Oral Morphine in Advanced Cancer

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Preface

The regular use of morphine - the main active ingredient in opium - has done much to improve the management of pain in advanced cancer. However, despite widespread advocacy in favour of its use, morphine is still often not prescribed for patients who need it. Cheap preparations of oral morphine are not always available, and doctors and nurses are often afraid to use one of nature's best remedies. Although oral morphine is not the panacea for cancer pain, personal experience and published data confirm that its appropriate use revolutionises cancer pain management..

Since it was originally published by Beaconsfield Publishers Ltd in 1984, over 2 lakh copies of Oral Morphine in Advanced Cancer have been sold and distributed. This extensively revised version has been prepared specifically for doctors and other health professionals working in India. The use of oral morphine is placed within the much wider context of cancer pain management. In relation to drug therapy, the concept of 'broad-spectrum' analgesia is important. This acknowledges the analgesic potential of various classes of drugs and encourages the combined use of different drugs from different classes in scientific and rational way.

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Disclaimer

The recommendations contained in this book reflect the author's judgment regarding the state of general knowledge and practice in the field as of the date of publication. Recommendations such as those contained in this book can never be all-inclusive, and therefore will not be appropriate in all and every circumstance. Those who use this book must use their own clinical judgement in relation to each patient, taking into account social circumstances and what is locally available in terms of personnel, equipment, and capability for monitoring treatment. The Institute of Palliative Medicine cannot be held responsible for any liability incurred as a consequence of the use or application of any of the contents of this book. Mention of specific product brands does not imply endorsement. As always, doctors are advised to make themselves familiar with manufacturer's recommendations and precautions before prescribing what is, for them, a new drug.

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Abbreviations

b.i.d.	twice a day
h.s.	at bedtime
IM	intramuscular
IV	intravenous
o.m.	in the morning
p.r.n.	as needed
PO	by mouth
q.i.d.	four times a day
q4h, q6h	every 4 hours, every 6 hours, etc.
SC	subcutaneous
t.i.d.	three times a day

Oral Morphine in Advanced Cancer

1. What are the indications for morphine in advanced cancer?

Main

- pain
- dyspnoea (See 62and 63)

Subsidiary

- cough
- diarrhoea

NOTE: sedation is not an indication for morphine

2. Why use morphine? What about other strong opioids?

Morphine is a versatile drug. By mouth, it has a plasma half-life of 2–2.5 hours and, apart from patients with renal failure, there is no danger of drug cumulation. Pethidine (meperidine USA) by mouth is not much better than codeine and has a shorter duration of action. Its main metabolite is norpethidine which can cause tremor, twitching, agitation, and even seizures. The total daily dose of pethidine should be limited to 600mg. Toxic manifestations occur with lower doses in patients with poor renal function.

Tramadol 400mg/day by mouth and buprenorphine 1.2mg/day sublingually are both equivalent to about morphine 80mg/day by mouth (see Question 15) and can therefore substitute for morphine up to this level. Theoretically, higher doses of buprenorphine can be given, maybe up to 4.8mg/day, or even more. However, taking six 200micrgram tablets sublingually four times a day is generally not acceptable to patients. Fentanyl is a full alternative to morphine but, like tramadol and buprenorphine, is considerably more expensive (Table 1).

Table 1 Comparison of opioid analgesics

	Opioid receptor affinity			*Non-opioid properties*	*Bio-availability*	*Plasma halflife*
	Mu	*Kappa*	*Delta*			
Buprenorphine	pA	Ant	A	None	50–60% SL	3h
Codeine	a	_	_	None	12-84%	3h
Dextropropoxyphene	a	_	_	None	40%	6-12h[a]
Fentanyl	A	_	_	None	_	3h (IV) 24h(TD)
Morphine	A	_	_	None	15-64%	2.5h
Pethidine	a	_	_	Antimuscarinic	33%	7h[b]
Tramadol	a	_	_	Inhibits presynaptic re-uptake of noradrenaline and serotonin	>90%	6h[c]

a. increases to >2 days in the elderly
b. despite a relatively long plasma halflife, analgesia is relatively short-lasting
c. active metabolite = 7h

Key

A= strong agonist; pA = partial agonist; a = weak agonist; Ant = strong antagonist; ⁻ = no activity; IV = intravenous; TD = transdermal

3. But what about addiction?

Provided morphine is used within the context of 'whole-person' care (attending to psychological, social and spiritual concerns as well as physical ones), addiction does not occur in patients prescribed morphine for cancer pain (Box A). Occasionally, a patient is admitted who appears to be addicted because he is demanding an injection every 2-3 hours. Typically such a patient has a long history of poor pain management, and for several weeks will have been receiving fairly regular (every 6 hours as needed) but inadequate injections of one or more opioid analgesics.

In this situation, given time, it is usually possible to relieve the pain adequately, prevent the clock-watching and demanding behaviour, and eventually change to an oral preparation. Even here it cannot be said that the patient is addicted. The demand for the opioid is not in order to experience its psychological effect but to be relieved from pain for a few hours.

Box A Definitions[a]

Addiction
Addiction is a primary, chronic, neurobiological disease, with genetic, psychosocial, and environmental factors influencing its development and manifestations. It is characterised by behaviours that include one or more of the following: impaired control over drug use, compulsive use, continued use despite harm, and craving.

Physical Dependence
Physical dependence is a state of adaptation that is manifested by a drug class specific withdrawal syndrome that can be produced by abrupt cessation, rapid dose reduction, decreasing blood level of the drug, and/or administration of an antagonist.

Tolerance
Tolerance is a state of adaptation in which exposure to a drug induces changes that result in a diminution of one or more of the drug's effects over time.

a. American Academy of Pain Medicine, American Pain Society & American Society of Addiction Medicine

Physical dependence develops in most patients who have taken an opioid regularly by mouth for more than 3-4 weeks. This is not a problem for dying patients, because they usually continue on regular morphine until they die.

Some patients live for much longer than expected. If their pain disappears, the dose of morphine can be decreased and possibly stopped altogether in the following way:

- if a patient has been entirely pain-free for 4+ weeks on a regular unchanged dose of morphine, decrease the dose on a trial basis by 20–50%
- if the pain recurs, increase the dose back to the original level
- if the pain does not return, the dose of morphine should be decreased every 1-2 weeks until the morphine is completely curtailed, or until the pain recurs
- when the pain recurs, increase the dose to the previously satisfactory dose.

Response to Morphine

4. What is the best way of giving morphine by mouth?

In practice, the choice is between a solution or tablet of morphine sulfate and slow-release tablets. Solutions and ordinary tablets are administered *every 4 hours*; slow-release tablets *every 12 hours*. A twice-a-day regimen makes slow-release morphine an attractive option, but it is more expensive.

Initial dose titration with morphine solution or ordinary tablets is advisable in patients with a history of poor pain management. Even so, at some centres, slow-release tablets are used from the start.

