European Society of
Regional Anaesthesia
& Pain Therapy
ESRA ITALIA

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XXIX CONGRESSO NAZIONALE

ESRA Italian Chapter

CESENA, Cesena fiere

7-9 Novembre 2024

Presidente del congresso
Vanni Agnoletti
Domenico Pietro Santonastaso
Andrea Tognù

MZ EVENTS

European Society of Regional Anaesthesia & Pain Therapy
ESRA ITALIA
ESRA Italian Chapter
XXIX CONGRESSO NAZIONALE
7-9 Novembre 2024
CESENA, Cesena fiere

IL RUOLO DELL'OSSICODONE IN FIALE NEL DOLORE POST-OPERATORIO

Dott.ssa Elisabetta Pusceddu
Responsabile SSD T.I.P.O.
Arnas G. Brotzu Cagliari

AOBrotzu

Dichiarazione conflitto di interessi

In qualità di relatore, ai sensi dell'art. 3.3 sul Conflitto di Interessi, pag. 18-19 dell'Accordo Stato Regione del 19 aprile 2012, dichiaro che negli ultimi due anni non ho avuto rapporti anche di finanziamento con soggetti portatori di interessi commerciali in campo sanitario.

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ARNAS G. BROTZU CAGLIARI

I numeri del Brotzu

LETTI INTERVENTI	**752** N° posti letto	**642** N° PL regime ordinario	**2,45** Peso medio DRG	**7636** N° interventi	**184** N° trapianti
ACCESSI	**55.026** N° tot. accessi PS	**34.951** N° accessi PS Adulti	**20.075** N° accessi PS Pediatria	**1.387.095** N° prestazioni ambulatoriali	**38.689** N° ricoveri per anno
DIPENDENTI	**3.475** N° dipendenti	**64,9%** Incarichi SC	**39,06%** Incarichi SS-SSD	**58.478** N° ore formazione personale	

E-mail: elisabetta.pusceddu@aob.it

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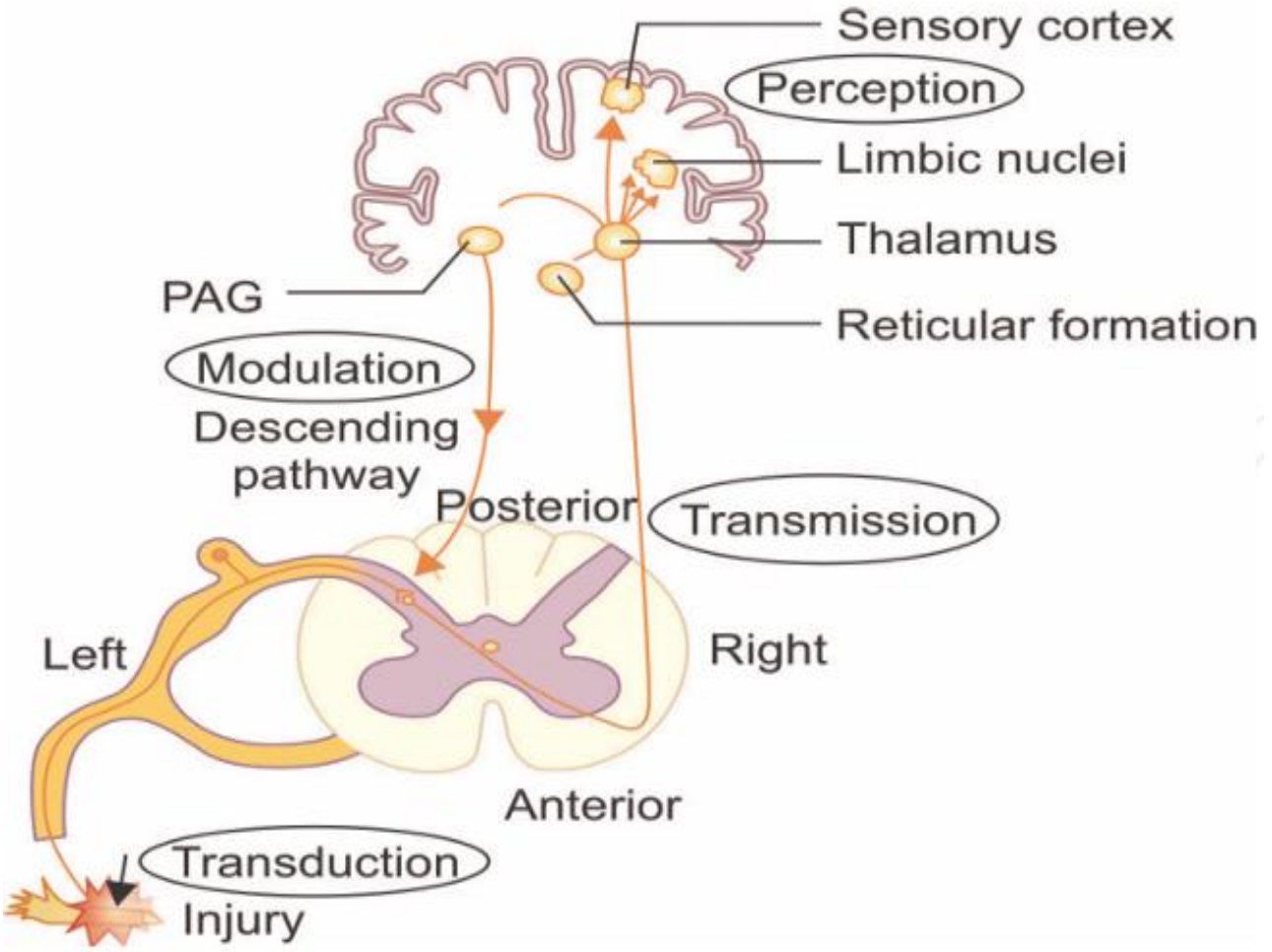
PAIN PATHWAY

