

Inhaled opioids for cancer pain relief

A narrative review

Magdalena Osowicka, MD, PhD^{a,*}, Piotr Janowski, MD, PhD^b, Agnieszka Gorzewska, MD, PhD^a, Monika Lichodziejewska-Niemierko, MD, PhD^a

Abstract

Despite the many new possibilities, cancer pain treatment is not always effective and often poses a challenge for practitioners. At the end-of-life care, both oral and subcutaneous drug delivery very often are not attainable. The increasing number of patients in terminal stage of chronic diseases forced us to look for the alternative ways of administration of pain treatment. In this context, the potentially rapid onset of action and ease of use make aerosolized drug delivery an attractive option in palliative care settings. The objective of this review was to identify literature on pain relief with inhaled opioids. The evidence suggests that nebulized opioids might be effective in the treatment of pain in various aetiologies; however, randomized controlled studies on nebulization therapy for cancer pain are lacking.

Abbreviations: CIV = continuous intravenous infusion, ED = emergency department, M3G = morphine-3-glucuronide, M6G = morphine-6-glucuronide, NRS = numeric rating scale, RCT = randomized controlled trial, VAS = visual analogue scale.

Keywords: aerosolized, analgesia, analgesic, inhalation, inhaled, nebulized, nebulized, pain

1. Introduction

Pain is one of the most important symptoms of advanced cancer.^[1] Insufficient therapy negatively affects quality of life, sleep, and physical function, and severely impairs normal daily activity.^[2,3] Therefore, effective pain management is a priority in palliative care. In moderate and severe pain, the treatment of choice is opioids.^[4] Although opioids are highly effective in relieving acute pain, their clinical utility can be limited by their side effects or the inability to administer them orally.^[2,5] The latter necessitates the search for alternative forms of drug administration. Commonly employed subcutaneous delivery might be complicated by local skin reactions and is contraindicated in patients with thrombocytopenia or blood coagulation disorders. In severe cases, subcutaneous injections may even result in phlegmon.^[7] In this context, the delivery of analgesics by nebulization might be an attractive alternative, considering that it is a preferred and effective route of opioid delivery in patients with episodic breathlessness.^[8,9] Thus, a literature review was performed to identify studies which assessed the effectiveness of nebulized opioids in the treatment of pain.

2. Methods

The MEDLINE database was searched using the following terms: inhaled, inhalation, nebulized, nebulized, aerosolized, pain, analgesia and analgesic. Studies on pain relief using nebulized opioids were included in this review. A single study on nebulized fentanyl in cancer patients was added to the review despite its absence in the MEDLINE database. Studies analysis is preceded by a short discussion on the significance of inhaled opioid pharmacokinetics. This is the literature review so the ethical approval was not necessary.

3. Results

The literature search provided 11 prospective studies on nebulized morphine and 11 on nebulized fentanyl. Tables 1 and 2 list the significant information on the aforementioned trials.

3.1. Inhaled opioids pharmacokinetics

The antinociceptive effect of opioids is related to their action on the μ , κ , and δ receptors located in the central nervous system

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The datasets generated during and/or analyzed during the current study are not publicly available, but are available from the corresponding author on reasonable request.

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Opioids In Cancer Pain

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Opioids In Cancer Pain:

Opioids in Cancer Pain Mellar P. Davis, 2009-05-28 Opioids can be effective in relieving pain in more than 90% of cancer patients. However, often irrational fears from both patients and clinicians persist about the potential for addiction, meaning treatable pain continues to be tolerated. This book offers clear guidelines on the use of opioids when managing cancer pain.

