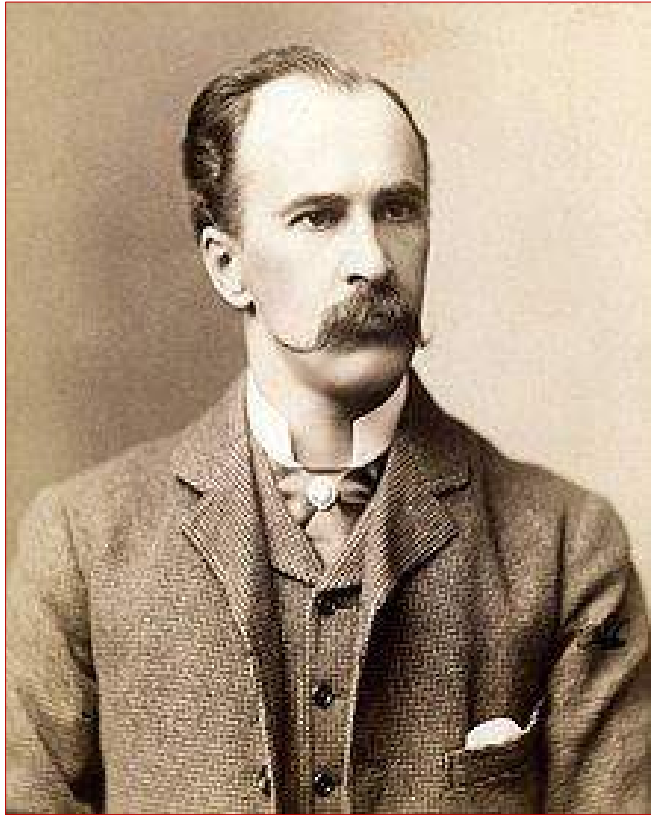


	
Modulo 507_K08 - UCC/NESTOR - Revisione n. 3 - Data di emissione: 12 settembre 2017 - Approvato dal comitato di controllo	
S.S. FORMAZIONE PERMANENTE E AGGIORNAMENTO	
Evento Formativo Residenziale	
CURE PALLIATIVE NEI MALATI ONCOLOGICI	
DATE	
Ediz.1: 19 giugno 2018	
ORARIO	
Dalle ore 9.30 alle ore 16.30	
SEDE	
Aula Dipartimento Rete Oncologica, Torino	
ECM REGIONE PIEMONTE	
CODICE: 30044 - Crediti: 7	

Il trattamento dei sintomi a domicilio

Alessandro Valle
Torino





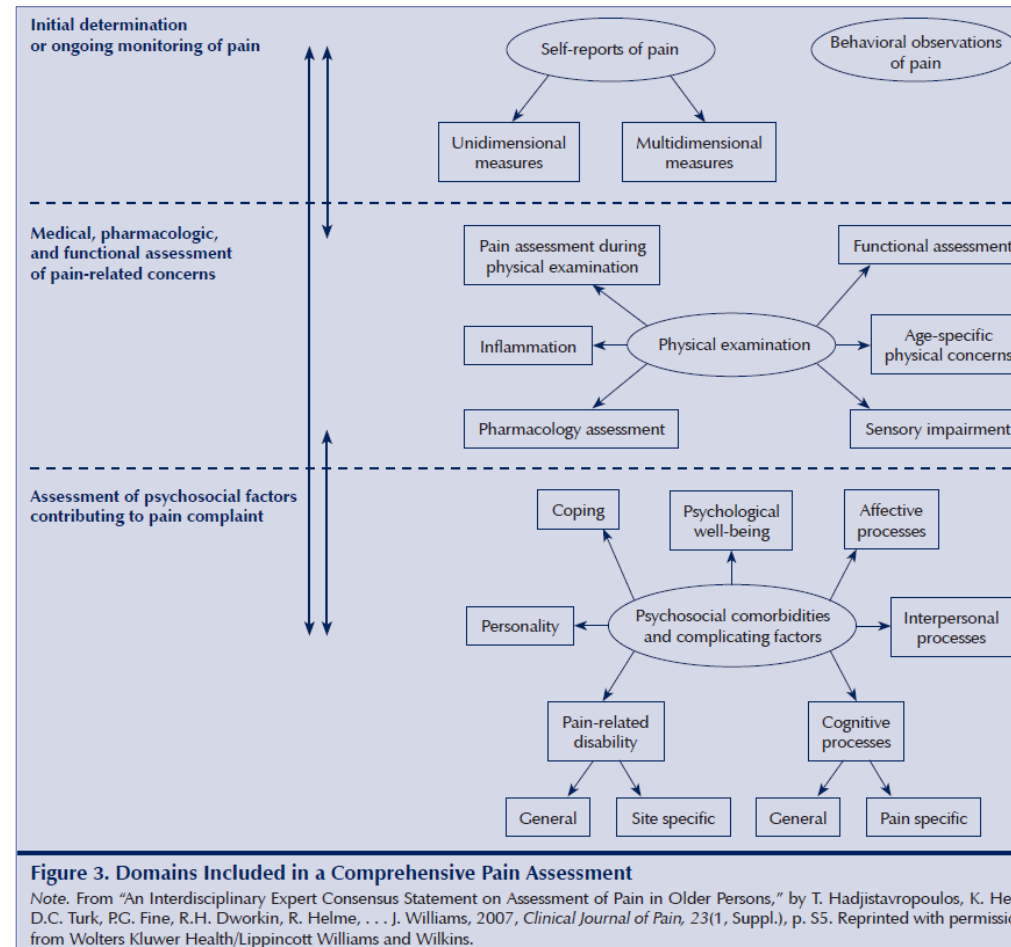
E' più importante sapere che tipo di persona ha una malattia, piuttosto che sapere che tipo di malattia ha una persona

Sir William Osler (1849-1919)

Problematiche ambientali e organizzative delle Cure Palliative domiciliari

- **Aumento dell'età media della popolazione (e quindi anche del caregiver)**
- **Fragilità familiare nella società moderna**
- **Difficoltà ad accettare la situazione ed oppiofobia**
- **Impiego di assistenti familiari stranieri con possibili difficoltà linguistiche**
- **Narrazione delle problematiche sintomatologiche a cura del caregiver o dell'assistente familiare (se paziente con deterioramento cognitivo)**
- **Procedure assistenziali non specialistiche affidate al caregiver**
- **Personale di assistenza non presente fisicamente 24h/24h (a differenza delle strutture residenziali)**

Dalla teoria....



Ala pratica
«domiciliare»...



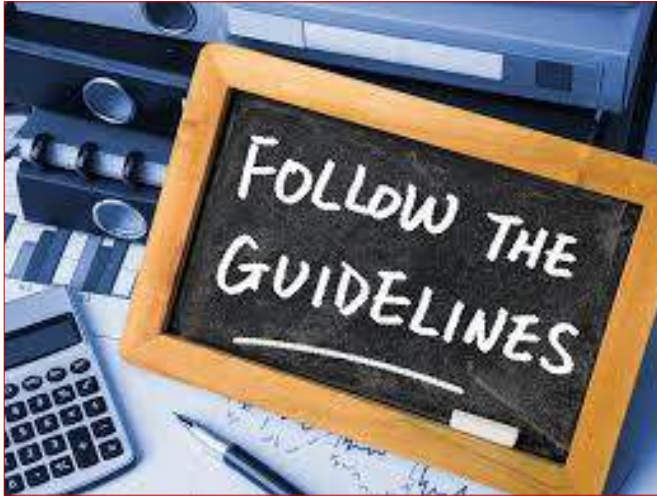


Table 2

Symptom prevalence in descending order at T1, with number and percentages of patients experiencing a symptom, symptom scores and scores for frequency, severity and distress.

Symptom	No. of patients with symptom N = 103 ^a	% of patients with symptom	Symp. score (0–4)	Freq. score (1–4)	Severity score (1–4)	Distress score (0–4)
Lack of energy ^b	82	80.4%	2.81	3.13	2.74	2.60
Feeling drowsy ^b	79	77.5%	2.51	2.96	2.58	1.96
Worrying	75	72.8%	2.39	2.55	2.43	2.18
Pain ^b	72	71.3%	2.98	3.12	2.96	2.98
Dry mouth ^b	65	65.0%	2.38	2.66	2.44	2.03
Lack of appetite	63	61.8%	2.58	3.06	2.73	1.90
Difficulty sleeping	54	52.9%	2.67	2.85	2.74	2.44
Feeling sad	51	51.0%	2.19	2.20	2.42	2.00
Weight loss ^b	49	48.0%	1.93	n. a.	2.35	1.53
Difficulty concentrating	48	47.1%	2.09	2.25	2.06	1.98
Feeling nervous	48	47.1%	2.19	2.38	2.19	2.06
Shortness of breath	46	44.7%	2.60	2.76	2.64	2.42
Sweats	45	43.7%	2.12	2.27	2.32	1.78
Nausea	43	42.2%	2.19	2.33	2.28	1.98
Constipation	43	42.2%	2.33	n. a.	2.52	2.19
"I don't look like myself" ^b	41	40.6%	1.92	n. a.	2.25	1.57
Cough	40	39.2%	2.10	2.33	2.13	1.89
Feeling bloated	40	39.2%	2.57	2.75	2.60	2.35
Dizziness ^b	38	37.3%	2.23	2.39	2.34	1.95
Change in the way food tastes	36	35.3%	2.39	n. a.	2.58	2.19
Numbness/tingling in hands/feet ^b	33	32.4%	2.20	2.58	2.19	1.84
Feeling irritable	33	32.7%	2.14	2.39	2.05	2.03
Swelling of arms or legs	31	30.1%	2.26	n. a.	2.53	1.92
Diarrhea	30	29.4%	2.27	2.43	2.39	2.14
Problems with urination	25	24.5%	2.24	2.36	2.28	2.08
Vomiting	25	24.5%	1.89	1.84	2.04	1.80
Mouth sores	25	24.3%	2.04	n. a.	2.12	1.96
Itching	24	23.3%	1.73	2.04	1.87	1.37
Difficulty swallowing	22	21.6%	2.45	2.86	2.32	2.18
Changes in skin	19	18.8%	2.01	n. a.	2.24	1.83
Hair loss	17	17.0%	2.10	n. a.	2.59	1.62

Abbreviations: Symp., symptoms; Freq., frequency; n. a., not applicable.

^a For single symptoms, data from 100 to 103 patients were available due to missing values.

^b For these symptoms, some correlations of frequency, severity and distress scores were >0.5, for dry mouth and feeling drowsy >0.4, while correlations for all other symptoms were >0.6.

**Coniugare semplicità ed
appropriatezza diagnostica e
terapeutica**

Magari non così ...

DA GIUGNO 2015 ACCIUNO
LENDICULIDE 100 mg PRANZO
VARESE 10 PRANZO 10 NOV
SOSPESO E RIFRESCA DAL
20 LUGLIO 2015

COLAZIONE:

- NEXIUM 40mg prima di colazione 1cp
- ~~CARDURA 2mg~~ 1cp
- PRITOR PLUS 80/25mg 1cp
- GLICABIDE 30 1cp

DOPO PRANZO:

- CARDIOASPIRIN 1cp
- FENO FIBRATO 145 mg 1cp

POMERIGGIO:

- ~~LEXOTAN~~ 5 gocce ~~ALBISOL~~
NON HA

PRIMA DI CENA:

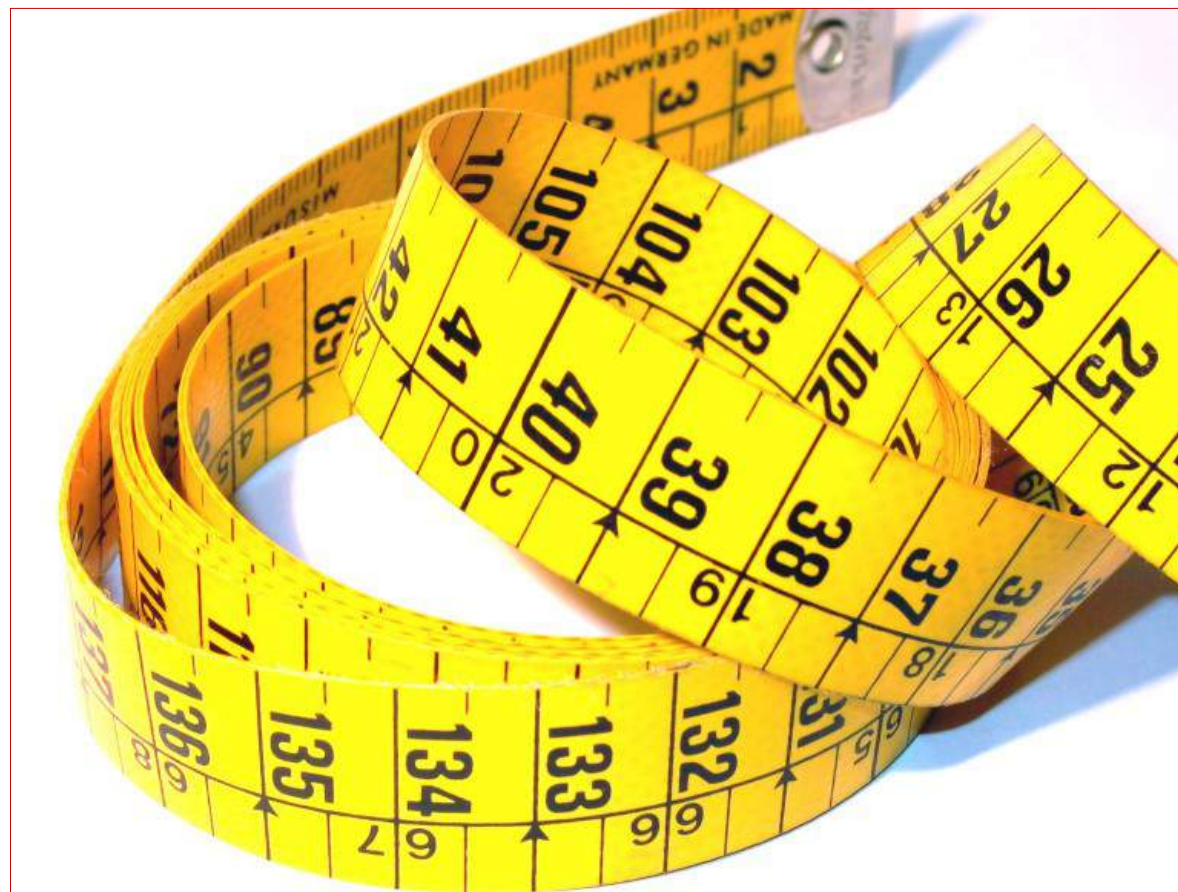
- METFORAL 850mg ½ cp (divisa in due)

DOPO CENA:

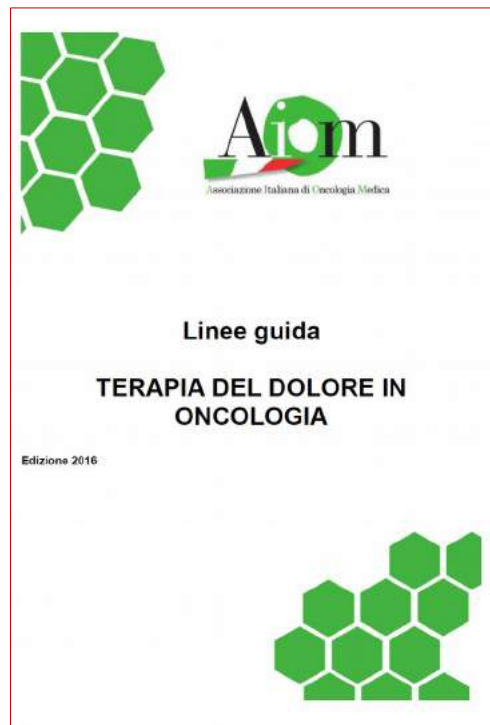
- ~~CARDURA 2mg~~ 1cp
- NORVASC 10mg ½ cp (divisa in due)
- ~~FENO FIBRATO 145mg~~ 1cp
- LEXOTAN 10 8 gocce

**Garantire il tempo necessario per la
relazione con la famiglia**

Partendo
dall'assessment....



