Clinical Oncology 22 (2010) 199–207

Contents lists available at ScienceDirect

Clinical Oncology

journal homepage: www.elsevier.com/locate/clon

Original Article

Frequency of Opioid Use in a Population of Cancer Patients During the Trajectory of the Disease

L. Jarlbaek*†, D.G. Hansen *, E. Bruera ‡, M. Andersen *

* The Research Unit of General Practice, Institute of Public Health, University of Southern Denmark, Winsloewsvej 9A, 5000 Odense, Denmark
† Department of Oncology, Herlev Hospital, Herlev, Denmark
‡ Department of Palliative Care & Rehabilitation Medicine, M. D. Anderson Cancer Center, Houston, Texas, USA

Received 23 August 2009; received in revised form 17 November 2009; accepted 19 November 2009

Abstract

Aims: Bearing in mind that Denmark has one of the world's highest legal uses of strong opioids per capita, the aim of the present study was to describe the frequency of opioid use in a complete, population-based cohort of cancer patients at different time points during the trajectory of the disease, and to analyse the influence of different factors on opioid use close to death.
Materials and methods: All incident cancer patients registered in 1997–1998 (n = 4006) from a population of 470 000 were followed individually from diagnosis to death (non-survivors) or for 5 years (survivors). The use of opioids was obtained from a prescription database covering the whole population.
Results: Among the 43% cancer patients who survived for 5 years, 12% used opioids at diagnosis, 38% during follow-up and 10% after 5 years. For the non-survivors, 80% used opioids sometime during follow-up. At diagnosis, use related inversely to the cancer type's 5-year survival, and ranged from 20 to 46%; before death 64–76% used opioids. The odds ratios for opioid use at death were smaller for breast cancer (0.53; confidence interval 0.33–0.85), haemopoietic cancer (0.28; confidence interval 0.17–0.44) and the group of miscellaneous cancers (0.54; confidence interval 0.36–0.83) compared with colorectal cancer. Older age, longer disease duration and male gender (0.76; confidence interval 0.59–0.99) reduced the odds of opioid use at death.
Conclusions: Judged by the use of opioids, moderate to severe pain is frequent throughout the trajectory of the cancer disease. The frequency of opioid use was in accordance with the frequency of moderate to severe cancer-related pain described in published studies. This completely population-based data set enables analyses of the actual practice regarding cancer patients' use of opioids, and it can serve as a more effective template for the management of cancer pain than the traditional measures, such as opioid consumption per capita, for international comparisons.

Key words: Cancer patients; cohort study; disease duration; opioids; pain treatment; pharmaco-epidemiology

Introduction

Many cancer patients suffer moderate to severe pain. The prevalence increases as the disease progresses [1,2] and the undertreatment of cancer pain has been described as a frequent and worldwide problem [3,4]. Cancer pain frequently goes untreated; when it is treated, relief is often inadequate. Pain experts are aware of a treatment gap between what can be done and what is done about cancer pain. Education, training of health care workers and accessibility to pain relief are thought to narrow this treatment gap [5]. The size of this gap has been difficult to establish, and one reason may be the lack of community-based systems for data gathering to enable studies on pain epidemiology and treatment in whole populations of cancer patients [6]. Opioids are effective drugs in the treatment of moderate to severe cancer-related pain [7], but the extent to which opioids are actually prescribed to the cancer population is poorly elucidated. The overall opioid consumption in various countries has been used to highlight trends and possible problem areas in pain treatment [8], and a high consumption has been interpreted as an indicator of good cancer pain management [9], even without the ability to separate the use between cancer patients and non-cancer patients. For many years, Denmark has been among the countries in the world with the highest legal use of strong opioids per capita [8,10], partly due to few restrictions in

Author for correspondence. L. Jarlbaek, The Research Unit of General Practice, Institute of Public Health, University of Southern Denmark, Winsloewsvej 9A, 5000 Odense C, Denmark. Fax: +45-6550-3980.
E-mail address: ljarlbaek@health.sdu.dk (L. Jarlbaek).