Cancer Pain Relief World Health Organization, 1996 The second edition of a guide which introduced a simple yet highly effective method for the relief of cancer pain. Thoroughly revised and updated, the new edition further refines the WHO method which advocates the use of a small number of relatively inexpensive drugs including morphine. Revisions draw on experiences with millions of patients around the world as well as new knowledge about the specific pain syndromes unique to cancer. Completely new are chapters describing the international system by which morphine and other opioids are made available for medical purposes. The book has two parts. Part one provides a practical guide to the relief of cancer pain, concentrating on drug treatment as the mainstay of pain management. The most extensive section sets out detailed guidelines for the selection and prescribing of non-opioid analgesics, opioid analgesics, drugs for neuropathic pain, and adjuvant drugs for the treatment of adverse effects, the enhancement of pain relief, and the management of concomitant psychological disturbances. Information ranges from explanations of how specific drugs work through the precautions to take in the presence of certain disorders to a list of factors that influence the effectiveness of opioids. Concerning the use of opioids, readers are reminded that psychological dependence does not occur in cancer patients and that the only correct dose of morphine is the one that relieves the pain. Part two provides a guide to opioid availability. A discussion of the reasons why opioids continue to be underprescribed or difficult to obtain is followed by an explanation of the Single Convention on Narcotic Drugs.

Opioids in Non-Cancer Pain Cathy Stannard, Michael Coupe, Tony Pickering, 2013-03-21 Opioids have been used as analgesics for many years and their use in the management of acute pain related to trauma and surgery is well established. However, patients with persisting pain need a pain management plan that brings relief of symptoms without adverse effects in both the short and longer terms. The prescribing of opioids for chronic non-cancer pain has increased substantially since the first edition of this pocketbook was published, prompting considerable debate regarding the appropriateness of prescribing for this indication and the potential harms to individuals and to society that may result from this trend. This second edition of *Opioids in Non-Cancer Pain* brings clinicians up to date on the current use of opioid drugs in patients with non-cancer pain and highlights the potential benefits of therapy as well as the problems that can occur. The edition includes new chapters on the history of opioids to help contextualize the following discussions and a new chapter covering the emerging field of pharmacogenomics which provides explanations for differing responsiveness to opioids and propensity to adverse effects. An international perspective on opioid prescribing trends is also a valuable new addition.

Opioids in the Treatment of Cancer Pain Derek Doyle, 1990 Cancer Pain: From Molecules to Suffering Judith A.

Paice, Rae F. Bell, Eija A. Kalso, Olaitan A. Soyannwo, 2015-06-01 An in depth analysis of basic and clinical research on cancer pain *Cancer Pain From Molecules to Suffering* describes underlying mechanisms of cancer pain and reviews opioid treatment issues including tolerance This comprehensive new volume discusses current drug trials and research clinical trial designs common reactions including inflammation and hyperalgesia the psychology of cancer pain and disparities in the availability of cancer care worldwide Who should buy this book *Cancer Pain From Molecules to Suffering* is essential reading for Clinicians including physicians nurses physical therapists and psychologists Cancer researchers interested in studying the mechanisms and psychology of pain as well as clinical drug trials Global health care professionals who experience disparities in cancer treatment Medical students who want to improve their skills in cancer pain assessment and management *Demystifying Opioid Conversion Calculations: A Guide for Effective Dosing* Mary Lynn McPherson, 2009-08-24 Have you ever wondered if you calculated your patient's dosage correctly Against a backdrop of the growing scrutiny of appropriate dosages this textbook takes a fresh new approach to helping health professionals strengthen care to and possibly save the lives of patients living with pain This easy to understand and often humorous book is the most comprehensive to date on opioid calculations for pain management and palliative care It carefully walks clinicians through a five step process for performing opioid conversion calculations in the real world situations they often see The book has case examples simple charts and tables and practice problems throughout on topics such as difficult conversions for methadone fentanyl PCA and neuraxial opioid therapy conversions between routes and dosage formulations of the same opioids and different opioids titrating opioid dosages up and down to include dosage change and timing calculating doses for rescue opioid therapy Written by pain management expert Dr Mary Lynn McPherson the book gives helpful tips that practitioners should incorporate into their practices It is a must for clinicians at all levels hospice and palliative care physicians physician's assistants nurses nurse practitioners and pharmacists Clinicians will come away with more confidence in doing the calculations and higher service levels from the improvement in care *Cancer Pain* Dermot R. Fitzgibbon, John D. Loeser, 2012-03-28 This book provides in a single cohesive source all the information a health care professional needs to diagnose and select appropriate treatments for the patient with pain associated with cancer The book is clinically oriented and comprehensively addresses all the issues surrounding modern cancer pain management The authors provide detailed information on common but difficult to treat cancer pain scenarios Coverage includes state of the art information on treatment options and discussions of the impact of radiation chemotherapy and surgery on pain management This authoritative comprehensive clinical reference is essential for all clinicians who treat patients with cancer including medical oncologists radiation oncologists surgeons pain specialists anesthesiologists primary care physicians internists and nurses ***Cancer Pain Relief and Palliative Care*** WHO Expert Committee on Cancer Pain Relief and Active Supportive Care, 1990 Considers what can and should be done to comfort patients suffering from the distressing symptoms of advanced cancer Prepared by nine renowned experts in oncology

