Medicines management in the palliative care of cancer patients

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Educational aims

- To provide information on the conventional and off licence use of medicines
- To provide the rationale behind choices of drug treatment of common symptoms
- To update on the precautions to be taken with respect to different medicines and highlight recent drug safety issues
- To empower pharmacists to be more active in the education and support of palliative care patients and their carers

Key words
Palliative care, pain, constipation, nausea and vomiting, oropharyngeal complications

Abstract

Cancer is one of the leading causes of death in Malta. Palliative care is a mainstay in the care of such patients. Commonly encountered symptoms include pain, nausea and vomiting, constipation and oropharyngeal complications. All of these bear an impact on the quality of life of the patient and also of the carers. Drug treatment is an integral part of the management of these symptoms. Patients and their carers may have concerns regarding their medication. The community pharmacist is well positioned and competent to support the needs of these patients as part of their holistic care.

Introduction

Palliative care involves the care of patients with advanced terminal disease, taking a holistic approach to dealing with issues that patients and their relatives encounter in their day-to-day activities.

This paper specifically focuses on palliative care for cancer patients. During 2014, 932 (or 28.5%) of the total number of deaths registered in Malta were due to cancer, with people over the age of 65 years accounting for almost 75% of cancer deaths. Over 80% of these deaths occurred in hospital, just under 10% at their residence and another 6% in care homes.[1] This paper will focus on the control of common symptoms - pain, nausea and vomiting, constipation and oropharyngeal complications. The general principles of such management can be applied to other advanced non-malignant conditions with terminal outcomes, such as neurological disorders. However cancer patients remain the main beneficiaries of such care offered both in hospital as well as the community.

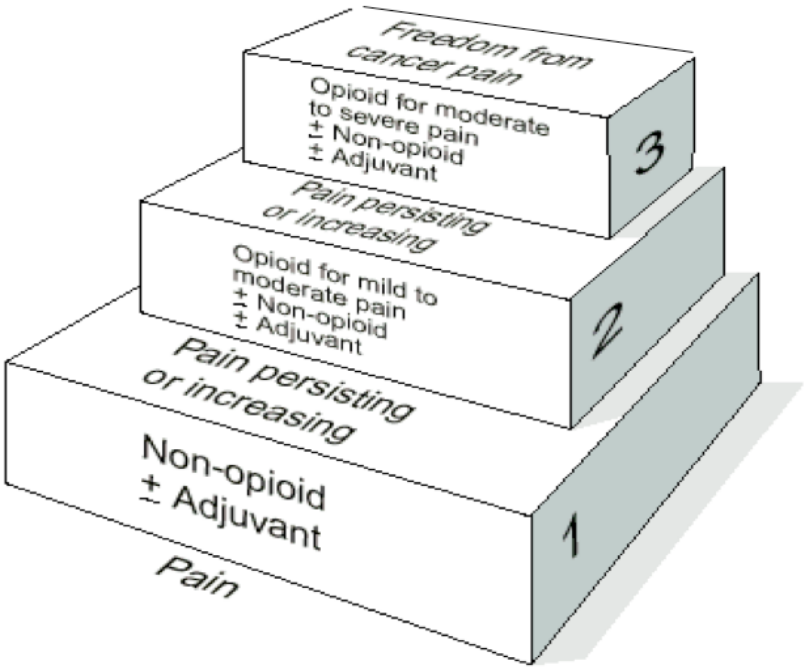
Hospice for terminally ill patients has been established for over 150 years, with the first hospice founded in France back in 1842. During the past 50 years the concept of hospice has developed rapidly to also include care outside the hospital environment.[2]

This article does not focus on the "terminal phase", last few days or hours of life, where an increased level of care is required. During this phase, symptoms such as pain, nausea and constipation change little in prevalence but additional symptoms such as asthenia, dry mouth, confusion and breathlessness may take priority. During this phase the need for drug treatment including the routes by which drugs are administered requires careful evaluation. In such a setting clinical pharmacists' intervention in medicines management goes beyond drug reviews and will require particular expertise with regards to mixing of parenteral medicines and their subsequent stability.