POST-OPERATIVE PAIN

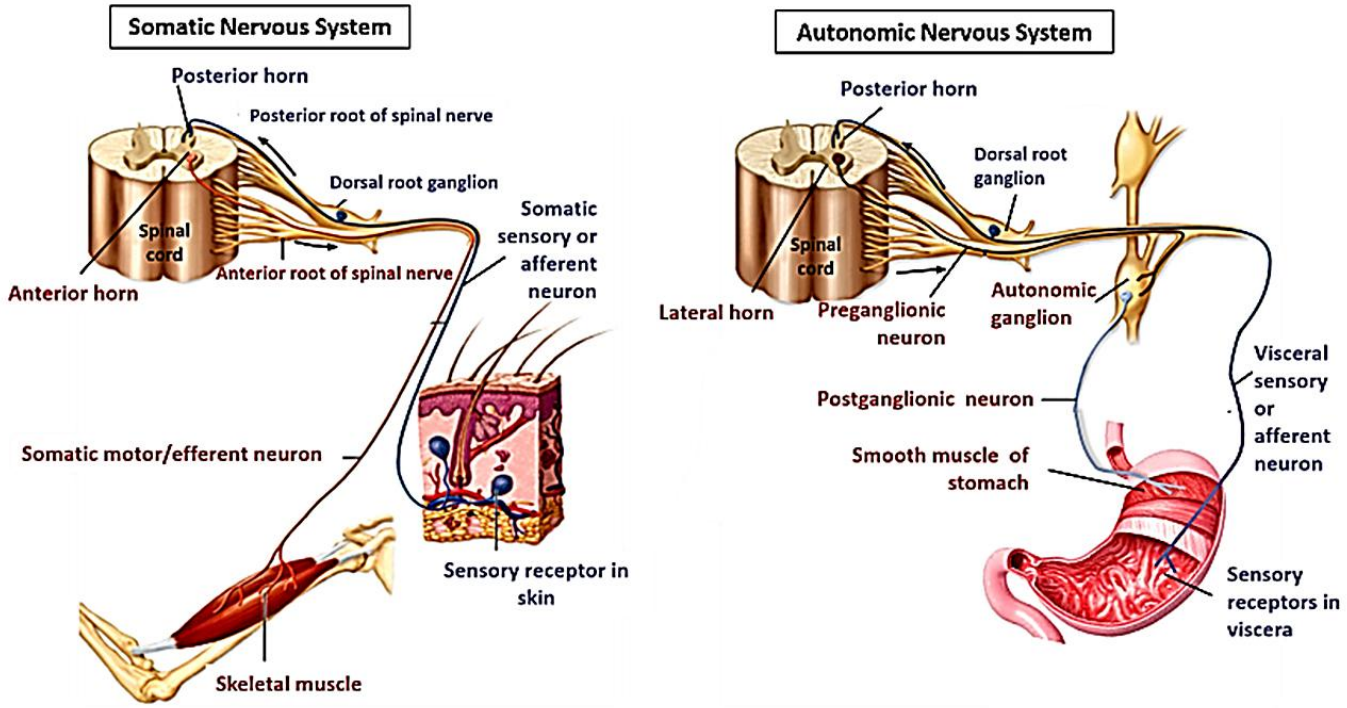
- **ACUTE**
- **CRONIC**



- Paracetamolo
- FANS
- Oppioidi

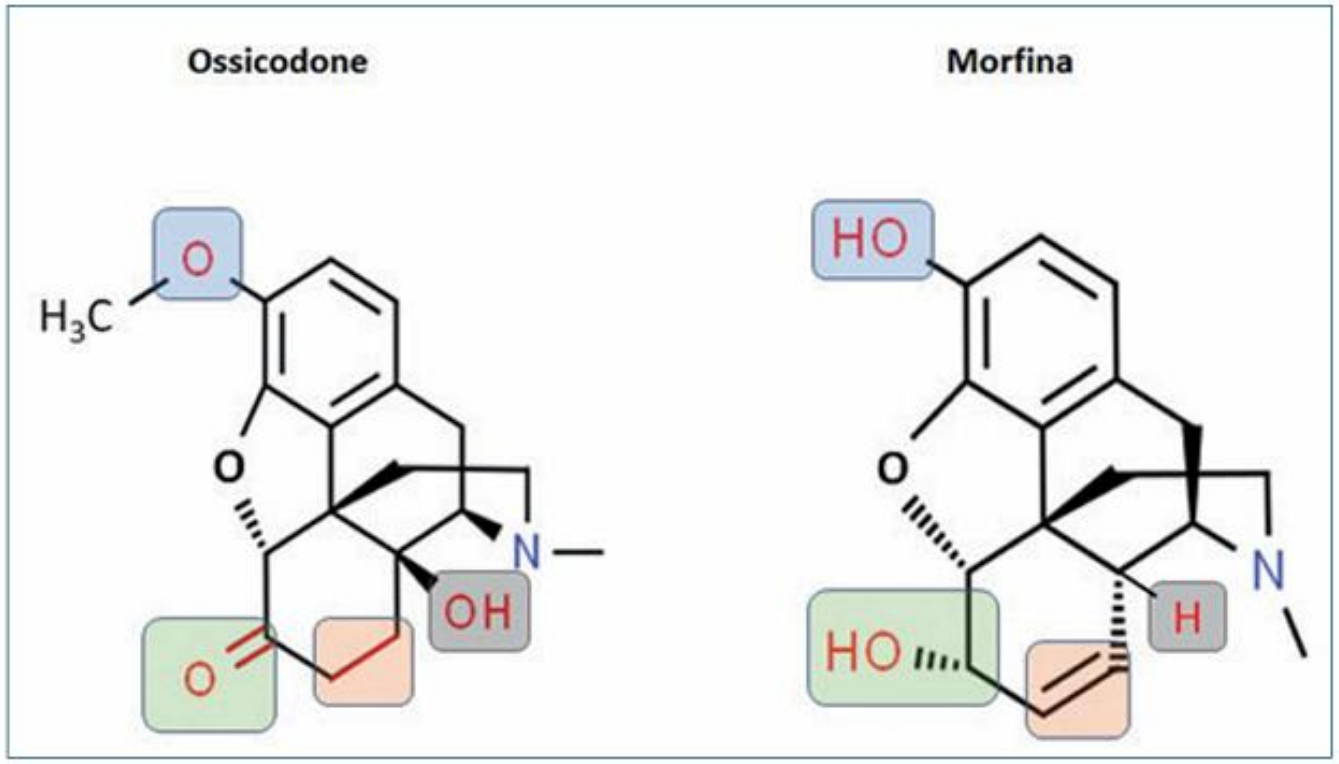
- Tramadolo
- Morfina
- Fentanyl

OSSICODONE CLORIDRATO



PERIOPERATIVE PAIN MANAGEMENT

OXYCODONE vs MORFINA



- gruppo metile (-CH3) anziché un gruppo idrossile (-OH) in posizione -3
- un gruppo idrossile (-OH) al carbonio -14
- l'ossicodone ha una funzione di 7,8-diidro, mentre la morfina ha un doppio legame tra i due atomi di carbonio
- l'ossicodone ha un gruppo carbonile (= O) al posto del gruppo idrossile in posizione -6

> 47,2% (2014-2016)

Bosetti C, Santucci C, Radrezza S, et al. Trends in the con sumption of opioids for the treatment of severe pain in Eu rope, 1990-2016. Eur J Pain 2019;23:697-707.

OXYCODONE: new 'old' drug

Oxycodone: new 'old' drug

Klaus T. Olkkola and Nora M. Hagelberg

Department of Anaesthesiology, Intensive Care, Emergency Care and Pain Medicine, University of Turku and Turku University Hospital, Turku, Finland

Correspondence to Klaus T. Olkkola, MD, PhD, Professor and Chairman, Department of Anaesthesiology, Intensive Care, Emergency Care and Pain Medicine, University of Turku and Turku University Hospital, PO Box 52 (Kiinamyllynkatu 4-8), FI-20521 Turku, Finland
Tel: +358 2 313 0000; fax: +358 2 313 3960;
e-mail: klaus.olkkola@utu.fi

Current Opinion in Anaesthesiology 2009, 22:459–462

1917

Purpose of review

Since the introduction of oral immediate release and controlled-release oxycodone preparations to the market in the 1990s, the clinical use and scientific interest in oxycodone has increased greatly.

Recent findings

Recent studies have shown that the pharmacokinetics of oxycodone are dependent on age of the patient and therefore individual titration of the dose is necessary, especially in the elderly. Oxycodone has good oral bioavailability and it produces more predictable plasma concentrations than morphine, which has a poor and more variable bioavailability. Oxycodone has clinically significant drug interactions with drugs affecting cytochrome P450 3A enzymes. Clinical studies have demonstrated that oxycodone is a useful opioid analgesic in acute postoperative pain, cancer pain, visceral pain and chronic nonmalignant pain.

Summary

The availability of oxycodone preparations has increased its clinical use exponentially during the last decade. Further clinical studies are still needed to fully understand its clinical pharmacology. Oxycodone is still a new 'old' drug whose pharmacology and clinical potential is not yet fully understood.

OSSICODONE PARENTERALE: indicazione terapeutica

INDICAZIONI TERAPEUTICHE

- Adulti sopra i 18 anni
- Per il trattamento del dolore da moderato a intenso in pazienti oncologici e nel dolore postoperatorio
- Per il trattamento del dolore intenso che richiede l'utilizzo di un oppioide forte

Dosaggi

10 mg/ml: fiale da 1ml, 2ml

50 mg/ml: fiale da 1 ml

Via di somministrazione

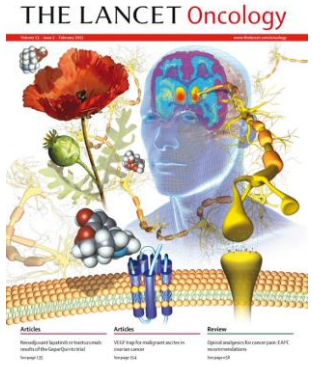
- Iniezione o infusione sottocutanea **(bolo, infusione)**
- Iniezione o infusione endovenosa **(Bolo, infusione, PCA)**

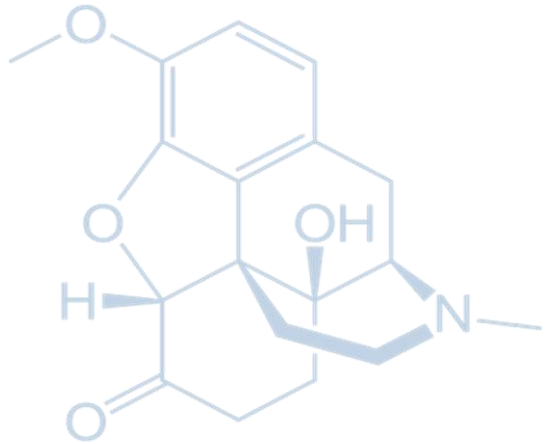
OSSICODONE INIETTABILE: in quali pazienti?

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

Augusto Caraceni*, Geoffrey Hanks*, Stein Kaasa*, Michael I Bennett, Cinzia Brunelli, Nathan Cherny, Ola Dale, Franco De Conno, Marie Fallon, Magdi Hanna, Dagny Faksvåg Haugen, Gitte Juhl, Samuel King, Pål Klepstad, Eivor A Laugsand, Marco Maltoni, Sebastiano Mercadante, Maria Nabal, Alessandra Pigni, Lukas Radbruch, Colette Reid, Per Sjogren, Patrick C Stone, Davide Tassinari, Giovambattista Zeppetella, for the European Palliative Care Research Collaborative (EPCRC), on behalf of the European Association for Palliative Care (EAPC)

Parenteral opioid administration might be necessary for patients who cannot swallow, those with nausea and vomiting, or those at the end of life who are unable to continue with oral medication because of weakness or debility.[59,60] A systematic literature review found





