful. Codeine, for example, is usually classed with the former which obscures its pharmacological relationship with morphine and other narcotics. Moreover, there are occasions when morphine (a 'strong analgesic') does not relieve pain which aspirin (a 'mild analgesic') does. Anti-pyretic and narcotic have much in their favour, although nefopam does not fit into either category. The basic division into non-narcotic (non-opioid) and narcotic (opioid) is important. The advent of drugs that have morphine-like (agonist) properties when used alone but act as antagonists when given after or in association with morphine has complicated matters. As agonists and agonist-antagonists should not be prescribed concurrently, the classification in Table 1 has much to commend it.

It is generally considered that aspirin and non-steroidal anti-inflammatory drugs (NSAID) act peripherally and narcotics centrally, that is, within the central nervous system. Paracetamol (acetaminophen) and nefopam also act centrally but via different mechanisms. Such concepts are almost certainly an oversimplification. Aspirin and related drugs appear to act at several sites in relation to prostaglandin synthesis, some peripheral and some central (Ferreira, 1981). Morphine also acts both centrally and peripherally, though the major analgesic effect is undoubtedly central.

TABLE 1. Classification of analgesics

Narcotic agonists	Non-narcotic	Narcotic agonist-antagonists
Weak	Aspirin	Weak
Codeine	Paracetamol	Pentazocine
Dihydrocodeine	Nefopam	
Dextropropoxyphene		
Ethoheptazine		
Strong		Strong
Morphine		Butorphanol
Diamorphine		Buprenorphine
Pethidine		Nalbuphine
Levorphanol		
Phenazocine		
Methadone		

Analgesics in perspective

There is always more to analgesia than analgesics. The importance of explaining in simple terms the mechanism(s) underlying the patient's pain should not be forgotten. Pain that does not make sense or, worse, is seen as a threat is always more intense than pain which is understandable.

Many drugs affect pain. Some affect it indirectly, for example, antibiotics in cystitis or sinusitis and penicillamine or gold in rheumatoid arthritis. These drugs act by modifying the pathological process, and fall outside the definition of analgesic. Spasmolytics, such as baclofen, diazepam (somatic muscle) and probanthine (smooth muscle), are another group of pain-modulating drugs.

Surgery is a commonly employed measure for the management of acute severe pain (e.g. appendicectomy), likewise, radiation therapy and cytotoxic chemotherapy in pain associated with cancer. The use of such measures does not preclude the use of analgesics. Best results are often obtained by adopting a 'broad spectrum' approach, using two or more treatments in combination. In some conditions, e.g. trigeminal neuralgia, a sequential approach may, however, be appropriate.

The use of analgesics is best seen as simply one way of elevating a patient's pain threshold. Analgesics, including narcotics, do not usually relieve pain caused by degenerative nerve damage (dysaesthetic and stabbing pains). The site of the neurological lesion and the type of pain determine which pharmacological measures are appropriate, if any (Table 2).

Principles of use

Persistent pain requires prophylactic (preventive) therapy

Analgesics should be given regularly, and prophylactically. The aim is to titrate the dose of the analgesic against the patient's pain, gradually increasing the dose until the patient is pain-free. The next dose is given before the effect of the previous one has fully worn off—and therefore before the patient may think it necessary (Fig. 1 and 2). In this way it is possible to erase the memory and fear of pain. If a drug ceases to be effective, do not transfer to an alternative of comparable efficacy but prescribe a drug that is definitely stronger.

If a strong analgesic other than morphine is used, the physician must be familiar with its pharmacology. For example, pethidine (meperidine) is effective for an average of 2–3 hr. Yet it is commonly prescribed every 4 or 6 hr. This is clearly insufficient, and forces the patient to be in pain for perhaps 3 out of every 6 hr.