Dolore oncologico



Qualità dell'evidenza SIGN	Raccomandazione clinica R3	Forza della raccomandazione clinica
D	Per la valutazione delle esacerbazioni si raccomanda di misurare la presenza di picchi di dolore più intenso nelle 24 ore precedenti la rilevazione. In caso di risposta affermativa, approfondire la valutazione al fine di arrivare ad una diagnosi di presenza o assenza di dolore episodico intenso secondo una definizione prestabilita. (4)	Positiva forte

Qualità dell'evidenza SIGN	Raccomandazione clinica R1	Forza della raccomandazione clinica
D	Per un'adeguata gestione del dolore da cancro si raccomanda la misurazione dell'intensità, delle eventuali esacerbazioni del dolore e del sollievo dato dalle terapie riferiti alle 24 ore precedenti; la valutazione di altri aspetti deve essere introdotta senza creare disagio al paziente. (4)	Positiva forte

Qualità dell'evidenza SIGN	Raccomandazione clinica R2	Forza della raccomandazione clinica
D	Per la misurazione dell'intensità dolore oncologico si raccomanda l'uso della scala numerica a 11 livelli (0= nessun dolore, 10 peggior dolore immaginabile); in pazienti con disfunzioni cognitive si consiglia l'uso della scala verbale a 6 livelli (Nessun dolore, dolore molto lieve, dolore lieve, dolore moderato, dolore forte, dolore molto forte). (2)	Positiva forte

Qualità dell'evidenza SIGN	Raccomandazione clinica R4	Forza della raccomandazione clinica
D*	Per la valutazione del sollievo dal dolore dato dai trattamenti si raccomanda l'uso di una scala specifica che rileva l'entità del sollievo nelle 24 ore precedenti la rilevazione; al fine di evitare confusione per il paziente, se l'intensità del dolore è stata rilevata con una scala numerica, per il sollievo si raccomanda di utilizzare una scala di valutazione verbale (nessun sollievo, sollievo leggero, sollievo moderato, sollievo elevato, sollievo completo).	Positiva forte

Journal of medical ethics, 1978, **4**, 112-116

The assessment of pain in advanced cancer

Robert G Twycross *The Churchill Hospital, Headington, Oxford*

Table 1 <i>The PQRST characteristics of pain</i> ¹	
‘Tell me about your pain.’	
‘Where is it?’	
<i>P</i> alliative rovocative factors	‘What makes it less intense?’
<i>Q</i> uality	‘What makes it worse?’
<i>R</i> adiation	‘What’s it like?’
<i>S</i> everity	‘Does it spread anywhere else?’
<i>T</i> emporal factors	‘How severe is it?’
	‘Is it there all the time, or does it come and go?’

¹Gray, J (1977). A pain in the neck – and shoulder.
Pain Topics, 1, No. 3, 6.

Vol. 23 No. 1 January 2002 *Journal of Pain and Symptom Management* 31

Original Article

Factors Associated with the Accuracy of Family Caregiver Estimates of Patient Pain

Ellen M. Redinbaugh, PhD, Andrew Baum, PhD, Carol DeMoss, RN, MSN, Maryann Fello, RN, MEd, and Robert Arnold, MD
University of Pittsburgh Cancer Institute (E.M.R., A.B.), University of Pittsburgh Medical Center Hospice Home Care (C.D.), Forbes Family Hospice (M.F.), and University of Pittsburgh School of Medicine (R.A.), Pittsburgh, Pennsylvania, USA

Table 2 Descriptive Statistics for Measured Variables (n = 31)		
Variable Name	Mean (SD)	Range
Patient Pain Rating	3.4 (2.9)	0-9
Caregiver Rating of Patient Pain	6.1 (3.4)	0-10

Higher caregiver pain ratings were related to poorer patient existential QOL, greater patient ADL care needs, greater caregiver distress, and greater caregiver burden.

A paired *t*-test compared patient ratings to caregiver ratings and indicated that caregivers' estimates were significantly higher than patients' pain ratings (*t* = -4.9, *P* < 0.01). These findings are consistent with previous studies that found that family members overestimate patient pain.⁶⁻⁹

Original Article

Family Caregivers' Assessment of Symptoms in Patients with Advanced Cancer: Concordance with Patients and Factors Affecting Accuracy

Christine J. McPherson, RN, PhD, Keith G. Wilson, PhD, CPsych, Michelle M. Lobchuk, RN, PhD, and Susan Brajtman, RN, PhD
School of Nursing (C.J.M., S.B.), Faculty of Health Sciences, University of Ottawa, Ottawa; Institute for Rehabilitation Research and Development (K.G.W.), The Rehabilitation Centre, The Ottawa Hospital, Ottawa; and Faculty of Nursing (M.M.L.), University of Manitoba, Winnipeg, Canada

Agreement Between Patients and Family Caregivers on Symptoms at the Individual Level

	Patient	Family Caregiver	Agreement
	Mean (SD)		ICC ^a
Pain			
Frequency	1.94 (1.55)	2.12 (1.37)	0.44
Severity	1.36 (1.09)	1.80 (1.17)	0.42
Distress	1.77 (1.41)	2.04 (1.37)	0.36
Total	1.69 (1.28)	1.94 (1.21)	0.44

Caregiver: fattori influenzanti negativamente la concordanza con quanto riferito dall'ammalato:

- Umore (depresso)
- Genere (maschile)
- «Burden» assistenziale



**World Health
Organization**

1. **'By mouth' – oral forms of analgesics is preferred wherever possible**
2. **'By the clock' – analgesic should be given at regular intervals rather than on demand.**
3. **'By the ladder' – The principles of the ladder should be adhered to.**
4. **'For the individual' – there is no standardised dosage and therapy and should be based around the level of the patient's reported pain.**
5. **'Attention to detail' – refers to the close monitoring of the patient's pain as well as the biopsychosocial factors that may be impacting upon their pain.**

Quando la via orale è utilizzabile, è preferibile a elastomeri e syringe driver (ed è anche meno costosa....)



TITOLAZIONE DEGLI OPPIACEI

R11. Le formulazioni orali di morfina, ossicodone, idromorfone a immediato e a lento rilascio possono essere utilizzate per la titolazione della dose. Gli schemi di titolazione per entrambi i tipi di formulazione dovrebbero essere integrati con oppioidi orali a rilascio immediato somministrati al bisogno.

RACCOMANDAZIONE POSITIVA DEBOLE

R12. La via sottocutanea è semplice ed efficace per la somministrazione di morfina e dovrebbe essere la prima scelta di via alternativa per pazienti che non possono ricevere oppioidi per via orale o transdermica; l'infusione endovenosa deve essere considerata quando l'infusione sottocutanea è controindicata (ad esempio, a causa di edema periferico, disturbi della coagulazione, deficit della circolazione periferica, esigenza di elevati volumi e dosi, ecc); la somministrazione endovenosa deve essere usata per la titolazione degli oppioidi, quando è richiesto un rapido controllo del dolore.

RACCOMANDAZIONE POSITIVA FORTE

TITOLAZIONE DEGLI OPPIACEI

Recommendation for opioid titration

The data permit a weak recommendation that immediate-release and slow-release oral formulations of morphine, oxycodone, and hydromorphone can be used for dose titration. The titration schedules for both types of formulation should be supplemented with oral immediate-release opioids given as needed.



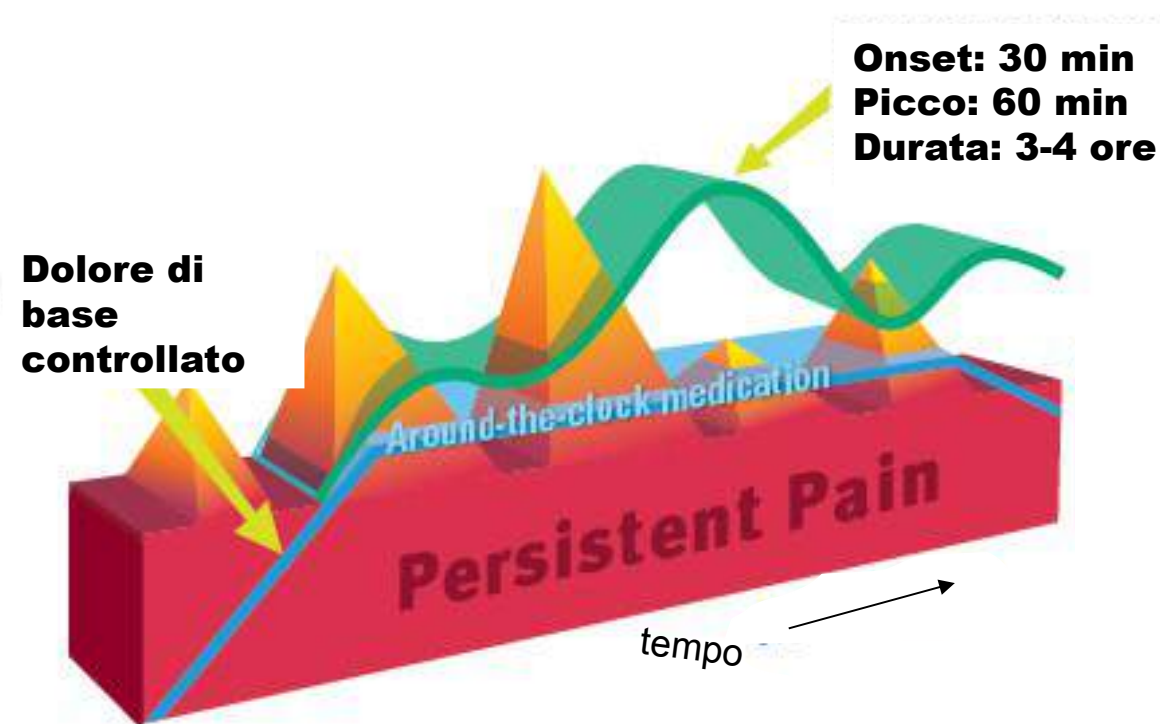
IL BREAKTHROUGH CANCER PAIN (BTcP)



An episode of severe pain intensity in patients receiving an adequate treatment with opioids that are able to provide at least mild background analgesia

TRATTAMENTO DEL BTcP: I SAO

“La farmacocinetica e la farmacodinamica degli oppioidi per via orale non rispecchiano il profilo temporale della maggior parte degli episodi di BTcP, ovvero una rapida insorgenza (pochi minuti) e una breve durata (30-60 minuti)”



TRATTAMENTO DEL BTcP: LA MORFINA ENDOVENOSA

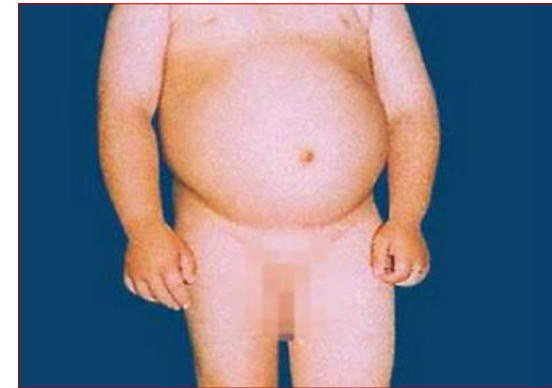
- **Inizio d'azione rapidissimo, pochi minuti (anche se, essendo idrofila, attraversa la barriera ematoencefalica meno rapidamente del fentanyl, lipofilo)**
- **Però, analogamente alla morfina solfato a rapido rilascio, la farmacocinetica della morfina endovenosa, soprattutto per l'emivita (circa 4 ore), può non rispecchiare il profilo temporale della maggior parte degli episodi di BTcP**
- **Inoltre, la morfina endovenosa può essere poco maneggevole in un setting domiciliare, ove dovrebbero (vorrebbero ...) essere assistiti la maggior parte dei pazienti oncologici in fase avanzata di malattia**

Davies AN et al. Eur J Pain. 2009

TRATTAMENTO DEL BTcP: LA MORFINA SOTTOCUTANEA

Onset intermedio tra morfina solfato a rapido rilascio e morfina endovenosa (ma attenzione al paziente gravemente cachettico, gravemente ipoteso o in stato anasarcatico)

Resta invariato il problema dell'emivita troppo lunga...



IL FARMACO IDEALE PER IL BTcP

- Efficace
- Inizio d'azione rapido
- Durata d'azione relativamente breve
- Ben tollerato
- Pratico da usare

Vol. 35 No. 5 May 2008

Journal of Pain and Symptom Management 563

Clinical Note

Opioids for Cancer Breakthrough Pain:
A Pilot Study Reporting Patient Assessment
of Time to Meaningful Pain Relief

Giovambattista Zeppetella, FRCP

St. Clare Hospice, Hastingswood, and Princess Alexandra NHS Trust, Harlow, United Kingdom

Zeppetella G. J Pain Symptom Manage. 2008

TRATTAMENTO DEL BTcP: I ROOs

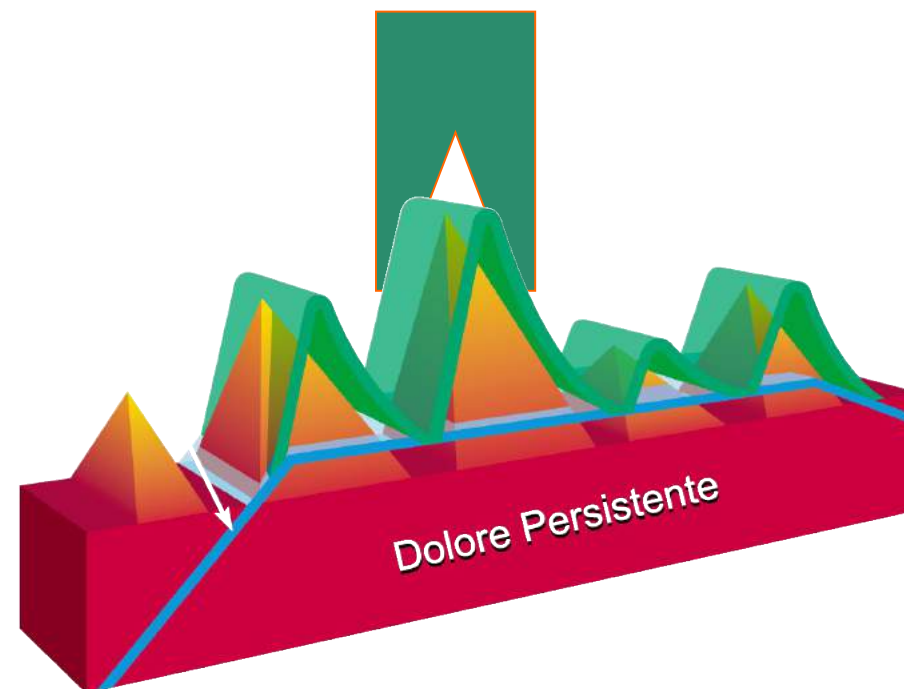
ROOs (Rapid Onset Opioids)

- Rapido inizio d'azione
- Buona efficacia
- Durata dell'effetto analgesico paragonabile a quello del BTcP
- Praticità d'uso

"Indeed the studies identified in this review suggest that fentanyl can be used successfully in patients using a variety of oral ATC opioids including morphine, oxycodone, hydromorphone, and methadone"



MIMANO L'ANDAMENTO NEL
TEMPO DEL BTcP



Zeppetella G. Palliat Med. 2011

LINEE GUIDA PER IL TRATTAMENTO DEL BTcP



**Linee guida
Association for Palliative
Medicine of Great
Britain and Ireland. 2009**

**Oral opioids are not the
optimal rescue
medication for most
breakthrough pain
episodes**

A variety of commercial buccal, sub-lingual, nasal and pulmonary opioid preparations are currently under development. It is likely that these new products will offer significant advantages over the current products

LINEE GUIDA PER IL TRATTAMENTO DEL BTcP

clinical practice guidelines

Annals of Oncology 23 (Supplement 7): vii139–vii154, 2012
doi:10.1093/annonc/mds233

Management of cancer pain: ESMO Clinical Practice Guidelines[†]

C. I. Ripamonti¹, D. Santini², E. Maranzano³, M. Berti⁴ & F. Roila⁵, on behalf of the ESMO Guidelines Working Group^{*}

[†]Supportive Care in Cancer Unit, Fondazione IRCCS, Istituto Nazionale Tumori, Milan, Italy; ²Oncologia Medica, Università Campus Bio-Medico, Rome, Italy;

³Department of Oncology, Radiation Oncology Centre, S. Maria Hospital, Terni, Italy; ⁴Anaesthesiology Intensive Care and Pain Therapy, University Hospital Parma, Parma, Italy; ⁵Department of Medical Oncology, S. Maria Hospital, Terni, Italy

**Linee guida
ESMO. 2012**

RECOMMENDATIONS

Intravenous opioids; buccal, sublingual and intranasal fentanyl drug delivery have a shorter onset of analgesic activity in treating BTP episodes in respect to oral morphine [I, A]

LINEE GUIDA PER IL TRATTAMENTO DEL BTcP

Review

Use of opioid analgesics in the treatment of cancer pain: evidence-based recommendations from the EAPC

Augusto Caraceni*, Geoffrey Hanks*, Stein Kaasa*, Michael J Bennett, Cinzia Bruzzi, Nathan Cherny, Olu Dalu, Franco De Conno, Marie Fallon, Magdi Hanna, Dagry Falkovig Haugen, Gitter Johl, Samuel King, Pål Klepstad, Eivor A Lousgaard, Marco Maltoni, Sebastiano Mercadante, Maria Nabel, Alessandra Pigni, Lukas Radbruch, Corlette Reil, Per Sjogren, Patrick C Stone, Davide Tassinari, Giovambattista Zepfella, for the European Palliative Care Research Collaborative (EPCRC), on behalf of the European Association for Palliative Care (EAPC)

Here we provide the updated version of the guidelines of the European Association for Palliative Care (EAPC) on the use of opioids for the treatment of cancer pain. The update was undertaken by the European Palliative Care Research Collaborative. Previous EAPC guidelines were reviewed and compared with other currently available guidelines, and consensus recommendations were created by formal international expert panel. The content of the guidelines was defined according to several topics, each of which was assigned to collaborators who developed systematic literature reviews with a common methodology. The recommendations were developed by a writing committee that combined the evidence derived from the systematic reviews with the panelists' evaluations in a co-authored process, and were endorsed by the EAPC Board of Directors. The guidelines are presented as a list of 16 evidence-based recommendations developed according to the Grading of Recommendations Assessment, Development and Evaluation system.