- **DOLORE non CONTROLLATO CON VIA ORALE O TRANSDERMICA**

- **IMPOSSIBILITA' ALLA DEGLUTIZIONE**

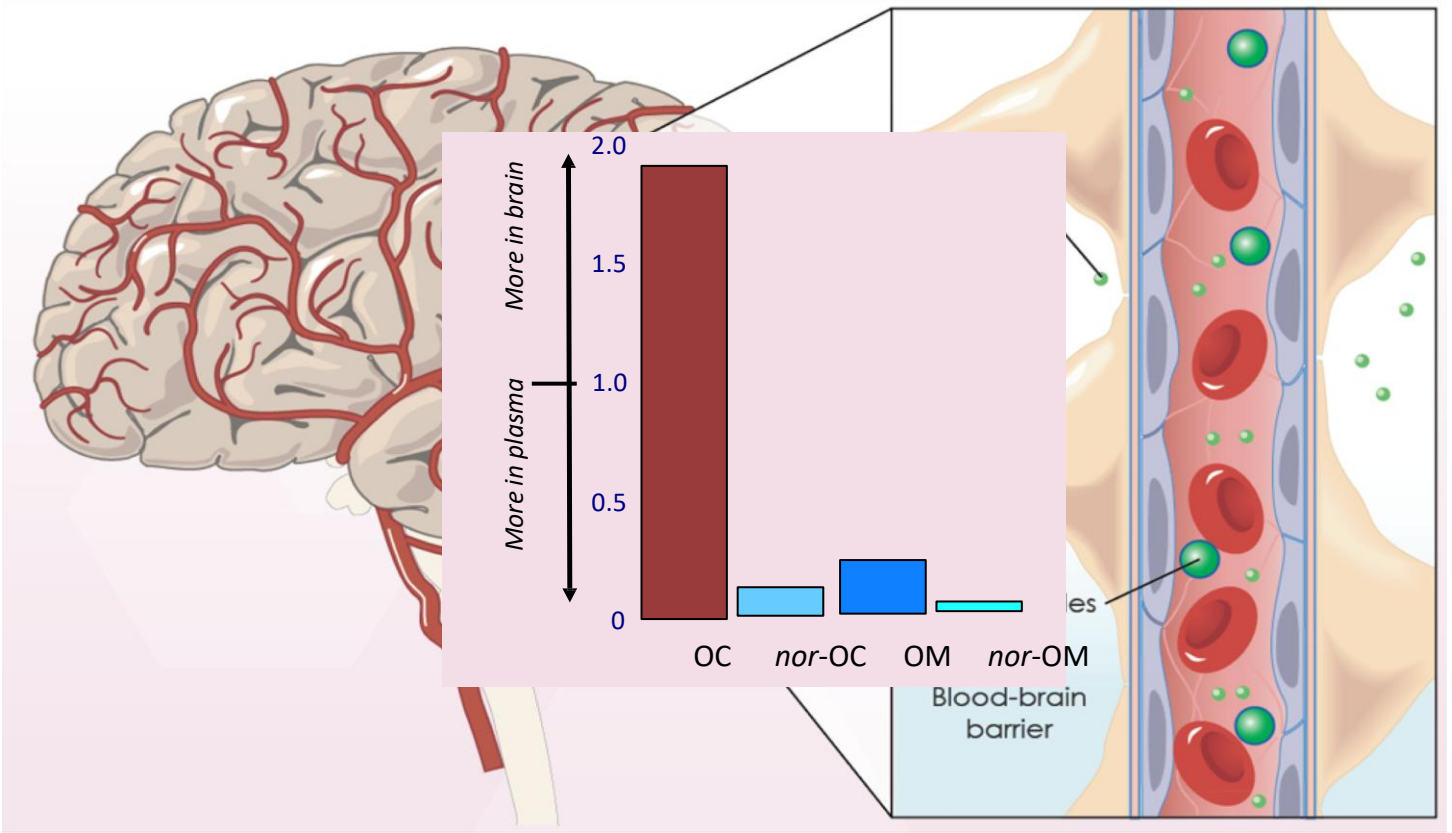
- **NAUSEA, VOMITO**

OSSICODONE: farmacocinetica

- **L'emivita ($T_{1/2}$), dopo somministrazione per via e.v. = 2/3 ore**
- **(Tmax) = 25 minuti** dall'iniezione
- **Equivalenza** della **disponibilità dell'ossicodone** quando **somministrato** per **e.v.** e **s.c.**, sia come **singola dose in bolo** sia come **infusione continua** per 8 ore
- Passaggio dall'ossicodone per via orale a quello per via parenterale: la dose va stabilita considerando che 2 mg di ossicodone orale equivalgono ad 1 mg di ossicodone parenterale
- Metabolizzato da: Citocromi **CYP3A4 e 2D6**
- **Attività analgesica attribuibile per il 94,7% al composto nativo**

Leppert W. Pharmacol Rep 2010;62:578-91.
Klimas et al. Expert Opin Drug Toxicol 2013; 9.517-28

Distribuzione dell'ossicodone e dei suoi metaboliti



Conclusions: CYP3A-mediated *N*-demethylation is the principal metabolic pathway of oxycodone in humans. The central opioid effects of oxycodone are governed by the parent drug, with a negligible contribution from its circulating oxidative and reductive metabolites. (Clin Pharmacol Ther 2006;79:461-79.)

Stabilità di ossicodone

Fisicamente e chimicamente stabile per un periodo superiore a 24 ore a temperatura ambiente se in contatto con siringhe di polipropilene o policarbonato, tubi di polietilene o PVC e sacche per infusione di PVC o EVA.

Non necessita di protezione dalla luce

ARTICLE

Stability of Oxycodone Hydrochloride for Injection in Dextrose and Saline Solutions

Kathy Turnbull, Monique Bielech, Scott E. Walker, and Shirley Law

Can J Hosp Pharm 2002;55:272-77

In conclusion, 100 mg/mL solutions of oxycodone hydrochloride dissolved in sterile water are stable and retain more than 95% of the initial concentration of the drug during 35 days of storage in plastic syringes at 4°C and 24°C. Furthermore, 5 and 50 mg/mL solutions prepared by dilution of the 100 mg/mL solution in NS or D5W also retained more than 95% of their initial concentration during 35 days of storage in PVC minibags at 4°C and 24°C.

Perché OSSICODONE è più efficace di morfina?

L'ossicodone mostra **un'affinità significativa per i recettori k** insieme all'effetto agonista sui recettori **μ**

Clinical Trial/Experimental Study

Medicine®

OPEN

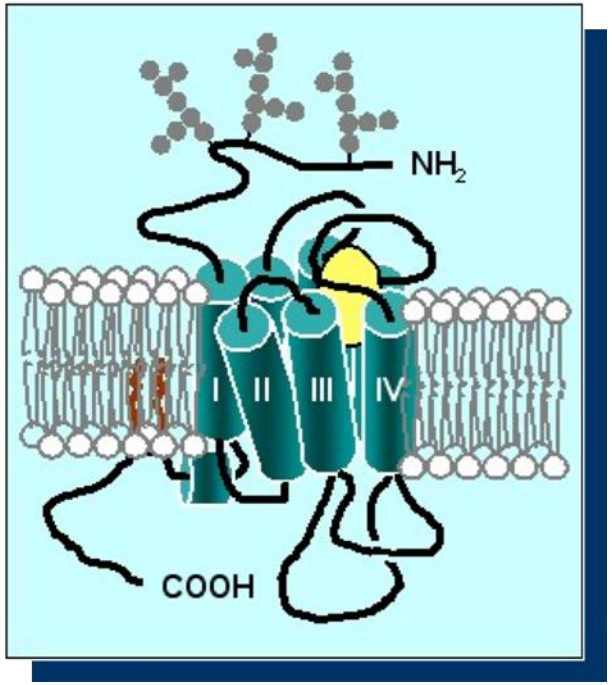
Efficacy and tolerability of oxycodone versus fentanyl for intravenous patient-controlled analgesia after gastrointestinal laparotomy

A prospective, randomized, double-blind study

Zhen Ding, MM[a,b], Kaiguo Wang, MD[b,*], Baosheng Wang, MD[b], Naibao Zhou, MD[b], Hao Li, MM[b], Bo Yan, MM[b]

Ding et al. Medicine (2016) 95:39

I recettori k sui nervi periferici possono giocare un ruolo importante nel sistema di antinocicezione del dolore viscerale. L'ossicodone, agendo anche su questo *pattern* recettoriale, ha **mostrato un'elevata efficacia terapeutica, specialmente nel dolore viscerale.**



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American Pain Society
RESEARCH
EDUCATION
TREATMENT
ADVOCACY

PUBLISHED BY ELSEVIER

The Journal of Pain, Vol 19, No 6 (June), 2018: pp 612-625
Available online at www.jpain.org and www.sciencedirect.com

A Kappa Opioid Receptor Agonist Blocks Bone Cancer Pain Without Altering Bone Loss, Tumor Size, or Cancer Cell Proliferation in a Mouse Model of Cancer-Induced Bone Pain

Katie A. Edwards,* Joshua J. Havelin,* Mary I. Mcintosh,† Haley A. Ciccone,† Kathlene Pangilinan,* Ian Imbert,* Tally M. Largent-Milnes,† Tamara King,* Todd W. Vanderah,† and John M. Streicher†

Abstract: **Breast cancer metastasizes to bone, diminishing quality of life of patients because of pain, fracture, and limited mobility. Cancer-induced bone pain (CIBP) is characterized as moderate to severe ongoing pain, primarily managed by mu opioid agonists such as fentanyl. However, opioids are limited by escalating doses and serious side effects. One alternative may be kappa opioid receptor (KOR) agonists. There are few studies examining KOR efficacy on CIBP, whereas KOR agonists are efficacious in peripheral and inflammatory pain. We thus examined the effects of the KOR agonist U50,488 given twice daily across 7 days to block CIBP, tumor-induced bone loss, and tumor burden. U50,488 dose-dependently blocked tumor-induced spontaneous flinching and impaired limb use, without changing tactile hypersensitivity, and was fully reversed by the KOR antagonist *nor*-binaltorphimine. U50,488 treatment was higher in efficacy and duration of action at later time points. U50,488 blocked this pain without altering tumor-induced bone loss or tumor growth. Follow-up studies in human cancer cell lines confirmed that KOR agonists do not affect cancer cell proliferation. These studies suggest that KOR agonists could be a new target for cancer pain management that does not induce cancer cell proliferation or alter bone loss.**

Perspective: ***This study demonstrates the efficacy of KOR agonists in the treatment of bone cancer-induced pain in mice, without changing tumor size or proliferation in cancer cell lines. This suggests that KOR agonists could be used to manage cancer pain without the drawbacks of mu opioid agonists and without worsening disease progression.***

Agonisti KOR nel dolore osseo

Gli agonisti dei rec K sono efficaci nel CIBP (dolore osseo indotto da cancro) nei topi **senza interferire con la grandezza del tumore** o la **proliferazione** delle linee **cellulari cancerose**

International Journal of *Molecular Sciences*

Int. J. Mol. Sci. **2019**, *20*, 6047

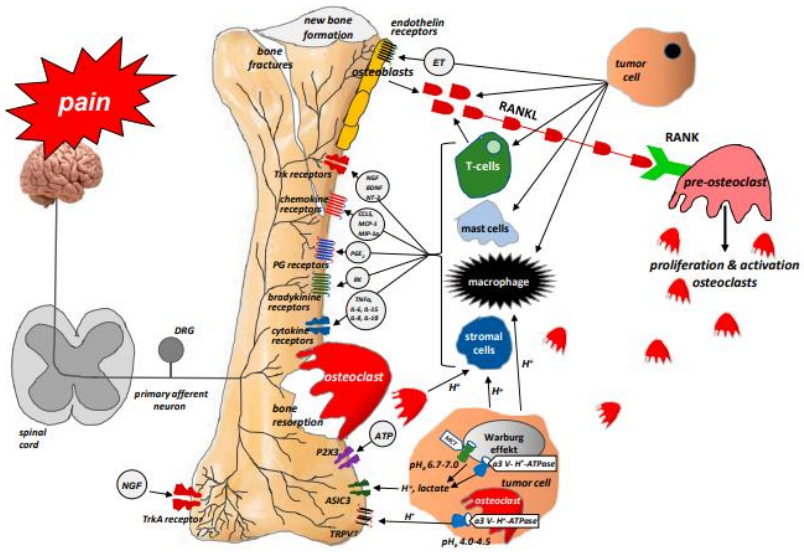
MDPI

Review

Bone Pain in Cancer Patients: Mechanisms and Current Treatment

Renata Zajączkowska [1,*], Magdalena Kocot-Kępska [2,*], Wojciech Leppert [3] and Jerzy Wordliczek [1]

Opioids are used widely in cancer patients, but studies have suggested that some of them may promote cancer progression. The main mechanisms responsible for this effect are the stimulation of angiogenesis and immunosuppression, mainly mediated by agonism at MOR [66]. Studies have suggested that morphine has the greatest immunosuppressive potential, and fentanyl has intermediate potential, whereas buprenorphine and tramadol have shown the lowest or no immunosuppressive effect [67]. Experimental studies have shown that KOR agonists are efficacious in the treatment of CIBP in mice, without changing tumor size or proliferation in cancer cell lines. These data suggest that KOR agonists could be used to manage cancer pain without the drawbacks of MOR agonists and without worsening disease progression [68].



