Physicians’ prescribing habits for cancer pain in Cyprus

H. Charalambous1*, E. Protopapa2, D. Gavrielidou1 & V. Avgousti1
1Bank of Cyprus Oncology Centre, Nicosia, Cyprus, 2Institute of Child Health, University College London, London, UK

Background: Prescription of opioids based on morphine equivalence data per capita is very low in Cyprus. Three studies were undertaken to evaluate the prescribing habits of physicians in Cyprus for cancer patients with pain.

Methods: Data were collected regarding the presence and severity of pain and prescription of analgesia in a cross-sectional study of 141 patients receiving outpatient chemotherapy within the Bank of Cyprus Oncology Centre (BOCOC), in a retrospective study of 90 new lung cancer patients referred to one Oncologist in the BOCOC, and in a prospective study of 100 new cancer patients referred to the BOCOC. In the first study, the results reflected the prescribing habits of oncologists within the oncology centre, whilst the second and third studies reflected the prescribing habits of physicians outside the oncology centre.

Results: In the three studies, 56.0%, 48.1% and 57.7%, respectively, of patients with pain were prescribed analgesia. The majority of patients were prescribed paracetamol and non-steroidal anti-inflammatory drugs, and only 8.6%, 11.5% and 0%, respectively, of patients were prescribed strong opioids. In the last two studies, following their oncology appointment the prescription of analgesia to patients with pain, increased to 80.8% and 73.1%, respectively, whilst the prescription of strong opioids, increased to 28.8% and 34.6%, respectively, reflecting oncologists’ practice.

Conclusion: There is under-treatment of pain in cancer patients, both within and outside a tertiary oncology centre in Cyprus. Particularly there is low prescribing of strong opioids. There is a need to look further into the barriers that prevent physicians prescribing opioids in Cyprus, as well as to patients’ attitudes towards analgesia and opioids, and to set up training programs to address these issues.

Key words: cancer pain management, physicians prescribing habits, opioids use and barriers

introduction

Pain is one of the main symptoms of cancer, perhaps the most troublesome. It is therefore of paramount importance, that health care systems and individuals working in cancer/palliative care provide adequate pain relief to all cancer patients [1]. A measure of appropriate pain management is the consumption of opioids. For this purpose, the morphine equivalence metric (ME) is being used, expressed in mg per person, as it allows for equianalgesic comparisons between countries of the aggregate consumption of all principal opioids. For Cyprus, the total ME was 17.9451 mg per person in 2009 [2], and is well below that of other European countries, e.g. United Kingdom 311.96 mg, France 191.44 mg, Germany 344.68 mg. It is even considerably less than the ME of other Southern Europe countries, e.g. Italy 128.79 mg, Spain 259.60 mg, Portugal 149.75 mg and Greece 94.57 mg.

This low consumption of opioids in Cyprus cannot be explained or be attributed to financial or political reasons. Cyprus has been an independent state since 1960, with a population of about 1 million. In 2004, Cyprus joined the European Union, and in 2008 it joined the Euro, with the latest estimate per capita GDP (adjusted for purchasing power) at $30,003 [3], i.e. around the average of the European Union (EU27). In terms of health care spending, in 2005 Cyprus spent just over 6% of its GDP for health care [4], which although lower than the 8.9% average of the European Union, cannot account for a 10-fold or more difference in opioid usage.

Therefore other reasons or barriers to explain the low opioid consumption in Cyprus need to be looked at. On a global scale, differences in opiate consumption are often due to availability problems and excessive regulatory restrictions [5, 6]. In Cyprus it appears that neither opioid availability nor regulatory restrictions are to blame. When looking at the availability of opiates in Cyprus in comparison to the essential drugs list of the World Health Organization (WHO) [7] and the International Association for Hospice and Palliative Care (IAHPC) list of essential medicines for palliative care [8], all four opioids on the WHO list are available and most from the IAHPC list (fentanyl transdermal patches, methadone, and hydromorphone). Examining the current legal framework in Cyprus for prescription of opiates compared to the guidelines for assessment of national opioid regulations of the WHO [9], there is no significant overregulation for opioids in Cyprus. However, there is no legal framework to facilitate emergency prescribing and dispensing.
In view of the lack of significant regulatory restrictions or problems with opioids availability, failure on behalf of the clinicians to prescribe opiates or patients refusal to accept opiates are likely to blame. To examine this hypothesis further, we carried out three studies to investigate the prescribing habits of physicians in Cyprus both for existing cancer patients on treatment and also for new cancer patient referrals.