Introduction
Moderate to severe pain in cancer is common and affects 70–80% of patients with advanced disease. We have the means and the knowledge to relieve most pain in cancer for most patients,¹ but evidence from surveys and observational studies shows that many patients have troublesome or severe pain and do not get adequate relief.²
The skilled use of opioid analgesics is crucial to the relief of cancer pain, but there is a shocking lack of evidence to support clinical practice. The so-called analgesic ladder is the central idea of the WHO 1996 guidelines on cancer pain relief,³ in which the choice of analgesic is determined by the severity of the pain. The WHO method has been adopted worldwide but the lack of up-to-date evidence, knowledge, and opioid availability have obstructed the path to effective relief of cancer pain.^{4,5}
Randomised controlled trials (RCTs) in patients with cancer pain are beset by difficulties.⁶ In the absence of hard evidence from RCTs, expert consensus and clinical guidelines might be helpful, because cancer pain relief is a specialist area but most care is delivered by non-specialist practitioners. The European Association for Palliative Care (EAPC) research network published its first guidelines on the use of morphine and alternative opioids in cancer pain in 1996,⁶ and published an update in 2001.⁷ In this Review we present further work done to strengthen the scope of the EAPC recommendations by the application of rigorous, evidence-based methodology.

Development of recommendations
A comprehensive list of relevant topics on opioid use for cancer pain was derived from a comparison of the previous EAPC recommendations with other available guidelines on cancer pain relief. This list was submitted to a formalised expert consensus process that led to 30 practical clinical questions being summarised in 22 topics.^{8,9} The subsequent guidelines development

process followed the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system.^{10–12}
Each of the 22 topics was assigned to a group of collaborators who did a systematic review according to a standardised method (appendix). The results were presented at the Fifth Bristol Opioids Conference, Bristol, UK, Feb 8–9, 2010. 19 reviews have since been published.^{8–9} Within each topic the evidence profile for each relevant outcome was determined and this formed the basis for a final recommendation.
In the review of opioids in liver failure¹³ and on the use of opioid combinations,¹⁴ evidence did not reach sufficient quality to support a recommendation and, therefore, these areas were not included in this guideline. Our literature review on the treatment of opioid-related constipation completely overlapped with a Cochrane review¹⁵ and it was not submitted for publication. Finally one topic on the role of ketamine was not included because of the lack of resources to complete the work. Thus, 16 recommendations have been included in this summary paper by the writing committee, on the basis of the evidence profiles, modified to take into account individual judgments and evaluations. They have been circulated to the Scientific Advisory Board of the European Palliative Care Research Collaborative, the Board of Directors of the EAPC and to each collaborator for comment and modification as necessary. With this feedback the recommendations were revised by the writing committee and circulated to the whole group once more for comment and final approval.
In this paper and associated publications we have adopted the terms step I opioids and step III opioids to differentiate between low-potency drugs, such as codeine and tramadol, and higher-potency drugs, of which morphine is the prototype. This terminology relates directly to the WHO cancer pain relief ladder and is widely understood.

USE OF OPIOIDS ANALGESICS IN THE TREATMENT OF CANCER PAIN: EVIDENCE-BASED RECOMMENDATIONS FROM THE EAPC. 2012

Recommendation for opioids for breakthrough pain
Breakthrough pain (eg, incident pain) can be effectively managed with oral, immediate-release opioids or with buccal or intranasal fentanyl preparations. In some cases the buccal or intranasal fentanyl preparations are preferable to immediate-release oral opioids because of more rapid onset of action and shorter duration of effect.

LINEE GUIDA PER IL TRATTAMENTO DEL BTcP

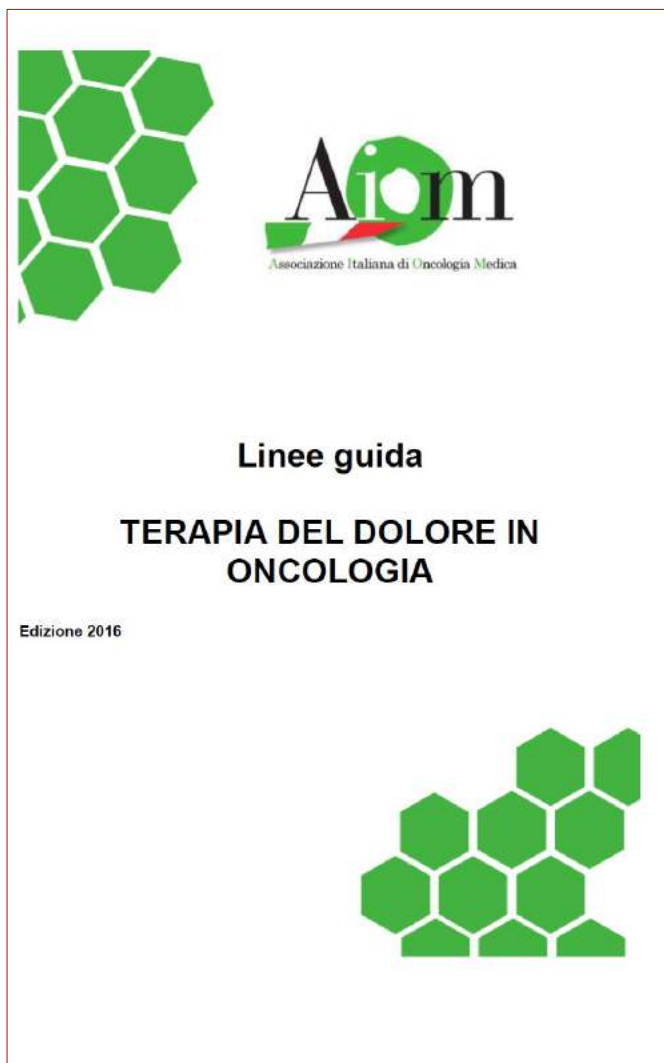


Position Paper SICP. 2010

R6. Nel trattamento del BTcP nuove formulazioni di fentanyl citrato, come quelle orosolubile, sublinguale e intranasale, offrono oggi sostanziali vantaggi dal punto di vista sia farmacocinetico (rapido assorbimento, maggiore biodisponibilità ed efficacia) sia della compliance (più facile via di somministrazione)

R5. La morfina orale può essere raccomandata solo per il trattamento di episodi che si instaurano lentamente, prevedibili o procedurali, della durata di oltre 60 minuti. La somministrazione deve avvenire circa trenta minuti prima dell'evento, per esempio prima di iniziare l'attività

LINEE GUIDA PER IL TRATTAMENTO DEL BTcP



Linee guida AIOM. 2016

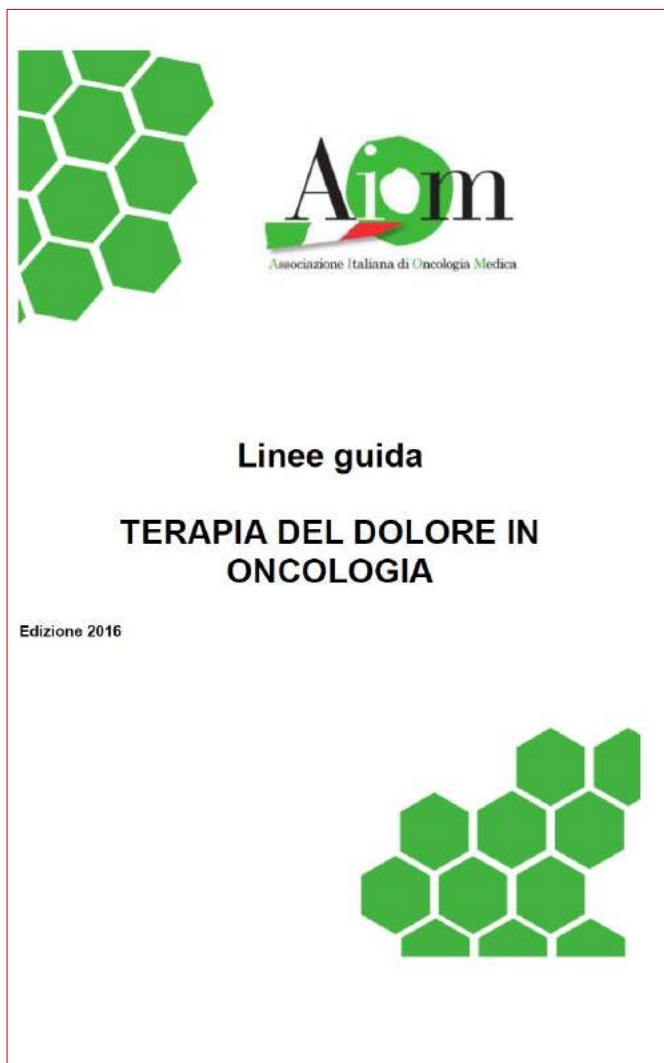
È raccomandabile l'utilizzo della morfina o di altri oppioidi nel trattamento del dolore episodico intenso?

R30. L'utilizzo della morfina o di altri oppioidi per via orale a rapido rilascio, o della morfina per via parenterale nel controllo del DEI dovrebbe essere preso in considerazione.

Raccomandazione Positiva DEBOLE

(metodo GRADE)

LINEE GUIDA PER IL TRATTAMENTO DEL BTcP



Linee guida AIOM. 2016

E' raccomandabile l'utilizzo del fentanyl transmucoale per il controllo del dolore episodico intenso?

R 28. L'utilizzo del fentanyl transmucoale nel controllo del dolore episodico intenso rispetto alla morfina dovrebbe essere preso in considerazione. Non vi sono al momento evidenze di letteratura sufficienti ad orientare nella scelta della formulazione di fentanyl.

Raccomandazione Positiva DEBOLE

(metodo GRADE)⁰

What to Do, and What Not to Do, When Diagnosing and Treating Breakthrough Cancer Pain (BTcP): Expert Opinion

Working Group Nientemale DEI · R. Vellucci¹ · G. Fanelli² · R. Pannuti³ · C. Peruselli⁴ · S. Adamo⁵ · G. Alongi⁶ · F. Amato^{7,8} · L. Consoletti⁹ · L. Lamarca¹⁰ · S. Liguori¹¹ · C. Lo Presti¹² · A. Maione¹³ · S. Mameli¹⁴ · F. Marinangeli¹⁵ · S. Marulli¹⁶ · V. Minotti¹⁷ · D. Miotti¹⁸ · L. Montanari^{19,20} · G. Moruzzi²¹ · S. Palermo²² · M. Parolini²³ · P. Poli²⁴ · W. Tirelli^{25,26} · A. Valle²⁷ · P. Romualdi²⁸

healthcare resource management [13]. In the latter, it is essential to weigh the absolute cost of the drugs used to treat BTcP against those arising from poor management, which will entail more frequent and longer periods of hospitalisation and consultation, as well as indirect costs for the healthcare providers and patients [27, 28].

Support Care Cancer (2017) 25:333–340

DOI 10.1007/s00520-016-3371-3



SPECIAL ARTICLE

2016 Updated MASCC/ESMO consensus recommendations: Management of nausea and vomiting in advanced cancer

Declan Walsh^{1,2,3} · Mellar Davis⁴ · Carla Ripamonti⁵ · Eduardo Bruera⁶ ·
Andrew Davies⁷ · Alex Molassiotis⁸

Table 2 Antiemetic guidelines in advanced cancer

Recommendation	MASCC/ESMO level of evidence
Drugs of choice The antiemetic drug of choice in advanced cancer is metoclopramide (titrated to effect).	MASCC level of consensus: high MASCC level of confidence: moderate ESMO level of evidence: III ESMO grade of recommendation: C MASCC level of consensus: high MASCC level of confidence: low ESMO level of evidence: V ESMO grade of recommendation: D
Alternative options include haloperidol, levomepromazine, or olanzapine.	MASCC level of consensus: high MASCC level of confidence: high ESMO level of evidence: II ESMO grade of recommendation: A MASCC level of consensus: high (moderate for corticosteroids) MASCC level of confidence: moderate (low for corticosteroids) ESMO level of evidence: IV ESMO grade of recommendation: D
The use of cyclizine* or 5-HT₃ receptor antagonists is poorly defined to date and may be used where dopamine antagonists are contraindicated or ineffective.	MASCC level of consensus: low MASCC level of confidence: low ESMO level of evidence: V ESMO grade of recommendation: D
Bowel obstruction The drug recommended in a bowel obstruction is octreotide, dosed around the clock and given alongside an antiemetic (with the committee recommending haloperidol).	MASCC level of consensus: high MASCC level of confidence: high ESMO level of evidence: II ESMO grade of recommendation: A MASCC level of consensus: high (moderate for corticosteroids) MASCC level of confidence: moderate (low for corticosteroids) ESMO level of evidence: IV ESMO grade of recommendation: D
If Octreotide plus antiemetic is ineffective, the use of anticholinergic antisecretory agents (e.g., scopolamine butylbromide, glycopyrronium bromide) and/or corticosteroids is recommended as either adjunct or alternative interventions.	MASCC level of consensus: low MASCC level of confidence: low ESMO level of evidence: V ESMO grade of recommendation: D
The use of cyclizine* or 5-HT₃ receptor is poorly defined in this setting**. Metoclopramide should be used with caution in partial bowel obstruction and should not be used in complete bowel obstruction.	MASCC level of consensus: high MASCC level of confidence: low ESMO level of evidence: V ESMO grade of recommendation: D
Opioid-induced nausea and vomiting No recommendation can be made for specific antiemetics, although various antiemetics may help. Opioid rotation and route switching may be effective approaches. There is no data to support prophylactic antiemetics in this situation.	MASCC level of consensus: high MASCC level of confidence: low ESMO level of evidence: V ESMO grade of recommendation: D

*Unavailable in some countries

**Caution should be exercised because of the risk of drug interactions



Recommendation for treatment of opioid-related emesis

The data permit a weak recommendation that some antidopaminergic drugs (eg, haloperidol) and other drugs with antidopaminergic and additional modes of action (eg, metoclopramide) should be used in patients with opioid-induced emesis.

