Palliative Care

Dr. N. Steiner

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Palliative care: a global perspective

- Tens of millions of people worldwide are affected by lifethreatening illnesses such as HIV/AIDS and cancer.

- Majority of cases occur in the developing world, where access to prompt and effective treatment is often still difficult.

Cancer deaths:
Out of 9 Mo new cases worldwide in 1985, 55% were in the developing world.
In 2005, they will represent 15 Mo and 66% of cases.

Ref: Information and communication Unit. WHO regional office for Africa.

- Source of major suffering for patients and families as well as economical hardships
Palliative care: a global perspective

- There are major differences in access to palliative care services between regions and countries,

- .. as well as serious impediments to opioid availability in many countries
Palliative care: WHO’s definition (1)

- Palliative care is an approach that improves the quality of life of patients and their families facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.
Palliative care: WHO’s definition (2)

- Provides relief from pain and other distressing symptoms
- Affirms life and regards dying as a normal process
- Intends neither to hasten or postpone death
- Integrates the psychosocial and spiritual aspects of patient care
- Offers a support system to help patients live as actively as possible until death
- Offers a support system to help the family cope during the patient’s illness and in their own bereavement
- Uses a team approach to address the needs of patients and their families, including bereavement counselling, if indicated
- Will enhance quality of life, and may also positively influence the course of illness
## Symptom prevalence in cancer patients

- **275 consecutive advanced cancer patients**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Prevalence</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthenia</td>
<td>90</td>
<td>81-100</td>
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<tr>
<td>Anorexia</td>
<td>85</td>
<td>78-92</td>
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<tr>
<td>Pain</td>
<td>76</td>
<td>62-85</td>
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<tr>
<td>Nausea</td>
<td>68</td>
<td>61-75</td>
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<tr>
<td>Constipation</td>
<td>65</td>
<td>40-80</td>
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<tr>
<td>Sedation-confusion</td>
<td>60</td>
<td>40-75</td>
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<tr>
<td>Dyspnéa</td>
<td>12</td>
<td>8-16</td>
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</tbody>
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Prevalence of symptoms in advanced disease


  - There are statistically significant differences in symptom prevalence depending on primary site of cancer and the hospice:

    * Moderate to severe pain: 51%
      (43% in stomach cancer - 80% in gynecological cancer)

    * Nausea: most prevalent in gynecological (42%) and stomach (36%) cancers

    * Dyspnea most prevalent in lung cancer (46%)
Definition of pain

«Pain is an unpleasant sensory and emotional experience associated with actual and potential tissue damage or described in terms of such damage ». Pain is always subjective.

IASP (International Association for the Study of Pain)
Patient suffering from pain: what should we do?

1. Assess his/her/pain(s):

😊 history
   (ask patients, relatives and professional caregivers)

😊 validated assessment tools

😊 physical examination, including neurological

😊 complementary tests, if/when appropriate, in order to answer specific questions
Patient suffering from pain: what should we do?

2. Diagnose the pain(s):

- Origin(s): primary disease, treatments, other
- Type of pain: nociceptive, neuropathic
- Mecanism of pain
- Different dimensions of the pain experience and other symptoms
Origin of pain in cancer patients

- Underlying disease (78%)
- Treatments (19%)
  - Chemotherapy: e.g., mucositis, post-chemotherapy neuropathies
  - Radiotherapy: e.g., post-radiation plexopathies
  - Surgery: e.g., post-thoracotomy pain
- No direct relationship with one or the other (3%)
  - Ex: postherpetic neuralgias,
    inflammatory or degenerative arthropathies,
    diabetic neuropathies,...
Types of pain

**Nociceptive pain**
Activation of nociceptors in the different tissues/organs by tissue damage

**Somatic pain**
Well localised

**Visceral pain**
Poorly localised, deep, dull, cramping, referred

Modified from Mazzocato, Sylvana 02
**Types of pain**

**Neuropathic pain**
- Peripheral or central alteration of nerve conduction
- Dysesthesias: burning sensation, numbness, tingling, as well as sharp and shooting, paroxystic exacerbations
- Associated with a sensory deficit, hyperesthesia, allodynia; in the region innervated by the affected nerve structure (dermatoma, radicular distribution, etc.)