TABLE 2. Neuromuscular classification of pain: implications for therapy

Type of pain	Treatment
(1) Muscle spasm	Baclofen Diazepam
(2) Nociceptive	Analgesics
(3) Nerve compression	Analgesics Corticosteroids Nerve blocks
(4) Nerve destruction (dysaesthetic)	Psychotropic drugs (especially antidepressants)
peripheral nerve—occasionally useful;	Narcotics Corticosteroids Nerve blocks
cord lesion—of no benefit	Cordotomy
(5) Mixed nerve compression and destruction (partly dysaesthetic)	Treated as mixed 3 and 4 (?)Stellate ganglion block for upper limb pain

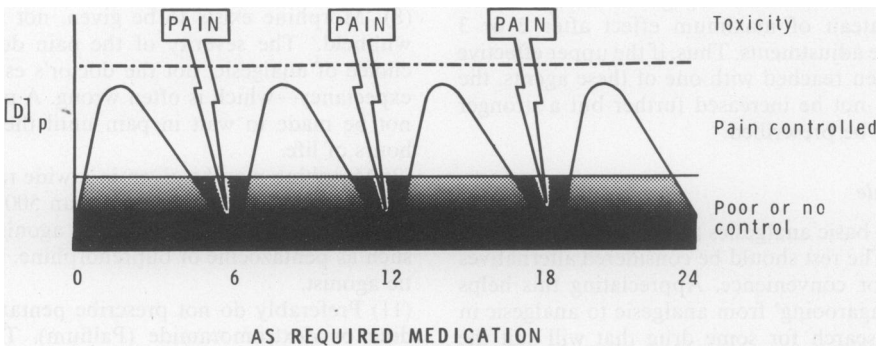

FIG. 1. Diagram to illustrate the result of 'as required' morphine sulphate. [D]p = plasma concentration of drug.

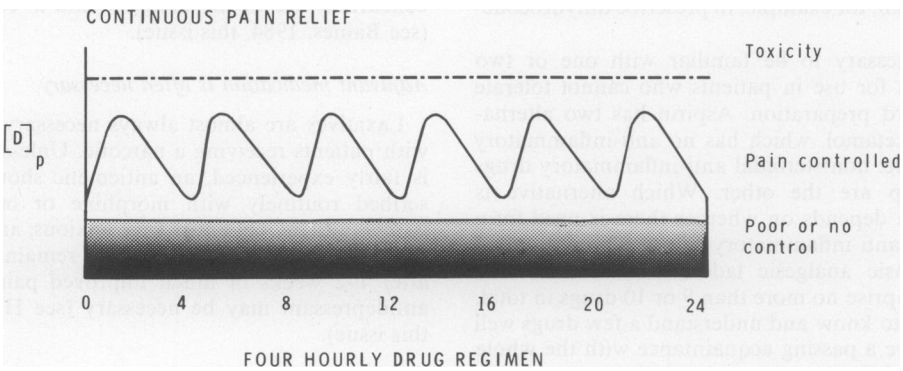

FIG. 2. Diagram to illustrate the result of regular 4-hourly morphine sulphate. [D]p = plasma concentration of drug.

Use oral medication whenever possible

The route of administration is a significant consideration because it has substantial impact on the patient's way of life. The patient taking oral medication is free to move around, travel in a car and, most important, be at home. Injections promote dependence on the person administering the drug. Oral administration eliminates muscle trauma, and enables the patient to maintain control over his own drug administration.

Doses should be determined on an individual basis

The effective analgesic dose varies considerably from patient to patient. The right dose of an analgesic is that which gives adequate relief for at least 3 and preferably 4 or more hours. 'Maximum' or 'recommended' doses, derived mainly from post-operative parenteral single-dose studies, are not applicable in cancer. The dose of morphine and other strong narcotic agonists can be increased almost indefinitely. On the other hand, the non-narcotics, weak narcotic agonists and narcotic agonist-antagonists all reach a plateau of maximum effect after 2 or 3 upward dose adjustments. Thus, if the upper effective dose has been reached with one of these agents, the dose should not be increased further but a stronger drug should be prescribed.