neurology pain management and nursing care the book draws together the evidence and arguments needed to define clear lines of action whether on the part of the medical and nursing professions or in the form of national legislation Throughout arguments for palliative care take their force from the magnitude of unrelieved suffering currently borne by the majority of terminally ill patients Although methods for the relief of pain are emphasized other physical psychological and spiritual needs for comfort are also included in the report s comprehensive recommendations The concept of palliative care is explained in terms of its concern with quality of life and comfort before death emphasis on the family as the unit of care dependence on teamwork and relationship to curative interventions Subsequent sections concentrate on measures for the relief of pain and other physical symptoms the psychosocial needs of the patient and family and the need for spiritual comfort A section devoted to ethics provides several important statements concerning the legal and ethical distinction between killing the patient and killing the patient and the need to recognize the limits of medicine crammed with very valuable information an altogether excellent book Family Practice a comprehensive report on cancer pain relief and active supportive care a valuable reference for those specializing in cancer care and for the generalist caring for dying patients Nursing and Health care WHO definition of palliative care

Clinical Pain Management : Cancer Pain Nigel Sykes,Michael Bennet,Chun-su

Yuan,2008-09-26 Now divided into four parts the second edition of Cancer Pain delivers broad coverage of the issues that arise in the management of malignancy related pain from basic science through end of life care and associated ethical issues to therapies both medical and complementary Part One reviews basis considerations in cancer pain management includ

Opioids and Pain Relief Marcia Meldrum,2003 Presents 14 papers from the second conference sponsored by the John C Liebeskind History of Pain Collection held in August of 2000 The conference brought together scientists and historians in order to examine the history of the opioids opium morphine heroin and others as a Janus drug showing two faces of therapeutics on the one hand and addiction and degradation on the other The focus is on the use of opioids within medicine and the growth of scientific understanding about them and their impact on human beings *Cancer Pain* Eduardo D.

Bruera,Russell K. Portenoy,2003-06-23 Nearly one in three people will be diagnosed with cancer and many of these patients will suffer from related cancer pain Cancer associated pain is widely feared by cancer patients but knowledge about the causes and management of cancer pain has increased dramatically in recent years and many new treatment options are available This comprehensive book discusses the unique characteristics of cancer pain including its pathophysiology clinical assessment diagnosis pharmacological management and nonpharmacological treatment The internationally recognized authors are leaders in cancer pain research and they apply their first hand knowledge in summarizing the principal issues in the clinical management of cancer pain This state of the art book cohesively addresses the full range of disciplines regularly involved in cancer pain management including pharmacology communication studies and psychology Cancer Pain is a scholarly but accessible text that will be an essential resource for physicians nurses and medical students who treat patients