Modified from Mazzocato, Sylvana 02
History of pain

- How did the pain begin?
- Localisation(s)
- Intensity
- Temporal characteristics
  Does it have a periodicity? How long?
- How is the pain described:
  words used by the patient (gives clue to the underlying etiology/sensation and emotional component)

- What improves the pain?
  Types of therapies tried and what benefit they had
- What makes the pain worse?
- How does the pain impact the patient’s life? (home, friends, work)
- Patient’s understanding of pain
- Important elements in past medical and psychological history
Assessment of pain intensity

- Visual analog scale:
  - No pain
  - _____________________________
  - Worst possible pain

- Numerical scale:
  - No pain
  - 0 1 2 3 4 5 6 7 8 9 10
  - Worst possible pain

- Categorical scale:
  - No pain  Week pain  Moderate pain  Severe pain  Very severe pain  Extreme pain
Benefits of a systematic pain assessment

- Identification of patients in pain, even if they don’t complain
- Active role for the patient, and an attentive ear
- Prescription of effective treatments
- Monitoring of treatment effects and pain evolution
- Facilitation of communication between doctors, nurses and other healthcare professionals
Treatment of pain

- Early identification and systematic multidimensional assessment
- Etiological treatments if benefits > disadvantages
- Symptomatic medical treatments
- Non-medical approaches
- Explanations to patients and family, patient and family education
- Communication between professionals: give the diagnosis to nurses and tell them what to look for and when to tell you what!
- Reassessments at regular intervals
Symptomatic pain treatments

- By the mouth
- By the ladder

By the clock
WHO analgesic ladder

**Step 1**
Non-opioïd:
Paracetamol, AINS
+/- adjuvants

**Step 2**
Codeine, tramadol
+/- non-opioïds
+/- adjuvants

**Step 3**
Reference: oral morphine
Hydromorphone
methadone, fentanyl,
+/- non-opioïds
+/- adjuvants

*WHO, in collaboration with IASP 1999*
Step 2: Codein

- Biotransformation into morphine by Cyt. P450.

Iso-enzyme absent in 7-10% caucasians. In those cases, codein will probably be poorly effective.

Dose: 30-60 mg/4h
Step 2: tramadol

- Opioïd (week affinity for the µ recept) + noradrenergic effect (noradrenaline and serotonin)

- Peak plasma concentration: approx. 70 min, prolonged in the elderly T1/2 env 6 h, prolonged in liver failure

- Kidney elimination of tramadol and its metabolites

- Doses:
  - initially: 50 mg/6-8h and 15-20 mg breakthrough (analgesic effect: 3-7h with chronic administration)
  - maximal studied dose: 400 mg/d. In the elderly > 75 yrs: 300 mg
Step 2: tramadol

- **Side effects:**
  - frequent nausea/vomiting
  - dizziness
  - sweating
  - dry mouth
  - constipation
  - convulsions
Step 2: tramadol

- Potentially dangerous drug interactions with antidepressants: SSRIs, tricyclics, IMAO:

  serotoninergic syndrome

Schaad, Med et Hyg 2001;2346
# Serotonergic syndrome

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<thead>
<tr>
<th>Gastro-intestinal</th>
<th>Cramps</th>
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<tr>
<td></td>
<td>Diarrhea</td>
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<tr>
<td>Neurological</td>
<td>Headaches</td>
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<td>Dysarthria</td>
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<td></td>
<td>Incoordination</td>
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<td></td>
<td>Myoclonia</td>
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<td>Cardiovascular</td>
<td>Tachycardia</td>
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<td></td>
<td>Hypo/hypertension</td>
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<td></td>
<td>Cardiovascular collapsus</td>
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<tr>
<td>Psychiatric</td>
<td>Confusion</td>
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<tr>
<td></td>
<td>Dysorientation</td>
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<tr>
<td>Other</td>
<td>Sweats</td>
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<tr>
<td></td>
<td>Hyperthermia</td>
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<td>Hyperreflexia</td>
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Step 3: initiation of treatment

- **Morphine is the narcotic of first choice, since it is the most cost-effective**

  Give explanations to the patient, patient and family education

- Start with a short acting substance; oral morphine
  
  A. **Opioid naive patient:**  
  5 mg/4h  
  Breakthrough, if pain in between regular dose: 4-hourly dose, to be repeated if needed up to every hour. Monitor treatment response (analgesic as well as possible adverse effects)

  B. **Patient previously treated with another opioid (ex.: step2):**  
  Start at least by the equianalgesic dose!
Step 3: dose titration

A/ Increases by approx. 30%  
   Regular doses + breakthroughs taken in 24h

B/ ________________________________ = new 4 hourly dose
   6

😊 Adjust breakthrough doses (4 hourly dose)

😊 Reassess if need for more than 3 breakthroughs/day
Step 3: when stable and well controlled pain

- Switch to a slow-release form if necessary: for eg MST
  24h dose in slow-release form = 24h dose in short acting form
  Slow release morphine tablets: q 12h