Ossicodone iniettabile: in quali pazienti?

PAZIENTI con DOLORE POST-OPERATORIO

Chirurgia addominale

Chirurgia pelvica/uro-ginecologica

Chirurgia ortopedica maggiore e neurochirurgia

SIAARTI GUIDELINES

Postoperative pain treatment
SIAARTI Recommendations 2010
Short version*

G. SAVOIA [1], D. ALAMPI [2], B. AMANTEA [3], F. AMBROSIO [4], R. ARCIONI [2], M. BERTI [5], G. BETTELLI [6], L. BERTINI [7], M. BOSCO [8], A. CASATI [9], I. CASTELLETTI [10], M. CARASSITI [11], F. COLUZZI [12], A. COSTANTINI [13], G. DANELLI [5], M. EVANGELISTA [8], G. FINCO [14], A. GATTI [15], E. GRAVINO [16], C. LAUNO [17], M. LORETO [1], R. MEDIATI [18], Z. MOKINI [13], E. MONDELLO [19], S. PALERMO [17], F. PAOLETTI [20], A. PAOLICCHI [21], F. PETRINI [22], Q. PIACEVOLI [23], A. RIZZA [24], A.F. SABATO [15], E. SANTANGELO [3], E. TROGLIO [5], C. MATTIA [12*]

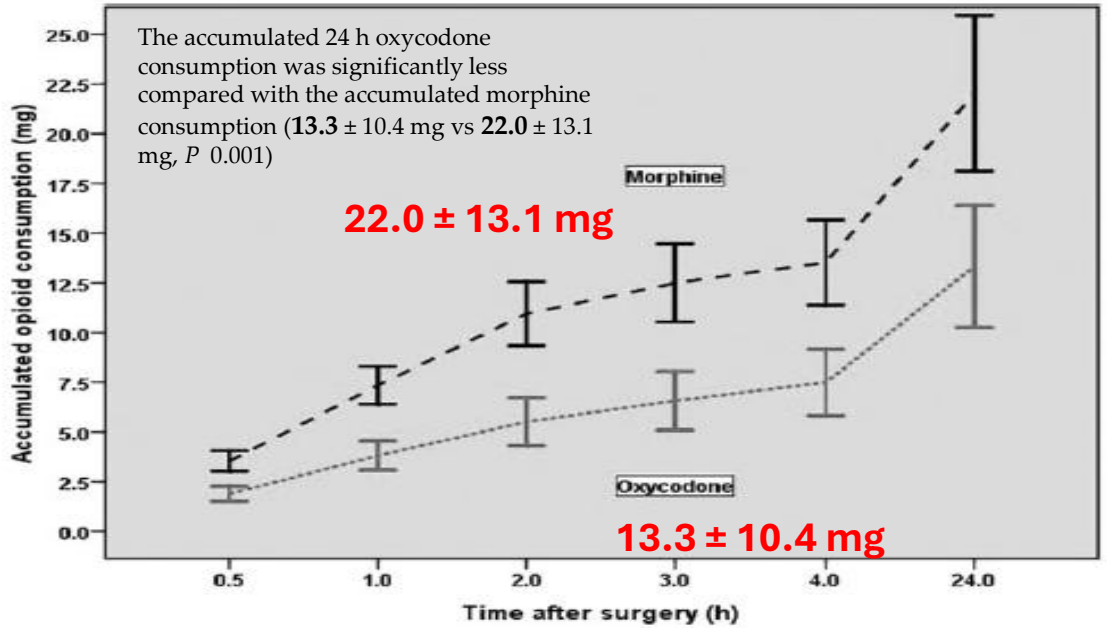
Postoperative pain

Analgesia is a fundamental right of the patient. The appropriate management of postoperative pain (POP) is known to significantly reduce perioperative morbidity, including the incidence of postoperative complications, hospital stay and costs, especially in high risk patients (ASA III-V), those undergoing major surgery and those hospitalized in a critical unit (Level A).[12]

Ossicodone iniettabile: meno consumo di oppioide

A Comparison of Intravenous Oxycodone and Intravenous Morphine in Patient-Controlled Postoperative Analgesia After Laparoscopic Hysterectomy

Lenz, Anesth. Analg 2009 Oct;109(4):1279-83



Rapporto equianalgesico

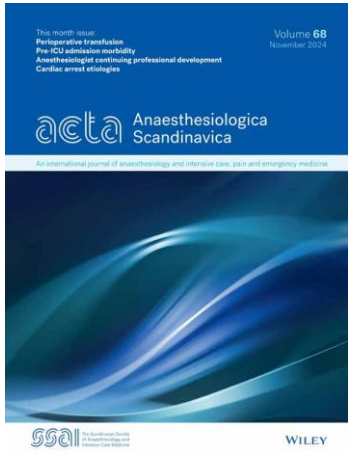
OSSICODONE : MORFINA
2 : 3

- Studio randomizzato doppio cieco
- OXY PCA EV vs MORF PCA EV
- **91 pazienti post isterectomia per via laparoscopica**

Ossicodone iniettabile: rapidità d'azione

RAPIDITÀ D'AZIONE

SOLLIEVO DAL DOLORE OTTENUTO PIÙ RAPIDAMENTE
rispetto a morfina (27 min vs 39 min, p < 0,05)



Intravenous morphine and oxycodone for pain after abdominal surgery

E. Kalso, R. Pöyhiä, P. Onnela, K. Linko, I. Tigerstedt and T. Tammisto
Department of Anaesthesia, Helsinki University Central Hospital, Helsinki, Finland

group 7 ± 1.7 min (range 0–29 min). In the OX-group the first state of relative pain relief was achieved significantly ($P < 0.05$) faster (28 ± 4.8 min, range 5–73 min) than in the MO-group (46 ± 6.9 min; range 5–110 min). It also seemed to last longer (39 ± 6.8 min; range 5–95 min) in the OX-group than in the MO-group (27 ± 3.8 min; range 14–67 min), but this difference was not statistically significant. This state was char-

- Studio randomizzato doppio cieco
- **39 pazienti**
- chirurgia addominale maggiore
- OXY EV vs MORF EV
- boli incrementali EV di 0.05 mg/kg

Kalso et al. Acta Anaesthesiol Scand 1991: 35: 642-646

Ossicodone iniettabile: rapidità d'azione

A Comparison of Intravenous Oxycodone and Intravenous Morphine in Patient-Controlled Postoperative Analgesia After Laparoscopic Hysterectomy

Harald Lenz, MD*†
Leiv Sandvik, MSc, PhD*‡
Erik Qvigstad, MD, PhD*§
Carl Eivind Bjerkelund, MD†
Johan Raeder, MD, PhD*†

INTRODUCTION: In this study, we investigated the dose requirements, pain relief, and side effects of oxycodone versus morphine after surgery with visceral pain.
METHODS: Ninety-one women received IV oxycodone or morphine before the end of laparoscopic hysterectomy and then continued with patient-controlled analgesia for 24 h postoperatively.
RESULTS: The accumulated oxycodone consumption was less (13.3 ± 10.4 mg vs 22.0 ± 13.1 mg, $P = 0.001$) than morphine. With oxycodone, the visual analog scale scores were significantly lower in the first hour postoperatively and sedation was less during the 24-h postoperative period, $P = 0.006$.
CONCLUSIONS: Oxycodone was more potent than morphine for visceral pain relief but not for sedation.
(Anesth Analg 2009;109:1279-83)

- Studio randomizzato doppio cieco
- OXY PCA EV vs MORF PCA EV
- **91 pazienti post isterectomia per via laparoscopica**

Il gruppo trattato con ossicodone si è mostrato **più efficace a 30 e a 60 min** dopo l'intervento chirurgico rispetto a morfina , sia nella riduzione del **dolore al riposo** che **dopo la tosse**

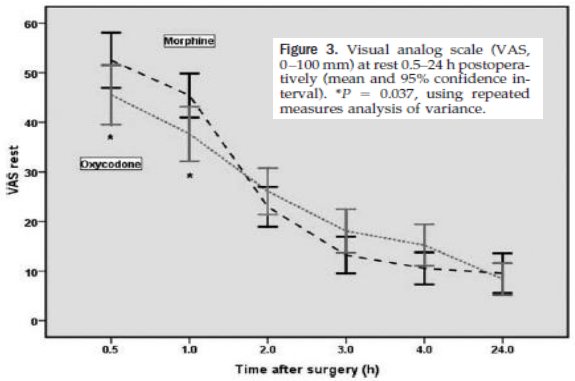


Figure 3. Visual analog scale (VAS, 0–100 mm) at rest 0.5–24 h postoperatively (mean and 95% confidence interval). *$P = 0.037$, using repeated measures analysis of variance.

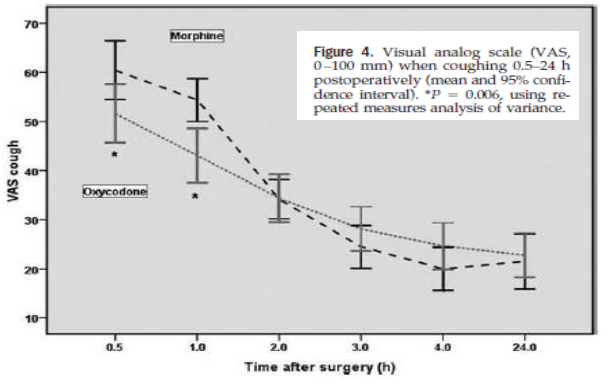


Figure 4. Visual analog scale (VAS, 0–100 mm) when coughing 0.5–24 h postoperatively (mean and 95% confidence interval). *$P = 0.006$, using repeated measures analysis of variance.