suffering from cancer pain **Opioid Therapy in the 21st Century** Howard S. Smith, 2008-02-27 Over the last thirty years the concern of Pain Medicine practitioners about the potential for their patients to develop a dependence on opioids has left opioid therapy as a largely underutilized treatment While there is no simple answer to chronic pain opioids remain the only class of drugs capable of providing relief to patients experiencing serious pain Opioid Therapy in the 21st Century Second Edition fills a dearth of clinical knowledge about analgesics to aid practitioners in weighing the risks versus the benefits of opioid therapy for their chronic pain patients This second edition provides updated information on recently approved opioids as well as approved indications for older opioids and clinical trials Part of the Oxford American Pain Library this concise guide serves as a practical accessible reference for physicians across the range of primary care and medical specialties It includes an overview of appropriate clinical applications of opioids covering such topics as opioid pharmacology route selection and individualization of therapy as well as strategies for managing and mitigating the risk of abuse addiction and diversion There are also special sections dedicated to the unique needs of pediatric geriatric and palliative care patient populations **Clinical Pain Management Second Edition: Cancer Pain** Nigel Sykes, Michael Bennet, Chun-su Yuan, 2008-09-26 Now divided into four parts the second edition of Cancer Pain delivers broad coverage of the issues that arise in the management of malignancy related pain from basic science through end of life care and associated ethical issues to therapies both medical and complementary Part One reviews basic considerations in cancer pain management including epidemiology pharmacology history taking and patient evaluation and teamworking Part Two brings together the drug therapies for cancer pain their underlying basis and potential side effects Part Three covers the non drug therapies including nerve blocks stimulation induced analgesia radiotherapy complementary therapies and psychological interventions The control of symptoms other than pain so critical to cancer patients is also considered here Part Four describes special situations Cancer pain management in children and older patients and in the community setting and pain in the dying patient and the cancer survivor are all covered here Opioid Therapy in the 21st Century Howard S. Smith, 2013-02-21 Over the last thirty years the concern of Pain Medicine practitioners about the potential for their patients to develop a dependence on opioids has left opioid therapy as a largely underutilized treatment While there is no simple answer to chronic pain opioids remain the only class of drugs capable of providing relief to patients experiencing serious pain Opioid Therapy in the 21st Century Second Edition fills a dearth of clinical knowledge about analgesics to aid practitioners in weighing the risks versus the benefits of opioid therapy for their chronic pain patients Part of the Oxford American Pain Library this concise guide serves as a practical user friendly reference for physicians across the range of primary care and medical specialties It includes an overview of appropriate clinical applications of opioids covering such topics as opioid pharmacology route selection and individualization of therapy as well as strategies for managing and mitigating the risk of abuse addiction and diversion There are also special sections dedicated to the unique needs of pediatric geriatric and palliative care patient