5. In relation to pain, when should morphine be used?

From a therapeutic point of view, pain in cancer can be divided into three categories:

- morphine responsive, i.e. pain relieved by morphine, *generally in conjunction with a non-opioid*
- morphine poorly-responsive, i.e. pain relieved by the concurrent use of morphine and an adjuvant analgesic (co-analgesic)
- morphine non-responsive, i.e. pain that is not relieved by morphine (Table 2).

Table 2 Mechanisms of pain and implications for treatment

Type of pain	*Mechanism*	*Examples*	*Response to opioids*	*Typical treatment*
Nociceptive	Stimulation of nerve endings			
muscle spasm		Cramp	_	Muscle relaxant
Somatic		Soft tissue, bone pain	+/-	NSAID + opioid
Visceral		Hepatic capsule pain	+	Opioid ± NSAID
Neuropathic				
nerve compression	Stimulation of nervi nervorum		+/-	Opioid + corticosteroid (if cancer)
nerve injury de-afferentation pain	Peripheral nerve injury	Neuroma or nerve infiltration, e.g. brachial or lumbosacral plexus	+/-	Opioid; NSAID (if cancer); tricyclic antidepressant; anti-epileptic, local anaesthetic congener; NMDA receptor-channel blocker; spinal analgesia; transcutaneous electrical nerve stimulation
central pain	CNS injury	Spinal cord compression or post-stroke pain		

For morphine-responsive pains, morphine is generally prescribed when the concurrent use of a *weak opioid* (i.e. codeine or dextropropoxyphene) *and an NSAID* fails to provide satisfactory relief. However, some centres prefer instead to start morphine at a lower dose when an NSAID alone is no longer adequate, rather than move 'up the ladder' via a weak opioid.

Although functional gastro-intestinal pains are generally morphine-responsive, they should be treated more specifically:

- gastric distension → dietary advice, antiflatulent (simethicone), prokinetic (metoclopramide or domperidone)
- irritable bowel syndrome → bulk-forming agent, antispasmodic
- constipation → laxatives.

These are morphine-responsive pains for which morphine should not be used.

6. Which pains are only poorly-responsive to morphine?

Pain associated with the following are often (although not always) poorly responsive to morphine:

- raised intracranial pressure
- bone metastasis (and some soft tissue pains)
- neuropathic (i.e. nerve compression and nerve injury).

A partial response calls for adjuvant medication and consideration of non-drug treatments:

- raised intracranial pressure → corticosteroid
- bone and soft tissue pain → NSAID; radiotherapy (treatment of choice for bone pain)
- nerve compression → corticosteroid; neurolytic block (sometimes).

For nerve injury pain not associated with cancer, adjuvant analgesics should be tried first, i.e. an antidepressant and/or an anti-epileptic drug. If associated with cancer, such drugs should be introduced only after the combined use of an NSAID and morphine has proved inadequate.

If such pain remains only poorly-responsive despite the addition of appropriate adjuvant analgesics (e.g. pain caused by lumbosacral plexopathy), a good response can often be achieved with a combination of oral ketamine and oral morphine or with spinal analgesia (e.g. a continuous infusion of epidural morphine and bupivacaine). Unfortunately, these treatments are available only at a limited number of centres in India.

7. What do you mean by morphine non-responsive pains?

Not all pains respond equally well to morphine. The following pains should be regarded as morphine non-responsive:

- tension headache
- migraine
- muscle spasm (cramp).

Movement-related pain often does not respond well to oral morphine. So much morphine is required for relief during activity that the patient becomes unacceptably drowsy at rest. The dose of morphine is therefore titrated against rest pain rather than pain on movement.

8. Are there any other important morphine non-responsive pains?

There are several other circumstances in which pain appears to be non-responsive to morphine. These include:

- underdosing (dose too small or given only as needed)
- poor alimentary absorption (rare)
- ignoring psychological, social and spiritual factors.

9. Can psychological factors really inhibit the action of morphine?

Morphine (or any other opioid) should be given only within the context of comprehensive biopsychosocial (whole-person) care. If psychological factors are ignored, pain may well prove intractable.

> A 55 year-old man with cancer of the oesophagus was still in pain despite receiving slow-release morphine tablets 6000mg *(sixty 100mg tablets!!)* twice a day. Following inpatient admission, he became pain-free on 30mg twice a day and diazepam 10mg at bedtime. When he returned home, he converted an under-used room into a workshop, and spent many happy hours there. The key to success was *listening, explaining and setting positive rehabilitation goals.*

The first step is to break the vicious cycle of pain, sleeplessness, exhaustion, increasing pain and increasing distress. Achieving a good night's sleep may require a night sedative or anxiolytic as well as morphine.

An antidepressant should be prescribed if the patient is clinically depressed. Initially it is impossible to distinguish between clinical depression and demoralisation secondary to insomnia and exhaustion caused by long-continued pain and despair. Generally, clinical depression should be diagnosed only after steps have been taken to relieve persistent severe pain and the associated insomnia. With pains expected to respond to morphine, lack of success is one pointer to depression, or another major negative psychological factor.

10. Can I ever be confident that the use of morphine will result in complete relief?

Yes: if the pain is morphine-responsive. Partial relief obtained with a weak opioid or when morphine is first prescribed often indicates whether the pain is morphine-responsive.

Doctor 'With your present tablets [weak opioid], how soon do you get relief?'

Patient 'After 20-30 minutes.'

Doctor 'How long does the relief last?'

Patient 'About one and a half to two hours.'

Doctor 'How much of the pain is relieved by the tablets? 25%, 50%, 75%?'

Patient 'I would say about 50%; they make it bearable.'

Doctor 'That's good, because it means that you have a pain which responds to this type of pain killer. What we have to do now is to use something stronger, something which will get rid of 95% of your pain.'

In this situation, the doctor can be confident that the use of morphine will achieve much greater, possibly complete, relief.

Starting Treatment with Morphine

11. What are the basic principles governing the use of morphine in advanced cancer?

- use within the context of comprehensive biopsychosocial (whole-person) care
- use when a weak opioid and an NSAID are no longer adequate
- continue to prescribe an NSAID, unless there is a major contra-indication
- administer by mouth
- administer regularly by the clock, with additional as needed or rescue doses
- titrate the dose according to individual need
- anticipate and treat vomiting and constipation
- monitor the response
- use adjuvant analgesics or non-drug treatments if the pain remains poorly-responsive.

12. Is it better to start with morphine solution/ordinary tablets or with slow-release tablets?

It is often easier to begin with morphine solution or ordinary tablets every 4 hours and convert to slow-release tablets when the dose has stabilised. However, this is not an absolute rule, and some centres titrate with slow-release morphine backed up with *rescue doses* of morphine solution or ordinary tablets (see Question 17).