**methods**

Data regarding the prescribing habits of clinicians in Cyprus was sourced from three different studies.

The first study investigated the prescribing habits of oncologists by looking at prescription of analgesia in patients receiving outpatient chemotherapy in the BOCOC, the main tertiary oncology referral centre in Cyprus. This was a cross-sectional study, in which the presence of pain and analgesic prescriptions were documented in 145 outpatients attending the BOCOC in Nicosia. Ethics approval was obtained from the University of Surrey, Faculty of Arts and Human Sciences Ethics Committee, as well as the Cyprus Bioethics Committee. All patients attended the day care unit for chemotherapy including targeted therapy and intravenous zolendronic acid infusions. Patients over the age of 18, with any type of cancer, with or without pain, were eligible to participate following explanation of the study and provided they gave their informed consent. Assessment measures completed by patients included the Brief Pain Inventory (BPI) questionnaire [10]. The BPI is an instrument that measures pain severity and pain interference with function. It uses 11-point (0–10) numerical scales to assess worst, least, average and current pain, in addition to pain’s interference with general activity, mood, walking ability, normal work, relations with others, sleep and life enjoyment. The BPI also takes into account the percentage of pain relief experienced by patients. All analgesics used by the patients were recorded by the researcher (EP). Four of the 145 patients were excluded due to incomplete responses, for analysis purposes. Therefore a total of 141 patient records were available for analysis.

The other two studies collected data regarding the prescription of analgesia for new cancer patient referrals to the BOCOC. The second study was a retrospective study of 90 consecutive patients with lung cancer referred to one oncologist (HC) in 2009–2010, whilst the third study was a prospective study of 100 new patients referred in 2011 to the BOCOC. Ethics approval was obtained from the Cyprus National Bioethics committee for the prospective study. Both the second and third studies looked at the pain treatment of new patient referrals, which reflected the prescribing habits of physicians outside the oncology centre. The presence and severity of pain was documented, in addition to the type of cancer, stage of disease, treatment and the type of any analgesia that was prescribed to the patients prior to their referral to the BOC Oncology Centre. In the prospective study the BPI questionnaire was used. Furthermore, the analgesia prescribed following their oncology appointment (and up to 1 month after their initial appointment) was documented (reflecting oncologists' prescribing habits).

**results**

**cross-sectional study with existing cancer patients at the BOCOC**

In the first cross-sectional study of cancer patients receiving chemotherapy at the BOCOC, there were 141 patients (105 females, 36 males) with various types of cancer, predominantly breast (51.1%), gastrointestinal (19.1%) and lung cancer (9.9%) aged between 18 and 80 [mean, 56.6; standard deviation (SD), 12.3]. Forty-nine patients (34.8%) had metastatic disease.

Based on responses to the BPI question on average pain, most patients enrolled in this study experienced pain. Only 25 out of the 141 (17.7%) patients did not have any pain. Regarding pain severity, patients’ average pain scores have been divided into four categories using the BPI scores (0 = no pain, 1–4 = mild pain, 5–6 = moderate pain, 7–10 = severe pain). Most patients had either mild or moderate pain severity; 63 patients (44.7%) had mild pain, 39 patients (27.7%) had moderate pain and only 14 patients (9.9%) had severe pain.

Regarding pain treatment, whilst only 25 (17.7 %) patients reported no pain, 74 (52.5%) patients were not prescribed analgesics. Paracetamol and non-steroidal anti-inflammatory drugs (NSAIDs) was prescribed to 53 patients (37.6%), weak opioids to 2 patients (1.4%) and strong opioids to 10 patients (7.1%).