Panel 1: WHO definition of palliative care

"The active total care of patients whose disease is not responsive to curative treatment. Control of pain, of other symptoms, and of psychological, social and spiritual problems is paramount. The goal of palliative care is achievement of the best quality of life for patients and their families."

Figure 1: WHO Pain Relief Ladder[4]



Management of cancer pain

Pain is a frequent symptom in patients with cancer, with substantial impact on their quality of life. Despite the availability of opioid analgesics and updated guidelines, under treatment is still frequently encountered.[3] Careful assessment of the patient, including factors that aggravate or relieve the pain, is essential if adequate analgesia is to be achieved. Patients also have concerns with regards to side-effects including dependence and addiction. Such misconceptions can lead to refusal of pain relief and a reduction in patients' quality of life. Palliative patients should have adequate pain relief medication and fear of addiction should not restrict adequate pain relief treatment. Counselling is thus an important component in ensuring effective pain management.

Principles of treatment of cancer pain

The World Health Organization (WHO) pain ladder, originally devised for the treatment of cancer pain, is a well established guideline for the management of patients with chronic pain. The analgesic treatment should start with drugs indicated by the WHO analgesic ladder appropriate for the severity of pain. This guideline recommends the use of conventional analgesics including non-steroidal anti-inflammatory drugs (NSAID's), paracetamol and opioids. Opioids are classified into two categories according to their efficacy (strong and weak opioids). Adjuvant analgesics can be used at any step if indicated (Refer to Figure 1).[4]

Step 1: Mild pain - Non-opioid analgesics such as paracetamol or non-steroidal anti-inflammatory drugs are indicated. To improve outcomes, patients should be advised to take their pain relief medication at regular intervals rather than on an "as required" basis.[4,5,6]

Step 2: Mild to moderate pain - A weak opioid (codeine, tramadol), should be used in combination with a non-opioid analgesic. The prescribing of combinations of weak opioids is not recommended. If a patient is not responding to maximum doses of a weak opioid/ non-opioid combination then it is appropriate to move up to step 3.[4,5,6]

Step 3: Moderate to severe pain - Strong opioid analgesics are required. Once a patient is stabilised on a dose of immediate-release opioid, he/she should be switched to the equivalent dose of a modified-release preparation if possible. An immediate-release formulation should also be prescribed on an "as-required" basis for breakthrough pain episodes. The equivalent dose should be approximately 1/6th of the daily dose.[4,5,6]

Measurement of cancer pain

A number of validated pain assessment scales have been developed to enable the making of consistent, repeated assessments. Complex tools such as the McGill pain questionnaire are generally too time-consuming for daily use and simpler scales such as visual analogue scales (VAS), verbal rating scales (VRS) or numerical rating scales (NRS) are routinely used.

The equivalence of each category in the WHO classification of pain intensity on the numerical rating scale and the relevant pharmacological management is shown in Table 1.[5,6]

Drugs used for analgesia

Non-opioids

Paracetamol remains the main non-opioid used for the treatment of cancer pain. Non-steroidal anti-inflammatory drugs (NSAIDs) may also be prescribed. There is no evidence to support the preference of one NSAID over another. Prescribing of NSAIDs should be based on knowledge of the side-effect profile and previous response to individual drugs. NSAIDs should be used with caution in patients with cardiovascular disease. In the presence of gastro-intestinal (GI) risk factors a proton pump inhibitor should be co-prescribed with all NSAIDs including COX-2 inhibitors. The long-term use of NSAIDs