13. How do I decide the initial dose of oral morphine?

If weak opioids have not been used or small doses only (e.g. codeine 30mg every 4 hours), 5–6mg every 4 hours (or slow-release morphine 10-15mg every 12 hours) may be adequate. However, if the patient has been taking codeine 60mg every 4 hours, morphine 10mg every 4 hours is the correct starting dose (or slow-release morphine 30mg every 12 hours).

If the patient has been taking dextropropoxyphene hydrochloride 65mg with paracetamol 650mg (Proxyvon) 1 tablet q.i.d., and is well pain-controlled, start with morphine 5mg every 4 hours (or slow-release morphine 10-15mg every 12 hours). However, if the patient is still in pain, then start with morphine 10mg every 4 hours (or slow-release morphine 30mg every 12 hours).

But if the weak opioid has been taken only three or 4 times a day *as needed* and has given good intermittent relief, the first step may be not to prescribe morphine but to take the weak opioid regularly every 4 hours. If the patient is pain-free the next day, the regular use of the weak opioid every 4 hours should be continued: *morphine is not indicated.* If the patient is only 75–90% comfortable, treatment with morphine should be started.

With alternative strong opioids (i.e. tramadol, buprenorphine, fentanyl), if the patient has previously had good relief but is now 'getting used to the tablets', it may only be necessary to increase the dose in order to re-establish good relief. However, a decision to change to morphine may be made because of cost and convenience.

14. Is morphine 10mg every 4 hours the right starting dose for a patient previously receiving an alternative strong opioid?

No! If morphine 10mg (or slow-release morphine 30mg twice a day) is prescribed in these circumstances, the patient will soon be in severe pain. This is unnecessary and

damages the morale of both patient and family. It may also lead to the false conclusion that 'morphine is no good for Mr Kumar's pain: it doesn't work for him.'

15. What is the right starting dose for patients changing from an alternative strong opioid?

The dose of morphine to be prescribed is calculated as follows:

- add up the total 24-hour dose of the alternative strong opioid
- multiply this by the potency of the strong opioid in question (Table 3). This is the *total daily dose of morphine* which will give comparable relief
- if the patient has been in pain despite the use of the alternative strong opioid, the total daily dose of morphine should be increased by 30–50 per cent
- if using ordinary morphine tablets or solution, divide the calculated total daily dose by 6 and round up to the nearest convenient 5mg or 10mg. This is the correct 'every 4 hours' starting dose of morphine (which could be 60mg or even more)
- if using slow-release tablets, divide by 2 and round up to the nearest convenient twice-a-day dose (which could be as much as 200mg).

Table 3 Preparations available and potency ratio

	Preparations available in India					*Oral potency ratio with morphine*[a]
	Oral solution	*Tablet/ capsule*	*Trans-mucosal*	*SR*	*Injection*	
Buprenorphine	_	_	Tab SL	TD	+	60
Codeine	_	_				1/10
Dextropropoxyphene						1/10[b]
Fentanyl	_	_	Loz	TD	+	100
Pethidine						1/8
Tramadol						1/5

a. these are all debatable but represent safe 'transfer factors'; for discussion, see respective monographs in the Palliative Care Formulary (www.palliativedrugs.com)
b. multiple doses; single doses are less potent

Key
SR = slow-release; Loz = lozenge; SL = sublingual; TD = transdermal.

Example
- patient taking tramadol 100mg q.i.d. = 400mg/day
- multipy by potency ratio with morpine(1/5) = 80mg/day of morphine
- divide by 6 to obtain 4-hourly dose = 10-15mg every 4 hours
- depending on the circumstances, prescribe either 10mg [patient comfortable but cachectic] or 15mg [patient in pain and physical status reasonably good]
- advise patient on appropriate p.r.n. dose [e.g. 10mg up to every 2 hours].

16. Overwhelming pain

Some patients present a picture of 'It's all pain, doctor.' They are often highly anxious, demoralised, and exhausted from pain-related insomnia. In this situation there is no way of estimating what a patient will need to achieve relief.

Initially an anxiolytic (e.g. diazepam) and morphine should be prescribed concurrently. The nurses should be instructed to repeat the initial combined medication after one hour if the patient is not much more comfortable. Review by the doctor after two hours and 4 hours is not excessive. Subsequent doses of both drugs depend on the initial response.

Overwhelming pain is usually the result of weeks or months of unrelieved severe pain. *It should be regarded as a medical emergency*. Best results are obtained if *one doctor* (or at most two) accepts responsibility for frequent review and prescribing. Spinal cord compression may cause widespread pain in the lower half of the body and must be distinguished from the syndrome of overwhelming pain.

17. How soon should a patient be re-evaluated after starting oral morphine?

Ideally after two hours and again after four hours! This is rarely possible if the patient is at home. Monitoring progress must be seen as the shared responsibility of the patient, family, nurses and doctor. Provided everyone plays their part, it is unlikely that anything will go seriously wrong.

The patient and family should be advised that the starting dose may not completely relieve the pain. Various strategies can be adopted to cope with this. The most straightforward is to advise the patient, if necessary, to use an extra *rescue dose* between the regular doses:

> 'If the morphine solution/tablet does not give more than 75% relief, take a *rescue dose* after 2 hours. If you do this, you must still take the next regular dose on time.' (Here the rescue dose will be the *same* as the regular every 4 hours dose.) *or*
>
> 'If the effect of the slow-release tablets wears off in less than 12 hours, take a *rescue dose* of morphine solution or ordinary tablets.' (Here the rescue dose will be approximately *one-third* of the every 12 hours dose.)

The aim, however, is to increase the regular dose progressively until the patient's pain is relieved (dose titration). The patient should therefore be advised to increase the dose by 30–50% on the second day if the pain is not 90% relieved (even if he feels moderately drowsy), and again 2-3 days later.

Ideally, as the regular dose increases, the need for rescue doses will decrease. However, for most patients, rescue doses continue to be necessary, at least occasionally.. After every dose adjustment the patient should be told what is the right rescue dose for him. (See also Question 23.)

18. What other general advice should a patient be given?

It is important to tell the patient:

> 'If you are unhappy about the new medication, contact me at (name and telephone number of doctor or nurse)' *or*
>
> 'I (or nurse) will be in touch later today/tomorrow to review progress' *or*
>
> 'Please phone me tomorrow and let me know how things are going?'

When an unknown team member is to be on duty, give the patient the name of the person and a few words of introduction and re-assurance:

> 'Dr X./Nurse Y. is on call tonight. We work closely together, and I will tell him/her about you before I go off duty.'

It should be exceptional for a patient not to be contacted on the second day of treatment by either a doctor or nurse familiar with oral morphine therapy. The dose of morphine and the laxative, in particular, may need to be adjusted over the first few days.

The patient and family often have questions they want to ask about morphine, e.g. 'Will I become addicted?' Professional time must be made for discussion.

Professional support is necessary to encourage the patient and family during the initial period. Also, only the trained professional can recognise when the dose of morphine should be reduced temporarily or when morphine intolerance cannot be circumvented (see Question 36).