Keep it simple

The three basic analgesics are aspirin, codeine and morphine. The rest should be considered alternatives of fashion or convenience. Appreciating this helps prevent 'kangarooing' from analgesic to analgesic in a deperate search for some drug that will suit the patient better. If a non-narcotic or weak narcotic preparation, such as aspirin-codeine or paracetamol-dextropropoxyphene, fails to relieve, it is usually best to move directly to a small dose of oral morphine sulphate than, for example, to prescribe dihydrocodeine.

It is necessary to be familiar with one or two alternatives for use in patients who cannot tolerate the standard preparation. Aspirin has two alternatives: paracetamol, which has no anti-inflammatory effect, is one: non-steroidal anti-inflammatory drugs as a group are the other. Which alternative is appropriate depends on whether there is need for a peripheral anti-inflammatory effect. The individual doctor's basic analgesic ladder, with alternatives, should comprise no more than 9 or 10 drugs in total. It is better to know and understand a few drugs well than to have a passing acquaintance with the whole range. The following points should be noted:

(1) With mild or moderate pain, use a non-narcotic in the first instance.

(2) It may be appropriate to prescribe aspirin in addition to a narcotic, especially in patients with bone pain.

(3) It is logical to combine analgesics that act via different mechanisms, for example: aspirin and paracetamol; paracetamol and codeine; aspirin and morphine. However, it is not always wise from the point of view of patient compliance, nor is it always therapeutically necessary.

(4) It is pharmacological nonsense to prescribe either two weak or two strong narcotics simultaneously.

(5) There is sometimes a place for a patient on a strong narcotic to have another narcotic (weak or strong) as a second as required analgesic for occasional troublesome pain, though generally patients should be advised to take an extra dose of their regular medication if 'breakthrough' pain occurs.

(6) If one weak narcotic preparation does not control the pain, do not waste time by prescribing an alternative; move to something definitely stronger.

(7) Morphine or an alternative strong narcotic should be used when non-narcotics and weak narcotics fail to control the pain (Table 3).

(8) 'Morphine exists to be given, not merely to be withheld.' The severity of the pain determines the choice of analgesic, not the doctor's estimate of life expectancy—which is often wrong. A patient should not be made to wait in pain until the last days or hours of life.

(9) Morphine may be given in a wide range of doses from as little as 5 mg to more than 500 mg.

(10) Do not prescribe a narcotic agonist-antagonist, such as pentazocine or buprenorphine, with a narcotic agonist.

(11) Preferably do not prescribe pentazocine, pethidine or dextromoramide (Palfium). The first is a weak narcotic by mouth and frequently causes unpleasant mental effects. All three tend to be short-acting (2–3 hr).

(12) Many cancer pains respond better to the concurrent use of an analgesic and a 'co-analgesic' (see Baines, 1984, this issue).

Adjuvant medication is often necessary

Laxatives are almost always necessary, especially with patients receiving a narcotic. Unless the doctor is fairly experienced, an antiemetic should be prescribed routinely with morphine or other strong narcotic. If the patient is very anxious, an anxiolytic should be prescribed. If a patient remains depressed after 1–2 weeks of much improved pain relief, an antidepressant may be necessary (see Hanks, 1984, this issue).

Do not use mixtures routinely

At some centres, for cancer pain, morphine is

TABLE 3. Strong narcotic analgesics: approximate oral equivalents to morphine sulphate

Analgesic	Proprietary name	Potency ratio with morphine sulphate‡		Duration of action (hr)§
Pethidine/meperidine	Demerol	1/8	*1/12*[a]	2–3
Dipipanone*	Diconal	1/2	*1/3*	3–5
Papaveretum	Omnopon, Pantopon	2/3	*1/2*	3–5
Oxycodone†**	Percodan	1	*2/3*	3–5
	Percocet			
	Tylox (capsule)			
Dextromoramide*	Palfium	2††	*1·5*	2–4
Methadone	Physeptone, Dolophine	3–4‡‡	*2–3*	6–8
Levorphanol	Dromoran, Levo-dromoran	5	*3*	4–6
Phenazoine*	Narphen	5	*3*	4–6
Hydromorphone†	Dilaudid	6	*4*	3–4

*Not available in the U.S.A.

