SUPPORTIVE CARE IN ONCOLOGY

Supportive care in oncology

- **best supportive care**
- **Term in late 80s to describe the treatment of a control group that did not have specific oncological treatment**

Supportive care in oncology

- Supportive Care (symptomatic/substitutional/supportive care-treatment)

It is the one that optimizes the comfort, functioning (physical, psychological and social) of the patient and his family in all stages of the disease

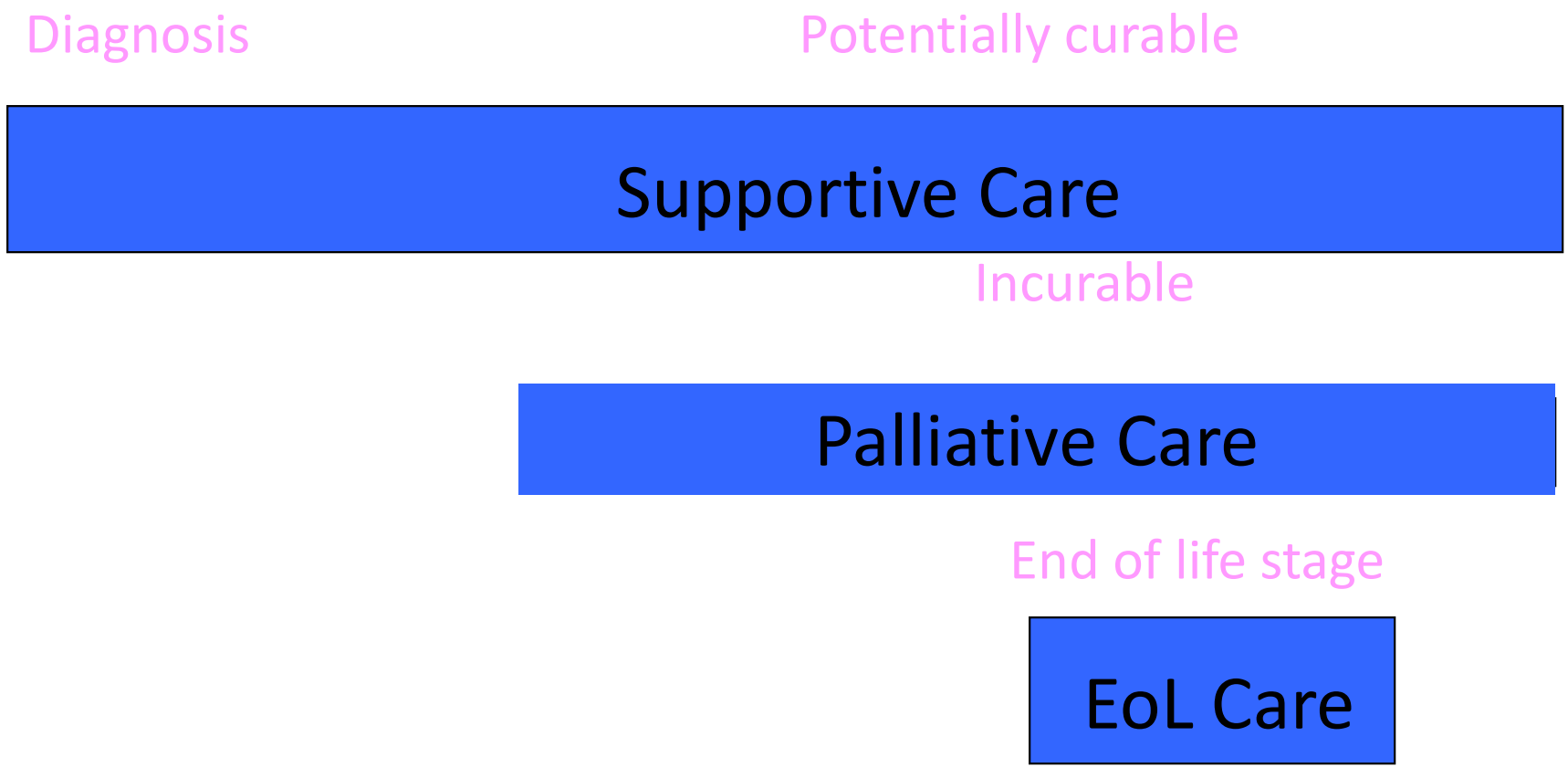
- Palliative Care (symptomatic care-treatment)