It is irresponsible to prescribe morphine and not make arrangements for close supervision by somebody familiar with its use.

19. How soon should the patient become pain-free?

Total immediate success is a bonus. It is best, therefore, to agree on a series of sequential goals:

- a good night's sleep free of pain (normally achieved in 2-3 days)
- comfort at rest (sitting or lying) during the day (normally achieved in 3-5 days)
- comfort when active (normally achieved in 3-7 days); *in patients with multiple vertebral or pelvic metastases, this third level of relief may not be possible*
- for patients with persisting movement-related pain, suggest ways in which the patient might modify his way of life so as to reduce activities which cause or exacerbate pain.

In patients with more than one pain, each pain should be re-evaluated. Some respond more readily than others. Re-evaluation remains an ongoing necessity. Old pains may get worse and new ones may develop. If the patient is very anxious or depressed, it may take 3-4 weeks to achieve a satisfactory result.

20. What should be done if morphine does not completely relieve the patient's pain?

If there is little relief after one or two increments, it is possible that the patient has a morphine non-responsive pain. In this circumstance, an alternative strategy is necessary.

Alternatively, a poor response may indicate that the pain has a higher than average psychological component. This will demand more time, more psychotherapeutic support, and possibly the prescription of an anxiolytic or an antidepressant.

21. By how much should the dose of morphine be increased?

A 50% increase is generally appropriate, but certainly no less than 33%. Each adjustment takes time; and time and confidence are lost if an adjustment yields little benefit. It is important to be equally decisive when increasing the dose of slow-release tablets.

22. Is oral morphine really effective?

Yes. Morphine sulfate has been used in doses ranging from less than 5mg to more than 1200mg every 4 hours. However, mega-doses are uncommon. Published data show that for ordinary morphine tablets and aqueous solution:

- the median maximum dose is 15–20mg every 4 hours
- few patients ever need more than 200mg every 4 hours
- patients with inadequate relief on 100mg every 4 hours may obtain benefit at higher doses.

Controlled trials have shown that slow-release tablets are equally effective. This means that for slow-release morphine, the median maximum dose is likely to be about 60mg

twice a day, and few patients will need more than 600mg twice a day. Further, as a general rule, if a pain does not respond to oral morphine, it will not respond to SC or IV morphine (though may respond to spinal morphine).

23. How good is morphine for episodic (intermittent) pain?

For patients who continue to experience episodic (intermittent) pain despite regular morphine (and an NSAID), it is important to differentiate between pain which is:

- *predictable* (incident), i.e. an exacerbation of pain caused by physical activity (including coughing, defaecation, dressing change, etc.)
- *unpredictable* (spontaneous), i.e. pain unrelated to activity (e.g. colic, stabbing nerve injury pain)
- *end-of-dose failure*, i.e. pain which occurs regularly 30-60 minutes before the next dose of four-hourly morphine is due, or 1-2h before the next dose of slow-release morphine.

End-of-dose failure pain generally responds to an increase in the dose of morphine. With predictable (incident) pain, management will depend on the precipitating cause, certainly in the case of pain caused by coughing or defaecation. Morphine by mouth obviously does not take effect instantly. Even with a solution of morphine sulphate there is likely to be a latent interval of at least 15-30 minutes. Thus, it might help to time a dressing change for 1-2h after the last regular dose of morphine.

For pain brought on by movement, many patients adopt an attitude of 'grin and bear it', because they have learned that it quickly eases after movement ceases. Some patients, if they anticipate a period of sustained activity may either time it for 1-2h after the last dose of morphine or take an extra prophylactic dose (e.g. 50% or more of their regular four-hourly dose).

For patients experiencing unpredictable (spontaneous) pain, management is likely to depend on the cause (e.g. abdominal massage for moderate visceral colic). However, the unpredictability often makes the pain more fearful, and therefore more intense. Most patients in this situation feel the need to take extra medication. Again, there is scope for working out individual solutions to ease the impact of distressing unpredictable pain. But if extra morphine is used, the dose is generally 50-100% of the regular four-hourly dose.

Coping with Undesirable Effects

24. What are the main undesirable effects of morphine?

Initial

- nausea and vomiting
- drowsiness
- confusion (delirium)
- unsteadiness

Continuing

- constipation

Other

- dry mouth (common)
- sweating
- myoclonus (associated with neurotoxicity)
- urinary retention (uncommon)

NOTE: respiratory depression is not listed (see Question 35).

25. Is the use of morphine limited by undesirable effects?

Generally *No*

Occasionally *Yes.*

Undesirable effects are minimised by close supervision and by the use of an appropriate anti-emetic and a laxative.

26. Is an anti-emetic always necessary?

If the patient vomits after taking morphine, the morphine will not be absorbed, the patient remains in pain, and confidence will be lost. To avoid this, some doctors prescribe an anti-emetic routinely when morphine is prescribed. Although this is good advice for the inexperienced prescriber, once a doctor and the team feel confident in the use of oral morphine, a more selective approach is possible.

The following patients should be prescribed an anti-emetic prophylactically:

- those who are already experiencing nausea and vomiting from another cause
- those who are experiencing nausea and vomiting with codeine or other weak opioid
- those who vomited when given a strong opioid in the past.

The following patients need not be prescribed an anti-emetic prophylactically:

- those with no nausea and vomiting
- those taking a weak or alternative strong analgesic regularly without nausea or vomiting.

One third of all patients prescribed morphine never need an anti-emetic.

27. Which anti-emetic is best?

For morphine-induced vomiting, an anti-emetic which acts on the chemoreceptor trigger zone in the area postrema of the brain stem is generally a good choice. For example, haloperidol 1mg at bedtime (or 0.5mg b.i.d.) or metoclopramide 10mg t.i.d. (or every 4 hours). Metoclopramide is the better choice if the patient's symptoms suggest a degree of delayed gastric emptying.

Some centres in India use a $5HT_3$-receptor antagonist, e.g. ondansetron 8mg b.i.d., if haloperidol and/or metoclopramide are unsatisfactory, or as their preferred choice in this circumstance. However, in most countries the cost of $5HT_3$-receptor antagonists is such that their use in palliative care is not encouraged.

28. Can the anti-emetic be stopped?

For many patients, vomiting with morphine is an initial effect. If an anti-emetic was prescribed prophylactically, and not to relieve pre-existing nausea and vomiting, it is good practice to stop it after the patient has been on a steady dose of morphine for one week. Remember: about 1/3 of patients receiving morphine never need an anti-emetic. If necessary, the anti-emetic can be restarted, and continued indefinitely.

29. Do patients become drowsy on morphine?

Like nausea and vomiting, drowsiness tends to be troublesome during the first few days, and subsequently if the dose is increased. Patients should be warned about initial drowsiness and encouraged to persevere in the knowledge that it will lessen after 4-5 days on a steady dose. Occasionally, in elderly or frail patients, it is necessary to reduce the dose of morphine and then increase it again more slowly, every 2-3 days until adequate relief is obtained.