†Not available in Britain.

‡Multiply dose of stated drug by the potency ratio to determine the equivalent dose of morphine sulphate.

§Dependent to a certain extent on dose, often longer lasting in very elderly and those with liver or renal dysfunction.

[a] Column of figures in italics refer to approximate potency ration with *diamorphine* (Heroin).

** Oxycodone is available in Britain only as oxycodone pectinate suppositories.

†† Dextromoramide single 5 mg dose is equivalent to morphine 15 mg (diamorphine 10 mg) in terms of *peak* effect but is generally shorter acting; overall potency rate adjusted accordingly.

‡‡ Methadone—single 5 mg dose is equivalent to morphine 7·5 mg (diamorphine 5mg). It has a prolonged plasma half-life which leads to cumulation when given repeatedly. This means it is several times more potent when given regularly.

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always prescribed with a second drug, either cocaine (a stimulant) or a phenothiazine (a tranquillizer). Sometimes both are added. In these circumstances, increasing the dose of morphine can be hazardous if, by increasing the volume of the mixture taken, the dose of the adjunctive medication is automatically increased also, regardless of need. Depending on the adjunctive drug, this can lead to agitation and restlessness or to somnolence. It is far better to give adjunctive medication separately, either as a syrup or tablet/capsule. The dose of each pharmcologically active substance can then be adjusted individually to patient need.

Insomnia must be treated vigorously

Discomfort is worse at night when the patient is alone with his pain and his fears. The cumulative effect of many sleepness, pain-filled nights is a substantial lowering of the patient's pain threshold with a concomitant increase in pain intensity. Sometimes it is necessary to use morphine at night in patients well-controlled during the day by a weak narcotic; or to use a considerably larger dose of morphine at bedtime to relieve pains that are particularly troublesome when lying down for a prolonged period.

It is sometimes necessary to balance the degree of relief against unwanted side effects

Examples include aspirin and gastric irritation, and morphine and gastric stasis. Generally, there are two ways round these problems but occasionally a compromise is necessary.

Admission is sometimes necessary to achieve pain control

Particularly in a hospice, a patient is affected by far more than drug changes. He is surrounded by a team of people who are confident that the pain will come under control. Peer support comes from the other patients in the four or five bed unit who relate their own stories of having achieved good pain control. The patient sees the other people receiving regular medication and observes that, except for the very ill, they are alert and functioning normally.

Attention to detail

Analgesic regimens should be simple to understand and easy to administer. It is only necessary to adopt a 4-hourly regimen if morphine or a comparable analgesic is being used. With other patients, 'with meals and at bedtime' will cover all other drug requirements. Variations include: 'on waking, after lunch and tea, and at bedtime', and 'after breakfast and at bedtime'.

If some drugs are best given before meals and others after, it is usually advisable to forsake pharmacological purity and to opt for one or other time so as to avoid an impossibly complex schedule. It is necessary to look at boxes and other containers to check that the pharmacist has not given the patient contrary or complicating advice.

When a 4-hourly regimen is adopted, the first and last doses are linked to the patient's waking and bedtimes. The best additional times during the day are usually 10 a.m., 2 p.m., and 6 p.m. unless the patient wakes exceptionally late. The list of drugs and doses for the patient (and family) to work from should be written out clearly. It is useful to add what the different preparations are for, even if this seems obvious to the doctor.

Capsules should be described as capsules and tablets as tablets, not vice versa. Doses should not be described simply as 'spoonfuls'. Patients have been known to use a tablespoon (15 ml) instead of a teaspoon (3·5–5 ml). A plastic medicine cup with each 5 ml clearly marked is generally the best way for the patient to self-administer liquid preparations. Sometimes, if the above recommendations are carried out, the patient can cope immediately with a new regimen. Not infrequently, however, the patient is found to be in confusion when reviewed the next day.

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