1 compressa di domperidone ~ 0,15 Euro

1 compressa di metoclopramide ~ 0,25 Euro

1 compressa di ondansetron 4mg ~ 4,50 Euro



1 fiala di metoclopramide ~ 0,30 Euro

1 fiala di ondansetron 4mg ~ 6,80 Euro

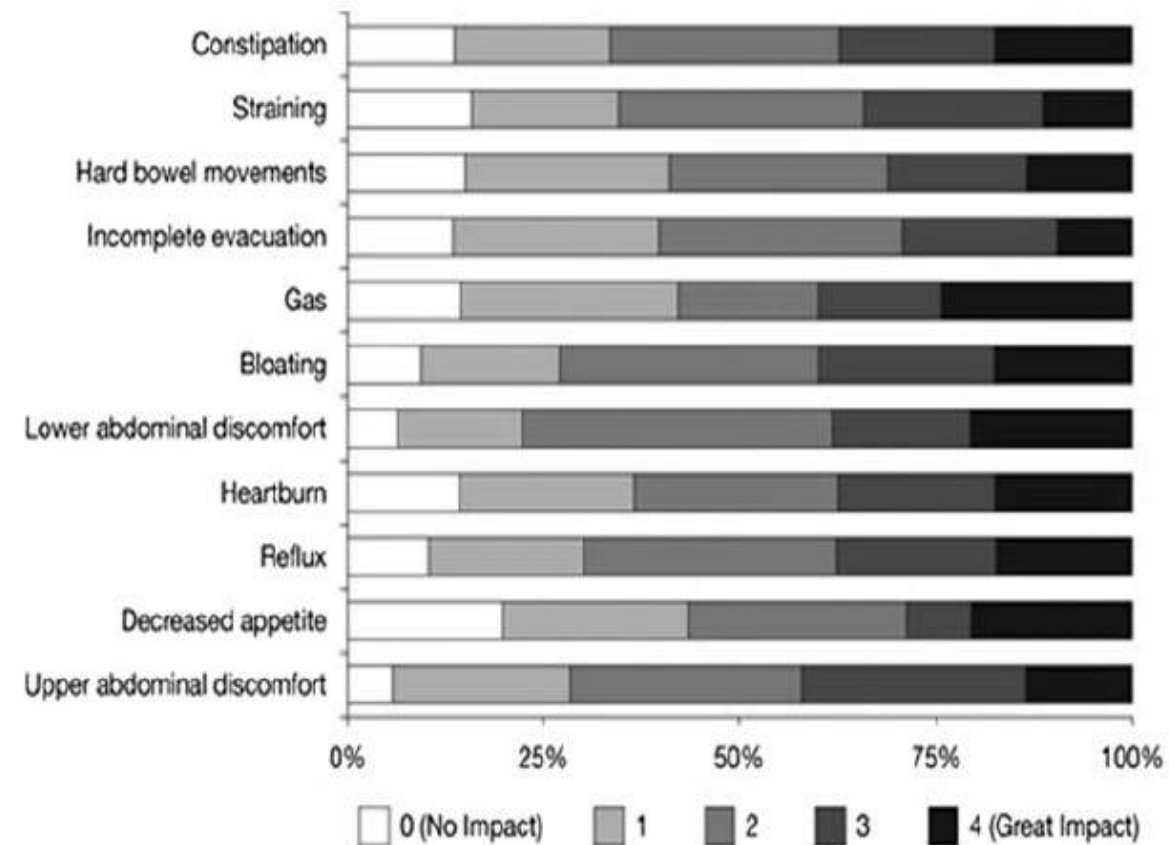


Opioid Induced Bowel Disease: a Twenty-first Century Physicians' Dilemma

Considering Pathophysiology and Treatment Strategies

Ankush Sharma · M. Mazen Jamal

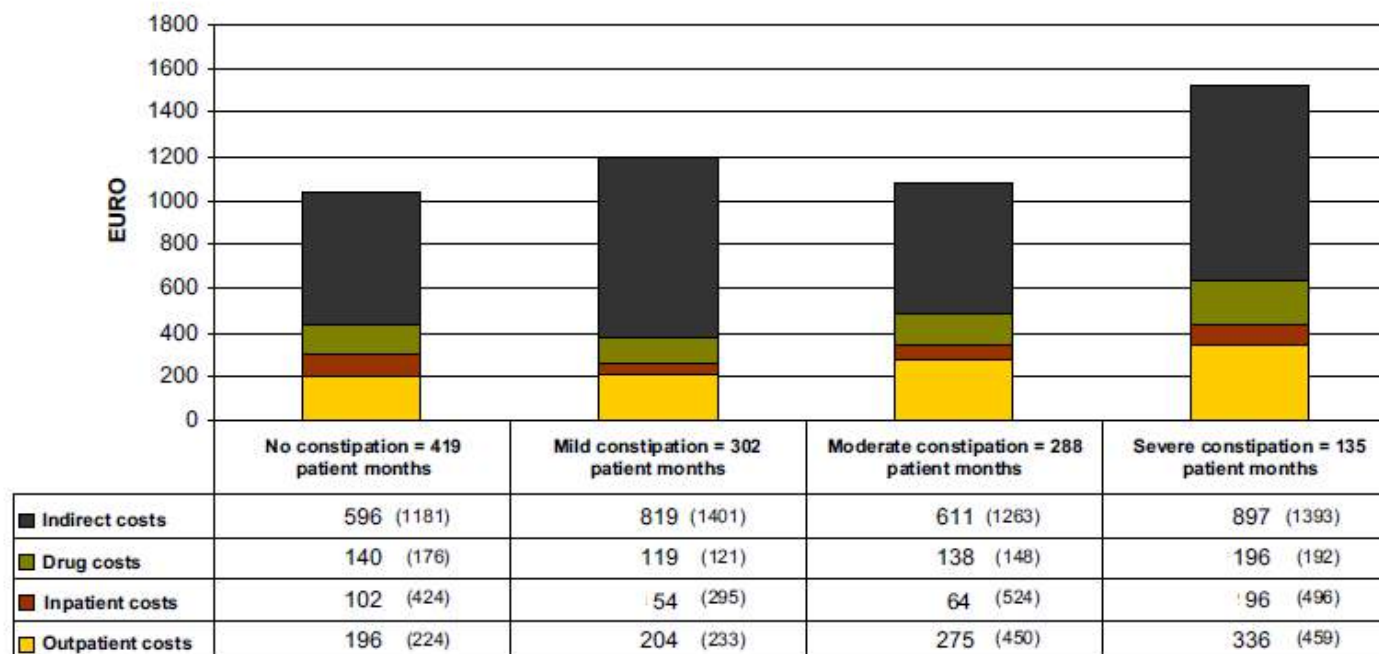
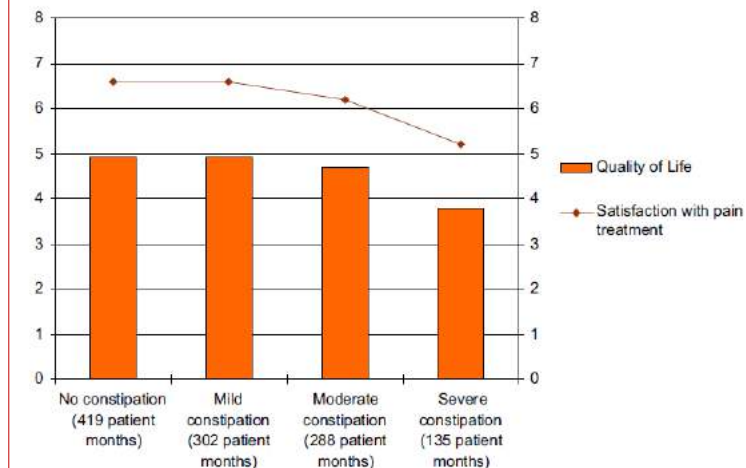
Fig. 2 Impact of the most common symptoms of OBD on ADL. (Reprinted from Bell et al., with permission from American Academy of Pain)



Original Article

The Direct and Indirect Costs of Opioid-Induced Constipation

Frida Hjalte, MSc, Anna-Carin Berggren, MSc, Henrik Bergendahl, MD, and Catharina Hjortsberg, PhD
The Swedish Institute for Health Economics (FH., C.H.), Lund; Mundipharma AB (A.-C.B.), Gothenburg; and Department of Anaesthesiology, Intensive Care and Pain Medicine (H.B.), Karolinska University Hospital, Huddinge, Stockholm, Sweden



- (1) Lack of awareness among clinicians about OIC in patients on opioid therapy.
- (2) If clinicians are aware, they may not ask patients questions about constipation.
- (3) Patients might feel ashamed to disclose their symptoms to clinicians.
- (4) Absence of universal diagnostic criteria for OIC.
- (5) Efforts to screen patients based on Rome III criteria may not cover the whole spectrum of OIC that might present with abdominal pain.
- (6) Absence of a standard protocol for the treatment of OIC.



Bowel Function Index (BFI)

Please complete all items in this assessment.

1. Ease of defecation (NAS) during the last 7 days according to patient assessment:

0 = easy / no difficulty

100 = severe difficulty



Ask the subject: "During the last 7 days, how would you rate your ease of defecation on a scale from 0 to 100, where 0 = easy or no difficulty and 100 = severe difficulty?"

If the subject requires clarification, ask: "During the last 7 days, how easy or difficult was it to have a bowel movement on a scale from 0 to 100, where 0 = easy or no difficulty and 100 = severe difficulty?"

2. Feeling of incomplete bowel evacuation (NAS) during the last 7 days according to patient assessment:

0 = not at all

100 = very strong



Ask the subject: "During the last 7 days, how would you rate any feeling of incomplete bowel evacuation on a scale from 0 to 100, where 0 = no feeling of incomplete evacuation and 100 = a very strong feeling of incomplete evacuation?"

If the subject requires clarification, ask: "During the last 7 days, how strongly did you feel that you did not empty your bowels completely? Please indicate how strong this feeling was on a scale from 0 to 100, where 0 = not at all and 100 = very strong"

3. Personal judgement of patient (NAS) regarding constipation during the last 7 days:

0 = not at all

100 = very strong



Ask the subject: "During the last 7 days, how would you rate your constipation on a scale from 0 to 100, where 0 = not at all and 100 = very strong"

If the subject requires clarification, ask: "During the last 7 days, how would you rate how constipated you felt on a scale from 0 to 100, where 0 = not at all and 100 = very strong"

Stipsi

Table 4. Laxatives and opioid antagonists dosage refers to symptom control in cancer patients				
Mode of action	Group	Substance	Dosage ^a	Latency [h]
I Bulking agents		Wheat bran Indian flax seed (Plantago) Linseed	10–30 mg	Initially 24–72, afterwards 8–24
		Sodium sulfate = Glauber's salt		
	Sugar alcohols	Mannit/mannitol sorbitol, glycerol	1 clysm	0.5–2
II Antireosorptive and hydragogue laxatives	Sugar	Lactulose	1 clysm	0.5–2
			10–40 g	Initially 10–72, afterwards 8–24
	Polyethylenglycol	Macrogol 3350	13–40 g	Initially 48–72, afterwards 8–24
	Anthraglycoside	Sennoside B	2–3 pills	12
	Phenolphthalein	Bisacodyl	10 mg	Per rectum 5–10
		Sodium picosulfate	15–40 drops	Per rectum 15–60 min
				2–4 [–8]
	Castor oil	Castor oil	4–6 g	2–6
V Laxatives with effect on the defecation reflex	Alcohols	Laxamin	10–30 ml	6–12
		Sorbitol	1 clysm	0.5–1
		Glycerol	1 suppository	0.5–1
Binds to mu-opioid receptor in the gastrointestinal tract	Peripherally acting mu-receptor antagonist	Methylnaltrexone bromide	8–12 mg/0.6 ml s.c	30–60 min

REVIEW	
	Pharmacological treatment of constipation in palliative care
Karin E. Clements ^a , Matteo Piccoli ^a , Shoji Isayama ^b , and Elad Mizus ^c	
Regimen of review	
The treatment of constipation in palliative care patients varies. There is controversy about the choice between laxative and antidiarrhoeal agents. The purpose of this review was to evaluate the current recommendations of therapy guidelines and to determine the effectiveness and safety of laxative administration for the management of constipation in palliative care patients.	
Recent findings	
Despite the clinical importance, there are limited data on the efficacy and safety of laxatives in palliative care patients. The most comprehensive studies used to be conducted in healthy, but elderly, patients. Thus, the evidence for most laxatives is weak. However, there are some data on the efficacy and safety of laxatives in palliative care patients. The most comprehensive studies used to be conducted in healthy, but elderly, patients. Thus, the evidence for most laxatives is weak. However, there are some data on the efficacy and safety of laxatives in palliative care patients.	
Summary	
There are limited data available on the conventional pharmacological treatment of constipation in palliative care patients. The most comprehensive studies used to be conducted in healthy, but elderly, patients. Thus, the evidence for most laxatives is weak. However, there are some data on the efficacy and safety of laxatives in palliative care patients.	
Keywords	
constipation, laxative, methylnaltrexone bromide, palliative care	
INTRODUCTION	
In advanced stages of tumour disease, constipation, often because of dysmotility, is a common problem. It is a symptom of advanced disease and is a source of significant discomfort and distress for patients. It is a common problem in palliative care, particularly those with advanced cancer [1]. The prevalence of constipation in palliative care ranges from 70% to 80% [2,3], and therefore is the most common symptom after pain and anorexia [4]. Constipation refers to bowel movements that are infrequent and/or hard to pass [5], and has a number of clinical (functional, morphological, and anatomical) causes, including opioid and laxative [6,7]. Constipation is a common problem in palliative care, particularly those with advanced cancer [1]. The prevalence of constipation in palliative care ranges from 70% to 80% [2,3], and therefore is the most common symptom after pain and anorexia [4]. Constipation refers to bowel movements that are infrequent and/or hard to pass [5], and has a number of clinical (functional, morphological, and anatomical) causes, including opioid and laxative [6,7].	
For severe patients, additional causes (such as dehydration, hypokalaemia, hypomagnesaemia, hypocalcaemia, and/or hypoproteinaemia) should be considered. In addition, the use of opioid analgesics or other drugs, decreased mobility, and decreased fluid intake may also contribute to constipation [8]. Constipation can be a source of significant discomfort and distress for patients. It is a common problem in palliative care, particularly those with advanced cancer [1]. The prevalence of constipation in palliative care ranges from 70% to 80% [2,3], and therefore is the most common symptom after pain and anorexia [4]. Constipation refers to bowel movements that are infrequent and/or hard to pass [5], and has a number of clinical (functional, morphological, and anatomical) causes, including opioid and laxative [6,7].	
The aim of this review was to evaluate the current recommendations of therapy guidelines and to determine the effectiveness and safety of laxative administration for the management of constipation in palliative care patients.	
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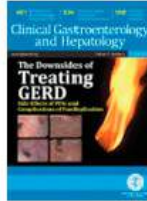
Terapia aspecifica

- Prescrizione sostenuta da pochi studi e di modesta qualità
- Caratteristiche organolettiche sgradite a numerosi pazienti
- Effetti collaterali fastidiosi (crampi addominali, flatulenza, ecc.)
- Necessità frequente di somministrare di alti dosaggi, non sempre efficaci

Accepted Manuscript

Efficacy of Treatments for Opioid-induced Constipation: A Systematic Review and Meta-Analysis

Judy Nee, Mohammed Zakari, Michael A. Sugarman, Julia Whelan, William Hirsch, Shahnaz Sultan, Sarah Ballou, Johanna Iturrino, Anthony Lembo



PII: S1542-3565(18)30087-9

DOI: 10.1016/j.cgh.2018.01.021

Reference: YJCGH 55657

To appear in: *Clinical Gastroenterology and Hepatology*
Accepted Date: 11 January 2018

Three trials using lubiprostone and one using prucalopride demonstrated that both agents were efficacious in the treatment of OIC; however, both drugs were comparatively less efficacious when compared to u-opioid receptor antagonists, supporting previous findings.

The NNT of lubiprostone was higher at 15 compared to other u-opioid receptor antagonists.

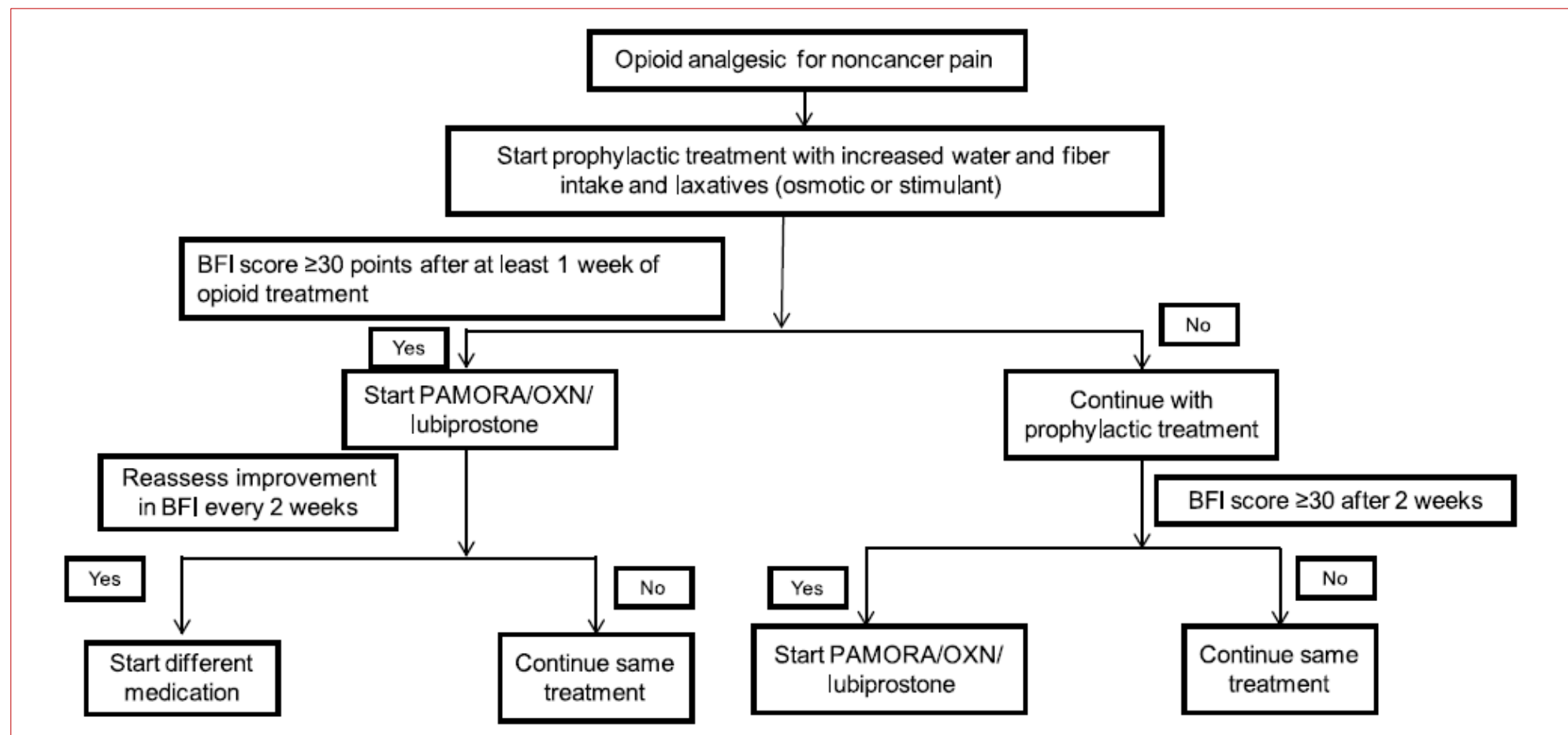
This meta-analysis confirms the overall safety of these medications in over 5,000 patients receiving u-opioid antagonists while maintaining opioid analgesic affect.