It is the one that optimizes the comfort, functioning (physical, psychological and social) of the patient and his family in a situation where healing is not possible

- End of Life Care (care of an oncology patient in the terminal phase of the disease)

Is symptomatic care-treatment of the patient when death is close and imminent

Supportive care in oncology



Supportive care in oncology

"Supportive care for cancer patients is the multi professional attention to the individual's overall physical, psychosocial, spiritual and cultural needs, and should be available at all stages of the illness, for patients of all ages, and regardless of the current intention of any anti-cancer treatment".

- *EORTC - Ahmed et al 2004*

Supportive care in oncology

- What is the modern concept of supportive care?
- Supportive (symptomatic/substitutional/supportive) treatment does not mean doing nothing
- Implies:
- Symptom control
- Psychological support
- Treatment of comorbidities
- Providing information about illness and treatment
- Family support

- And it depends on?
- The need, not the stage of the disease!

Supportive care in oncology

- To help the patient and his family go through the process of diagnosis, treatment, cure, prolongation of illness or death

- It helps the patient to maximize the benefit of treatment and to prolong life with the disease and treatment.

Supportive care in oncology

- Introduction to diagnosis and treatment
- Providing information about illness and treatment
- Learning about the disease is bad news for the patient
- *Bad news is any information that seriously affects the patient's vision of his future in a negative way*

- Disease prognosis
- Information about side effects of treatment
- Information about the impossibility of healing
- Recurrence of the disease
- Treatment failure
- Exhaustion of therapeutic options

Supportive care in oncology

- How to break bad news?

- Understand the patient's needs for information, his emotions, treatment attitudes
- Ensure the trust and cooperation of the patient

Supportive care in oncology

- Provide enough time
- Enable the presence of someone important to the patient (child, spouse, parent...)
- To find out what the patient already knows about his illness
- Assess what the patient wants to know (depending on education, age, religious beliefs, understanding...)

Supportive care in oncology

- Communicate information avoiding a monologue, checking if the patient has understood, giving him the opportunity to participate in the conversation
- Do not minimize the severity of the illness situation
- Monitor the patient's emotional reactions during exposure
- Encourage him to express his emotion
- Listen to patient

- Outline the treatment plan
- Schedule your next check-up
- Provide information to whom the patient can contact in case of need

Involvement of the family in the treatment process:

Make cooperation with mutual respect

Practice cooperation in case of any important events:

- Needs to break bad news
- Considerations for therapeutic options
- Making important medical decisions
- Determination of treatment goals
- Problem occurrences
- The family's information needs

Supportive care in oncology

- Symptom control
- Symptoms can be caused by the nature of the disease, as well as treatment, associated diseases and the patient's psychological state

Adverse events caused by cancer

- Bone metastases
- Metastases in the central nervous system
- Neurological dysfunctions caused by tumor
- paraneoplastic syndrome and iatrogenic
- Liver metastases and biliary obstruction
- Malignant effusions
- Intestinal obstruction
- Metabolic disorders
- Anorexia and cachexia
- Hematological disorders
- Sexual dysfunction

Common physical symptoms caused by advanced cancer

The pain
Dyspnea and cough
Exhaustion
Nausea and vomiting
Opstipation
Diarrhea
Insomnia

Common psychological problems associated with the disease

Anxiety

Sadness

Depression

Delirium

Suicidal toughts

Fear of death

End of Life Care (care of patients in the terminal phase of the disease)

Care, not cure

When the disease reaches its terminal stage, the focus of attention must be shifted from treatment to prolong life, to relief from symptoms and suffering, in order to improve the quality of the remaining life of both the patient and the family.