- Prescribe breakthrough doses (in short acting form):
  Equivalent to the 4 hourly dose, q 1h

- Reassess at regular intervals
  Adapt doses by approx. 30%
Indications for transdermal fentanyl

- Not a first choice!
- Stable pain
- Effective dose determined by a short acting opioid
- Swallowing difficulties, alteration of drug absorption or other intolerances to the oral route
Contratindications for transdermal fentanyl

- Economical considerations: expensive ++++
- Acute pain
- Unstable pain
- Skin problems
- Generalised edema
Morphine: feared effects

- **Addiction**
  Almost *never* in a well managed pain treatment

- **Physical dependance**
  Means withdrawal when medication abruptly stopped
  of in the case of administration of an antagonist

- **Tolerance**
  Need to increase doses in order to maintain the same effect
  Almost *never* a problem in clinical practice
Morphine: side effects

- Classical:
  - nausea, vomiting (prevent)
  - constipation (systematically prescribe laxatives)
  - drowsiness

Sometimes also:
- Sweating, itching, urinary retention
Morphine: side effects

- **Nausea/vomiting: prevent**
  for eg metoclopramide
  10 mg po if occasional episodes (breakthrough only)
  if necessary, 10 mg/4h + 10 mg breakthrough

  alternative: haloperidol
  1 mg po if occasional episodes
  if necessary, 1 mg/12h + 1 mg breakthrough

  NB: both metoclopramide and haloperidol can be given sc
Morphine: side effects

- **Constipation: to be systematically prevented:**

  *stimulant laxative:*
  eg: Na picosulfate 10 drops morning + evening, to be adjusted
  alternatives: bisacodyl, senne derivatives

  +

  *osmotic:*
  eg. lactilol: 10 mg tds

  reassess min. twice a week and adjust
Morphine: adverse effects

- **Neurotoxicities:**
  myoclonias,
  delirium,
  hyperalgesie/allodynia,
  hallucinations

mainly in the case of renal failure
Opioid neurotoxicities

- **Hydrate**
  If oral route not possible/sufficient, prefer sc route: NaCl 0.9% or min 1/3 NaCl, eg 80-100cc/h

- **If possible, change opioid**
  eg: switch from morphine to hydromorphone

- **Rule out other aggravating factors**
  eg: renal failure, hypercalcemia, etc.

- **Treat symptoms**
  haloperidol for hallucinations/agitation
Buprenorphine

- Not a first choice
- Partial mu receptor agonist, week intrinsic activity and efficacy, ceiling effect
- Maximal effective dose unknown in humans
  30-70 times more potent than morphine
  Duration of action: 6-9h
- Metabolised by the liver. No modification of pharmacokinetics in renal
- Possible indications: severe renal failure, need for relatively low doses of opioids.
- Do not associate it with a pure agonist!
**meperidine / pethidine**

- Contraindicated for chronic administration:
  - neurotoxicities (normeperidine) with risks of myoclonus/seizures
  - short duration action
Co-analgesics

- **NSAIDS:**

  Particularly in bone metastasis

  Beware of adverse effects, and of the increased risks of opioid toxicity through renal failure
Co-analgesics

Corticosteroids:

- Intracranial hypertension
- Tumor compressions, eg epidur spinal cord compression
- Nerve infiltrations
- Distension of the liver capsule

Eg: dexamethasone 12-16 mg/d
Decrease gradually to determine minimal effective dose

Beware of side effects!
Co-analgesics

- **Antidepressants**: (tricyclics or SSRIs)

  Neuropathic pain

  Beware of side effects as well as drug interactions
Co-analgesics

Anticonvulsants:

gabapentine (Neurontin®)
Initial doses: 100 mg/8h
Increase progressively and monitor clinical effects

clonazepam (Rivotril®)
Initial doses: 0.5 mg nocte
Increase carefully. Risks of drowsiness, confusion, falls

carbamazepine (Tegretol®)
Side effects (liver, haematological, drowsiness, etc.)
Co-analgesics

- NMDA antagonists, eg:
  - methadone
  - dextrometorphan
  - ketamine

Neuropathic and resistant pain
Co-analgesics

- Bisphosphonates:

  Decreased « bone events » due to bone mets.