Despite Food and Drug Administration (FDA) approval for the u-opioid antagonists naloxegol, methylnatrexone, fixed-dosage oxycodone/naloxone, and naldemedine no formal guidelines exist for their usage in clinical practice; thus, making them underutilized. While some consensus is developing in regards to utilizing these agents in clinical practice for those patients with chronic pain on opiate treatment, this provides further evidence demonstrating the efficacy and safety of u opioid receptor antagonists and lubiprostone in the treatment of OIC

Opioid-induced constipation: advances and clinical guidance

Alfred D. Nelson and Michael Camilleri

Ther Adv Chronic Dis
2016, Vol. 7(2) 121–134
DOI: 10.1177/
2040622315627801
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Dispnea

JOURNAL OF PALLIATIVE MEDICINE
Volume 14, Number 10, 2011
© Mary Ann Liebert, Inc.
DOI: 10.1089/jpm.2011.0109

Dyspnea Review for the Palliative Care Professional: Assessment, Burdens, and Etiologies

Arif H. Kamal, M.D.,¹ Jennifer M. Maguire, M.D.,² Jane L. Wheeler, MSPH,¹
David C. Currow, M.P.H.,³ and Amy P. Abernethy, M.D.^{1,3}

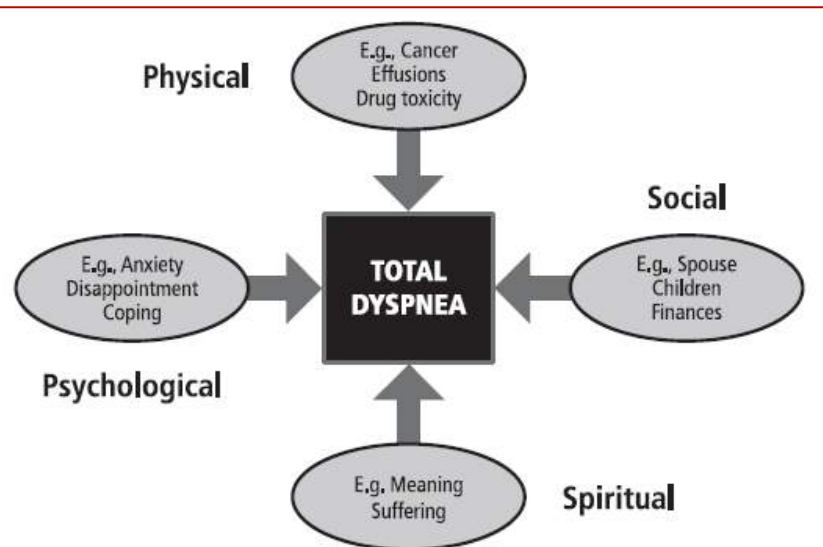


FIG. 1. Elements of the biopsychosocial model of "total dyspnea."

Depression, sadness

Yearning (for peace, rest, forgiveness, etc)

Social issues (with family, community, etc)

Physical problems

Nonacceptance or spiritual distress

Economic or financial distress

Anxiety, anger

FIG. 2. Mnemonic of the biopsychosocial elements of dyspnea.

**Non è solo il dolore ad
essere «totale»...**

Dispnea



Interventi
specifici

REVIEW

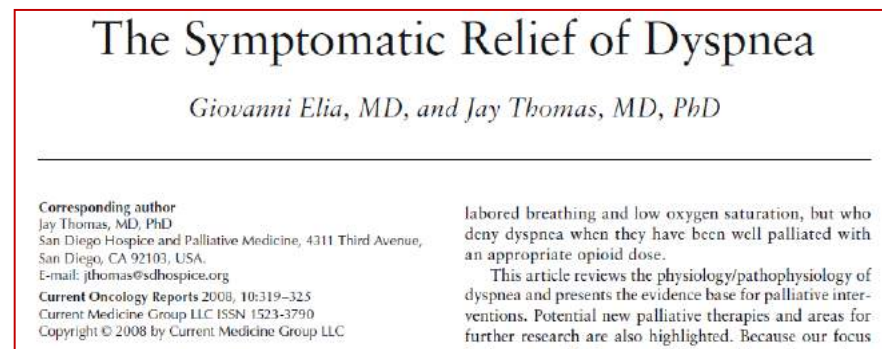
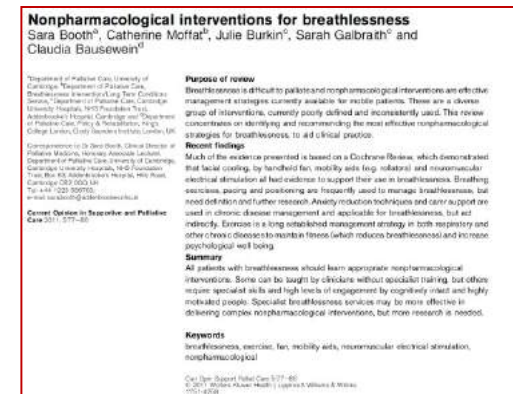
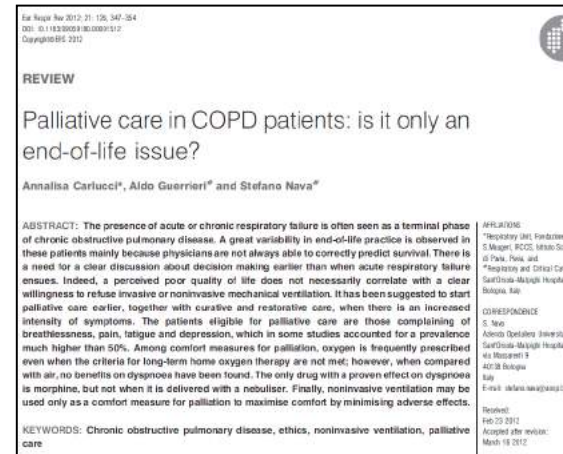
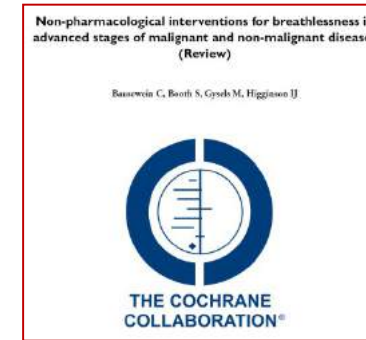
www.nature.com/clinicalpractice/onc

The etiology and management of intractable breathlessness in patients with advanced cancer: a systematic review of pharmacological therapy

Sara Booth*, Shakeeb H Moosavi and Irene J Higginson

Table 1 The causes of breathlessness in advanced cancer.	
Causes in patients with cancer	Specific management
Infection/pneumonia	Antibiotics and other standard therapies when appropriate
Comorbid conditions associated with increased dead space, e.g. pulmonary vascular disease, COPD	Optimize medical management of pre-existing/ coincident conditions
Deconditioning (lack of exercise)	Rehabilitation (see text)
Anemia	Erythropoietin, blood transfusion where appropriate
Cachexia possibly leading to breathlessness by an unknown mechanism	Prevention of cachexia: activity plus possibly some dietary supplements
Comorbidities associated with respiratory muscle weakness, e.g. myasthenia gravis	Optimum treatment of all comorbid conditions
Respiratory muscle syndromes associated with cancer, e.g. Lambert–Eaton syndrome	Treatment of underlying disease is most effective treatment
COPD associated with lung (and therefore thoracic) hyperinflation, leading to inefficiency of respiratory muscles	Optimum treatment and palliation of COPD
Lymphangitis carcinomatosa	Treatment of cancer, often palliative care, although trial of high-dose steroids (60 mg prednisolone then taper) often used
Tumor obstructing an airway, pleural effusions, pleural disease, e.g. mesothelioma	Standard oncological/surgical treatment according to patient's condition, e.g. radiotherapy and/or stenting, etc.
Fibrosis following pulmonary emboli, radiotherapy, chemotherapy (e.g. bleomycin)	Prevention of fibrosis where possible by early standard intervention in these conditions (e.g. anticoagulation or steroids) or prevention by surveillance during cancer therapy and careful control of chemoradiation dosage
Conditions affecting the compliance of the chest wall/ diaphragm, such as hepatomegaly/ascites splinting diaphragm, pleural disease, e.g. mesothelioma, or chest wall infiltration by tumor	Treat as appropriate
Comorbid conditions, e.g. asthma, COPD, interstitial lung disease	Ensure optimum treatment of comorbid conditions
Pulmonary congestion, e.g. from SVCO, heart failure, pulmonary emboli, pericardial effusion	Standard therapy for underlying cancer or treatment of complication of cancer, prevention where possible (e.g. LMWH in high-risk patients)
Hypoxia is a consequence of many conditions associated with cancer including pulmonary emboli, pleural effusions, lymphangitis carcinomatosa, diaphragmatic splinting (e.g. in ascites or hepatomegaly), infections	Assess contribution of hypoxia to breathlessness in that individual and treat conditions as appropriate
Anxieties associated with dyspneic episode reminding the patient they have cancer and are very ill: ▪ Anxiety of dying gasping for breath ▪ Fear/anxiety provoked by idea that breathlessness is in itself harmful ▪ Fear/anxiety because breathlessness at some point may be uncontrollable ▪ Fear/anxiety provoked by the feeling of being breathless ▪ Memory of relative dying with unrelieved breathlessness	Anxiety management using the following alone or in combination: ▪ Nonpharmacological anxiety management strategies (see text) ▪ Pharmacological management of fear and anxiety by phenothiazines, butyrophenones, or benzodiazepines ▪ Cognitive approaches such as cognitive behavioral therapy or education ▪ Availability of clinicians skilled in the management of the symptom
Abbreviations: COPD, chronic obstructive pulmonary disease; LMWH, low-molecular-weight heparin; SVCO, superior vena cava obstruction.	

Dispnea



labored breathing and low oxygen saturation, but who deny dyspnea when they have been well palliated with an appropriate opioid dose.

This article reviews the physiology/pathophysiology of dyspnea and presents the evidence base for palliative interventions. Potential new palliative therapies and areas for further research are also highlighted. Because our focus

Authors' conclusions

Breathing training, walking aids, NMES and CWV appear to be effective non-pharmacological interventions for relieving breathlessness in advanced stages of disease.

Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases (Review)

Bausewein C, Booth S, Gysels M, Higginson IJ



This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2011, Issue 5

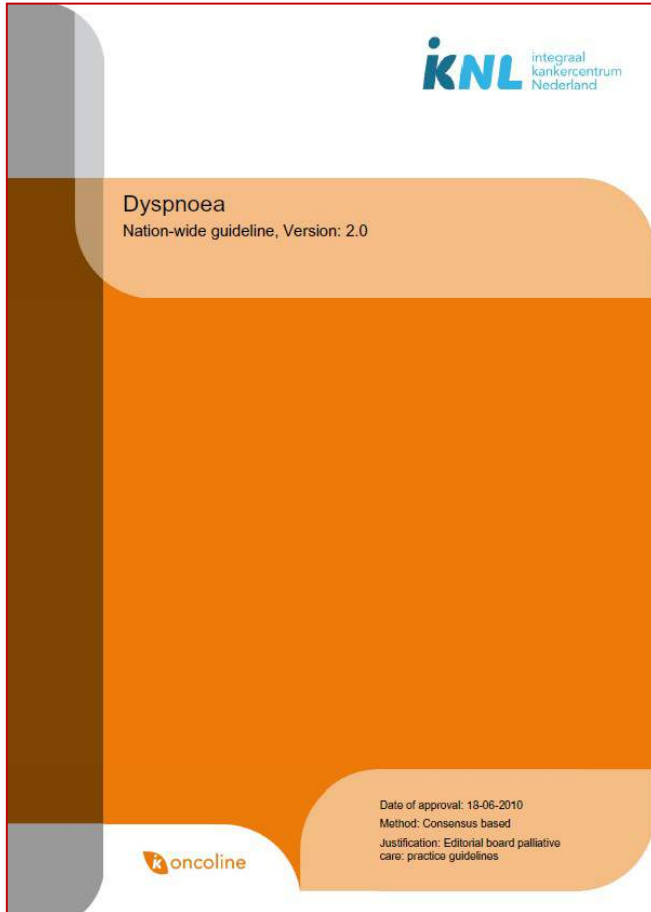
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Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases (Review)
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**Evidenze di efficacia (assai deboli,
nel paziente oncologico...)**

- **Ventilatore (stimolazione della branca mascellare del nervo trigemino)**
- **Fisioterapia respiratoria (respirazione diaframmatica)**
- **Tecniche di rilassamento muscolare**
- **Autoipnosi**
- **Supporto psico-sociale**



INDICAZIONI

- **Broncospasmo**
- **Sindrome della cava superiore**
- **Linfangite carcinomatosa**
- **BPCO e fibrosi polmonare**

**Attenzione alla miopatia
da steroidi ed agli effetti
psicomimetici!**

Miopatia da steroidi, con coinvolgimento della muscolatura respiratoria



THE BASOPHIL ADENOMAS OF THE PITUITARY BODY* AND THEIR CLINICAL MANIFESTATIONS (PITUITARY BASOPHILISM)¹

HARVEY CUSHING, M.D.

Professor of Surgery, Harvard Medical School

Introduction. In a long since superseded monograph on the pituitary body and its disorders, published in 1912, a section was devoted to a group of cases which showed peculiar and sundry polyglandular syndromes. It was stated at the time that the term "polyglandular syndrome" implied nothing more than that secondary functional alterations occur in the ductless-gland series whenever the activity of one of the glands becomes primarily affected; and further, that the term, as employed, was restricted to those cases in which it was difficult to tell where the initial fault lay.

That a primary derangement of the pituitary gland, whether occurring spontaneously or experimentally induced, was particularly prone to cause widespread changes in other endocrine organs was appreciated even at that early day, and it was strongly suspected that this centrally placed and well protected structure in all probability represented the master-gland of the endocrine series. The multiglandular hyperplasias of acromegaly, so evident in the thyroid gland and adrenal cortex, were already known, and the no less striking atrophic alterations in these same glands brought about by the counter state of pituitary insufficiency were coming to be equally well recognized. But in spite of these hopeful signs, we were still groping blindly for an explanation of many other disorders, obviously of endocrine origin, like those associated with pineal, parathyroid or suprarenal tumors. Out of this obscurity, those seriously interested in the subject have, step by step, been feeling their way in spite of pitfalls and stumbling blocks innumerable.

¹ The subject matter of this paper was ventilated at the New York Academy of Medicine, January 5, 1932; at the Yale Medical School, February 24, 1932, and at the Johns Hopkins Hospital Medical Society, February 29, 1932.