Goals and methods?

- Relieve the patient of pain and other symptoms
- Avoid all procedures that are not necessary
- Maintain nutrition and oral medication as long as possible, and when this is not possible, find alternative ways
- Do not insist on parenteral or nasogastric feeding
- Prepare the family

How to provide quality symptomatic and supportive therapy?

Patients must be under constant surveillance to register the occurrence and severity of physical and psychological symptoms that require intervention

We can achieve this by:

- By monitoring and determining the quality of life
- By monitoring and measuring pain and other symptoms
- By monitoring mental and psychological symptoms
- Once the presence and degree of symptoms is determined, it is necessary to start treating them immediately

- The goal of supportive care is not only to relieve symptoms, but also to improve the quality of life
- Therefore, supportive therapy should be started immediately after the diagnosis of a malignant disease, and should be continued during the entire treatment and after it.
- Palliative (symptomatic) treatment should be reserved only for the terminal stages of the disease

PAIN

an unpleasant sensory and emotional experience associated with actual or potential tissue damage

(*International Association for the Study of Pain, 1986.*)

The patient has the right to the highest level of alleviation of suffering and pain in accordance with generally accepted professional standards and ethical principles

- **Acute pain has a well-defined onset, is associated with subjective and objective physical signs and hyperactivity of the autonomic nervous system. Responds to analgesics and treatment of underlying causes of pain**

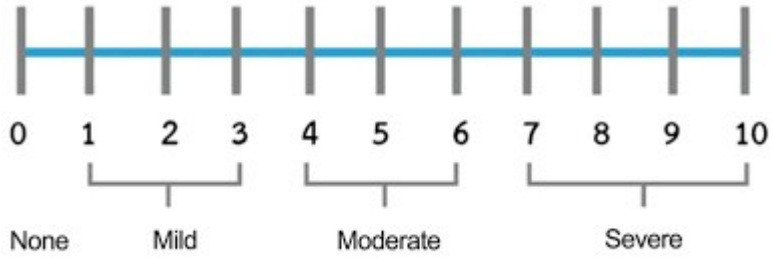
- **Chronic pain lasts for weeks or months, and can be associated with significant changes in lifestyle, functional ability, and personality. Treatment of chronic pain is complex**