Table 1: Pharmacological management of cancer pain

Pharmacological management		
Mild	**Mild to moderate**	**Moderate to severe**
Numerical rating scale 1-3	**Numerical rating scale 4-6**	**Numerical rating scale 7-10**
Non-opioids Paracetamol NSAID's Non-selective NSAIDs COX-2 selective inhibitors	**Titration of weak opioid** Codeine Tramadol	**Strong opioids** Morphine Fentanyl
	+/- NSAIDs/paracetamol	
+/- adjuvant analgesic		

including COX-2 inhibitors has to be carefully monitored and reassessed periodically because they can provoke severe toxicity such as GI bleeding, platelet dysfunction and renal failure. COX-2 selective inhibitors may increase the risk of thrombotic cardiovascular adverse reactions and do not protect against renal failure.[5,6,7]

Opioids

The opioids are classified as the weak opioids (e.g. codeine, tramadol) and the strong opioids (e.g. morphine, fentanyl).

Prescribing a high dose of a weak opioid can result in an opioid load comparable to a low dose of a strong opioid (i.e., 100mg of codeine is roughly equivalent to 10mg of oral morphine). Weak opioids can have the same adverse effects as strong opioids, so patient counselling should be the same.

A ceiling analgesic effect is observed with weak opioids. Increasing the dose of a weak opioid beyond the maximum licensed dose will not improve analgesia but expose the patient to more pronounced adverse effects. A maximal ceiling analgesic effect is not observed with strong opioids.[5,6,7]

Panel 2: Codeine, dihydrocodeine and tramadol

Codeine is a pro-drug and has to be metabolised to morphine mainly via CYP2D6 liver enzyme in order to have an analgesic effect.[8,9] Up to 7% of Caucasian populations may have a deficiency in CYP2D6 resulting in an inadequate analgesic effect.[9]

Dihydrocodeine is an active substance. It is also a substrate for CYP2D6, however there is no evidence that inhibition of this enzyme reduces analgesic effect.[8]

Tramadol has clinically relevant serotonergic activity. It should be avoided in patients taking TCA and SSRIs due to the risk of serotonin toxicity. It also lowers seizure threshold.[8]

The range of strong opioids available to prescribers locally is limited, with morphine being the most frequent prescribed opioid for the relief of severe pain. At the initiation of treatment or when changing treatment the patient's dose should be titrated until an adequate maintenance dose is reached. Patients should be prescribed maintenance treatment on a regular basis at the appropriate dose which relieves pain throughout the dosing interval without causing unmanageable adverse effects.

The dose should be titrated with caution in patients with risk factors: impaired renal function, impaired hepatic function, chronic respiratory disease, compromised upper airway, sleep apnoea. Dose increments should be based upon total opioid dose taken in the previous 24 hours. The rapidity of the dose escalation should be related to the severity of the symptoms. Opioid switching can also improve response by at least 50 per cent.

The appropriate formulation should be used for maintenance dose. When tolerated, morphine via the oral route of administration should be advocated as first choice, unless the patient is nil by mouth. Transdermal fentanyl patches are a useful option in patients unable to swallow. Patches are also useful in patients with worsening renal function, intolerable side-effects (e.g. intractable constipation) and patients with poor concordance.

Management of breakthrough pain

Breakthrough pain should be managed using short acting medication (refer to Table 2). Typically "as required" doses are calculated as one sixth of the 24 hour oral regular dose given every 4 hours as needed. Whereas this approach is useful for titration of the background opioid dose it may not be appropriate for breakthrough pain characterised by quick onset and short duration.[10]

Table 2: Causes of breakthrough pain and their management

Causes of breakthrough pain	Management
Incidental to specific activities (e.g. dressing change, physiotherapy)	Potentially managed with short-acting opioids given in anticipation of these events
End of dose failure pain	Potentially managed by increasing the dose of regularly scheduled opioid
Uncontrolled persistent pain	Potentially managed by increasing the dose of regularly scheduled opioid