Alternatively this could be expressed as a percentage of the number of patients with pain. Considering the 116 patients with pain, only 65 (56%) patients were prescribed any analgesics. From those patients prescribed analgesics, the majority of patients were prescribed paracetamol/NSAIDs, while only 10 out of the 116 patients with pain (8.6%) were given strong opioids. Furthermore there were many patients with both moderate and severe pain receiving no analgesia, or just taking paracetamol/NSAIDs, as can be seen in Figure 1. It was of particular concern that 11 out of 14 patients (78%) with severe pain were either on the first step of the WHO ladder (paracetamol/NSAIDs) or not receiving any analgesia at all.

**studies of new cancer patients referrals**

Two studies were undertaken to examine the presence of pain and prescription of analgesia for new cancer patient referrals to the BOCOC. The analgesic regime on referral was considered to reflect the prescribing habits of physicians outside the BOCOC, and was compared to the analgesic regime following their first appointment (and up to 1 month later), considered to reflect BOCOC oncologists’ prescribing habits.

The first study was retrospective in nature and assessed 90 consecutive new patients with lung cancer referred between 2009 and 2010 to one oncologist (HC) at the BOCOC. There were 70 men and 20 women, age range (26–84), mean age 62.4 (SD, 12.2). Forty-two patients (46.7%) had metastatic disease.

![Figure 1. Pain treatment according to pain severity (cross-sectional study of patients receiving chemotherapy).](image-url)
Data were collected regarding the presence of pain and the prescription of analgesia from patients' notes. Regarding the presence of pain, 38 patients (42.2%) had no pain, 29 patients (32.2%) mild pain, 13 patients (14.4%) had moderate pain and 10 patients (11.1%) had severe pain. Out of the 52 patients with pain only 25 (48.1%) had been prescribed analgesics and only 6 (11.5%) had been prescribed strong opioids.

Following their initial appointment, the prescription of analgesia in the BOCOC was reviewed again after 1 month of follow-up had elapsed. The number of patients being prescribed analgesics increased to 39 out of 52 patients with pain (75%), with 15 patients (28.8%) being on strong opioids (Figure 2). Furthermore, looking at patients with moderate and severe pain, the prescription of weak and strong opioids increased from 10 out of 23 patients (43.5%) to 18 patients out of 23 patients (78.3%), respectively, strong opioids from 6 patients (26.1%) to 14 (60.9%).

Finally a prospective study of 100 new cancer patients (all cancer diagnoses) referred to the BOCOC was undertaken. There were 59 men and 41 women, age range (33–96), mean age 63.3 (SD, 12.9). The most common cancers were genitourinary cancer with 24 patients (24%), gastro-intestinal cancer 19 patients (19%), breast cancer 16 patients (16%), skin cancer 13 patients (13%), and lung cancer 10 patients (10%). Twelve patients (12%) had metastatic disease.

The BPI questionnaire was used to collect data regarding the presence of pain and the prescription of analgesia. In this study 26 out of the 100 patients had pain, 10 patients had mild pain (10%), 7 (7%) had moderate pain and 9 (9%) had severe pain.

Of the 26 patients with pain, 15 (57.6%) were offered analgesics, which they all accepted. Analgesics prescribed was predominantly on the first step of the WHO ladder, with 12 out of 15 patients on paracetamol/NSAIDs, and 3 on weak opioids. No patients were on strong opioids prior to their referral to the oncology centre.

Following their initial appointment, the prescription of analgesia in the BOCOC was reviewed again after 1 month of follow-up had elapsed. The number of patients being prescribed analgesics increased to 19 out of 26 patients with pain (73%), with 9 patients (34.6%) being on strong opioids. Furthermore looking at patients with moderate or severe pain 14 out of 16 patients were on either on no treatment or on paracetamol/NSAIDs prior to their oncology appointment and only 2 patients (12.5%) were on weak opioids. After their oncology appointment 8 out of 16 patients (50%) were prescribed strong opioids (Figure 3).

**discussion**

In these three studies, respectively 56.0%, 48.1% and 57.7% of patients with pain were prescribed analgesia, therefore between 42.3% and 51.9% of cancer patients in Cyprus with pain did not receive any analgesia at all (Table 1). When looking at the analgesia prescribed, the majority of patients were prescribed paracetamol and NSAIDs, and respectively only 8.6%, 11.5% and 0% of patients were prescribed strong opioids. In fact, even for patients with moderate and severe pain, weak and strong opioids were offered to 15%, 43% and 16%, respectively (Table 2), confirming under-treatment of pain in Cyprus.