Types of pain

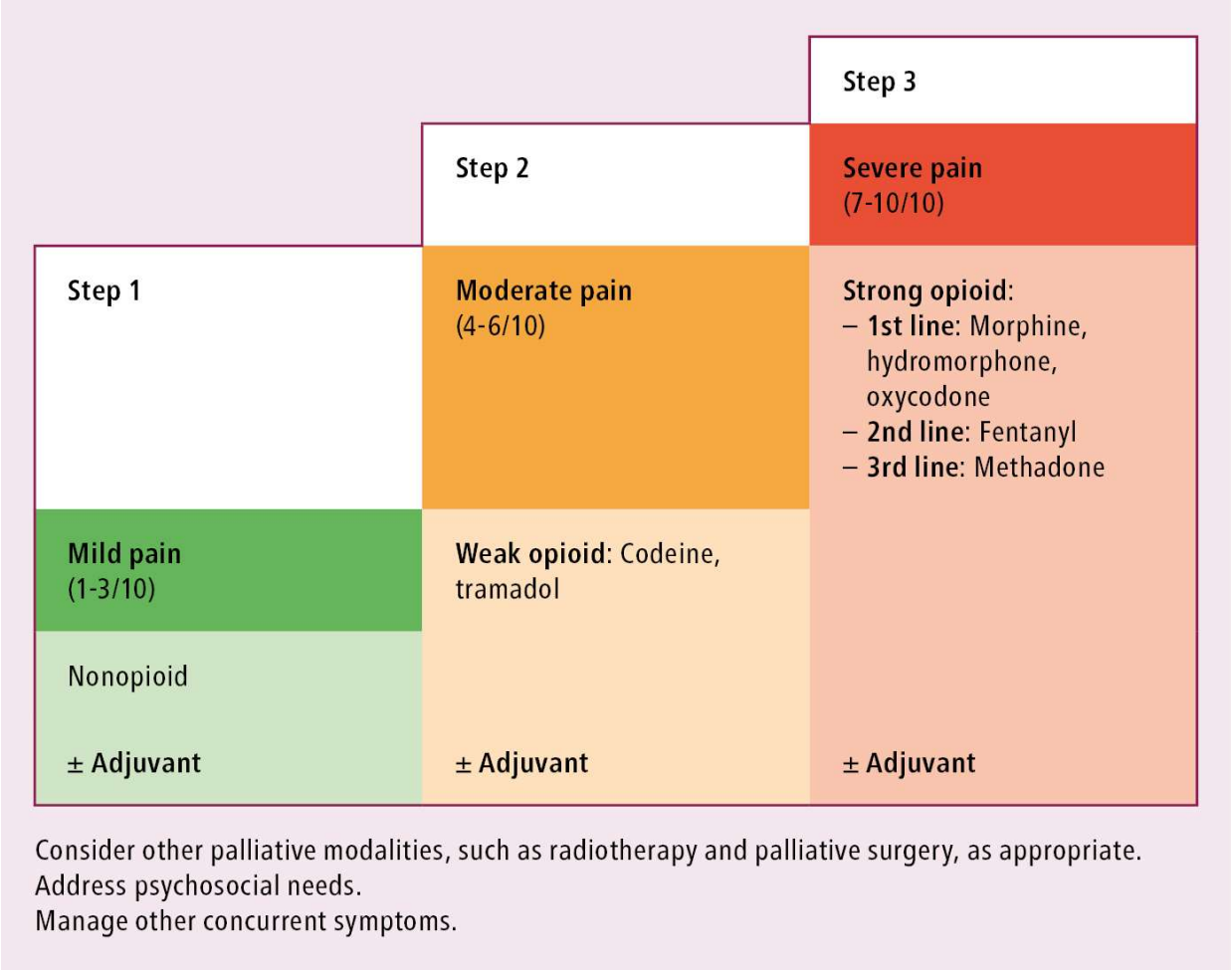
Type of Pain	Pharmacologic Interventions
Somatic (nociceptive)	Nonopioids • Acetaminophen • NSAIDs Opioids
Neuropathic	Opioids (may require higher doses) Adjuvant analgesics • Antiepileptics • Antidepressants • Corticosteroids • Local anesthetics • NMDA antagonists
Visceral	Opioids Corticosteroids Adjuvant analgesics?

Vitals

- ***1. Temperature***
- ***2. BP***
- ***3. Pulse***
- ***4. Respirations***
- ***5. Pain***



WHO


Step 3
Step 2
Severe pain
(7-10/10)
Step 1
Moderate pain
(4-6/10)
Strong opioid:
– 1st line: Morphine, hydromorphone, oxycodone
– 2nd line: Fentanyl
– 3rd line: Methadone
Mild pain
(1-3/10)
Weak opioid: Codeine, tramadol
Nonopioid
± Adjuvant
± Adjuvant
± Adjuvant
Consider other palliative modalities, such as radiotherapy and palliative surgery, as appropriate.
Address psychosocial needs.
Manage other concurrent symptoms.

Basic principles of pain reduction

- Per os administration of drugs
- Hourly rate
- By step (if applicable)
- According to the patient
- Attention to detail
- Drugs of the second step are considered, skip them when necessary.

- Recommend an adequate dose
- Titrate the dose according to each patient
- Recommend medicine according to the hourly rate
- Give instructions for the use of drugs to relieve pain
- Warn about possible side effects (prevention)
- Recommend the simplest application of analgesics
- Use the oral route whenever possible
- Constantly evaluate pain therapy

Initial pain treatment

- Mostly self-initiated at home (NSAIDs, caffeine, Analgin,...)
- At the GP/specialist
- At the oncologist
- Clinic for cancer pain
- Home treatment service
- Other.