Lenz et al. Anesth Analg. 2009 Oct;109(4):1279-83.

Ossicodone iniettabile: durata d'azione

Richiesta di **PCA più dilazionate nel tempo** (20 vs 16 min) rispetto a morfina.

A Comparison of Intravenous Oxycodone and Intravenous Morphine in Patient-Controlled Postoperative Analgesia After Laparoscopic Hysterectomy

Harald Lenz, MD*†
Leiv Sandvik, MSc, PhD*‡
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CONCLUSIONS: Oxycodone was more potent than morphine for visceral pain relief but not for sedation.
(Anesth Analg 2009;109:1279–83)

the groups (Table 1). Mean VAS at rest at the first PCA request was similar between the groups, 53 mm in Group O and 54 mm in Group M ($P = 0.71$), but the mean time from emergence to first use of PCA was different, mean 20 min in Group O and 16 min in Group M ($P = 0.038$). The accumulated 24 h oxycodone consumption was significantly less compared with the accumulated morphine consumption (13.3 ± 10.4 mg vs 22.0 ± 13.1 mg, $P = 0.001$) (Fig. 2).

- Studio randomizzato doppio cieco
- OXY PCA EV vs MORF PCA EV
- **91 pazienti post isterectomia per via laparoscopica**

Lenz, Anesth. Analg 2009 Oct;109(4):1279-83

Perché OSSICODONE è più rapido di morfina?

Nel modello animale l'ossicodone **penetra la barriera ematoencefalica molto rapidamente** e la sua concentrazione nel cervello è **3 volte più alta** di quella nel sangue

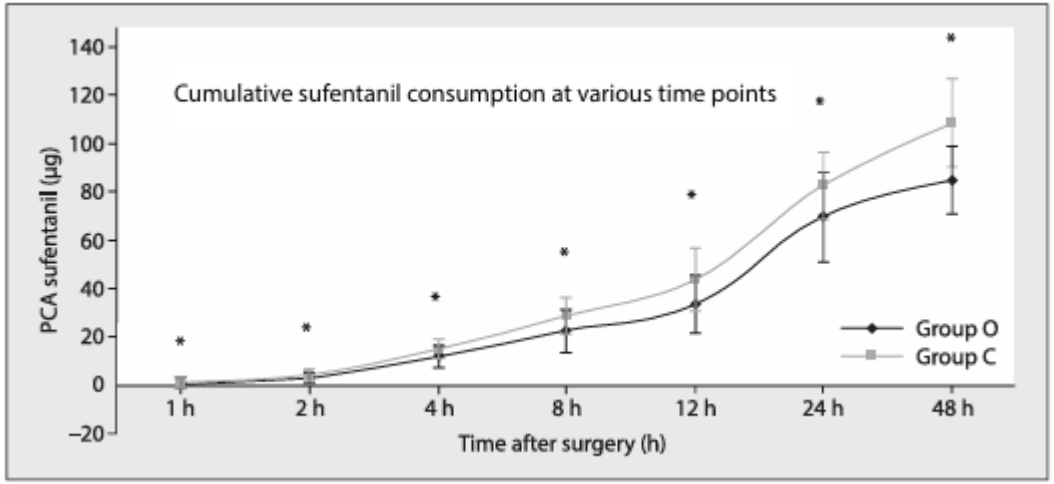
- Studi in modelli animali indicano che la ***permeabilità*** dell'ossicodone attraverso la barriera ematoencefalica è ***7 volte maggiore*** rispetto alla ***morfina***.
- Dopo somministrazione e.v., la **concentrazione dell'ossicodone nel sistema nervoso centrale (SNC) è 6 volte maggiore di quella della morfina**
- Si suppone che l'accumulo cerebrale di ossicodone è dovuto a un **meccanismo di trasporto attivo**.
- La ***glicoproteina P*** **non** ha un ruolo nella regolazione della permeabilità della barriera ematoencefalica per l'ossicodone a differenza di morfina e metadone che sono substrati per la glicoproteina P.

Leppert W. Pharmacol Rep 2010;62:578-91.
Olkkola et al. Trends Pharmacol Sci 2013;34:206-14
Boström et al, Anesthesiology 2008;108:495-505

Ossicodone iniettabile: meno consumo di oppioide

Effect of preoperative intravenous oxycodone administration on sufentanil consumption after retroperitoneal laparoscopic nephrectomy

Jinguo Wang[1], Haichun Ma[2], Honglan Zhou[1], Yang Gao[2], Yaowen Fu[1], Na Wang[2]



Cumulative sufentanil consumption by PCA was **lower in Group O** (Oxycodone) than in Group C (placebo) **at all the time points**.

Anaesthesiol Intensive Ther 2016, vol. 48, no 5, 300–304

The Effect of Oxycodone on Post-operative Pain and Inflammatory Cytokine Release in Elderly Patients Undergoing Laparoscopic Gastrectomy

Wei-long Lao[1†], Qi-liang Song[2†], Zong-ming Jiang[2], Wen-di Chen[2], Xian-he Zheng[2] and Zhong-hua Chen[1,3]*

[1] Shaoxing University School of Medicine, Shaoxing, China, [2] Department of Anesthesia, Shaoxing People's Hospital, Shaoxing, China, [3] Department of Anesthesia, The First Affiliated Hospital of Shaoxing University, Shaoxing, China

- 60 pazienti
- 65 anni
- Gastrectomia laparoscopica

- **PONV**
- **NRS viscerale**
- **infiammazione**

OPEN ACCESS

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Lao W-l, Song Q-l, Jiang Z-m, Chen W-d, Zheng X-h and Chen Z-h (2021) The Effect of Oxycodone on Post-operative Pain and Inflammatory Cytokine Release in Elderly Patients Undergoing Laparoscopic Gastrectomy. Front. Med. 8:700025. doi: 10.3389/fmed.2021.700025

Background: To evaluate the effect of oxycodone on post-operative pain and inflammation in elderly patients undergoing laparoscopic gastrectomy.

Methods: Sixty patients who were of both sexes, American Society of Anesthesiologists Physical Status (ASA-PS) Class I or II, over 65 years of age and undergoing an elective laparoscopic radical gastrectomy were randomly divided into two groups: an oxycodone group (Group O) including 20 males and 10 females and a sufentanil group (Group S) including 21 males and 9 females. The post-operative analgesia regimen was as follows: 40 mg of parecoxib sodium and 0.1 mg/kg of oxycodone was intravenously injected into Group O before the abdomen closure, while 40 mg of parecoxib sodium and 0.1 μg/kg of sufentanil was injected intravenously into Group S. Both groups were infiltrated with 20 ml of 1% ropivacaine at the end of the operation. The level of serum IL-6 and IL-10 were assayed immediately at the following timepoints: at the conclusion of surgery (T1), 1 h (T2), 6 h (T3), and 24 h (T4) after the completion of the surgery. The numerical rating scale (NRS), the Ramsay sedation score, analgesic-related adverse events, post-operative pulmonary inflammation events and the post-operative stay were recorded.

Results: Compared with Group S, the serum IL-6 concentrations of Group O decreased at T_3 and T_4, while the serum IL-10 concentrations increased ($P < 0.05$). In Group O, the serum IL-6 concentrations at T_3 and T_4 were lower than those at T_1 ($P < 0.05$). The incidence of post-operative nausea and vomiting (PONV) and pulmonary inflammation in Group O was lower than that in Group S ($P < 0.05$). At each time point, the NRS of visceral pain in Group O was lower than that in Group S. At 6 and 24 h after extubation, the NRS of incision pain in Group O was lower than that in Group S ($P < 0.05$).

Conclusion: Oxycodone can regulate the level of inflammatory cytokines and reduce post-operative inflammatory response.

Keywords: oxycodone, post-operative analgesia, inflammatory cytokine, laparoscope, gastric cancer

Lao, 2021 Sep 1;8:700025

Translated Title

Efficacy of an Oxycodone-Propofol Combination versus a Fentanyl-Propofol Combination in Conscious Sedation during Therapeutic Endoscopic Retrograde Cholangiopancreatography in Elderly Patients

Gerontology 2021 **67 :1** (9 - 16)

Translated Abstract

Background: With a rapidly aging population, the need for endoscopic retrograde cholangiopancreatography (ERCP) is increasing. The commonly used sedation anesthesia in ERCP is a combination of propofol and fentanyl, even though fentanyl may cause some adverse reactions such as respiratory depression. Objectives: This study aimed to evaluate the efficacy of oxycodone combined with propofol versus fentanyl combined with propofol for sedation anesthesia during ERCP. Methods: A total of 193 patients aged from 65 to 80 years undergoing ERCP were enrolled and randomized into two groups: an "oxycodone combined with propofol"group (group OP, n = 97) and a "fentanyl combined with propofol"group (group FP, n = 96). The rate of perioperative adverse events as well as the recovery time, patients' satisfaction, and endoscopists' satisfaction were noted. Results: There was no difference in the frequency of hypotension or bradycardia between the two groups, but there were more episodes of desaturation (SpO2 <90% for >10 s in 8.3%), postoperative nausea (7.3%), and vomiting (5.2%) in group FP than in group OP. Patients' satisfaction in group FP was lower than that in group OP. The recovery time was longer in group FP than in group OP. Conclusions: Oxycodone combined with propofol was effective in ERCP, with a low incidence of perioperative adverse events.