Management of opioid adverse effects

Opioids have a number of adverse effects. The management of these side-effects is an integral part of palliative care (refer to Table 3). Constipation and nausea are the two most commonly encountered side-effects of opioids. The management of such adverse effect involves the prophylactic use of stimulant laxatives and faecal softeners for the duration of opioid treatment plus possibly anti-emetics for the first few days of opioid treatment.[8, 11]

Table 3: Adverse effects of opioids and their management

Adverse effect	Management
Constipation Very common (≥ 1/10)	Stimulant laxative ± stool softener (titrate stool softener/ laxative as needed to get bowel movement every one to two days) If impacted consider phosphate enema Laxatives only treat constipation and can exacerbate other symptoms of opioid-induced bowel dysfunction; they do not address the cause of the problem. For intractable chronic constipation, consider an alternative opioid e.g. switch to fentanyl Ensure adequate hydration
Nausea Very common (≥ 1/10)	Prochlorperazine 10mg qds PRN PO Metoclopramide 10mg-15mg qds PRN PO Haloperidol 0.5mg-1.0mg tds or qds PRN PO Domperidone 10mg tds PO Change PRN to regular if nausea persists
Pruritus Common (>1%)	Antihistamines e.g. promethazine 10mg-20mg bd to tds PO; Hydroxizine 25mg up to qds PO Consider changing to another opioid
Respiratory depression and sedation Uncommon (<1%)	Naloxone can be used in case of respiratory depression. Administer by iv injection, 0.4 -2.0mg, if no response to be repeated at intervals of 2 to 3minutes to a maximum of 10mg. Further doses may be necessary if respiratory function deteriorates. Consider dose reduction of opioid

Adjuvant analgesia

The choice of a category of drugs, or a specific drug for adjuvant analgesia depends on a number of factors including type of pain (i.e. nociceptive or neuropathic), source of pain, co-morbidities and current medication (refer to Table 4). It is quite common to use low starting doses of adjuvants for neuropathic pain. Adjuvants can have opioid-sparing effects and the dose of the opioid should be carefully reviewed as the adjuvant is titrated.[5,11]

Panel 3: Bisphosphonates

About 50% of patients benefit, typically in one to two weeks, and this may last for 2 to 3 months. In those who respond, continue to treat PRN for as long as there is benefit.

Benefits are seen mainly with intravenous bisphosphonates. Bisphosphonates are poorly absorbed when given orally, and this is reduced further by food. Oral bisphosphonates are contra-indicated in patients with oesophageal abnormalities, strictures and achalasia and inability to stay upright for 60 minutes.[11]

Panel 4: Systemic corticosteroids

Systemic corticosteroids are used off-label for pain relief for pain caused by a tumour in a confined organ or body cavity, for example raised intracranial pressure and bone pain. Dexamethasone is the most frequently used corticosteroid for disease suppression.

Cautions with corticosteroids: Diabetes mellitus, psychotic illness. Although there is only a small increase in risk of peptic ulceration with corticosteroids alone, when given concurrently with NSAIDs the risk increases up to 15 times. Prolonged courses of corticosteroids increase susceptibility to infections and their severity.[11]

Table 4: Indications for adjuvant analgesics

Indication	Treatment
Inflammation	Trial of NSAIDs or corticosteroids
Bone	NSAIDs and titrate analgesic to effect Consider trial of bone-modifying agents (bisphosphonates) For diffuse bone pain consider hormonal therapy or chemotherapy, corticosteroids (and/or systemic administration of radioisotopes) For local bone pain consider non-pharmacological interventions such as radiotherapy and nerve block
Neuropathic pain	Tricyclic antidepressants (Amitriptyline and nortriptyline) Anti-convulsants (carbamazepine, gabapentine, pregabaline) Corticosteroids

Management of nausea and vomiting

Nausea and vomiting are common symptoms experienced by patients who are receiving palliative care. The prevalence of such symptoms tends to increase as disease progresses and is estimated to be up to 70% in patients with advanced cancer.[12]

Pharmacological management is the mainstay in treatment of these symptoms; however good health care strategies such as maintenance of oral hygiene and regularising bowel habit should be ensured. Such measures may also help postpone the need for anti-emetics. Where appropriate any reversible causes of nausea and vomiting should be treated.[13]

Optimal emetic control in the acute phase is essential to prevent nausea and vomiting in the delayed phase. Treatment of nausea and vomiting in palliative care cancer patients depends on the cause of the symptoms and patient's preference.