The questions the doctor faces are:

1. Which drug to choose as an initial agent,
2. How to effectively increase the analgesic effect,
3. How to eliminate side effects,
4. How and when to change the medicine,
5. Patient preferences
6. Education of the doctor

Type of Pain	Pharmacologic Interventions
Somatic (nociceptive)	Nonopioids • Acetaminophen • NSAIDs Opioids
Neuropathic	Opioids (may require higher doses) Adjuvant analgesics • Antiepileptics • Antidepressants • Corticosteroids • Local anesthetics • NMDA antagonists
Visceral	Opioids Corticosteroids Adjuvant analgesics?

Nonopioid analgesics

- ✓ Analgesics
- ✓ Analgoantipyretics
- ✓ non-steroidal anti-inflammatory drugs

These drugs work by a common mechanism, which is the inhibition of cyclooxygenase and the prevention of prostaglandin synthesis, and have a peripheral effect.

PGE2!

Table 2. Nonopioid Analgesic Agents for Acute and Chronic Pain.*

Drug	Dose†	Indication	Side Effects and Risks‡	Other Information
Acetaminophen	650 mg orally every 4 to 6 hr; maximum dose, 4000 mg/day; also available as injection	Mild-to-moderate pain	Overdose can cause liver damage	No evidence of an effect on neuropathic pain
Aspirin	350–650 mg orally every 4 hr; maximum dose, 3600 mg/day; individual doses for rheumatic diseases	Mild pain (temporary use), inflammatory rheumatic diseases	Nausea, dyspepsia, abdominal pain, bleeding tendency, tinnitus, headache, dizziness, insomnia, hypersensitivity reactions; risk of gastrointestinal bleeding	Contraindicated in patients with known hypersensitivity; should not be used in children under 16 yr of age (risk of Reye's syndrome); no evidence of an effect on neuropathic pain
NSAIDs	Dose depends on the specific drug	Mild-to-moderate pain, pain associated with inflammation	Nausea, dyspepsia, diarrhea, constipation, headache, dizziness, somnolence, hypersensitivity reactions; risks of gastrointestinal bleeding, myocardial infarction, stroke	Contraindicated in patients with known hypersensitivity; recommended dose is the lowest effective dose for the shortest period; no evidence of an effect on neuropathic pain
Amitriptyline§	25–150 mg orally once daily or in two divided doses;¶ maximum single dose, 75 mg; daily doses above 75 mg/day should be used with caution in patients >65 yr of age	Neuropathic pain (first-line therapy), fibromyalgia, prevention of tension-type headache or migraine	Somnolence, tremor, dizziness, headache, drowsiness, tachycardia, orthostatic hypotension, dry mouth, constipation, nausea, micturition disorder, weight gain, hyperhidrosis, decreased libido; increased risk of suicidal thoughts	Patients with poor metabolism of CYP2D6 require lower doses; abrupt discontinuation should be avoided; contraindicated in patients with recent myocardial infarction or cardiac rhythm disorders; caution required if used with other serotonergic agents
Duloxetine	60–120 mg orally once daily or in two divided doses¶	Neuropathic pain (first-line therapy), chronic musculoskeletal pain, fibromyalgia	Nausea, headache, dry mouth, somnolence, dizziness, increased blood pressure; increased risk of suicidal thoughts	Abrupt discontinuation should be avoided; caution required if used with other serotonergic agents
Gabapentin	900–3600 mg/day orally in three divided doses¶	First-line therapy for neuropathic pain	Dizziness, somnolence, peripheral edema, fever, infection, nausea, lack of coordination, blurred vision; increased risk of suicidal thoughts	Dose adjustment required in patients with compromised renal function; misuse, abuse, and dependence have been reported
Pregabalin	300–600 mg/day orally in two divided doses¶	Neuropathic pain (first-line therapy), fibromyalgia	Dizziness, somnolence, headache, peripheral edema, nausea, weight gain, disorientation, blurred vision; increased risk of suicidal thoughts	Dose adjustment required in patients with compromised renal function; misuse, abuse, and dependence have been reported
Lidocaine, 1.8% or 5% patch	1–3 Patches applied to intact skin for up to 12 hr/day	Peripheral neuropathic pain	Application-site pain, pruritus, erythema, and skin irritation	Approved by FDA and EMA for postherpetic neuralgia only
Capsaicin, 8% patch	1–4 Patches applied to intact skin for 30 or 60 min every 3 mo	Peripheral neuropathic pain	Application-site pain and erythema, transient increase in blood pressure; risk of reduced sensation	Applied by a health care professional wearing nitrile gloves