Colangio-pancreatografia retrograda endoscopica
193 pazienti
Tra 65-80 anni
Propofol/ossicodone (gruppo OP)
vs propofol/fentanil (gruppo FP)

Per gruppo OP
< episodi di desaturazione
< nausea e vomito
> soddisfazione
< tempo di recupero

Ossicodone iniettabile: TOLLERABILITÀ NAUSEA E VOMITO

Attenuation of Morphine-Induced Delirium in Palliative Care by Substitution With Infusion of Oxycodone

Table 3

Analogue Scale Observations for Pain, Nausea, and Vomiting in 12 Patients (Excluding Poor Metabolizer), All Converted to Scale of 0–10

Observation	Baseline (mean ± SD)	Steady state (mean ± SD)	End point (mean ± SD)
Pain	3.0 ±3.24	1.43±1.65	1.62±1.68
Nausea/ Vomiting	3.56±2.21	1.09±1.78*	0.72±1.15*

Significant $P < 0.05$ compared with baseline.

- Studio prospettico (fino a 6 gg di somministrazione di ossicodone)
- **13 pazienti** con delirio acuto da morfina ruotati a OXY SC
- Valutaz. a baseline (inizio di ossicodone), 24h (steady state) e dopo 6 gg

Miglioramento significativo di nausea/vomito (p=0,006)

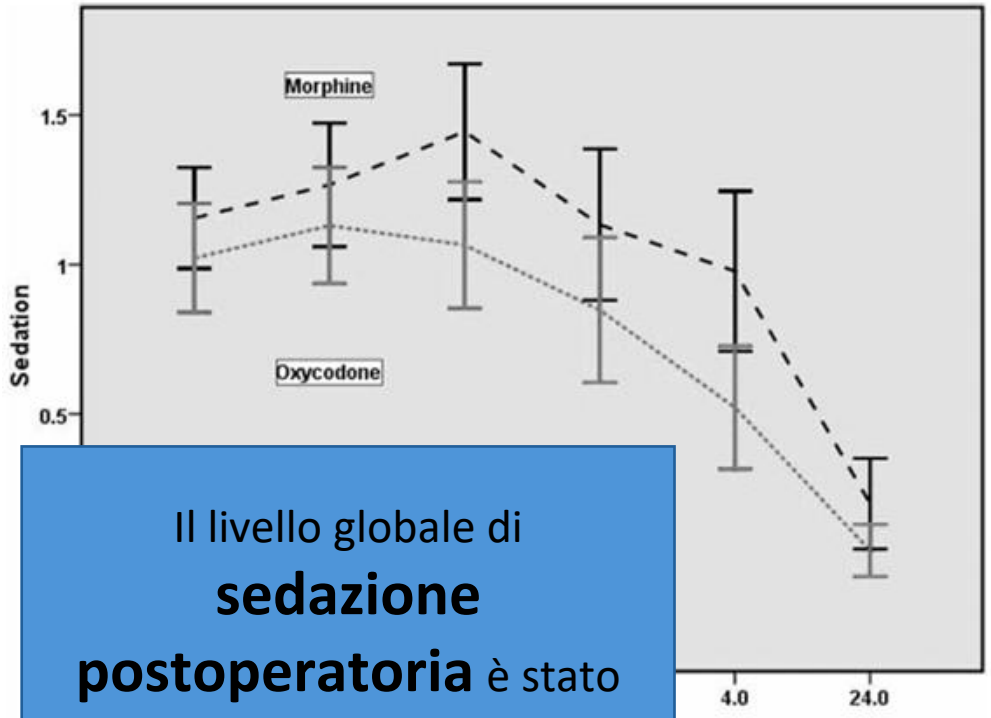
Maddocks et al., 1996 J Pain Symptom Management

Ossicodone iniettabile: TOLLERABILITÀ SEDAZIONE

A Comparison of Intravenous Oxycodone and Intravenous Morphine in Patient-Controlled Postoperative Analgesia After Laparoscopic Hysterectomy

Harald Lenz, MD*†
Leiv Sandvik, MSc, PhD*‡
Erik Qvigstad, MD, PhD*§
Carl Eivind Bjerkelund, MD†
Johan Raeder, MD, PhD*†

INTRODUCTION: In this study, we investigated the dose requirements, pain relief, and side effects of oxycodone versus morphine after surgery with visceral pain.
METHODS: Ninety-one women received IV oxycodone or morphine before the end of laparoscopic hysterectomy and then continued with patient-controlled analgesia for 24 h postoperatively.
RESULTS: The accumulated oxycodone consumption was less (13.3 ± 10.4 mg vs 22.0 ± 13.1 mg, $P = 0.001$) than morphine. With oxycodone, the visual analog scale scores were significantly lower in the first hour postoperatively and sedation was less during the 24-h postoperative period, $P = 0.006$.
CONCLUSIONS: Oxycodone was more potent than morphine for visceral pain relief but not for sedation.
(Anesth Analg 2009;109:1279–83)



Il livello globale di **sedazione postoperatoria** è stato **significativamente inferiore** nel gruppo trattato con **OXY** vs al gruppo trattato con MORF (p=0,006)

Lenz, Anesth. Analg 2009 Oct;109(4):1279-83

Ossicodone iniettabile: TOLLERABILITÀ DELIRIO

Attenuation of Morphine-Induced Delirium in Palliative Care by Substitution With Infusion of Oxycodone

Ian Maddocks, MD, FRACP, FAFPHM, Andrew Somogyi, PhC, MSc, PhD, Fay Abbott, AUA (Pharmacy), BA, Peter Hayball, BPharm, BSc (Hons), PhD and Deborah Parker, BA

In 8 pz su 12, il **DELIRIO è migliorato** ed in nessun paziente è peggiorato passando ad OXY SC

Support Care Cancer (1999) 7:265–270
DOI 10.1007/s005209900031
ORIGINAL ARTICLE

Bruno Gagnon
Monique Bielech
Sharon Watanabe
Paul Walker
John Hanson
Eduardo Bruera

The use of intermittent subcutaneous injections of oxycodone for opioid rotation in patients with cancer pain

Nel 34% di 38 pazienti che erano stati trattati con ossicodone a causa di delirio, il DELIRIO si **era annullato**

Miglioramento del delirio con ossicodone

Maddocks et al., 1996 J Pain Symptom Management
Gagnon, 1999 Supp Care Cancer 7: 265-270

Ossicodone iniettabile: TOLLERABILITÀ ALLUCINAZIONI E PRURITO

Morphine and oxycodone hydrochloride in the management of cancer pain

Kalso and Vainio Clin Pharmacol Ther, 1990

Perhaps the most interesting result was the absence of hallucinations during the administration of oxycodone hydrochloride in those patients who had had hallucinations during treatment with morphine. This result

Pain Practice, Volume 16, Issue 7, 2016 924–934

REVIEW ARTICLE

Perspectives on Intravenous Oxycodone for Control of Postoperative Pain

Joseph V. Pergolizzi Jr., MD*,†; Francis Seow-Choen, MBBS, FRCSEd, FAMS, FRES‡; Steven D. Wexner, MD, PhD (Hon), FACS, FRCS, FRCSEd§; Gianpietro Zampogna, MD¶; Robert B. Raffa, PhD**; Robert Taylor Jr., PhD¶

than has morphine.[65] Compared to morphine, pruritus may occur with less frequency and less severity with oxycodone.[66] This may be due to the fact that histamine release is less pronounced with oxycodone than with morphine.

Ossicodone iniettabile: DOSAGGI

e.v. (bolo): diluire a 1mg/ml in soluzione fisiologica 0,9%, destrosio 5% o acqua per preparazioni iniettabili. ***Somministrare in bolo una dose da 1 a 10 mg, lentamente per 1-2 minuti. Le dosi non devono essere somministrate più frequentemente di ogni 4 ore***.

e.v. (infusione): diluire a 1mg/ml in soluzione fisiologica 0,9%, destrosio 5% o acqua per preparazioni iniettabili. ***Si consiglia una dose iniziale di 2 mg/ora***.

e.v. (ACP): diluire a 1mg/ml in soluzione fisiologica 0,9%, destrosio 5% o acqua per preparazioni iniettabili. ***La dose in bolo da 0,03 mg/kg deve essere somministrata con un intervallo di blocco minimo di 5 minuti*.**

s.c. (bolo): **usare la concentrazione 10 mg/ml tal quale**. ***Si consiglia una dose iniziale da 5 mg, ripetere ad intervalli di 4 ore ove necessario.***

s.c. (infusione): diluire in soluzione fisiologica 0,9%, destrosio 5% o acqua per preparazioni iniettabili ove necessario. Nei pazienti non trattati precedentemente con oppioidi ***si consiglia una dose iniziale di 7,5 mg/giorno, titolando gradualmente in base al controllo dei sintomi***. Nei pazienti oncologici che assumevano ossicodone per via orale possono essere necessarie dosi molto più alte.

Ossicodone iniettabile: SWITCH da EV/SC a ORALE

Opiate	Morphine[17]	Morphine[13,17]	Morphine[17]	Morphine[17]	Morphine[17]	Codeine[17]	Tramadol[17,33]	Tramadol[33]	Tapentadol[16,34]	Oxycodone[2,13,16-18,25-26,35]	Oxycodone[2,13,16-18,25-26,35]	Hydromorphone[2,13, 16, 17,32]	Fentanyl[13,36]	Buprenorphine[27,37]	Fentanyl[1,2,17,28-31]	Buprenorphine[17,27,37]	Sufentanil[39]
Form	OS ATC	SC	IV	PD	SA	OS	OS	IM/IV	OS	OS	SC/IV	OS	IV	IM/IV	TTS	TTS	SL
Unit	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	mg	µg/h	µg/h	µg
	7.5	3.75*	2.5*	0.38*	0.04*	30*	37.5*	25*	25*	3.75*	1.88*	1.5*	0.1*		3*	5	7.5*
	15	7,5*	5*	0.75*	0.08*	60*	75*	50*	50	7.5*	3.75*	3*	0.2*		6*	10	15*
	22.5	11.3*	7.5*	1.13*	0.11*	90*	113*	75*	75	11.3*	5.63*	4.5*	0.3*		9*	15	22.5*
	30	**15**	**10**	**1.5**	**0.15**	**120**	**150**	**100**	**100**	**15**	**7.5**	**6**	**0.4**	**0.3**	**12**	**20**	**30**
	60	30	20	3	0.3	240	300	200	200	30	15	12	0.8	0,6	25	35	60
	90	45	30	4.5	0.45	#	#	300**	300	45	22.5	18	#	0.9	37.5*	52.5	90
	120	60	40	6	0.6	#	#	400**	400	60	30	24	#	1.2	50	70	120
	180	90	60	9	0.9	#	#	#	600	90	45	36	#	1.8	75	#	180
	240	120	80	12	1.2	#	#	#	#	120	60	48	#	2.4	100	#	240
	300	150	100	15	1.5	#	#	#	#	150**	75	60**	#	#	#	#	300

*Arithmetically extrapolated, below therapeutic range. **Arithmetically extrapolated, within therapeutic range. #Above therapeutic range. *Abbreviations:* ATC, around the clock; IM, intramuscular; IV, intravenous; OS, oral form; PD, peridural; SA, subarachnoid; SC, subcutaneous; SL, sublingual; TTS, transdermal system.

rale

nterale

Analgesia MULTIMODALE

Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Recommendations and Reports / Vol. 71 / No. 3
November 4, 2022

CDC Clinical Practice Guideline for Prescribing Opioids for Pain — United States, 2022

Multimodal Therapy for Subacute and Chronic Pain

rehabilitation (9). Multimodal therapies should be considered for patients not responding to single-modality therapy, and combinations should be tailored depending on patient needs, cost, convenience, and other individual factors.