* By the kind permission of The Johns Hopkins Press, pages 180 and 181 of this issue of the *Annals* are facsimiles of the title page and a concluding page from Cushing's review of his cases published in 1932 in the *Bulletin of the Johns Hopkins Hospital*, vol. 50, pages 137 *et seq.*

Dispnea

REVIEW

Mechanisms of glucocorticoid-induced myopathy

O Schakman, H Gilson and J P Thissen

Unité de Diabétologie et Nutrition, Faculté de Médecine, Université Catholique de Louvain, 54 Avenue Hippocrate, B-1200 Brussels, Belgium
(Correspondence should be addressed to J P Thissen; Email: jeanpaul.thissen@ucclouvain.be)

Abstract

Glucocorticoid-induced muscle atrophy is characterized by fast-twitch or type II muscle fiber atrophy illustrated by decreased fiber cross-sectional area and reduced myofibrillar protein content. Muscle proteolysis, in particular through the ubiquitin-proteasome system (UPS), is considered to play a major role in the catabolic action of glucocorticoids. The stimulation by glucocorticoids of the UPS is mediated through the increased expression of several atrogenes (genes involved in atrophy), such as atrogin-1 and MuRF-1, two ubiquitin ligases involved in the targeting of protein to be degraded by the proteasome machinery. Glucocorticoids also exert an anti-anabolic action by blunting muscle protein synthesis. These changes in protein turnover may result from changes in the production of two growth factors which control muscle mass, namely IGF-1 and myostatin respectively

anabolic and catabolic toward the skeletal muscle. The decreased production of IGF-1 as well as the increased production of myostatin have been both demonstrated to contribute to the muscle atrophy caused by glucocorticoids. At the molecular level, IGF-1 antagonizes the catabolic action of glucocorticoids by inhibiting, through the PI3-kinase/Akt pathway, the activity of the transcription factor FOXO, a major switch for the stimulation of several atrogenes. These recent progress in the understanding of the glucocorticoid-induced muscle atrophy should allow to define new therapies aiming to minimize this myopathy. Promising new therapeutic approaches for treating glucocorticoid-induced muscle atrophy are also presented in this review.

Journal of Endocrinology (2006) 192, 1–10

Joint Bone Spine 78 (2011) 41–44.



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Review

Glucocorticoid-induced myopathy

Rosa Maria Rodrigues Pereira*, Jozélio Freire de Carvalho

Rheumatology Division, Faculdade de Medicina, Universidade de São Paulo, Avenida Dr. Arnaldo, 455, 3 andar, sala 3105, São Paulo, 01246-903, Brazil

ARTICLE INFO

Article history:
Accepted 3 February 2010
Available online 14 May 2010

Keywords:
Myopathy
Glucocorticoid
Muscle weakness
Muscle
Type II fiber atrophy

ABSTRACT

Glucocorticoid-induced myopathy, characterized by muscle weakness without pain, fatigue and atrophy, is an adverse effect of glucocorticoid use and is the most common type of drug-induced myopathy. This muscle disturbance has a frequency of 60%, and it has been most often associated with fluorinated glucocorticoid preparations. Glucocorticoids have a direct catabolic effect on muscle, decreasing protein synthesis and increasing the rate of protein catabolism leading to muscle atrophy. In clinical practice, it is important to differentiate myopathy due to glucocorticoid from muscle inflammatory diseases. The treatment is based on reduction or, if possible, on discontinuation of the steroid. Fluorinated glucocorticoids such as dexamethasone should be replaced with nonfluorinated glucocorticoids such as prednisone. Other experimental treatments may be tried such as IGF-1, branched-chain amino acids, creatine, androgens such as testosterone, nandrolone and dehydroepiandrosterone (DHEA), and glutamine.

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LA MIOPATIA DA STEROIDI....

È la più frequente miopatia indotta da farmaci

Compare in circa il 60% dei pazienti in trattamento e non risparmia la muscolatura respiratoria

Gli anziani, i pazienti fisicamente inattivi e quelli oncologici sono maggiormente predisposti

È più frequentemente determinata dai composti fluorinati (desametasone, betametasone) che dai non fluorinati (prednisone, metilprednisolone)

Pur senza una rigida correlazione dose/effetto, si manifesta più spesso con posologie sostenute

Il trattamento consiste nella riduzione graduale della posologia sino a sospensione (se possibile) e/o “rotazione” a composti non fluorinati

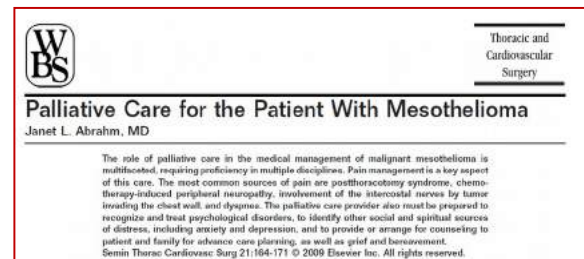
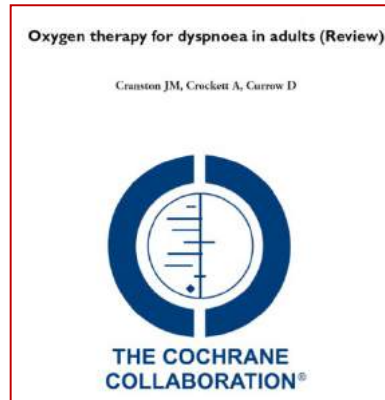
Sono stati tentati trattamenti sperimentali con IGF-1, aminoacidi ramificati, androgeni (testosterone, nandrolone, DHEA), glutamina, attività fisica, con risultati dubbi. Si tratta però di interventi per la maggior parte improponibili in un contesto di cure palliative

Dispnea



O2 terapia

Dispnea



Nessuno nega il valore “simbolico” dell'O₂, però il paziente dispnoico può non essere ipoossico (componente ansiosa) o viceversa (meccanismi di compenso)...

- **Mancano prove consistenti nel sostenere con forza l'uso dell'O₂ con finalità sintomatica (vs aria)**
- **Gli studi disponibili (più numerosi, nel paziente non oncologico) evidenziano la possibilità di ottenere un beneficio sintomatico SOLTANTO NEL PAZIENTE IPOSSICO, A RIPOSO E SOTTO SFORZO, E CON DISPNEA SEVERA**
- **Può essere opportuno un tentativo a breve termine (qualche giorno), valutandone i benefici, con un flusso di 1-5 l/min**
- **Nel caso, la maschera garantisce una minore dispersione dell'O₂, ma è poco tollerata dalla maggior parte dei pazienti in fase avanzata di malattia**
- **Vi sono studi randomizzati che evidenziano la superiorità della morfina nel controllare la dispnea, rispetto all'O₂, in pazienti**

Dispnea



**Benzodiazepine ed
altri farmaci
psicotropi**

Dispnea

JOURNAL OF PALLIATIVE MEDICINE
Volume 15, Number 1, 2012
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DOI: 10.1089/jpm.2011.0110

Palliative Care Review
Feature Editor: Vyjayanthi S. Periyakoil

Dyspnea Review for the Palliative Care Professional: Treatment Goals and Therapeutic Options

Arif H. Kamal, M.D.¹, Jennifer M. Maguire, M.D.², Jane L. Wheeler, MSPH¹,
David C. Currow, M.P.H., FRACP³ and Amy P. Abernethy, M.D.^{1,3}

REVIEW

www.nature.com/statelpractice/onc

The etiology and management of intractable breathlessness in patients with advanced cancer: a systematic review of pharmacological therapy

Sara Booth*, Shakeeb H Moosavi and Irene J Higginson

Support Care Cancer (2008) 16:329–337
DOI 10.1007/s00520-007-0389-6

REVIEW ARTICLE

The management of dyspnea in cancer patients: a systematic review

Raymond Viola · Cathy Kiteley · Nancy S. Lloyd ·
Jean A. Mackay · Julie Wilson · Rebecca K. S. Wong ·
Supportive Care Guidelines Group of the Cancer Care
Ontario Program in Evidence-Based Care

Received: 1 May 2007 / Accepted: 5 December 2007 / Published online: 24 January 2008
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Applicability and generalizability of palliative interventions for dyspnoea: one size fits all, some or none?

Marie Williams

School of Health Sciences, University of South
Australia, Adelaide, South Australia, Australia

Correspondence to: Marie Williams, PhD, B. App Sc.
(Physio), Associate Professor, School of Health
Sciences, University of South Australia, City East
Campus, North Terrace, Adelaide, SA 5000, Australia
Tel: +61 08 8302 2554; fax: +61 08 8302 2766;
e-mail: mariewilliams@unisa.edu.au

Current Opinion in Supportive and Palliative
Care 2011, 5:92–100

Purpose of review

Determining which palliative interventions are appropriate within and between groups
remains difficult because of the lack of prospective studies and heterogeneity in
dyspnoea control, assessment and reporting. This review presents an evaluation of
dyspnoea theories, summarizes literature published during 2010 concerning
intervention effectiveness between conditions and highlights the lag between emerging
research evidence and dyspnoea assessments in clinical trials.

Recent findings

With few exceptions, first-line pharmacological agents prescribed to modify the disease
with palliation of dyspnoea as consequence were unlikely to be generalizable between
conditions and contexts. Two agents (supplemental oxygen in people without resting
hypoxemia and benzodiazepines in advanced disease) did not significantly reduce
dyspnoea. Exercise training palliated dyspnoea across conditions and contexts. Short-
term reductions in dyspnoea were reported for a variety of adjunctive strategies
(breathing training, electrophysical agents and psychological approaches).

Summary

Multiple interventions exist for palliation of dyspnoea in different contexts. The majority of
studies assessed emotional and behavioural consequences of dyspnoea rather than
dyspnoea sensation (intensity, sensory quality, unpleasantness). As a more detailed
understanding of the mechanisms leading to perceptions of dyspnoea evolve, a 'back to
basics' strategy for clinical assessment might provide a means of determining which
interventions can be generalized or are best suited to various forms of dyspnoea.

Keywords

dyspnoea, management strategies, palliation, sensation of breathlessness

Cur Opin Support Palliat Care 5:92–100
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1753–4020



The Symptomatic Relief of Dyspnea

Giovanni Elia, MD, and Jay Thomas, MD, PhD

Corresponding author

Jay Thomas, MD, PhD
San Diego Hospice and Palliative Medicine, 4311 Third Avenue,
San Diego, CA 92103, USA
E-mail: jthomas@sdhospice.org

Current Oncology Reports 2008, 10:319–325
Current Medicine Group LLC ISSN: 1523-3790
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labored breathing and low oxygen saturation, but who
deny dyspnea when they have been well palliated with
an appropriate opioid dose.

This article reviews the physiology/pathophysiology of
dyspnea and presents the evidence base for palliative inter-
ventions. Potential new palliative therapies and areas for
further research are also highlighted. Because our focus

American Thoracic Society Documents

An Official American Thoracic Society Statement: Update on the Mechanisms, Assessment, and Management of Dyspnea

Mark B. Parshall, Richard M. Schwartzstein, Lewis Adams, Robert B. Banzett, Harold L. Manning,
Jean Bourbeau, Peter M. Calverley, Audrey G. Giff, Andrew Harver, Suzanne C. Lareau,
Donald A. Mahler, Paula M. Meek, and Denis E. O'Donnell; on behalf of the ATS Committee on Dyspnea

THIS OFFICIAL STATEMENT OF THE AMERICAN THORACIC SOCIETY (ATS) WAS APPROVED BY THE ATS BOARD OF DIRECTORS, October, 2011.

Dispnea



Authors' conclusions

Since the last version of this review, we have identified one new study for inclusion, but the conclusions remain unchanged. There is no evidence for or against benzodiazepines for the relief of breathlessness in people with advanced cancer and COPD. Benzodiazepines caused more drowsiness as an adverse effect compared to placebo, but less compared to morphine. Benzodiazepines may be considered as a second- or third-line treatment, when opioids and non-pharmacological measures have failed to control breathlessness. There is a need for well-conducted and adequately powered studies.

Palliative Care in advanced Lung Disease

Benzodiazepines:

May relieve anxiety/ panic associated with severe breathlessness, but are less effective than opioids for breathlessness and should be a 3rd line treatment for patients with symptoms unresponsive to non-pharmacological measures and opioids.

- **Beneficio limitatissimo e molto discusso**
- **Possono essere indicate quando coesiste importante componente ansiosa e/o per favorire il sonno**
- **Non possono essere considerate la monoterapia di prima scelta della dispnea cronica (contrariamente a quanto avviene di solito...), anche per gli effetti avversi, come la sonnolenza**
- **Viceversa, rivestono un ruolo fondamentale NELLA SEDAZIONE PROFONDA TEMPORANEA (CRISI ASFITTICA) E CONTINUA (DISPNEA REFRATTARIA)**

Dispnea



Oppiacei

Dispnea

Opioids for the palliation of breathlessness in advanced disease and terminal illness. (Review)

Jennings AL, Davies AN, Higgins JPT, Antunes-Cabre J, Broadley KE



THE COCHRANE
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REVIEW

www.cochrane.org/10.1002/rev.10000

The etiology and management of intractable breathlessness in patients with advanced cancer: a systematic review of pharmacological therapy

Sara Booth¹, Shakeeb H Moosavi¹ and Irene J Higginson

doi:10.1002/rev.10000

www.cochrane.org/10.1002/rev.10000

REVIEW

Palliative care in COPD patients: is it only an end-of-life issue?

Kristina Carter¹, Aldo Gasmon² and Stephen Hunt³

ABSTRACT: The presence of acute or chronic respiratory failure is often seen as a terminal phase of chronic obstructive pulmonary disease. A great variability in end-of-life practice is observed in these patients likely because physicians are not always able to identify predictability. There is a need for a clear discussion about disease severity rather than about respiratory failure status. Indeed, a perceived poor quality of the data not necessarily correlates with a clear difference in disease severity or end-of-life practice. There have been suggestions to date that palliative care is often together with curative and rehabilitative care, when there is an increased severity of symptoms. The patients eligible for palliative care are those completing or completing palliative care, those with end-of-life issues, and those with end-of-life issues much higher than 50%. Amongst current measures for palliation, oxygen is frequently prescribed even when the criteria for long-term home oxygen therapy are not met. However, when compared with air, no benefit in oxygenation has been found. The only drug with a proven effect on dyspnea is morphine, but not when it is delivered with a nebulizer. Finally, non-pharmacological measures may be used only as a constant measure for palliation to enhance comfort by minimizing adverse effects.

KEYWORDS: Chronic obstructive pulmonary disease, illness, non-pharmacological, palliative care

INTRODUCTION: The presence of acute or chronic respiratory failure is often seen as a terminal phase of chronic obstructive pulmonary disease. A great variability in end-of-life practice is observed in these patients likely because physicians are not always able to identify predictability. There is a need for a clear discussion about disease severity rather than about respiratory failure status. Indeed, a perceived poor quality of the data not necessarily correlates with a clear difference in disease severity or end-of-life practice. There have been suggestions to date that palliative care is often together with curative and rehabilitative care, when there is an increased severity of symptoms. The patients eligible for palliative care are those completing or completing palliative care, those with end-of-life issues, and those with end-of-life issues much higher than 50%. Amongst current measures for palliation, oxygen is frequently prescribed even when the criteria for long-term home oxygen therapy are not met. However, when compared with air, no benefit in oxygenation has been found. The only drug with a proven effect on dyspnea is morphine, but not when it is delivered with a nebulizer. Finally, non-pharmacological measures may be used only as a constant measure for palliation to enhance comfort by minimizing adverse effects.

KEYWORDS: Chronic obstructive pulmonary disease, illness, non-pharmacological, palliative care

VOLUME 26 • NUMBER 14 • MAY 10 2008

JOURNAL OF CLINICAL ONCOLOGY

REVIEW ARTICLE

Interventions for Alleviating Cancer-Related Dyspnea: A Systematic Review

Irit Ben-Aharon, Anat Gafner-Gvili, Mical Paul, Leonard Leibovici, and Salomon M. Stemmer



JOURNAL OF PALLIATIVE MEDICINE
Volume 15, Number 1, 2012
© Mary Ann Liebert, Inc.
DOI: 10.1089/jpm.2011.0110

Palliative Care Review

Feature Editor: Vjeyanthi S. Periyakoti

Dyspnea Review for the Palliative Care Professional: Treatment Goals and Therapeutic Options

Arif H. Kamal, M.D.¹, Jennifer M. Maguire, M.D.², Jane L. Wheeler, MSPH¹,
David C. Currow, M.P.H., FRACP³ and Amy P. Abernethy, M.D.^{1,3}

American Thoracic Society Documents

An Official American Thoracic Society Statement: Update on the Mechanisms, Assessment, and Management of Dyspnea

Mark B. Parshall, Richard M. Schwartzstein, Lewis Adams, Robert B. Banzett, Harold L. Manning, Jean Bourbeau, Peter M. Calverley, Audrey G. Giff, Andrew Harver, Suzanne C. Lareau, Donald A. Mahler, Paula M. Meek, and Denis E. O'Donnell; on behalf of the ATS Committee on Dyspnea

THIS OFFICIAL STATEMENT OF THE AMERICAN THORACIC SOCIETY (ATS) WAS APPROVED BY THE ATS BOARD OF DIRECTORS, OCTOBER, 2011

CHEST

Official publication of the American College of Chest Physicians

American College of Chest Physicians Consensus Statement on the Management of Dyspnea in Patients With Advanced Lung or Heart Disease

Donald A. Mahler, Paul A. Sealeck, Christopher G. Harrod, Joshua O. Beroff, Virginia Carter-Kohman, J. Randall Curtis, Harold L. Manning, Richard A. Muzanski, Basil Verkey, Margaret Campbell, Edward R. Carter, Jun Nishimura, Chong E. Wesley, John Hansen-Flaschen, Denis E. O'Donnell, and Alexander Walker

Chest 2010;137:674-691

ACP
American College of Physicians
GUIDELINES

CLINICAL GUIDELINES

Evidence-Based Interventions to Improve the Palliative Care of Pain, Dyspnea, and Depression at the End of Life: A Clinical Practice Guideline from the American College of Physicians

Ann Casper, MD, PhD, MPH, Vanessa Stone, MD, Paul Stohler, MD, PhD, Donald E. Coker Jr., MD, MPH, MBA,
Thomas Conz, Jr., MD, MPH, and Douglas L. Cramer, MD, MS, for the Clinical Efficacy Assessment Subcommittee of the American College of Physicians

Recommendation 1: In patients with serious illness at the end of life, clinicians should regularly assess patients for pain, dyspnea, and depression. (Grade: strong recommendation, moderate quality of evidence.)