Principles of antiemetic treatment

Antiemetics are to be selected according to the likely cause of emesis. A combination of two or more antiemetics is needed in over 25% of cases of chronic nausea.[14] Drug combinations may be used as long as the drugs chosen do not act on the same receptor. Drug combinations having the same mode of action increase the risk of side-effects without additional clinical benefit.[11,15]

The emetic risk with intravenous chemotherapy is divided into four categories (high, moderate, low and minimal) based on the Grunberg classification. Antiemetics are commenced before chemotherapy, if indicated. Oral doses are to be administered at least 30 minutes before chemotherapy is initiated. Domperidone is usually started on the evening of chemotherapy. Patients who receive highly emetogenic agents receive ondansetron or Aprepitant and dexamethasone as their pre- and post-chemotherapy schedule. For patients who receive chemotherapy with a moderate risk of causing nausea and vomiting the two-drug combination of a $5HT_3$ antagonist (ondansetron) and dexamethasone is recommended. For chemotherapy that carries a low risk of producing nausea, a single dose of dexamethasone is recommended prior to chemotherapy. No antiemetic agent is routinely recommended before or after low risk chemotherapy to prevent nausea and/or vomiting.

For patients who receive high risk radiation therapy a 5 HT_3 antagonist before each radiation fraction, and at least 24 hours after completing radiation therapy is recommended. Patients should also be given a 5 day course of dexamethasone during fractions 1 to 5 of radiation.

Dexamethasone should be prescribed prophylactically when indicated and not as a treatment for emesis. The risk and benefits of the use of steroids in diabetic patients and in patients who are immunosuppressed are to be carefully considered before prescribing. Dexamethasone should be given no later than 2.00pm to minimise wakefulness in the night.[16,17,18]

Drugs used for the treatment of nausea and vomiting

Various classes of drugs are used to control symptoms of nausea and vomiting (Refer to Table 5). The most commonly used drugs are prokinetic agents (e.g. metoclopramide and domperidone) as well as agents acting principally on the chemoreceptor trigger zone (e.g. haloperidol and domperidone). Drugs with prokinetic action are blocked by anticholinergic drugs (example amitriptyline, hyoscine and ondansetron) and thus such combinations are not recommended.[11,15]

Table 5. Medicines used as antiemetics: indications, side-effects and contra-indications

Class	Examples	Indications
Dopamine antagonists	Haloperidol	Mainly used for drug-induced nausea and vomiting
Histamine/ anticholinergic antagonists	Cyclizine	Mainly used when there is raised intracranial pressure, motion sickness or mechanical bowel obstruction.
Serotonin antagonists	Ondansetron	Prevention and treatment of nausea and vomiting induced by cytotoxic chemotherapy and radiotherapy.
Prokinetics	Metoclopramide Domperidone	Radiotherapy-induced nausea and vomiting as well as for delayed (but not acute) chemotherapy-induced nausea and vomiting.
NK-1 receptor antagonists	Aprepitant	Chemotherapy induced nausea and vomiting and inhibits both the acute and delayed phases of cisplatin-induced emesis. Augments anti-emetic activity of 5HT3 receptor antagonists and Dexamethasone
Corticosteroids (adjuvant use)	Dexamethasone (off-label use)	Adjuvant in the prevention of nausea and vomiting
Antipsychotics *	Levomepromazine (off-label use)	Levomepromazine by injection can be used in terminally ill patients requiring an anti-emetic and a sedative

*Benzodiazepines may be used in the management of nausea and vomiting due to their anxiolytic action.