30. Do some patients go on feeling very drowsy and drugged?

Occasionally, yes (Box B). It is important to distinguish between persistent drowsiness and inactivity or boredom drowsiness. Most patients receiving morphine catnap with ease. This means that they tend to drop off to sleep if sitting quietly, particularly if alone.

Box B Checklist for excessive drowsiness in patients receiving oral morphine

General factors

Is the patient still recuperating from prolonged fatigue?

Is the patient more ill than I thought?

- renal failure
- hypercalcaemia
- hyponatraemia
- hyperglycaemia
- hepatic failure
- cerebral metastases
- septicaemia
- cardiac failure

Drug factors

Is the patient completely pain-free?

- if yes, reduce the dose and review both drowsiness and pain relieve.

Is the patient on a sedative psychotropic drug such as a benzodiazepine (e.g. diazepam) or a phenothiazine (e.g. chlorpromazine)? Is it necessary?

- if no, cut it out.
- if yes, can the dose be reduced?

If the patient is taking a phenothiazine anti-emetic, can it be changed to haloperidol or metoclopramide?

As many of these patients have little stamina, they need more rest and sleep than when healthy. Provided that they rouse easily when joined by family or friends, continuing inactivity drowsiness can generally be regarded as a bonus. Indeed, many patients find that it helps to cope with what otherwise might be a long and exhausting day. But, if stamina is not limited, the patient can live a normal active life because any continuing drowsiness is related to inactivity.

On the other hand, patients with renal failure may become drowsy because of cumulation of an active metabolite, morphine-6-glucuronide. This necessitates a reduction in dose of morphine, and possibly a reduction in frequency of administration from every 4 hours to every 6-8 hours.

Moderate hepatic insufficiency does *not* affect the metabolism of morphine; severe hepatic failure does (patient with history or evidence of hepatic encephalopathy), and may necessitate a reduction in dose or frequency.

31. Do patients become confused?

Yes, a few. Particularly the elderly, who are more sensitive to the effects of morphine. It will be necessary to titrate the dose of morphine more slowly in these patients, possibly starting on a lower dose, or prescribing every 6–8 hours initially. Patients over 70 years old should be warned that they may become muddled at times during the first few days, but to persevere.

Confusion (delirium) may be caused by the concurrent use of morphine and psychotropic drugs and/or antimuscarinic drugs. If the confusion persists, a reduction in concurrent medication should be considered (Box B).

32. Is postural hypotension a problem?

No. Advise those over 70 years old that they may experience dizziness or feel unsteady for a few days, but to persevere.

33. Constipation

Generally, constipation is the most troublesome undesirable effect of morphine and other opioids. However, in some parts of India it is less of a problem, e.g. in Tamil Nadu, possibly because of dietary factors. Even so, constipation should be anticipated when a patient is prescribed regular morphine, and the situation monitored. Remember: correcting constipation is occasionally more difficult than relieving pain.

Opioids cause constipation by decreasing propulsive intestinal activity and increasing non-propulsive ring contractions, and by enhancing the absorption of fluid and electrolytes. Colonic contact (stimulant) laxatives such as senna and bisacodyl (Dulcolax) reduce ring contractions in the colon, and thereby facilitate propulsive activity. They therefore provide a logical approach to the correction of opioid-induced constipation. Patients receiving an opioid often need a higher dose of a contact laxative than that recommended for general use by the manufacturers (Figure 1).

- bulk-forming drugs, because they have no direct intestinal propulsive action, have little to offer in the management of opioid-induced constipation, and can make the situation worse
- some patients receiving morphine need continuing rectal measures (laxative suppositories, enemas, digital evacuation) .

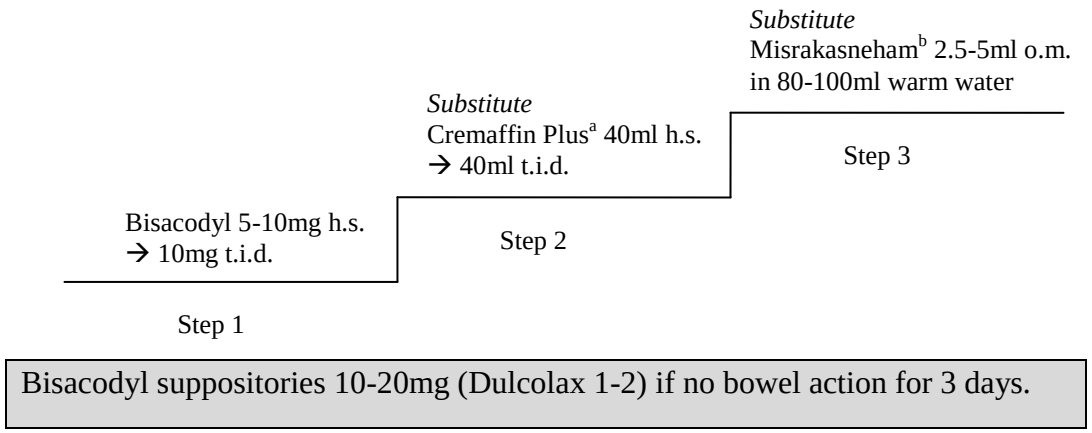

Figure 1 A possible therapeutic step-ladder for opioid-induced constipation, with safety net (rectal measures).

a. Contains liquid paraffin and sodium picosulfate (a potent stimulant laxative); alternatively use Cremaffin Pink (liquid paraffin, magnesium sulphate, phenolphthalein).
b. Misrakasneham is an Ayurvedic preparation and can only be recommended to patients, rather than prescribed. Its efficacy has been confirmed in a randomized controlled trial in which it was compared with senna (Ramesh et al. 1998 JPSM 16; 240-244).

34. Sweating

Some patients complain of sweating. This can be profuse and tends to be more troublesome at night. It probably occurs more in patients with extensive liver metastases. Sleeping lightly clad and in a cool room may be all that one can suggest to the patient. Most patients put up with the sweating as an acceptable price to pay for freedom from pain, particularly when they understand that it has no sinister meaning.

35. Do patients die of morphine-induced respiratory depression?

No, because pain antagonises the central depressant effects of morphine. When morphine is used in the way described here, clinically important respiratory depression is rarely seen. Should it occur:

- reduce the dose of morphine if the patient is pain-free
- consider using an opioid antagonist, e.g. naloxone 20 microgram IV every 2 minutes until the patient's respiratory status is satisfactory; this is rarely necessary.

NOTE: the dose of naloxone in this circumstance is only 20 microgram; to give more risks precipitating severe pain and a major withdrawal syndrome. Improvement is measured in terms of respiratory function; level of consciousness is only of secondary importance. The patient can sleep off the excess sedation; in itself sedation is not life-threatening.