Depending on patient comorbidities and benefit-to-risk ratios in individual patients, combinations of medications (e.g., two nonopioid medications with different mechanisms of action or a nonopioid with an opioid medication) also might be used. In some cases, medication combinations might provide complementary or synergistic benefits and facilitate lower dosing of individual medications, as has been demonstrated in trials of patients with neuropathic pain (7). However, this approach should be used with

Deborah Dowell et al., CDC Guideline 2022

La terapia multimodale dovrebbe essere considerata nei pazienti che non rispondono alla terapia singola, e le combinazioni di terapie dovrebbero essere personalizzate.

Terapie NON-OPPIOIDI con differenti meccanismi di azione o terapie NON-OPPIOIDI in combinazione con OPPIOIDI per ottenere un **effetto sinergico e ridurre la dose**

Gaffney et al, 2017Orthop Clin North Am. 2017 Oct;48(4):407-419 .
Jin et al., J Clin Anesth. 2001 Nov;13 (7): 524-39.
Savoia, Minerva Anestesiol 2010 Aug;76(8):657-67

Combinazione OXY-PARACETAMOLO

meccanismi d'azione:

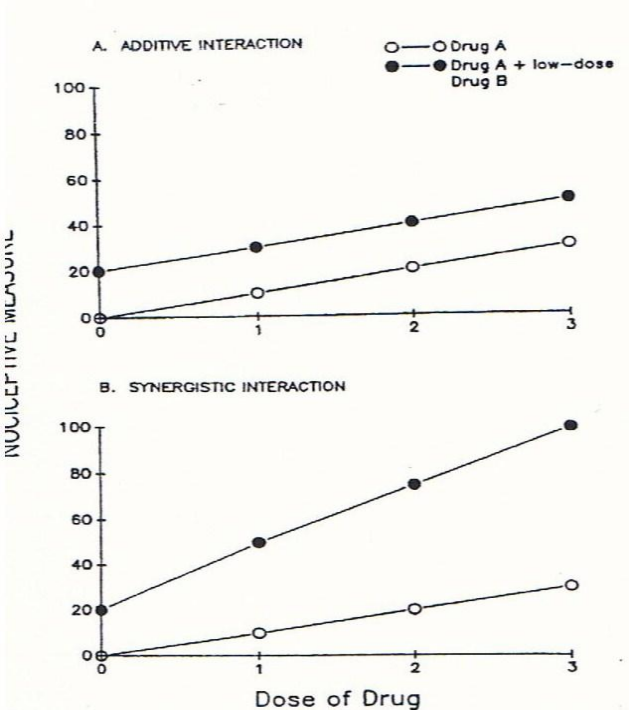
- inibizione ciclo-ossigenasi (COX)-3
- stimolazione delle vie discendenti inibitorie serotoninergiche a livello del midollo spinale
- inibizione della ricaptazione di ANANDAMIDE, agonista dei recettori CB1 e CB2

be the first report to support this notion. Another potential mechanism could be a direct antiemetic effect of acetaminophen. In fact, acetaminophen is metabolized in the brain into AM404, a metabolite that is able to inhibit the reuptake of anandamide, a known cannabinoid CB1 and CB2 receptor agonist. It has been shown that decreased anandamide levels are associated with an increased rate of nausea and vomiting in humans [14]. Therefore, it is possible

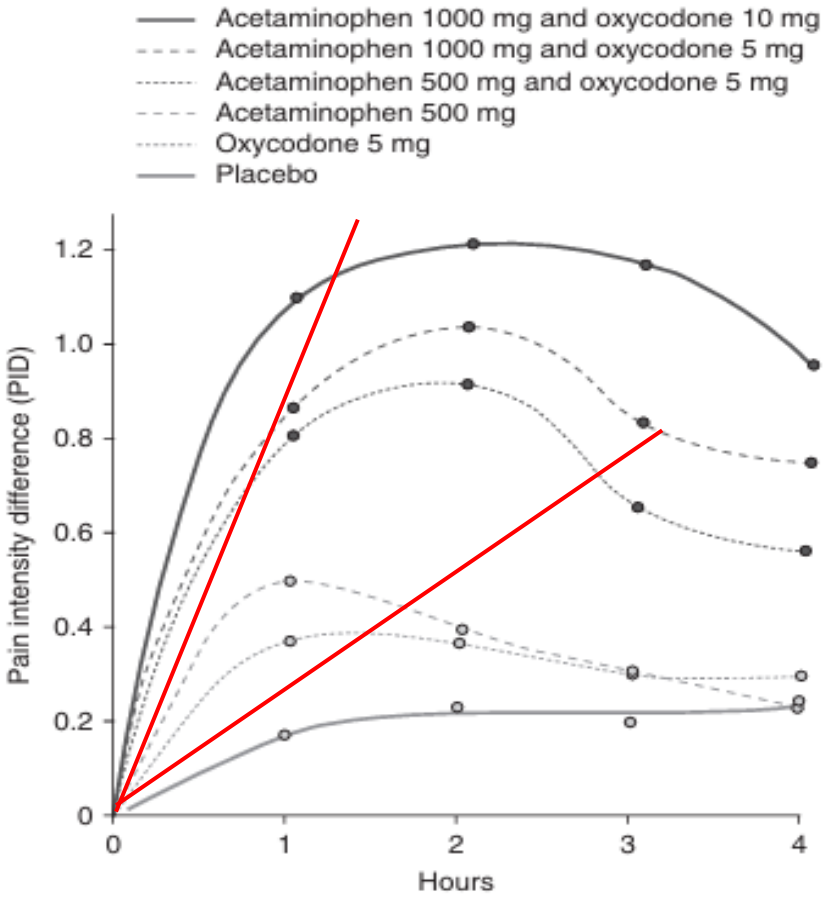
La combinazione di ossicodone con paracetamolo può alleviare non solo il dolore nocicettivo ma anche il dolore neuropatico

Gatti A. et al. Clin Drug Investig 2010; 30 Suppl. 2: 3-14.
Apfel CC Pain. 2013 May;154(5):677-894.
Ding et al. Medicine 2016 Sep;95(39):e4943

Sinergia d'azione



Miaskowski C et Al, Pain 1992; 49: 137-144



Gatti A et al. Clin Drug Invest 2010; 30(suppl 2): 3-14

Randomized, Double-Blind, Placebo-Controlled Comparison of the Analgesic Efficacy of Oxycodone 10 mg/Acetaminophen 325 mg versus Controlled-Release Oxycodone 20 mg in Postsurgical Pain

J Clin Pharmacol 2003;43:296-304

Arnold R. Gammaitoni, PharmD, Bradley S. Galer, MD, Scott Bulloch, DDS, Peter Lacouture, PhD, Frank Caruso, PhD, Tina Ma, PhD, and Thomas Schlagheck, PhD

FORMULAZIONE IR → RAPIDITA'
COMBINAZIONE → OPIOID SPARING EFFECT

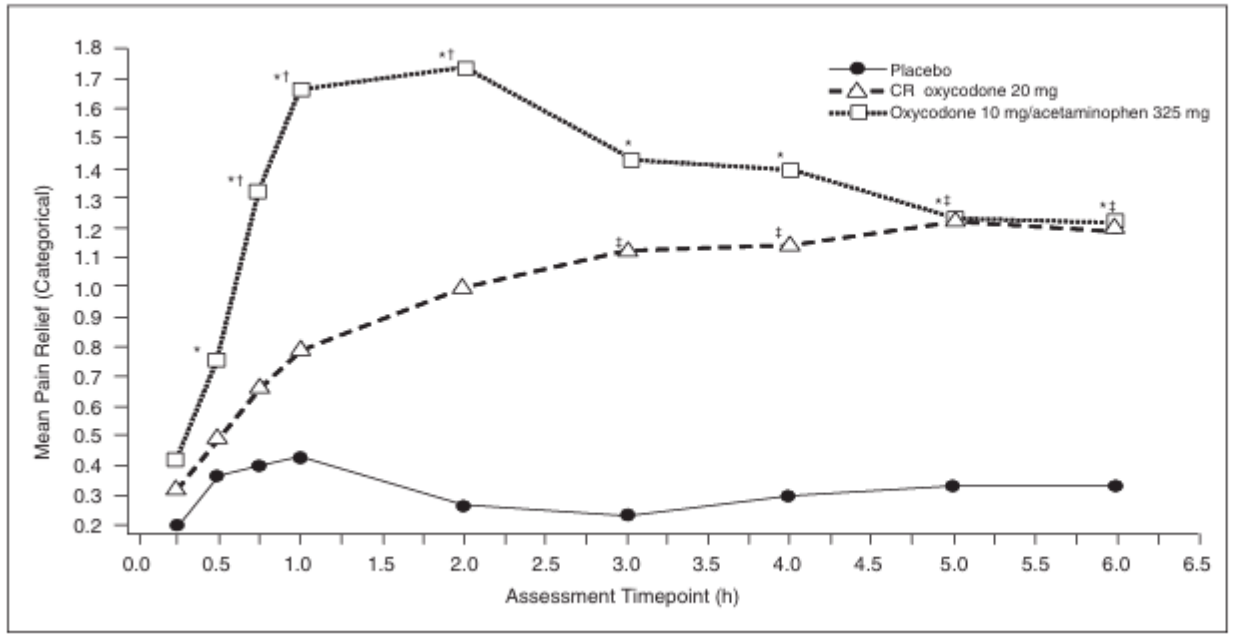


*Figure 2. Categorical pain relief (0-6 h). Measured on a 5-point scale (4 = complete relief, 0 = no relief). *Oxycodone 10 mg/acetaminophen 325 mg significantly better than placebo ($p < 0.05$). †Oxycodone 10 mg/acetaminophen 325 mg significantly better than CR oxycodone 20 mg ($p < 0.05$). ‡CR oxycodone 20 mg significantly better than placebo ($p < 0.05$). CR, controlled release.*