Recommendation 2: In patients with serious illness at the end of life, clinicians should use therapies of proven effectiveness to manage pain. For patients with cancer, the inclusion of nonsteroidal anti-inflammatory drugs, opioids, and biologic therapies. (Grade: strong recommendation, moderate quality of evidence.)

Recommendation 3: In patients with serious illness at the end of life, clinicians should use therapies of proven effectiveness to manage dyspnea, which include oxygen in patients with unmet oxygen and oxygen for short-term relief of hypoxemia. (Grade: strong recommendation, moderate quality of evidence.)

Recommendation 4: In patients with serious illness at the end of life, clinicians should use therapies of proven effectiveness to manage depression. For patients with cancer, the inclusion of antidepressants, selective serotonin reuptake inhibitors, or psychological intervention. (Grade: strong recommendation, moderate quality of evidence.)

Recommendation 5: Clinicians should ensure that advance care planning, including completion of advance directives, occurs for all patients with serious illness. (Grade: strong recommendation, low quality of evidence.)

Ann Intern Med 2008;148:140-146
For author affiliations, see end of text.

www.acponline.org

Advances in the pharmacological management of breathlessness

David C. Currow¹, Alicia M. Ward² and Amy P. Abernethy^{1,3}

Purpose of review: To explore advances in the pharmacological management of refractory breathlessness and the physiological evidence for treatments.

Recent findings: The evidence for the role of oral and parenteral opioids in the reduction of breathlessness continues to strengthen from individual studies and from systematic reviews. Importantly, more data are emerging about a lack of benefit in oxygenation or carbon dioxide retention with opioid therapy. In healthy volunteers and those with refractory dyspnea, reduced breathlessness appears to be worthy of further investigation with adequately powered phase III studies.

Summary: Opioids prescribed regularly can help to predictably and safely reduce breathlessness for people with a range of end-stage illnesses.

Keywords: dyspnea, dyspnea drug therapy, benzodiazepines, morphine, palliative care

Currow DC, Ward AM, Abernethy AP (2012) Advances in the pharmacological management of breathlessness. *Journal of Palliative Medicine* 15:1-10.

Ann Oncology, 2012; 23: 996-1008

informa
healthcare

ORIGINAL ARTICLE

Interventions for alleviating cancer-related dyspnea: A systematic review and meta-analysis

IRIT BEN-AHARON^{1,2}, ANAT GAFNER-GVILI^{1,2}, LEONARD LEBBOVICI^{1,3} & SALOMON M. STEMMER^{1,3}

¹Institute of Oncology, ²Department of Cancer Rehabilitation, ³Department of Medicine, ⁴Rabin Medical Center, Petach Tikva, Israel, and ⁵Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

Support Care Cancer (2008) 16:329-337
DOI 10.1007/s00262-007-6389-6

REVIEW ARTICLE

The management of dyspnea in cancer patients: a systematic review

Raymond Viola • Cathy Kiteley • Nancy S. Lloyd • Jean A. Mackay • Julie Wilson • Rebecca K. S. Wong • Supportive Care Guidelines Group of the Cancer Care Ontario Program in Evidence-Based Care

Received: 1 May 2007 / Accepted: 5 December 2007 / Published online: 24 January 2008
© Springer-Verlag 2007

Molta strada è stata percorsa dagli studi di Bruera negli anni '90...

- Sono oramai numerosi gli studi a sostegno dell'efficacia degli oppiacei (in particolare della morfina) per via orale o parenterale nel trattamento sintomatico della dispnea (al contrario della via inalatoria)
- **LA MORFINA È IL FARMACO CON MAGGIOR EVIDENZA DI EFFICACIA NEL TRATTAMENTO DELLA DISPNEA NEL PAZIENTE ONCOLOGICO E NON ONCOLOGICO IN FASE AVANZATA**
- Il farmaco è assolutamente sicuro se si rispettano le “buone pratiche” di titolazione ed uso degli oppiacei. **SE RISPETTATE QUESTE CONDIZIONI, IL TIMORE DELLA DEPRESSIONE RESPIRATORIA È INFONDATA**
- Probabilmente sono efficaci anche altri oppiacei maggiori (fentanyl, idromorfone, ossicodone, metadone), ma mancano prove sufficienti a sostegno (in genere non vale la proprietà “transitiva”...)

LA MORFINA NEL TRATTAMENTO SINTOMATICO DELLA DISPNEA

MECCANISMO D'AZIONE

- ❖ Riduce la risposta ventilatoria all'ipossia/ipercapnia ed all'esercizio fisico
- ❖ Riduce il precarico cardiaco
- ❖ Induce una riduzione della frequenza respiratoria rendendo più efficiente la ventilazione
- ❖ Riduce la percezione della dispnea e l'ansia correlata
- ❖ Nessun problema di depressione respiratoria, se usata correttamente

EFNS guidelines on the Clinical Management of Amyotrophic Lateral Sclerosis (MALS) – revised report of an EFNS task force

The EFNS Task Force on Diagnosis and Management of Amyotrophic Lateral Sclerosis: Peter M. Andersen^a, Sharon Abrahams^b, Gian D. Borasio^c, Mamede de Carvalho^d, Adriano Chio^e, Philip Van Damme^f, Orla Hardiman^g, Katja Kollewe^h, Karen E. Morrisonⁱ, Susanne Petri^j, Pierre-François Pradat^k, Vincenzo Silani^l, Barbara Tomik^l, Maria Wasner^m and Markus Weberⁿ

^aUmeå University, Umeå, Sweden; ^bUniversity of Edinburgh, Edinburgh, UK; ^cCentre Hospitalier Universitaire Vaudois, University of Lausanne, Lausanne, Switzerland; ^dHospital de Santa Maria, Lisbon, Portugal; ^eUniversity of Turin and San Giovanni Hospital, Turin, Italy; ^fUniversity of Leuven and VIB, Leuven, Belgium; ^gTrinity College and Beaumont Hospital, Dublin, Ireland; ^hMedizinische Hochschule Hannover, Germany; ⁱSchool of Clinical and Experimental Medicine, University of Birmingham and Queen Elizabeth Hospital, Birmingham, UK; ^jHôpital de la Salpêtrière, Paris, France; ^kUniversity of Milan Medical School, Milan, Italy; ^lJagiellonian University Medical College, Krakow, Poland; ^mMunich University Hospital, Munich, Germany; and ⁿKantonsspital St Gallen and University Hospital Basel, Basel, Switzerland

12. The medical treatment of intermittent dyspnoea should involve:

a for short dyspnoeic bouts: relieve anxiety and give lorazepam 0.5–2.5 mg sublingually;

b for longer phases of dyspnoea (> 30 min): give morphine 2.5 mg orally or s.c. (GCPP)

13. For the medical treatment of chronic dyspnoea, start with morphine 2.5 mg orally four to six times daily. For severe dyspnoea, give morphine s.c. or as an i.v. infusion. Start with 0.5 mg/h and titrate. If needed, add midazolam (2.5–5 mg) or diazepam for nocturnal symptom control and to relieve anxiety (GCPP).

TABLE 4
Suggested protocol for managing dyspnea with opioid therapy in advanced chronic obstructive pulmonary disease patients

- Initiate opioid therapy with oral immediate-release morphine syrup – titrate slowly at weekly intervals over a 4- to 6-week period
- Start therapy with morphine 0.5 mg orally twice daily for 2 days, and then increase to 0.5 mg orally every 4 h while awake for remainder of week 1
- If tolerated and indicated, increase to morphine 1.0 mg orally every 4 h while awake in week 2, increasing by 1.0 mg/week or 25% dosage increments/week until the lowest effective dose that appropriately manages the dyspnea is achieved
- Once a stable dosage is achieved (ie, no significant dose change for 2 weeks and dyspnea managed), a sustained-release preparation at a comparable daily dose could be considered for substitution
- If patients experience significant opioid-related side effects such as nausea or confusion, substitution of an equipotent dose of oral hydromorphone could be considered (1 mg hydromorphone = 5 mg morphine)
- Stool softeners and laxatives should be routinely offered to prevent opioid-associated constipation

Adapted from references 1, 109 and 115

SPECIAL ARTICLE

Managing dyspnea in patients with advanced chronic obstructive pulmonary disease: A Canadian Thoracic Society clinical practice guideline

Darcy D Marciniuk MD FRCPC FCCP¹*, Donna Goodridge RN PhD¹, Paul Hernandez MDCM FRCP²*, Graeme Rocker MHS DM FRCPC FCCP³, Meyer Balter MD FRCPC FCCP⁴*, Pat Bailey RN PhD⁴, Gordon Ford MD FRCP⁵*, Jean Bourbeau MD MS, FRCP⁶*, Denis E O'Donnell MD FRCP FRCP⁷*, Francois Maltais MD FRCP⁸*, Richard A Mulinski MD MSHS MCR FCCP⁹*, Andrew J Cave MB ChB FCFP¹⁰*, Irvin Mayers MD FRCP¹⁰*, Vicki Kennedy RN BN CRE¹¹, Thomas K Oliver BA^{12,13}, Candice Brown MSc CEP¹², Canadian Thoracic Society COPD Committee Dyspnea Expert Working Group

DD Marciniuk, D Goodridge, P Hernandez, et al; Canadian Thoracic Society COPD Committee Dyspnea Expert Working Group. Managing dyspnea in patients with advanced chronic obstructive pulmonary disease: A Canadian Thoracic Society clinical practice guideline. Can Respir J 2011;18(2):69-78.

La prise en charge de la dyspnée chez les patients atteints de maladie pulmonaire obstructive chronique avancée : des directives cliniques de la Société canadienne de thoracologie

La dyspnée est un symptôme courant de maladie pulmonaire obstructive

Review Article

Recommendations for Bowel Obstruction With Peritoneal Carcinomatosis

Guillemette Laval, MD, Blandine Marcelin-Benazech, MD, Frédéric Guirimand, MD, Laure Chauvenet, MD, Laure Copel, MD, Aurélie Durand, MD, Eric Francois, MD, Martine Gabolde, MD, Pascale Mariani, MD, Christine Rebischung, MD, Vincent Servois, MD, Eric Terrebbonne, MD, and Catherine Arvieux, MD, on behalf of the French Society for Palliative Care, with the French Society for Digestive Surgery, the French Society for Gastroenterology, the French Society for Digestive Cancer, and the French Association for Supportive Care in Oncology

Palliative and Supportive Care Mobile Unit (G.L.), Departments of Hepato-Gastroenterology (A.D.), Digestive Surgery (C.A.) and Oncology Day Hospital (C.R.), University Hospital Center, Grenoble; Palliative and Supportive Care Mobile Unit (B.M.-B.), HCL, Lyon; Medical House Jeanne Garnier (E.G.), Department of Medical Oncology (L.Ch.), Hospital Hôtel Dieu, APHP; Departments of Medical Oncology (L.Co.), Digestive Surgery (P.M.) and Radiology (V.S.), Institute Curie, Paris; Antoine Lacassagne Cancer Center (E.F.), Nice; Palliative Care Unit (M.G.), Hospital Paul Brousse, APHP, Villejuif; and Department of Hepato-Gastroenterology (E.T.), Hospital du haut Levêque, Pessac, France

Occlusionne intestinale

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Review Article

Recommendations for Bowel Obstruction With Peritoneal Carcinomatosis

Guillaume Laval, MD, Blaudius Marcello-Bernache, MD, Frederic Guiraud, MD, Laure Charette, MD, Laure Goyet, MD, Aurélie Durand, MD, Eric Trézou, MD, Martine Gohelle, MD, Pascale Mariani, MD, Christine Rebeschung, MD, Vincent Servin, MD, Eric Terribonne, MD, and Catherine Arvisou, MD, on behalf of the French Society for Palliative Care, with the French Society for Digestive Surgery, the French Society for Gastroenterology, the French Society for Digestive Cancer, and the French Association for Supportive Care in Oncology

Palliative and Supportive Care: Main Unit (S.G.), Department of Hepato-Gastroenterology (S.D.), Digestive Surgery (C.A.) and Oncology (M. Mariani) (C.R.), University Hospital Center, General, Palliative and Supportive Care (S.M.B.), HCL, Lyon Medical School, France; Cancer (F.G.), Department of Medical Oncology (L.G.), Hospital Saint Louis, APHP, Department of Medical Oncology (L.G.), Digestive Surgery (P.M.) and Radiology (S.S.), Institut Gustave Roussy, France; Cancer Center (C.A.), Non-Palliative Care Unit (M.G.), Hospital Paul Brousse, APHP, Villejuif; and Department of Hepato-Gastroenterology (F.T.), Hospital de Saint Louis, Paris, France.

Summary. When feasible, endoscopic procedures should be preferred to surgery as they have lower morbi-mortality rates (Grade C). The lesion must be accessible with the endoscopic device.

Table 3 Poor Prognostic Factors for Surgical Treatment of Bowel Obstruction

- Advanced age
- Poor performance status (OMS 3 or 4)
- Poor nutritional state
- Extent of the malignant disease: diffuse peritoneal carcinomatosis, ascites, palpable masses, multiple obstacles on the small bowel...
- Obstruction of the small bowel rather than colic obstruction
- Previous abdominal or pelvic radiotherapy

Summary. NGTs relieve intractable vomiting and gastric distension. They are absolutely necessary in patients with enteral obstruction. NGTs should not be removed if secretions exceed 1 L/24 h as abundant vomiting will result. Physicians should aim to remove the NGT as soon as possible to minimize patient discomfort (expert consensus).

Occlusion intestinale

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Review Article

Recommendations for Bowel Obstruction With Peritoneal Carcinomatosis

Guillaume Laval, MD, Blaudius Marcello-Bernache, MD, Frédéric Guiraud, MD, Laure Charette, MD, Laure Goyet, MD, Aurélie Durand, MD, Eric Trézouin, MD, Martine Gohelle, MD, Pascale Mariani, MD, Christine Rebeschung, MD, Vincent Servot, MD, Eric Terribonne, MD, and Catherine Arvisou, MD, on behalf of the French Society for Palliative Care, with the French Society for Digestive Surgery, the French Society for Gastroenterology, the French Society for Digestive Cancer, and the French Association for Supportive Care in Oncology

Palliative and Supportive Care: Main Unit (G.L.), Department of Hepato-Gastroenterology (B.B.), Digestive Surgery (C.A.) and Oncology Unit Hospital (C.R.), University Hospital Center, Gaudeluc, Palliative and Supportive Care Main Unit (B.M.B.), HCL, Lyon, Medical Research Center (F.G.), Department of Medical Oncology (E.G.), Hospital Saint-Denis, APHP, Department of Medical Oncology (L.G.), Digestive Surgery (P.M.) and Radiology (V.S.), Institut Gustave Roussy, Antoine Lacaze Cancer Center (C.F.), Non-Palliative Care Unit (M.G.), Hospital Paul Brousse, APHP, Villejuif and Department of Hepato-Gastroenterology (E.T.), Hospital de Saint-Louis, Paris, France

Summary Venting gastrostomy can be considered as a long-term alternative to maintain an NGT. It must be considered and indicated promptly providing it is feasible and the patient has agreed to undergo the procedure. Percutaneous endoscopic gastrostomy should be preferred although there are some contraindications, principally ascites. Surgical indications remain rare (experts consensus).

Summary. Even if evidence is lacking, steroid use may be suggested at the time of diagnosis. They should be administered in short courses of 5–10 days to help manage symptoms and resolve the obstruction. The mean dose is 1–4 mg/kg/d for methylprednisolone or equivalent (expert consensus of opinion).