However, iatrogenic overdosage and respiratory depression can occur if the dose of morphine is increased automatically every few days, i.e. without appropriate clinical re-evaluation.

36. Are there any circumstances in which treatment with morphine has to be abandoned?

On rare occasions, yes (Table 4). Oral tramadol, sublingual or transdermal buprenorphine or transdermal fentanyl may need to be substituted for morphine in these circumstances.

Table 4 Potential intolerable effects of morphine

Type	*Effects*	*Initial Action*	*Comment*
Gastric stasis	Epigastric fullness, flatulence, anorexia, hiccup, persistent nausea	Metoclopramide 10-20mg q4h	If the problem persists, change to an alternative opioid
Sedation	Intolerable persistent sedation	Reduce dose of morphine; consider methylphenidate 10mg o.m.-b.i.d.	Sedation may be caused by other factors; stimulant rarely appropriate
Cognitive failure	Agitated delirium with hallucinations	Prescribe haloperidol 3-5mg stat & p.r.n.; reduce dose of morphine and if no improvement, switch to an alternative opioid	Some patients develop intractable delirium with one opioid but not with an alternative opioid
Myoclonus	Multifocal twitching± jerking of limbs	Prescribe diazepam/midazolam 5mg stat & p.r.n.; reduce dose of morphine but increase again if pain recurs	Unusual with typical oral doses; more common with high dose IV and spinal morphine
Hyperexcitability	Abdominal muscle spasms, symmetrical jerking of legs, whole-body allodynia, hyperalgesia (manifests as excruciating pain)	Prescribe diazepam/midazolam 5mg stat & p.r.n.; reduce dose of morphine; consider switching to an alterrnative opioid	A rare syndrome in patients receiving intrathecal or high-dose IV morphine; occasionally seen with typical PO and SC doses
Vestibular stimulation	Movement-induced nausea and vomiting	Prescribe dimenhydrinate *or* promethazine 25-50mg q6-8h	If intractable, switch to an alternative opioid
Pruritus	Whole-body itch with systemic morphine; localised to upper body or face/nose with spinal morphine	Ondansetron 8mg IV stat and 8mg PO b.i.d. for 3-5 days	This is a central phenomenon and does *not* respond to H_1-antihistamines; centrally-acting opioid antagonists also relieve the itch but antagonise analgesia
Histamine release	Bronchoconstriction → dyspnoea	Prescribe IV/IM antihistamine(e.g. chlorphenamine 5-10mg) and a bronchodilator; switch to an alternative opioid immediately	Rare

Morphine by Injection

37. What about rapid dose titration with intravenous morphine?

For patients in severe pain, particularly for several weeks or months, some centres gain rapid relief with morphine given intravenously (Box C). This has the advantage of also rapidly gaining the patient's confidence in the ability of the treating doctor to ease the pain. This approach has been used in several thousand patients in Kerala, mostly in people with advanced cancer. In no case has the technique been complicated by clinically significant respiratory depression.

However, the relief achieved after 24 hours is the same whether morphine is started in this way or if oral morphine is used without an initial graduated intravenous bolus.

Box C Dose titration with IV morphine[a]

Prerequisites
Pain ≥5/10 on a numerical scale.
Likelihood of a partial or complete response to morphine.[b]
Method
Obtain venous access with a butterfly cannula.
Give metoclopramide 10mg IV routinely.
Dilute the contents of 15mg morphine ampoule in a 10ml syringe.[c]
Inject 1.5mg every 10 minutes until the patient is pain free or complains of undue sedation.
If patients experience nausea, give additional metoclopramide 5mg IV.
Results
Dose required (with approximate percentages):
1.5-4.5mg (40%)
10.5-15mg (15%)
6-9mg (40%)
>15mg (5%).

Complete relief in 80%; none in 1%.
Drop outs 2%.
Undesirable effects: sedation 32%; other 3%.
Ongoing treatment

- prescribe a dose of oral morphine q4h which is similar to the IV requirement, rounded to the nearest 5mg, i.e. relief with morphine 3-6mg IV → 5mg PO etc;
- the minimum dose is 5mg q4h
- instruct patients to take p.r.n. doses and to adjust the dose the next day according to need.

a. Kumar S et al. Palliative Medicine 2000; 14: 183-188.
b. most patients will already be taking an NSAID
c. ampoule strength is determined by local availability.

38. What about the use of morphine by injection if an acute-on-chronic pain crisis occurs?

It is possible to adopt the same approach for an acute-on-chronic pain crisis as for initial dose titration, particularly if 2-3 *as needed* doses have not relieved the acute pain. However, the amount of morphine given for the first bolus should be increased to 3-6mg, followed by 3mg every 5 minutes thereafter.

39. Wouldn't injections generally be better?

No. Injections are *not* generally better, and can be uncomfortable. Regular injections tie the patient to a second person, generally a nurse, because someone else is needed to administer the medication.

40. What are the indications for injections?

Main

- intractable vomiting
- inability to swallow
- coma

Subsidiary

- psychological aversion to oral medication
- poor alimentary absorption (rare)

If regular injections become necessary, the best option is a *continuous subcutaneous infusion* of morphine (preferably using a battery-driven or clockwork portable syringe driver) but this is not always possible. An indwelling butterfly cannula to give injections every 4 hours is another option. *The dose of morphine should be halved when changing to the subcutaneous route.*

41. Once on injections, is it possible to change back successfully to the oral route?

Once vomiting has been relieved with parenteral anti-emetics, it is often possible to revert to the oral route. It may be wise to convert in stages, e.g. first change the anti-emetic, and then, the next day, change the morphine if there is no recurrence of vomiting.

42. Is it necessary to give more morphine by mouth than by injection?

Yes. The dose of morphine sulfate should be *doubled* when converting from the intravenous or subcutaneous to the oral route. Further adjustments *up or down* may then be necessary.

43. Can morphine be given by suppository?

Yes. Suppositories are a useful alternative to injections, particularly in the home. In some countries, suppositories of morphine sulfate are available in several strengths. They can also be made by a local pharmacist. The *oral to rectal potency ratio is 1:1*; i.e. the same dose is given per rectum as by mouth.

If administration every 4 hours proves difficult, it is possible to give slow-release morphine tablets *per rectum* every 12 hours. Pharmacokinetic studies have demonstrated that they are equally well absorbed by this route.

More Questions about Morphine

44. Why do some people need more morphine than others?

There are many reasons, including:

- differences in pain intensity
- older people tend to need less
- whether adjuvant drugs and non-drug measures are used
- pharmacokinetic differences:
  - absorption
  - 'first-pass' hepatic metabolism
  - plasma half-life
  - renal function
- genetic differences in patient's pain tolerance threshold (relates to CNS endorphin stores)
- acquired differences in patient's pain tolerance threshold (relates mainly to mood and morale)
- previously induced tolerance:
  - needless increases in dose
  - initial use of morphine by injection in excessive amounts
- duration of treatment (the dose tends to increase as the disease progresses)
- adequacy of management of other symptoms.