* The drugs listed are those commonly used, but the list does not include all analgesics used for all pain conditions. CYP2D6 denotes cytochrome P-450 2D6, EMA European Medicines Agency, FDA Food and Drug Administration, and NSAID nonsteroidal antiinflammatory drug.
† Doses are given for adults.
‡ For a comprehensive list of side effects, risks, contraindications, and warnings, refer to the product information for each drug.
§ Other tricyclic antidepressants (imipramine, desipramine, and nortriptyline) have not been evaluated as extensively for the treatment of pain but may be associated with more acceptable side-effects profiles.
¶ The starting dose is lower.

Source: *NEJM Knowledge*

- All drugs of this group can be given up to a certain, maximum dose, and a further increase in the dose does not lead to analgesia, but only to the intensification of side effects.

- Different non-steroidal drugs are not combined with each other because this only increases the incidence of analgesic neuropathy.

Weak opioids

Conversions from weak opioids to oral morphine		
Weak opioid dose	**Equivalent oral morphine dose**	**Conversion factor from weak oral opioid to morphine**
Oral codeine or oral dihydrocodeine 240mg/24hrs	≈ Oral morphine 24mg/24hrs	Divide by 10
Tramadol 400mg/24hrs*	≈ Oral morphine 40mg/24hrs	Divide by 10
Buprenorphine 7-day Patch 5micrograms/hr**	≈ Oral morphine 12mg/24hrs	

Source: https://www.palliativecareguidelines.scot.nhs.uk/guidelines/pain/choosing-and-changing-opioids.aspx

Precautions when using opioids

- *1. Liver and kidney diseases*
- *2. Emphysema, asthma, pneumonia, atelectasis*
- *3. Head injuries – ↑CO2 due to respiratory depression ↑ICP*
- *4. Allergic reaction*
- *5. Interaction with other drugs. Antihistamines, hypnotics, tricyclic antidepressants, sedatives. Antiemetics. Meperidine and MAO inhibitors*

- *Known problems from the GITa-persistent constipation anamnestic, occlusive disorders...*

Opioid[a]	Main mode of action	Attributes	Precaution	Typical starting dose
Morphine	μ-Opioid receptor agonist	May be administered by different routes: oral, SC, IV, IT, local	Active metabolites may accumulate and cause adverse effects in renal failure	5–10 mg q 4 h (IR); 20–30 mg q 12 h (CR)
Fentanyl	μ-Opioid receptor agonist	Less constipation than morphine; safe in patients with renal impairment	Fever may increase absorption; should not be used for quick dose titration (unstable pain)	One patch 25 μg/h q 72 h; 12.5 μg/h q 72 h for older patients with liver or hepatic impairment
Oxycodone	μ- and κ-Opioid receptor agonist	Less CNS adverse effects than morphine	May accumulate in renal failure	5 mg q 4–6 h (IR); 10–20 mg 12 h (CR)
Buprenorphine	Partial μ-Opioid receptor agonist, weak κ-opioid receptor antagonist	Less constipation than morphine; safe in patients with renal impairment	Fever may increase absorption; should not be used for quick dose titration (unstable pain)	One patch 35 μg/h q 84 h; 17.5 μg/h q 84–96 h for older patients with liver or hepatic impairment
Hydromorphone	μ-Opioid receptor agonist	Useful for patients requiring high opioid doses; less pruritus, nausea/vomiting, and sedation than morphine	Parent compound and metabolites may accumulate in renal failure	1–2 mg q 4 h (IR); 2–4 mg q 12 h (CR)
Methadone	μ - and δ-Opioid receptor agonist, NMDA-receptor antagonist, NOR- and 5HT-reuptake blocker	Useful for patients with severe neuropathic pain and renal failure	Possible QT interval prolongation; numerous drug interactions; long plasma half-life	3–5 mg q 8 h
Tapentadol	μ-Opioid receptor agonist and NOR-reuptake blocker	Less adverse effects from GI tract than oxycodone	May accumulate in renal failure	50 mg q 4–6 h (IR); 100 mg q 12 h (CR)