  Demonstrated particularly for breast carcinomas, myelomas, prostate cancer. Injection every 4 weeks

  Eg: pamidronate: 60-90 mg iv
  clodronate can be given sc
Treatment of a patient in pain: different approaches

- **Treat the cause:**
  - when possible and reasonable

- **Treat symptoms:**
  - systemic analgesics (WHO guidelines)
  - local measures: eg; cold, heat, position, local application of anaesthetics or opioids in painful ulcerations
  - invasive treatments: injection of trigger zones, blocks (eg coeliac plexus in painful pancreatic cancer), spinal analgesia, if specialist available and simple analgesics fail

- **Treat the patient as a whole human being** (body, mind and spirit)

- Consider the patient and his family as the unit of care
Crescendo pain: look for…

- Complications of the underlying disease
- Accumulation of opioid toxic metabolites
- Delirium (impaired capacity to express pain)
- Urinary retention/fecal impaction in a patient with cognitive failure or impaired capacity to communicate
- Somatisation; expression of a global suffering as pain
Epidural spinal cord compression

- An emergency; functional prognosis depends on neurological deficits at the time of initiation of treatment

- High suspicion if:
  * Vertebral pain that: changes, increases, worsens in recumbent position, with Lhermitte’s sign
  * Radiculopathy
  * Muscle weakness +/- sensory deficits, incontinence

- Dexamethasone 12-16 mg/d, emergency MRI if possible

- Radiotherapy +/- vertebroplasty +/- laminectomy
Edmonton symptom assessment

- No pain → Worst possible pain
- No fatigue → Worst possible fatigue
- No nausea → Worst possible nausea
- No depression → Worst possible depression
- No anxiety → Worst possible anxiety
- No drowsiness → Worst possible drowsiness
- Excellent appetite → No appetite
- Best sensation of well-being → Worst sensation of well-being
- No shortness of breath → Worst possible shortness of breath
Edmonton Symptom Assessment System

- No pain
- No fatigue
- No nausea
- No depression
- No anxiety
- No drowsiness
- Excellent appetite
- No shortness of breath
- Best sensation of well-being

Worst possible:
- Pain
- Fatigue
- Nausea
- Depression
- Anxiety
- Drowsiness
- Lack of appetite
- Shortness of breath
- Discomfort

No pain
No fatigue
No nausea
No depression
No anxiety
No drowsiness
Excellent appetite
No shortness of breath
Best sensation of well-being

No appetite
No shortness of breath
Best sensation of well-being
Schema of symptom construct

1. Production / construct

2. Perception

3. Expression

Treatment

Modulation

Cognitive status

Mood

Beliefs

Cultural

Biography

Bruera Cancer Treat Rev 1996;22(supp A):3-12
Total pain

Physical
- Functional capacity
- Fatigue, cachexia
- Sleep and recuperation
- Appetite, nausea, etc.

Psychological
- Apprehension, worries
- Grief, depression
- Pleasures, leisure
- Anxiety, anger
- Cognitive function

Social
- Communication with healthcare team
- Relationships with family and friends, capacity of giving
- Financial situation, insurance problems

Suffering

Spiritual
- Personal value as a human being
- Meaning of life/illness/pain
- Religious faith
- Existential perspectives
Palliative care: a global perspective

- The development of palliative care through effective and low cost approaches represents a priority in order to respond to the urgent needs of the sick and improve their quality of life.
Palliative care: a global perspective

There is a need to promote a public health approach in which comprehensive palliative care programs are integrated into existing healthcare systems and tailored to the specific cultural and social context of the target populations.
**Foundation measures:**

**little cost, big effect**

(Stjernswärd J. JPSM 2002;24(2)259)

**Education**
- Public, professionals
- Undergraduate education for doctors and nurses
- Postgraduate training
- Advocacy (policy makers, administrators, drug regulators)

**Drug availability**
- Changes in legislation to improve availability especially of cost effective opioids such as morphine sulfate tablets
- Prescribing made easier and distribution, dispensing and administration improved

**Governmental policy**
- National policy emphasizing the need to alleviate unnecessary pain and suffering of the chronically and terminally ill
- Governmental policy integrating PC into the healthcare system
- Separate systems of care are neither necessary nor desirable
Palliative care: useful international organisations

- WHO Programme on Cancer Control

- EAPC (European Association for Palliative Care)
  www.eapcnet.org and www.eapcare.org

- International Association for Hospice and Palliative Care
  www.hospicecare.com

- Hospice Information Service St Christopher’s Hospice
  London
  www.hospiceinformation.co.uk
Palliative care: some references

- WHO guidelines on Cancer pain, opioid availability, symptom control and palliative care:
  - Cancer pain relief (1996)
  - Symptom relief in terminal illness 1998
  - Cancer pain relief and palliative care in children 1998
- Journal of Pain and Symptom Management 42(2) August 2002