45. What's so special about 'every 4 hours'?

Clinical experience in countless countries has shown that increasing the dose of morphine solution to provide relief for 4 hours achieves the optimum balance between relief, practical convenience, and undesirable effects.

Giving more at less frequent intervals will provide comfort for a longer period, but only at the price of more troublesome undesirable effects, particularly drowsiness and nausea.

Giving less at more frequent intervals simply makes the regular taking of morphine more tedious for the patient, particularly at night. Compliance is then reduced and more pain is the result. The general rule is: *give morphine regularly every 4 hours (or twice a day if a slow-release preparation is used).*

46. For ordinary morphine tablets and solution, are there any exceptions to the 'every 4 hours' rule?

Regular morphine is indicated for continuous pain but not for occasional pain. Other circumstances in which it may be desirable to prescribe morphine solution *less often* include:

- the very old (80+)
- patients with night pain only
- patients with evening and night pain only
- patients in renal failure (when the plasma half-life of an active metabolite of morphine is prolonged by up to three times, from 2.5h up to 7.5h).

47. Is it ever necessary to give morphine more often than every 4 hours?

Yes. Very occasionally a patient appears to metabolise morphine exceptionally fast. Increasing the dose in an attempt to prolong relief from 3 to 4 hours does little except increase undesirable effects. If this is the case, the dose should be decreased again and given *every 3 hours*.

A comparable situation may be seen with slow-release morphine tablets. Here, the frequency of administration would be increased to *every 8 hours*.

48. How can I tell if administration every 3 hours is indicated?

The following questions will help you decide:

> 'Are you completely pain-free during the 4 hours between two doses of morphine?'
>
> If the answer is *No*, then ask:
>
> 'Does the pain completely go but come back before your next dose is due, or does the medicine just ease the pain but never make you pain-free?'

If it just eases the pain, a morphine increment is clearly required. If it goes and returns, the patient *may* be a fast metaboliser. In this case, increase the dose of morphine, and monitor both relief and undesirable effects. If there is a minimal increase in the duration of the pain relief but a considerable increase in undesirable effects (drowsiness, vomiting), revert to the former smaller dose and increase the frequency to every three hours. *In practice, it is rarely necessary to give morphine every three hours.*

A comparable series of questions should be asked of patients receiving slow-release tablets to decide if administration should be every eight hours. This advice is given on the assumption that the doctor is treating a morphine-responsive pain and that appropriate non-drug measures are being used. As emphasized elsewhere, attempts to completely relieve movement-induced pains with morphine generally result in a marked increase in undesirable effects.

49. Should patients be awakened to take a dose in the middle of the night?

Theoretically yes, but in practice often no. A dose in the middle of the night is advisable if:

- a patient is already taking one and has established a satisfactory routine
- the patient wakes regularly to urinate sometime after midnight (the patient can take a dose then)
- attempts to achieve all-night relief have failed, and the patient continues to wake in pain in the second half of the night.

50. Can a dose in the middle of the night be avoided in other circumstances?

Yes. We regard it as the norm for the patient to sleep through the night without a dose at 0200h. This has been achieved by modifying the 'every 4 hours' regimen to: every 4 hours during the day (0600h, l000h, 1400h, 1800h) *and a double dose at bedtime* (2200h). The potential for drowsiness with the higher dose of morphine is turned to good effect by enhancing the patient's sleep.

51. Is a double dose more dangerous?

A double dose of morphine at bedtime is perfectly safe in most patients. In the very frail and/or elderly, particularly if there is a risk that they might wake in the night feeling drugged and disoriented, it would be wise to start with a 50% higher dose at bedtime, rather than a double dose.

52. What about driving?

Most patients receiving morphine are not well enough to drive, and have no wish to do so. Those who are stronger may still want to drive their car, particularly if they are continuing to work. Patients who wish to drive need specific advice (Box D).

Doctors have an ethical and legal responsibility to advise patients if a disability is likely to make them a danger when driving. In many states and countries, there is an obligation on the driver to report any such disability to the licensing authority, unless relatively short-term, e.g. less than three months. The patient can fulfil this obligation only if his doctor advises him appropriately.

Box D Advice for patients wishing to drive while taking oral morphine

The medicines you are taking do *not* automatically disqualify you from driving. However, the speed of your reactions and general alertness may be adversely affected by your medication.
It is important that you take the following precautions, particularly if you have not driven for some weeks because of ill health:

- do not drive in the dark or when conditions are bad
- do not drink alcohol during the day
- check your fitness to drive in the following way:
  choose a quiet time of the day when the light is good
  choose an area where there are several quiet roads
  take a companion (husband, wife, friend)
  drive for 10–15 minutes on quiet roads
  if both you and your companion are happy with your attentiveness, reactions and general ability, *then it is all right to drive for short distances*
- do not exhaust yourself by long journeys.

53. If morphine is prescribed more than a few weeks before the patient's death, what happens when tolerance develops?

Tolerance is not a practical problem when morphine is used regularly and prophylactically in individually optimised doses, and within the context of *total patient care*. After initial dose titration, many patients continue on an unchanged dose for weeks or months. In those who are not experiencing any breakthrough pain, it may be possible after several weeks to reduce the dose without the pain re-emerging. Rapid escalation of dose is hardly ever necessary when morphine is used properly.

54. Don't patients die quickly once morphine has been prescribed?

Many patients prescribed morphine are near to death and remain near to death. These will inevitably die fairly soon. On the other hand, many patients survive for weeks or

months after starting oral morphine, and occasionally for years. Patients survive for longer than expected because they are able to rest, sleep and eat more, and develop a renewed interest in life.

55. When the patient is close to death and unconscious, can morphine be stopped?

No, because unconscious patients in pain become restless. Further, physical dependence develops after several weeks of oral morphine therapy. Then, if morphine is stopped abruptly, the patient will become restless, sweaty, and might develop faecal incontinence secondary to rebound hyperperistalsis. However, only one quarter of the analgesic dose is needed to prevent opioid withdrawal phenomena.

56. If patients have morphine at home, won't it get stolen?

I know of no patient whose morphine was stolen by intruders. There have been rare reports of misappropriation by a relative or a friend.

57. Won't patients use their morphine to commit suicide?

I know of no case of self-poisoning by a cancer patient in which morphine was the agent used.

58. Isn't the use of morphine tantamount to prescribing a living death?

Many doctors and nurses have strongly negative attitudes towards the medicinal use of morphine. For example:

> 'What about the inoperable cancer patient who may not die for months and is suffering agonies from chronic pain? Is a doctor justified in prescribing morphine when he knows full well he will be sentencing his patient to a kind of living death?'
>
> 'I try to postpone giving morphia until the very end and am best pleased if the first dose is also the last.'