[a] Taken orally

Source: Leppert W. Curr Pain Headache Rep. 2011

TABLE 1

Recommendations on equianalgesic dose ratios*[1] (guidelines and aggregated evidence)

Active substances	Relative analgesic ratios	Evidence level
Morphine p.o. – oxycodone p.o.	1.5 : 1	Strong
Oxycodone p.o. – hydromorphone p.o.	4 : 1	Strong
Morphine p.o. – hydromorphone p.o.	5 : 1	Weak
Morphine p.o. – methadone p.o.	5 : 1 – 12 : 1*[2]	None*[2]
Morphine p.o. – buprenorphine t.d.	75 : 1	Weak
Morphine p.o. – fentanyl t.d.	100 : 1	Strong

*[1] Current recommendations on equianalgesic dose ratios based on (9) and on the recommendations of the EAPC (European Association for Palliative Care) [e1] or the S3 guideline on palliative medicine [e2].

*[2] The authors (EAPC und S3) make no recommendations for methadone; according to Mercadante et al., depending on the initial opioid dose the ratio can be higher than 12:1.

p.o. = per os, t.d. = transdermal

Equianalgesic doses

MORPHINE 24 hour dose		OXYCODONE[α] 24 hour dose A 2:1 ratio with morphine may also be used. See preparations outlined below.		HYDROMORPHONE 24 hour dose		FENTANYL
ORAL	IV/SC	ORAL	IV/SC	ORAL	IV/SC	TRANSDERMAL[#]
5mg	2.5mg	3.33mg	1.66mg	1mg	0.5mg	-
10mg	5mg	6.66mg	3.33mg	2mg	1mg	-
14.4mg	7.2mg	9.6mg	4.8mg	2.88mg	1.44mg	6 micrograms/hour
20mg	10mg	13.33mg	6.66mg	4mg	2mg	-
28.8mg	14.4mg	19.2mg	9.6mg	5.76mg	2.88mg	12 micrograms/hour
30mg	15mg	20mg	10mg	6mg	3mg	-
50mg	25mg	33.33mg	16.66mg	10mg	5mg	-
60mg	30mg	40mg	20mg	12mg	6mg	25 micrograms/hour
100mg	50mg	66.66mg	33.33mg	20mg	10mg	-