0936-6555/$36.00 © 2009 The Royal College of Radiologists. Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.clon.2009.12.002

national policy with regard to the prescribing of opioids. Several comprehensive population-based databases with high data quality exist in Denmark [11]. Linkage between the Danish Cancer Register [12,13] and the Odense University Pharmacoepidemiologic Database (OPED) [14,15], enabled us to create a complete population-based data set with information of each individual cancer patient's use of opioids. Cancer patients' share in the population's use of opioids [15] and changes in cancer patients' use of different opioids over time [16] have previously been studied using the data set. In the present study, incident cancer patients were followed individually from the time of diagnosis until death or for 5 years with regard to the use of opioids. The aim was to demonstrate the frequency of opioid use during the trajectory of illness with regard to disease duration and cancer type, and to analyse the influence of certain factors on the use of opioids before death.

Materials and Methods

Individual data on cancer patients and their use of opioids were obtained by linkage between two comprehensive, population-based databases: the Danish Cancer Register [12,13] and the prescription database OPED [14,15]. The identifier in both databases was the Central Person Registration (CPR) number, which is a unique number provided to every citizen in Denmark.

Databases

The Danish Cancer Register has, for all practical purposes, full coverage of the Danish cancer population, dating back to 1942. The register provides information on each cancer with CPR number, anatomic site and histological classification according to a modified version of ICD7, month and year of diagnosis, stage at the time of diagnosis, and date of death. In this study, the date of diagnosis was defined as the 15th of the month. OPED is a prescription database with full coverage of all prescriptions redeemed in Funen County since 1992. Each record contains the CPR number of the patient, the date of purchase, a full account of the dispensed product, including substance, formulation, brand name, Anatomical Therapeutic Chemical (ATC) code, dose unit and quantity [17]. The World Health Organization ATC code is a seven-digit system for the classification of drugs [18]. Dosing instructions and indication for prescribing are not recorded in the database. By use of a demographic module in OPED, holding information on all citizens in Funen County (covering 9% of the Danish population, ~470 000 inhabitants), including dates of migration and deaths, the linkage procedure with the Cancer Register enabled the identification of all patients in the county with a diagnosis of invasive cancer.

Patient Cohort

All patients diagnosed with cancer for the first time, i.e. incident cancer patients, during the 2-year period, 1997–1998, were identified. Only incident cancer patients who had been inhabitants in the county for at least 1 year before the date of the cancer diagnosis and until death or for the following 5 years were included in the cohort. Patients with common skin cancer as the only cancer diagnosis were not included. Survivors were defined as patients who were alive 5 years after the date of diagnosis. Non-survivors were patients who died during the 5-year follow-up after diagnosis.

From the time of diagnosis, each patient in the cohort was followed until death or for 5 years with regard to their redemption of opioid prescriptions from the pharmacies.

Cancer Types

Primarily, the cancers were categorised in 18 groups. In order to carry out more valid and robust analyses, the number of groups was reduced to eight. On the basis of the number of patients, each of the five most frequent organ-confined cancers (breast, colorectal, lung, haemopoietic and prostate cancer) were assigned their own group in the analyses. A group termed 'poor 5-year survival' included the remaining cancer diagnoses, apart from lung cancer, having a 5-year survival less than 20% (Table 1). These cancers are often advanced or metastatic at the time of diagnosis, and the prevalence of pain in this group is assumed to be high. A group termed 'lower abdomen' included carcinomas with the primary tumour localised in the lower part of the abdomen, excluding colorectal and prostatic cancer, and with a 5-year survival exceeding 20%. Pain experienced in this group was assumed to be similar and with a high frequency of visceral pain. The last group, termed 'miscellaneous', included the remainder of the cancers.

Opioid Use

Here, the term 'opioid use' equals the redemption of opioid prescriptions. The same practice is used when the country's legal uses of opioids are described, and in several other pharmaco-epidemiological studies. The opioids were identified in OPED using N02A, the first four digits in the seven-digit ATC code [18]. Single-entity drugs and ketobemidone combined with an antispasmodic were included in the study. Each patient's use of opioids was followed from the time of diagnosis until death or for 5 years. A patient was defined as an opioid user if redemption of at least one opioid prescription was recorded in OPED in the time intervals chosen for analysis. For the evaluation of opioid use at the time of death, only patients with disease duration exceeding 2 months were included. Patients with very short survival are usually hospitalised all or most of the time until death. Therefore, their opioid use cannot be evaluated using a prescription database such as OPED.

The proportions of opioid users were calculated

- during follow-up — as the percentage of cancer patients with opioid records in OPED from 3 months before the date of diagnosis until death or until 5 years later;