Panel 5 Antiemetics: drug safety updates

Domperidone [19]	There is a small increased risk of serious cardiac side effects particularly in the elderly, patients on total daily doses of more than 30 mg, or taking QT-prolonging medicines or potent CYP3A4 inhibitors. The cardiac risk profile of domperidone should be taken into account if there is a clinical need to use this drug.
Metoclopramide [20,21]	A recent EU review has confirmed the well known risks of neurological effects such as short-term extrapyramidal disorders and tardive dyskinesia. The review concluded that these risks outweigh the benefits in long-term or high-dose and recommended changes that include a restriction to the dose and duration of use to help minimise the risk of potentially serious neurological adverse effects.
Ondansetron [22,23,24]	Dose- dependent prolongation of QTc interval and cardiac arrhythmia, including Torsade de Pointes, are known risks with ondansetron. Thus caution must be used if administering ondansetron to patients with such risk factors.

Management of constipation in cancer care

Constipation in advanced cancer is generally a multi-factorial issue. It can be affected by the nutritional status of the patient, weakness, the underlying disease and drugs.

Principles of treatment

The aim of drug management is to restore the amount of water in the faeces and improve rectal evacuation.

Traditionally a combination of a bowel stimulant with a faecal softener is used. The concurrent use of several different laxatives is not recommended. Laxative doses should be titrated every couple of days according to response. If the maximum recommended or tolerated dose is not effective, an alternative preparation is to be used.[25]

Rectal products (suppositories or enemas) are sometimes indicated when oral treatment has failed or in patients with specific conditions such as paralysis, frailty or immobility. Rectal products should be avoided in patients who are neutropenic or thrombocytopenic because of the risk of infection or bleeding.[11]

Drugs used for the constipation

Commonly prescribed laxatives include osmotic laxatives (e.g. lactulose syrup and macrogols) and stimulant laxatives (e.g. senna and bisacodyl). Osmotic laxatives retain water in the gut with a subsequent increase in faecal volume. Stimulant laxatives improve intestinal motility by a direct contact with the submucosal and myenteric plexus causing muscle contraction. They also increase water secretion into the bowel lumen.

Management of oropharyngeal complications

Palliative patients, particularly those receiving chemotherapy and/or head and neck radiation may have various oral complications. Such complications can occur as a direct result of malignancies or as a result of the treatment that the patient might have had. Complications include: mucositis, xerostomia (dry mouth), gum disease and tooth decay.[26]

Elimination of oral disease and implementation of oral care protocols designed to maintain maximum oral health must be components of care before, during and after chemotherapy and radiation therapy. Regular, systematic oral care hygiene, including a combination of tooth brushing using a soft-toothbrush, flossing and one or more bland non-medicated oral rinses and moisturisers are to be used to maintain oral hygiene for all cancer treatment modalities.

Ongoing oral assessment and treatment of complications are essential. Nutritional issues as well as drug administration should also be considered. The alterations of formulations of oral medication (tablet crushing, capsule opening) to assist patients with swallowing difficulties are in most cases unlicensed.

Treatment of oropharyngeal complications

Oral ulceration (mucositis)

Simple mouthwashes e.g. 0.9% saline can be soothing, help maintain oral hygiene and prevent secondary infection. Advising to use at a tepid temperature may be more soothing. Alcohol-based mouth rinses should be avoided.

Protecting the ulcerated area by coating agents are of limited value because they can be difficult to apply and they do not relieve persistent inflammatory pain.

As mucositis severity increases and topical pain management strategies become less effective, it becomes increasingly necessary to depend on systemic analgesics to manage oral radiation mucositis pain. Pain relief in the form of topical analgesics is available in various formulations including gels, sprays and oral rinses. These formulations include anaesthetics and NSAIDs. Benzydamine mouthwash (an NSAID) can be used to prevent oral mucositis in patients with head and neck cancer receiving moderate dose radiation therapy (up to 50 Gy) without concomitant chemotherapy. Topical anaesthetics or other agents should be considered to promote oral comfort and provide short-term pain relief.