Summary. Butylscopolamine helps to manage vomiting and colicky pain (Grade C). As it is not very expensive, it is frequently used as a first-line treatment. The mean dose is 60–120 mg/24 h (expert consensus). Scopol-

Occlusion intestinale

Journal of Pain and Symptom Management 25

Review Article

Recommendations for Bowel Obstruction With Peritoneal Carcinomatosis

Guillaume Laval, MD, Blaudius Marcello-Bernach, MD, Frédéric Guiraud, MD, Laure Charette, MD, Laure Goyet, MD, Aurélie Durand, MD, Eric Trézouin, MD, Martine Gohelle, MD, Pascale Mariani, MD, Christine Rebeschung, MD, Vincent Servin, MD, Eric Terretouze, MD, and Catherine Arvieux, MD, on behalf of the French Society for Palliative Care, with the French Society for Digestive Surgery, the French Society for Gastroenterology, the French Society for Digestive Cancer, and the French Association for Supportive Care in Oncology

Palliative and Supportive Care: Maiti Ohi (S.G.), Department of Hepato-Gastroenterology (S.D.), Digestive Surgery (C.A.), and Oncology (M. Gohelle) (C.R.), University Hospital Center, Grenoble; Palliative and Supportive Care: Maiti Ohi (S.M.B.), HCL, Lyon; Medical Palliative Care: Maiti Ohi (S.G.), Department of Medical Oncology (S.D.), Hospital Saint-Denis, APHM; Department of Medical Oncology (S.G.), Digestive Surgery (P.M.) and Radiology (S.S.), Institut Gustave Roussy; Institut Louis Pasteur Cancer Center (C.F.), Non-Palliative Care Unit (M.G.), Hospital Paul Brousse, APHM; Virology and Department of Hepato-Gastroenterology (S.T.), Hospital de Saint-Louis, Paris, France

Somatostatin analogues can be considered for the treatment of bowel obstruction with peritoneal carcinomatosis. They are more effective than anticholinergic antisecretory drugs in controlling obstruction-induced vomiting.

Summary. Gastric antisecretory drugs, like PPIs, seem relevant in patients with obstruction or partial obstruction to reduce gastric secretion or bile reflux and relieve upper digestive symptoms (expert consensus of opinion). They should be administered continuously over 24 hours, which is not always feasible in clinical practice. The IV injection of a bolus is the most frequently used (expert consensus). Omeprazole can be administered SC.

Summary. Haloperidol is usually considered as a first-line treatment. If it does not prove effective, physicians can switch to chlorpromazine although it induces sedative side effects. Droperidol also can be an option (expert consensus). Metoclopramide should be administered only in patients with incomplete obstruction (expert consensus). In patients with intractable vomiting, 5-HT₃ receptor antagonists can be considered as a second-line

treatment. They can be administered alone or together (expert consensus).

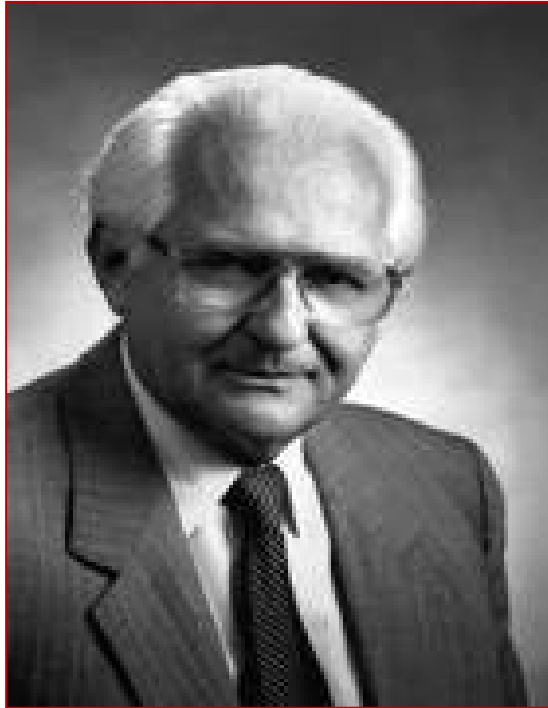
DETERMINAZIONE 18 maggio 2011.

Aggiornamento dell'elenco dei medicinali, istituito con il provvedimento della Commissione Unica del Farmaco dato 20 luglio 2000, erogabili a totale carico del Servizio sanitario nazionale, ai sensi della legge 23 dicembre 1996, n. 648.



Nome Composto	Indicazioni già autorizzate (AIC)	Estensione di indicazione relativa ad usi consolidati sulla base di evidenze scientifiche presenti in letteratura.
Octreotide	Trattamento delle sindromi da tumori endocrini gastro-entero-pancreatici in particolare: - Carcinoidi (sindrome del carcinoide); - VIPomi; - Glucagonomi; - Gastrinomi / sindrome di Zollinger-Ellison (eventualmente in associazione con farmaci anti-H2, con o senza antiacidi); - Insulinomi (per la prevenzione delle crisi ipoglicemiche pre-intervento e terapia di mantenimento); - GRFomi. Per il trattamento sintomatico e la riduzione dei livelli plasmatici di GH e Somatomedina-C nei casi di acromegalia non adeguatamente controllati con terapia chirurgica, radiante o farmacologica (con	Utilizzo nel trattamento di tumori neuroendocrini in fase evolutiva in pazienti non sindromici.
		Utilizzo nel trattamento dell'occlusione intestinale di pazienti con neoplasia avanzata (i.e.ovaio, colon) e carcinosi peritoneale.
		Utilizzo nella diarrea indotta da chemioterapia e resistente a trattamento con loperamide.

**Morfina, ossicodone, butilbromuro di
ioscina, octreotide, aloperidolo
miscelabili nello stesso sistema
d'infusione (elastomero, syringe driver)**



**SINDROME CEREBRALE ORGANICA
TRANSITORIA CARATTERIZZATA DA
COMPROMISSIONE ACUTA DELLA SFERA
ATTENTIVA, COGNITIVA, PSICOMOTORIA
E PERCETTIVA (Lipowski, *Am J
Psychiatry*, 1983)**

Table 1. Essential approaches and practical steps of an intervention programme for the prevention of delirium

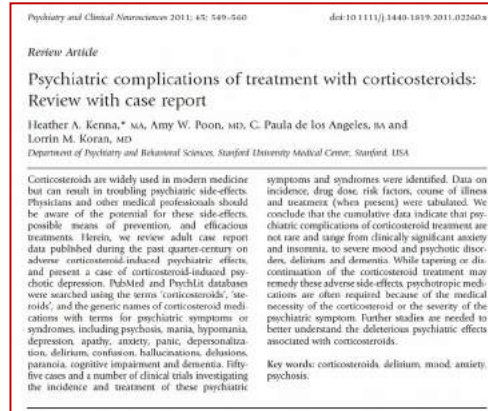
1. Identify high-risk individuals
 - Non-treatable delirium risk factors
 - Old age
 - Underlying dementia
 - Male gender
 - Previous history of delirium
 - Significant medical history
 - Poor eyesight and hearing
 - Frailty
 - Immobility
2. Initiate active preventive strategies (directed at all, but especially targeting those at high risk)
 - Identification and prompt management of any treatable delirium risk factor
 - Additional steps should include
 - Caring in an appropriately lit environment
 - Keeping number of staff caring for each individual to a minimum
 - Make patient familiar with clinical staff
 - Proper introduction and explanation by staff
 - Increase awareness among staff of delirium and its prevention
 - Increase awareness of sundowning syndrome
 - Ensure glasses and hearing aids are brought to hospital
 - Reminders to time and date
 - Review medications
3. Recognise delirium prodromal symptoms such as
 - Sudden and fine changes in mental state
 - Unexplained confusion
 - Shouting
 - Restlessness
 - Emerging hypoactivity
 - Sleeping difficulties

... non guasterebbe una valutazione dello stato cognitivo al momento della presa in carico (CAM, MDAS, intervista ai familiari)

Non vi sono evidenze sufficienti per consigliare un intervento farmacologico preventivo (Tabet, *Int J Geriatr Psychiatry*, 2009)

**Interventi farmacologici – Rivedere la
terapia in atto!
(ad esempio, corticosteroidi)**

Delirium



Riduzione o sospensione a seconda della situazione clinica, della possibilità di *restitutio quo ante*, della prognosi, ecc.

Occorrono studi clinici controllati per rispondere alle seguenti domande: come ridurre la posologia? come valutare il rischio di eventi indesiderati da sospensione?

“Treatment of corticosteroid-induced psychiatric symptoms should start whenever possible with dose reduction or stopping the drug.”

- Appenzeller. *Rheumatol Int* 2008.
- Brown. *J Clin Psychiatry* 2001.
- Lewis. *J Affect Disord* 1983.
- Ling. *Arch Gen Psychiatry* 1981.
- Patten. *Drug Saf* 2000.
- Sirois. *Gen Hosp Psychiatry* 2003.
- Warrington. *Mayo Clin Proc* 2006.

JOURNAL OF PALLIATIVE MEDICINE
Volume 12, Number 5, 2009
© Mary Ann Liebert, Inc.
DOI: 10.1089/jpm.2009.9628

Case Discussions
in Palliative Medicine

Feature Editor: James Hallenbeck

Can “Steroid Switching” Improve Steroid-Induced Psychosis in a Patient with Advanced Cancer?

Nao Okishiro, M.D.,¹ Hitoshi Tanimukai, M.D., Ph.D.,^{2,3}
Satoru Tsuneto, M.D., Ph.D.,⁴ and Noriyuki Ito, M.D.¹

In qualche caso potrebbe avere un ruolo la «rotazione» degli steroidi?



SOCIETÀ ITALIANA DI CURE PALLIATIVE SICP ONLUS

**Raccomandazioni della SICP
sulla
Sedazione Terminale /Sedazione Palliativa**



A CURA DEL GRUPPO DI STUDIO
SU CULTURA ED ETICA AL TERMINE DELLA VITA

Ottobre 2007

“Pratica volta ad alleviare sintomi refrattari riducendo lo stato di coscienza in misura adeguata e proporzionata alle necessità, effettuata quando la morte è attesa entro un lasso di tempo compreso tra poche ore e pochi giorni”

**CON IL CONSENSO DELL'AMMALATO!
(SE COMPETENT)**

SEDAZIONE PALLIATIVA A DOMICILIO: POSSIBILE?

SINTOMI REFRATTARI CHE
HANNO CONDOTTO ALLA
SEDAZIONE
(HOME CARE)

Brief Report

Palliative Sedation in Advanced Cancer
Patients Followed at Home: A Retrospective
Analysis

Sebastiano Mercadante, MD, Giampiero Porzio, MD, Alessandro Valle, MD,
Flavio Fusco, MD, Federica Aielli, MD, Claudio Adile, MD,
and Alessandro Casuccio, BS, on behalf of the Home Care–Italy Group (HOCMI)
Pain Relief and Palliative Care Unit (S.M., G.A.), La Maddalena Cancer Center, Palermo; Palliative
Medicine (S.M.), Department of Anesthesia & Intensive Care and Department of Experimental
Biomedicine and Clinical Neuroscience (A.C.), University of Palermo, Palermo; Home Care Program
(G.P., F.A.), L’Aquila per la vita, L’Aquila; Home Care Program (A.V.), Fondazione FARO, Torino;
and Home Care Program (F.F.), ASL 3 Genovese, Genova, Italy

Table 1
Indications to Start PS

Reasons to Start PS	Frequency	Percentage
Delirium	26	53.1
Delirium/pain	1	2
Delirium/dyspnea	7	14.3
Dyspnea	10	20.4
Dyspnea/O	1	2
Pain	1	2
Pain/dyspnea	2	4.1
Pain/dyspnea/psychological distress	1	2
Total	49	100

PS = palliative sedation; O = other.

Review Article

Palliative Sedation in Patients with Advanced Cancer Followed at Home: A Systematic Review

Sebastiano Mercadante, MD, Giampiero Porzio, MD, Alessandro Valle, MD, Flavio Fusco, MD, Federica Aielli, MD, and Veruska Costanzo, MD, on behalf of the "Home Care Italy" Group
Pain Relief and Palliative Care Unit (S.M.), La Maddalena Cancer Center, Palermo; Palliative Medicine (S.M.), Department of Anesthesia & Intensive Care, University of Palermo, Palermo; Home Care Program (G.P., F.A.), L'Aquila per la Vita, L'Aquila; Home Care Program (A.V.), Fondazione FARO, Torino; Home Care Program (F.F.), ASL 3 Genovese, Genova; and Home Care Program (V.C.), SAMO, Catania, Italy

FREQUENZA (HOME CARE)

Table 1
Published Articles on PS at Home

Authors/Year/Country	Design	Sample of Patients at Home, n (% Sedated)	Principal Drugs and Doses (mg/day)	Principal Indications	Mean Duration (days)
Ventafridda et al./1990/Italy ⁹	Prospective	154 (52)	NA	Dyspnea, pain	2
Peruselli et al./1999/Italy ⁷	Prospective, multicenter	100 (25)	NA	NA	NA
Bulli et al./2007/Italy ⁸	Prospective	1075 (12–14.2)	Neuroleptics Midazolam Opioids	NA	1
Rosengarten et al./2009/Israel ¹⁰	Retrospective	720 (5)	Morphine (12–240) Midazolam (12–144)	Pain, agitation	3
Porzio et al./2010/Italy ¹²	Retrospective	44 (36)	Midazolam (24–48)	Delirium, dyspnea	3.5
Alonso-Babarro et al./2010/Spain ¹¹	Retrospective	245 (12)	Midazolam (58–97)	Delirium, dyspnea	2.5

NA = not available.



In un servizio di cure palliative bisogna preoccuparsi se la sedazione è:

- **Troppo rara (riluttanza a metterla in atto quando indicato)**
- **Troppo frequente (incapacità di controllare i sintomi difficili ma non refrattari)**

FREQUENZA (HOME CARE)

860 *Journal of Pain and Symptom Management*

Vol. 47 No. 5 May 2014

Original Article

Palliative Sedation in Patients With Advanced Cancer Followed at Home: A Prospective Study

Sebastiano Mercadante, MD, Giampiero Porzio, MD, Alessandro Valle, MD, Federica Aielli, MD, and Alessandra Casuccio, BS, on behalf of the Home Care—Italy Group

Pain Relief and Palliative Care Unit (S.M.), La Maddalena Cancer Center, Palermo; Palliative Medicine (S.M.), Department of Anesthesia & Intensive Care and Department of Sciences for Health Promotion “G. D’Alessandro”—Hygiene Section (A.C.), University of Palermo, Palermo; Home Care Program (G.P., F.A.), L’Aquila per la vita, L’Aquila; and Home Care Program (A.V.), Fondazione FARO, Torino, Italy

“The palliative sedation was performed in 24 of 176 patients who died at home (13.6%).”

Elementi indispensabili per effettuare sedazione palliativa a casa:

- **Condivisione ed accordo con la famiglia**
- **Alta intensità assistenziale da parte della mini équipe domiciliare**
- **Disponibilità dei farmaci consigliati dalle linee guida**

Sedazione palliativa

 REGIONE
PIEMONTE

DIREZIONE SANITÀ
Settore ASSISTENZA FARMACEUTICA INTEGRATIVA E PROTESICA
settore.farmaceutico@regione.piemonte.it

Il Dirigente
Torino, 3.11.2016
Protocollo n. 33377 /A1404A
Classificazione 14.120.40

Direttori Generali
delle Aziende Sanitarie Regionali

Responsabili Servizi Farmaceutici
delle Aziende Sanitarie Regionali

LORO SEDI

OGGETTO: Dispensazione dei medicinali classificati H OSP -

La CTS ha ribadito, inoltre, che il regime di fornitura OSP individua farmaci utilizzabili ~~esclusivamente~~ in ambiente ospedaliero o ad esso assimilabile.

Come la mettiamo con il midazolam, farmaco di prima scelta per la sedazione palliativa?

Riflessioni conclusive...

- Numerose survey, effettuate intervistando persone sane e ammalate, hanno chiaramente evidenziato il desiderio prevalente di poter concludere i propri giorni a casa
- Trattare efficacemente a domicilio i sintomi dei pazienti oncologici in fase avanzata di malattia è possibile, non diversamente dai centri residenziali
- Per ottenere buoni risultati occorre équipe dedicata, in grado di garantire un elevato coefficiente di intensità assistenziale (LEA 2018, Accordo Stato-Regioni 2012) e flessibilità organizzativa
- Questi requisiti facilitano altresì la possibilità di dedicare tempo adeguato alla relazione con paziente e caregiver, quest'ultimo spesso in difficoltà nell'accettare la situazione ed a condividere i suggerimenti terapeutici («Il tempo di relazione è tempo di cura» Legge 219 - 2017).
- Per poter garantire risultati soddisfacenti occorre avere a disposizione i farmaci più efficaci, secondo i dati della letteratura più aggiornati: in caso contrario, il rischio è di accessi inappropriati in ospedale, con insoddisfazione dell'ammalato e netto incremento dei costi assistenziali



*Grazie per
l'attenzione*