OSSICODONE/PARACETAMOLO

1:1

OXY/PAR basse dosi

Adv Ther (2016) 33:1025–1032
DOI 10.1007/s12325-016-0339-0

ORIGINAL RESEARCH

Retrospective Evaluation of a Fixed-Dose Combination of Oxycodone and Acetaminophen to Manage Moderate Pain: The Lower the Better

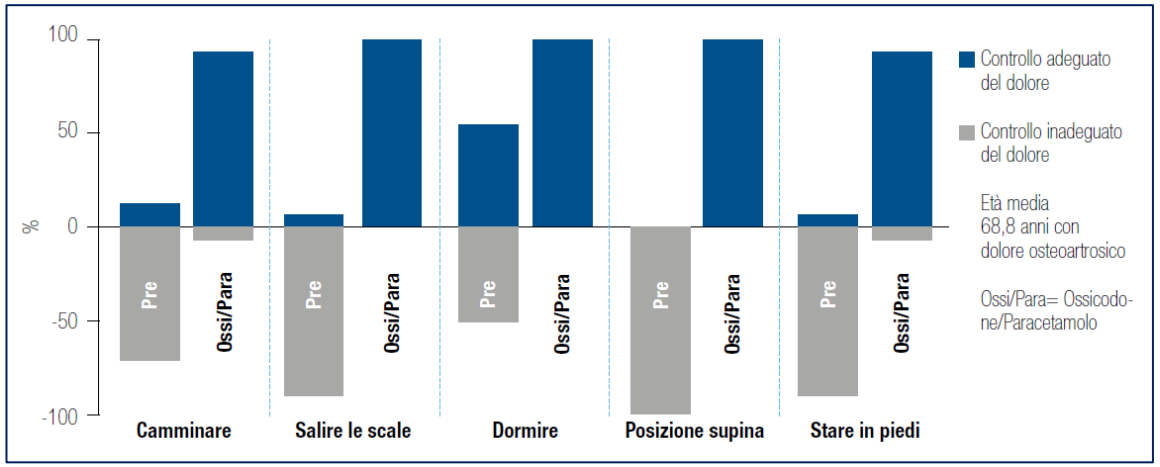
Silvia Natoli · Marzia Lazzari · Roberta Carpenedo · Elisa Palombo · Maria Beatrice Silvi · Massimo Mammucari · Mario Dauri

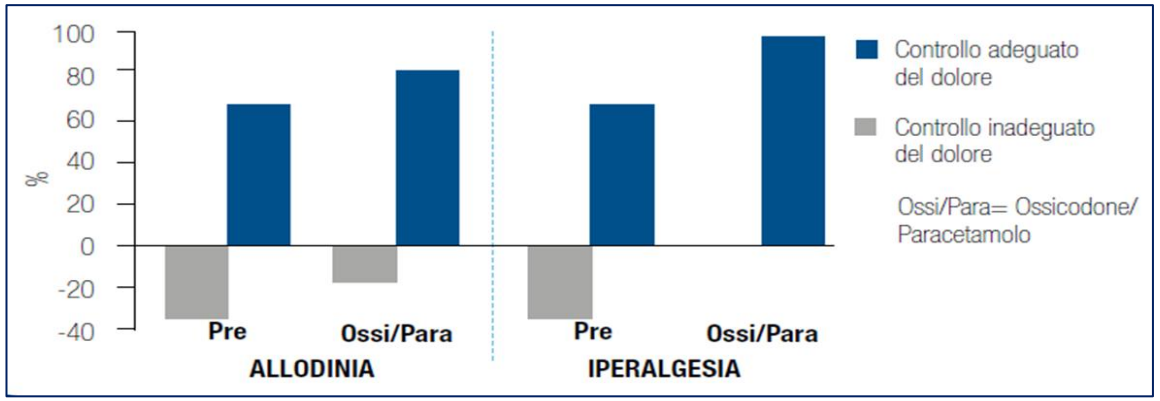
Table 2 Use of different available doses of oxycodone (5, 10, and 20 mg) in combination with acetaminophen fixed-dose (325 mg) and days of stable pain

Oxycodone/ acetaminophen dose	Patients, *n* (%)	Mean ± SD number of doses	Mean ± SD daily oxycodone dose, mg	Mean ± SD daily acetaminophen dose, mg	Mean ± SD days of stable pain NRS
5/325	476 (96.95)	1.61 ± 0.67	8.07 ± 3.38	523.00 ± 216.7	21.33 ± 5.96
10/325	12 (2.44)	2.50 ± 0.52	25.00 ± 5.22	812.50 ± 169.7	31.33 ± 3.73
20/325	3 (0.61)	2.00 ± 0.00	40.00 ± 0.00	650.00 ± 0.00	26.33 ± 7.77

RISULTATI:
NRS medio: 5,68±1,35 (baseline), FU 2,49±1,71 (Δ medio 3,17±1,31)
Dose media di oxy/par era 8,68±4,96 mg con 1,63 somm/die media.

Miglioramento della funzionalità fisica, allodinia e iperalgesia





78 paz (68 anni) con osteoartrosi dolorosa
ossicodone + paracetamolo (dose 5/325 mg x 3) per > 6mesi
Valutazione del questionario WOMAC (valutazione **dolore, rigidità e funzionalità fisica** con 24 domande)

Tutti i pazienti che hanno completato lo studio hanno mostrato
un notevole **miglioramento della sintomatologia dolorosa**

Gatti A et al. Clin Drug Investig 2009; 29 Suppl. 1:31-40.

PAZIENTE ANZIANO

REVIEW

Italian Intersociety Recommendations
on pain management in the emergency setting
(SIAARTI, SIMEU, SIS 118, AISD,
SIARED, SICUT, IRC)

Per il dolore lieve-moderato → **paracetamolo da solo**

Paracetamolo in combinazione con oppioidi deboli o con ossicodone

I **FANS non dovrebbero essere considerati come farmaci di prima linea**, e dovrebbero essere utilizzati con estrema cautela perchè associati a danno renale e aumentato rischio di sanguinamento gastrico. Tra i FANS, l'ibuprofene è da preferire. Negli anziani FANS e COXIB dovrebbero essere utilizzati insieme ad un inibitore di pompa.

I **Pazienti anziani rispetto ai giovani necessitano di una dose più bassa di oppioidi**

Ossicodone-Paracetamolo nel paziente anziano

Efficacy of oxycodone/acetaminophen and codeine/acetaminophen vs. conventional therapy in elderly women with persistent, moderate to severe osteoarthritis-related pain

Archives of Gerontology and Geriatrics 49 (2009) 378–382

Laura Corsinovi *, Elisa Martinelli, Gianfranco Fonte, Marco Astengo, Alessandro Sona, Antonia Gatti, Massimiliano Massaia, Mario Bo, Mauro Zanocchi, Giuliana Michelis, Gianluca Isaia, Mario Molaschi

Table 3
BDI-II, ADL and MMSE scores in the study groups at baseline and at the end of the study, mean ± S.D.

BDI-II			ADL			MMSE		
O/A	C/A	CT	O/A	C/A	CT	O/A	C/A	CT
Baseline								
19.1 ± 4.4	18.6 ± 4.5	19.4 ± 4.9	2.4 ± 1.2	2.4 ± 1.3	2.7 ± 1.2	27.0 ± 1.9	26.7 ± 2.0	27.3 ± 1.5
Week 6								
13.2 ± 3.1	13.4 ± 3.7	17.1 ± 4.7	1.3 ± 1.2	1.3 ± 0.9	2.3 ± 1.1	27.1 ± 2.0	26.9 ± 2.0	26.5 ± 2.7
Statistical comparison of the groups, Bonfer								
O/A vs. C/A: $p = 1.0$								
O/A vs. CT: $p < 0.05$								
C/A vs. CT: $p = 0.04$								
General linear model between groups								
$F = 3.9$, $p < 0.023$								
General linear model within groups								
$F = 8.7$, $p < 0.001$								

(p = ns). Treatment withdrawals due to AEs occurred in 4 subjects receiving O/A (7.7%), 10 subjects treated with C/A (19.2%) and 12 patients treated with CT (24%) (p = ns). Most frequent AEs responsible for drug discontinuation were nausea, vomiting and drowsiness in patients receiving opioid combined therapy and dyspepsia and worsening of renal function in patients treated with CT.

at the end of the follow-up, patients treated with O/A or C/A had significant lower BDI-II and ADL scores, than patients treated with CT.

PERIOPERATIVE PAIN MANAGEMENT

Ideal drug for the patient based on the type of surgery

Surgery

Post-operative shift

Follow-up

I

Intra-operatove

Post-operative

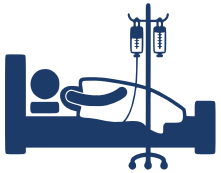
Hospital discharge

T0 T1 T2 T3 T4 T5 T6

Patient charge

Drug Shift
Sc-OS-IV
SR
IR

IV drug



European Society of
Regional Anaesthesia
& Pain Therapy
ESRA ITALIA

ESRA Italian Chapter

XXIX CONGRESSO NAZIONALE

7-9 Novembre 2024

CESENA, Cesena fiere

thank you!