An initial look at the data, especially of the cross-sectional study in the BOCOC reflecting oncologists prescribing habits, would suggest that under-treatment of pain is common in Cyprus, both within and outside the tertiary oncology centre, and hence that pain management by oncologists does not differ from other physicians in Cyprus. However, when examining the last two studies, following their oncology appointment the prescription of analgesia to patients with pain, increased from 48.1% and 57.7% to 80.8% and 73.1%, respectively, whilst the prescription of strong opioids, from 11.5% and 0% to 28.8% and 34.6%, respectively, suggesting an improvement in the practice of oncologists at the oncology centre (Table 1).

These findings are not surprising for oncologists in Cyprus. In fact these studies were initiated out of the observation that even patients with severe pain and metastatic disease were not offered opioids prior to their oncology appointment and the clinical experience that often pain was overlooked as a symptom, with more emphasis being placed on cancer diagnosis and treatment. More unexpected were the findings of...
the cross-sectional study that even patients on chemotherapy within the oncology centre, were not offered appropriate analgesics, with the only explanation here being that the majority of patients did not harbor metastatic disease and that most patients on this study had mild and moderate pain on the BPI scale.

It is therefore worth highlighting some of the differences between the three studies, especially in terms of percentage of patients with metastatic disease, patients with moderate and severe pain and prescription of opioids. Contrary to what one may have expected, in the cross-sectional study of patients on chemotherapy there were only 35% of patients with metastatic disease, hence most patients were receiving adjuvant as opposed to palliative chemotherapy, especially for breast cancer. This was the study with the highest percentage of patients with pain up to 83% (Table 1), but with the majority of patients experiencing mild pain (63/116 of patients with pain). Also indicative of poor practice was that only 15% of patients with moderate or severe pain were put on opioids (Table 2). The retrospective study of new lung cancer patients had fewer patients with pain (57.8%), which may be due to the retrospective nature of this study. This study had the highest percentage of patients (46.7%) with metastatic disease, but not a higher percentage of patients with moderate and severe pain compared to the cross-sectional study (Table 2). Interestingly this study had the highest percentage with 43% of patients with moderate and severe pain on opioids, which increased to 78.3% after the oncology appointment (Table 2). This may suggest that the knowledge of metastatic disease may affect prescribing habits of physicians in Cyprus. The prospective study of new patient referrals, had the lowest rate of pain prevalence of only 26%, with a predominance of moderate and severe pain on BPI, which is the opposite from the other two studies. This may suggest that patients, especially with mild pain, were more pre-occupied on their first appointment to discuss their diagnosis and treatment with their oncologists, than to record their pain on the BPI questionnaire. This study also had the lowest incidence of only 12% of patients with metastatic disease, and only 16% of patients with moderate and severe pain on opioids (Table 2).

Adequate pain relief is a basic human right, and every effort should be made to alleviate or eradicate this for cancer patients. It is well known that up to 90% of cancer patients’ pain can be effectively treated with analgesia [11]. Yet cancer patients in Cyprus still continue to experience pain without being provided with adequate analgesics, even though some of them may be terminally ill. It is therefore vital that we try to understand the reasons for this, and try to rectify them as a priority.

All studies support the suggestion that the underuse of opioids for cancer patients in Cyprus is predominantly due to physicians’ factors failing to prescribe appropriate analgesics and opioids for their patients, although to a smaller degree this may be due to patient factors. It is well documented in the literature that patient barriers to prescription of opioids include concerns about addiction and side effects, poor communication with physicians, reluctance to admit to pain (fear that this implies disease progression) and misconceptions about inevitability of pain [12]. Our studies cannot reliably answer to what degree the under-treatment of pain was due to negative attitudes of patients and their families toward opioid medications. Only in the last prospective study, there was a question asking patients if they were offered analgesia, and whether they declined or accepted it. All the patients replied that they accepted all analgesia offered, and whether they declined or accepted it. Further support that the underuse of opioids is predominantly due to physicians’ factors is, however, provided by the significant increase in the prescription of opioids in the last two studies after patients were seen by oncologists.