Antimicrobial lozenges should not be used to prevent oral mucositis in patients receiving radiation therapy for head and neck cancer. [27,28]

Xerostomia (dry mouth)

Saliva helps maintain a healthy balance of bacteria in the mouth. Without saliva pathogenic organisms can colonise the mouth. This can cause sores and mouth infection, including thrush that is caused by an overgrowth of yeast. Saliva also washes away acids and food particles left in the mouth after eating, which means that a lack of saliva can cause gum disease and cavities. Dry mouth may make it difficult to wear dentures.

Chemotherapy and radiation treatments cause dry mouth by damaging the salivary glands. Chemotherapy causes dry mouth by making saliva thicker, which is usually a temporary symptom that clears up about 2 to 8 weeks after treatment ends.

Dry mouth can also be a side-effect of treatment with certain medicines including antidepressants, diuretics and some analgesics. Other causes of dry mouth include mouth infections such as thrush and dehydration.[29]

The underlying cause should be treated, where possible. Unless a main salivary duct is blocked, a saliva stimulant is preferable. Chewing gum is useful. When advising on chewing gum a sugar free brand should be recommended. In addition a low tec brand is more suitable in patients with dentures.

Artificial saliva is a poor substitute for natural saliva. Artificial saliva with a neutral pH is an option for patients who cannot tolerate saliva stimulants. Pilocarpine (a muscarinic agent) is indicated for xerostomia after radiotherapy for head and neck cancer. After radiotherapy, up to 3 drops of 4% eye drops tds (equivalent to 6mg tds) can be administered. This is off-label use of the eye drops, pilocarpine tablets are not available locally.[11]

Oral candidiasis

Oropharyngeal candidiasis is a common oropharyngeal complication in palliative care patients, ranging from 13 to 30%. This may increase during head and neck radiation therapy and in patients who receive concurrent chemotherapy.[30]

Treatment of candidiasis

Topical antifungal agents such as nystatin or clotrimazole can be effective. These can be presented as gels or drops. In order to increase the contact time of the drug with the mucosa, food should not be taken immediately after drugs have been administered.

Patients using dentures should remove the denture before using a topical antifungal agent and should also treat the dentures to avoid repeat colonisation.[11]

For moderate to severe infections and persistent lesions, systemic agents such as fluconazole are preferred. Patients who receive oral antifungals should be asked to avoid eating, drinking or rinsing for at least 30 minutes after use.[11]

Preparations for the topical treatment of oral complications

There are various preparations for the topical treatment of oropharyngeal complications, including the use of off-label and extemporaneously prepared medicines (Table 6).[31]

Table 6: Topical therapies used for oral conditions

Preparation	Therapy	Recommended dose	Precautions
Saline mouthwash	Oral hygiene	Frequent intervals	Made up with warm water
Chlorhexidine 0.2% mouthwash (with alcohol)	Topical antiseptic	10ml rinsed in mouth for one minute twice a day	Alcohol-based mouth rinses should be avoided in mucositis and dry mouth
Chlorhexidine 0.2% alcohol free mouthwash	Topical antiseptic	10ml rinsed in mouth for one minute twice a day	Alcohol free preparation is to be used where there is oral ulceration
Benzydamine 0.15% mouthwash	Topical anti-inflammatory NSAID. Used for the relief of post-radiation mucositis	10-15ml rinsed in mouth every 1.5-3 hours when required. Not usually longer than seven days duration	Only used in patients aged 13 years and older
Benzydamine 0.15% oro-mucosal spray		Four to eight sprays applied to affected area every 1.5-3 hours	None relevant
Orabase	Mucoadhesive	Used as required	None relevant
Hydrocortisone mucoadhesive buccal tablets	Topical corticosteroid	2.5mg tablet dissolved slowly in the mouth four times a day	Increased risk of candidiasis
Beclometasone 50mcg inhaler (unlicensed indication)	Topical corticosteroid	50 – 100mcg twice daily on the oral mucosa	Increased risk of candidiasis
Lidocaine 5% ointment	Local anaesthetic	Rub sparingly and gently on affected area	Avoid prolonged use. Avoid anaesthesia of the pharynx before meals due to risk of choking
Choline salicylate dental gel	Analgesic for mild oral and perioral lesions	Apply gel with gentle massage. Not more often that every 3 hours	Contra-indicated in children under 16 years of age
Artificial saliva Spray Gel	Treatment of dry mouth	To be applied as required	