These views stem from ignorance about the correct use of morphine in cancer patients with pain. Indeed, the patients who are truly sentenced to a kind of living death are the ones who are not prescribed adequate doses of morphine. For example, one man had been bedbound for two months because of pain. His wife then found him crawling around the room on his hands and knees searching for his gun which she had hidden for fear he would shoot himself. The subsequent correct use of morphine enabled this patient to live a far more normal life than would otherwise have been possible. The same has proved true for many lakhs of others too.

59. Is oral morphine the panacea for cancer pain?

Definitely not! Oral morphine is a useful treatment without which life would be extremely uncomfortable for many patients with advanced cancer. It must be used correctly with an awareness of its limitations and with regular supervision for each patient.

60. What are the more important non-drug treatments?

- radiation therapy for bone pain; also for some nerve compression pains and fungating tumours
- inection of trigger points with local anaesthetic
- neurolysis (e.g. nerve destruction with alcohol or phenol-in-glycerol)

- modification of the patient's way of life (for pains exacerbated by weight-bearing or movement)
- psychological support of the patient and family.

In some centres, nerve blocks have been almost entirely replaced by spinal analgesia (epidural or imtrathecal) with a continuous infusion of morphine and bupivacaine, sometimes with addition of clonidine. There are, of course, many other non-drug treatments – too many to list here.

61. When treating the cancer patient in pain, what else must I bear in mind?

The International Association for the Study of Pain defines pain as *an unpleasant sensory and emotional experience*. Because pain is a somato-psychic experience, its intensity is modified by the patient's mood and morale, and the meaning of the pain for the patient.

Those caring for the patient with cancer must be aware of the many factors which influence the patient's perception of discomfort (Figure 2). If a doctor is not prepared to address the many factors influencing the perception of pain, it would be wise not to prescribe morphine but to ask a colleague who is willing to do so to care for the patient.

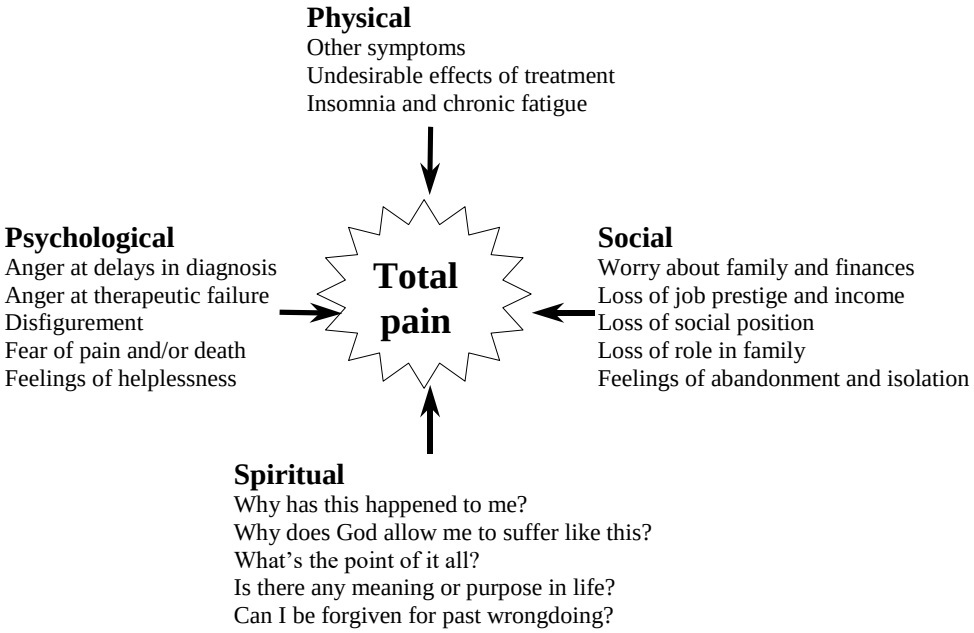

Figure 2 Factors influencing perception of pain

Other Uses of Morphine

62. How is morphine used to relieve dyspnoea?

Patients with dyspnoea caused by irreversible malignant chest disease often benefit from oral morphine. The aim is to reduce the *sensation* of breathlessness. If a resting respiratory rate of, say, 30/minute increases on mild exertion to a level which is distressing to the patient, it should be treated. The use of morphine for dyspnoea is not generally the first-choice treatment. Its use is appropriate only after:

- the impact of dyspnoea has been discussed with the patient and family and, when relevant, the nature of respiratory panic attacks has been explored and coping strategies devised
- general guidance about coping with activity-related dyspnoea has been given, e.g. introducing periods of rest between necessary activities (sometimes called 'pacing')
- as far as possible, reversible factors have been treated, e.g. bronchospasm and heart failure.

Much of the benefit from morphine may relate to a reduction of a futile physiological respiratory overdrive which is seen in some patients with diffuse pulmonary malignant disease, possibly in response to the respiratory stimulant effect of multiple small areas of atelectasis.

63. What is the right dose of morphine for dyspnoea?

The optimum dose of morphine for dyspnoea is generally less than that for pain relief:

- begin with a test dose of 5–6mg (or even less in an elderly frail patient)
- continue with 5–6mg every 4 hours during the daytime, and 10mg at bedtime
- if dyspnoea is limited to activity, anticipatory *as required* use is preferred by some patients, up to every 2h
- after 24-36h , if there is no benefit at all and no undesirable effects, increase the dose to 10mg every 4 hours, and 15–20mg at bedtime
- if there is some benefit, but the resting respiratory rate remains more than 24 per minute, increase the dose after two or three days and review
- consider further adjustment to morphine 15–20mg every 4 hours after 2-3 more days.

At each stage, benefits must be weighed against undesirable effects. The aim is a more relaxed patient who is not cyanosed and is mentally clear. If a patient is already receiving morphine as an analgesic, the dose should be increased by 50% on a trial basis.

64. Is oral morphine of value in other forms of terminal illness?

Yes. There are at least two other situations in which morphine should be considered:

- to ease the aches and discomforts of any patient who is bedbound and dying if paracetamol is insufficient or too difficult to swallow; morphine 5–6mg every 4 hours and 10mg at bedtime may make a big difference, or just a bedtime dose, depending on the circumstances
- as a cough sedative and/or night sedative in patients with motor neurone disease/amyotrophic lateral sclerosis.

Most patients with this disorder develop progressive impairment of the lower cranial nerves. This results in progressive dysarthria and dysphagia. Associated with the

dysphagia is a tendency to choke unpredictably when eating or drinking, and at night as a result of aspiration of saliva. The resulting terror and anticipatory fear is a major problem in the management of terminal motor neurone disease.

Although dietary advice and explanation may help, a pharyngeal sedative is generally necessary to prevent or minimize the bouts of choking. Begin with oral morphine 5–6mg at bedtime or twice a day and go on to titrate dose and frequency in the light of the initial response. Many patients need only 5–6mg three times a day before meals with perhaps a larger bedtime dose; a few take it every 4 hours.

Further Reading

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