Regarding physicians’ barriers/factors for underuse of opioids, these are due to misconceptions about medications and side effects, insufficient knowledge/training in pain management and lack of formal assessment procedures for pain [12], and hence all these barriers need to be tackled in a comprehensive training program for physicians in Cyprus. Lack of training of physicians in pain management and in

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients with metastatic disease</th>
<th>Moderate + severe pain as % of all patients with pain</th>
<th>Patients with moderate + severe pain on weak and strong opioids: Pre- and after oncology appointment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cross sectional</td>
<td>49/141 (34.8 %)</td>
<td>53/116 (45.7 %)</td>
<td>8/53 (15 %)</td>
</tr>
<tr>
<td>Lung cancer Retrospective</td>
<td>42/90 (46.7 %)</td>
<td>23/52 (44.2 %)</td>
<td>10/23 (43 %)</td>
</tr>
<tr>
<td>Prospective all diagnoses</td>
<td>12/100 (12 %)</td>
<td>16/26 (61.5 %)</td>
<td>2/16 (16 %)</td>
</tr>
</tbody>
</table>

Table 1. Summary table

<table>
<thead>
<tr>
<th>Study</th>
<th>Patients with pain</th>
<th>Patients with pain prescribed analgesia</th>
<th>Patients with pain prescribed strong opioids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cross sectional</td>
<td>116/141 (82.3%)</td>
<td>65/116 (56.0 %)</td>
<td>10/116 (8.6 %)</td>
</tr>
<tr>
<td>Lung cancer Retrospective</td>
<td>52/90 (57.8%)</td>
<td>25/52 (48.1 %)</td>
<td>42/52 (80.8 %)</td>
</tr>
<tr>
<td>Prospective all diagnoses</td>
<td>26/100 (26 %)</td>
<td>15/26 (57.7 %)</td>
<td>19/26 (73.1 %)</td>
</tr>
</tbody>
</table>

Table 2. Summary table
palliative care in general was highlighted also by Bingley and Clark [13] in their report about palliative care in Cyprus. This is further aggravated or even caused by the fact that there are only two palliative care specialists in Cyprus for a population of 1 million, hence this limited presence impacts negatively in teaching opportunities for other physicians working in Cyprus. Furthermore, currently the public health care system which caters for most (close to 80% of all patients) has no organized palliative care services, instead palliative care has been left to the not for profit NGOs (non-governmental organizations), whilst there is no official contact between staff of the public hospitals and palliative care staff working for the NGOs.

Even in countries with comprehensive palliative care programs and palliative care training opportunities, there are still problems with inadequate knowledge and practice regarding opioids prescription by physicians, and despite the availability of guidelines, e.g. the ASCO symptom management curriculum [14] and excellent web-based tools e.g. the EPEC: Education for Physicians in Palliative and End-of-Life Care Oncology [15]. A recent national survey of medical oncologists in the US [16] aiming to evaluate the knowledge and practice of US medical oncologists relating to cancer pain, found that there were major limitations in pain-related knowledge and practice. This was despite medical oncologists rating their specialty highly for the ability to manage cancer pain, and rating their peers lower.

The findings of these studies reinforce the need for further work that needs to be done in this field to improve pain management in Cyprus. Future research needs to focus on direct questionnaires to physicians enquiring about their knowledge and practice/prescribing habits, similar to the US study [16], and also on asking patients about knowledge regarding opioids, barriers / phobias, and preferences. It would be extremely useful to look at the effect of increasing physicians’ training (physicians’ prescribing habits questionnaire pre and after training), increasing patient–physician contact time and providing more pain and analgesia input/information from physicians and other healthcare professionals to patients, and how these measures impact into better pain management, prescription of analgesia and opioids in Cyprus.

disclosures

The authors declare no conflicts of interest.

references

2. Data of opioid consumption in Cyprus from the University of Wisconsin Pain and Policy Studies group. Available at: http://www.painpolicy.wisc.edu/internal/EURO/Cyprus/cyprusMEtable.pdf (20 April 2012, date last accessed).