populations This second edition discusses opioids approved for use since publication of the first edition such as Butrans buprenorphine patch fentanyl patch and nasal spray abuse resistant version of Oxycontin and Embeda morphine sulfate Approved indications for older opioids as well as clinical trial information have also been updated **Cancer Pain** Magdi Hanna,Zbigniew (Ben) Zylitz,2013-07-31 Cancer Pain provides a comprehensive practical guide to the management of pain in cancer patients Beginning with a discussion of current issues in the control of cancer pain the initial chapters provide a clear concise explanation of cancer pain syndromes an up to date understanding of the pathophysiological mechanism and recent developments in creating pre clinical cancer pain models The book offers the reader the wide and improved options for management of cancer pain in clinical practice including the use of opioid and non opioid drugs and the role of non pharmacological methods in pain control Subsequent chapters address particular challenges in pain control such as breakthrough pain neuropathic cancer pain as well as pain associated with cancer treatment which until recently has not been fully appreciated Recent issues relating to new adverse side effects to chronic opioid medications such as hyperalgesia and neurotoxicity are explained and best practice to reduce or avoid them is stated The book also aims to aid in the overall educational need for young doctors as well as established primary care physicians by highlighting the available tools and the importance of early pain interventions in the overall cancer treatment strategy *Cancer-related Breakthrough Pain* Andrew Davies,2012-08-23 This new edition in the Oxford Pain Management Library includes an extensive evaluation of opioids non opioid drugs and non pharmacological interventions for cancer related breakthrough pain This volume is a concise but rich resource for consultants GPs and specialist nurses interested in pain management *Fundamentals of Cancer Pain Management* Andrew Leitner,Christine Chang,2021-09-20 This book presents a timely and multidisciplinary update on the modalities currently available for treating the most feared symptom of patients diagnosed with cancer The various cancer pain syndromes are explored in detail covering those related directly to malignancy and those due to the after effects of cancer therapy Treatment modalities including pharmacologic approaches interventional procedures and palliative surgical options are discussed clearly and concisely with provision of recommendations for the practitioner Further topics include new and emerging treatments for cancer pain survivorship considerations pain management in special populations and implementation of systems based pain programs The book has been written by a multidisciplinary group of experts reflecting the evolution in pain and symptom management that has occurred in parallel with progress toward more targeted oncologic treatments Oncologists palliative care physicians allied health professionals and other practitioners involved in caring for cancer patients will find Fundamentals of Cancer Pain Management to be a rich source of evidence based insights into effective pain management *The MASCC Textbook of Cancer Supportive Care and Survivorship* Ian Olver,2018-09-25 This book is intended for medical students residents and fellows as well as medical oncologists radiation oncologists surgeons general practitioners nurses and allied health workers Complete with case vignettes key points and sidebar

summaries to further assist readers using practical tips and tricks this textbook provides current information on the management and prevention of cancer related side effects referring to up to date sources that are useful for conducting further research It also introduces new topics such as financial toxicity and complementary medicine as well as covering the new side effects of targeted therapies not covered in the last edition Additionally MASCC Textbook of Cancer Supportive Care and Survivorship 2nd edition assembles international multidisciplinary experts who focus on a comprehensive range of symptoms and side effects associated with cancer and its treatment Over the last five years much progress has been made in supportive care helping people cope with the symptoms of cancer and cancer treatment and addressing the physical and psychosocial matters of survivorship prior to during and after anticancer treatment This is central to a patient s wellbeing and the MASCC Textbook of Cancer Supportive Care and Survivorship 2nd edition explores not only the diagnosis and treatment but also the increasingly recognized complex and ongoing symptoms experienced by long term cancer survivors Significant advances have been made designing strategies to manage the side effects and symptoms of treatment and to prevent them from occurring maximizing the person s ability to pursue daily activities Reviews of the 1st edition This book reviews the management of cancer symptoms in patients and the side effects and late effects of treatment The focus of the book is on supportive care and survivorship of cancer patients The book covers symptomatology medication and treatment and system function of patients undergoing chemotherapy or radiation therapy Photographs and algorithm charts further illustrate key points This outstanding book is thorough in its explanations and easy to follow Arlenda C Thompson Doody s Review Service January 2011 *Strong Opioids and the Relief of Cancer Pain* ,2015-06 Supportive Care in Oncology Sebastiano Mercadante,2020-09-03 This text considers the concepts of cancer pain palliative care and supportive care leading the reader on an evolutionary journey parallel to changes in these disciplines It highlights new research in these fields reflecting the link between clinical activity primordial intuitions and scientific data

Unveiling the Magic of Words: A Overview of "**Opioids In Cancer Pain**"

In a world defined by information and interconnectivity, the enchanting power of words has acquired unparalleled significance. Their capability to kindle emotions, provoke contemplation, and ignite transformative change is truly awe-inspiring. Enter the realm of "**Opioids In Cancer Pain**," a mesmerizing literary masterpiece penned by a distinguished author, guiding readers on a profound journey to unravel the secrets and potential hidden within every word. In this critique, we shall delve in to the book is central themes, examine its distinctive writing style, and assess its profound effect on the souls of its readers.

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