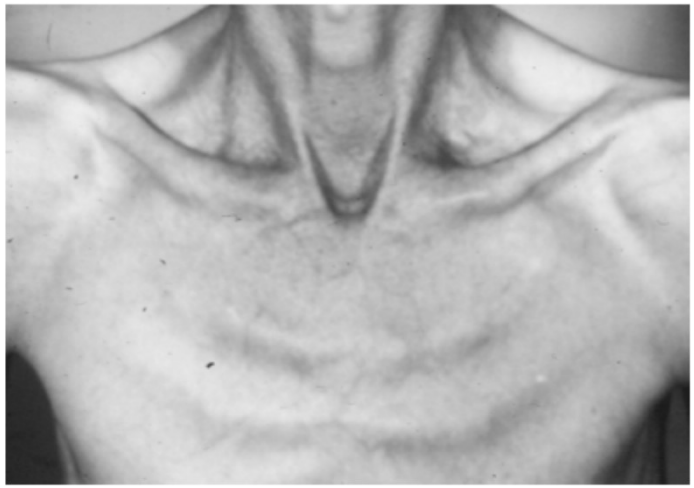
Type of drug	Daily recommended dose	Route	Indications
Antidepressants	Amitriptyline 10 to 25–150 mg/day Nortriptyline 25 mg/day Desipramine 10 to 25–150 mg/day Venlafaxine 37.5–150 mg/day Duloxetine 30–120 mg/day	Oral	Neuropathic pain
Anticonvulsants	Gabapentin 1200–3600 mg/day Pregabalin 150–600 mg/day	Oral	Neuropathic pain
Corticosteroids	Dexamethasone 4–24 mg/day	Oral/iv.	Neuropathic, bone, visceral pain, brain edema, spinal cord compression
Lidocaine	Patches 5%/day Bolus 1–2 mg/kg in 15–30 min. If effective, 2 mg/kg/h	Topical iv.	Neuropathic pain
NMDA antagonists	Ketamine: 0.04–0.3 mg/kg/h Amantadine Magnesium 1 g/day	iv./oral/sc./sl./topical Oral iv.	Neuropathic pain Tolerance to opioids
Bisphosphonates	Pamidronate 60–90 mg every 2–4 weeks Zoledronic acid 4 mg every 3–4 weeks Ibandronate 6 mg × 3 days, then every 3–4 weeks	iv.	Osteolytic bone pain

iv.: Intravenous; sc.: Subcutaneous; sl.: Sublingual.
Data taken from [12,43,50,51].

Source: Lara-Solares A et al. Pain Manag. 2017.

- **More than 80% of cancer patients with advanced disease develop cancer cachexia**
- **In more than 20% of cases, cachexia is the main cause of death**
- **Cachexia is a prognostic factor of poor survival!**

E. Bruera. Pharmacologiccal treatment of cachexia: any progress? Support Care Cancer 1998;6:109-113



- Cachexia - Greek word
- Cocos: bad Hexis: state

- Features:
- Pronounced and progressive loss of muscle and body mass
- Anorexia
- Chronic nausea
- Fatigue
- Weakness
- Change in physical appearance

Factors contributing to cachexia

Therapy factors

Chemotherapy: mucositis, nausea, vomiting, diarrhea, change in taste, constipation...

Radiotherapy: enteritis, diarrhea, dry mouth...

Surgery: malabsorption due to gastrectomy, short bowel syndrome...

Tumor factors

Tumor products

Mechanical obstruction

Humoral factors - release of procachectic cytokines

Pain, depression, old age, physical inactivity...

Diagnostic criteria for cahexia

- UNWANTED LOSS OF BODY MASS (≥ 5%)
- BMI< 20 IN PATIENTS < 65 YEARS OLD
- < 22 IN PATIENTS ≥ 65 YEARS OLD

- ALBUMINS < 3.5 g/dl
- LOSS OF MUSCULATION
- CRP INCREASE

- **Glucose metabolism**
- Increased gluconeogenesis (from muscle and fat tissue)
- Increased glycolysis in muscle and tumor tissue
- Increased production of lactate
- Increased activity of the Cori cycle (loss of energy 300 kcal/day
-)Glucose intolerance
- Insulin resistance
- Decreased uptake of glucose into muscle tissue

- **Protein metabolism**
- Increased protein catabolism
- Decreased protein synthesis
- Loss of muscle tissue: asthenia
- Increased synthesis of tumor proteins
- Increased protein synthesis in the liver
- Acute phase proteins

- **Lipid metabolism**
- Increased lipolysis
- Decreased lipogenesis
- Significant loss of fat tissue
- Decreased lipoprotein lipase
- Hypertriglyceridemia
- Low LDL, HDL

Intensive nutritional support (parenteral and enteral nutrition)

Parenteral nutrition is contraindicated in patients in the terminal phase of the disease

Parenteral nutrition does not improve body weight or prolong life

Enteral nutrition (nasogastric tube, gastrostomy) is indicated only in patients in whom we expect a clear improvement