Administration of medication to patients with swallowing difficulties

Patients or their carers may attempt to modify the medication without seeking advice from a health care professional. Pharmacists are competent to advise and optimise treatment in such situations. Although, in many cases, the modification of drugs (crushing of tablets, opening of capsules) is unlikely to cause harm to the patient evidence supporting this practice is currently limited. Certain medication such as modified release tablets, enteric coated tablets, hormonal and cytotoxic preparations should never be crushed or opened. The tampering with such medication may compromise the safety of the patient or the carer. Formulation tampering is in most cases unlicensed by the manufacturer.

Liquid formulations still remain the first choice alternative for solid dosage forms in patients who retain some ability to swallow. Alternative formulations that avoid the need of swallowing e.g. patches and oro-dispersable formulations are increasingly being made available.

Panel 6: Cytotoxic tablets - do not crush

All health care workers should avoid contact with cytotoxic drugs and hormones (e.g. methotrexate and tamoxifen). There is a risk of cytotoxic powder being aerosolized if cytotoxic tablets are crushed, exposing care workers to hazardous materials.

Conclusion

The pharmacist is in a strategic position to provide holistic care for palliative care patients and their carers. When dispensing and counselling about medicines pharmacists should consider the rationale behind choices of drug treatment. Aspects of patient behaviour which affect concordance should be given appropriate consideration. Pharmacists can support seamless care by improving access to medication, carrying out medication reviews and bridging communication between different health care professionals, patients and their carers.

Acknowledgements

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Key points

- Patients should be treated adequately for pain relief. Chronic pain should be treated with analgesics given at regular intervals and 'as required' medication for break through pain.
- Use of opioids should not be restricted due to fear of addiction to opioids.
- In additional to conventional analgesics, adjuvant medication is sometimes indicated in order to improve pain control. Such medication can have opioid-sparing effects.
- Opioids reduce bowel tone and contractility, predisposing patients to constipation. A combination of a faecal softener plus a stimulant laxative should be prescribed prophylactically on starting treatment with opioids.
- There are various causes of nausea and vomiting in palliative cancer patients and treatment of these symptoms will depend on their cause and the patient's preference.

Questions

1 In 2014 less than a quarter of deaths registered in Malta were due to cancer.

2 Dihydrocodeine is a prodrug which requires hepatic activation before an analgesic effect is achieved.

3 Tramadol is safe to use in patients with epilepsy.

4 Generally patients prescribed an opioid should also be prescribed a stimulant laxative and a faecal softener.

5 Therapeutic use of morphine should be restricted in palliative care patients because drug dependence is a commonly encountered problem in such patients.

6 Domperidone is contraindicated in patients with underlying cardiac conditions.

7 A combination of anti-emetic drugs with the same mode of action is indicated if symptom control is not achieved with a single agent.

8 Patients using dentures should remove the denture before using topical antifungals and should also treat the dentures to avoid repeat colonisation.

9 Alcohol-based mouth rinses should be avoided in patients with oral ulceration.

10 Crushing of tablets containing cytotoxic medication should be avoided.