Artykuł oryginalny

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Age influence on opioid consumption in terminally ill digestive cancer patients

Abstract

The aim of this work was to estimate the influence of the age and gender on the opioids usage in terminally ill digestive cancer patients. A retrospective files analysis of the 344 patients who had died in two palliative units, divided into three groups (< 60, 60–70, > 70 years old) was performed. Morphine Equivalent Daily Dose (MEDD) on admission, within the last 3 days, last 5 days and in the last day of life were compared. The number of patients receiving coanalgesics and the number of coanalgesics used per patient were also analyzed. The amount of opioids remained stable through the last 5 days. The mean daily MEDD values in every time intervals were significantly higher in the youngest group than in older ones. The number of coanalgesics used was the highest in the youngest group. Smaller number of patients received coanalgesics in the oldest group. Women < 60 years old required a significantly higher MEDD than men in each time interval, except of the admission. Study confirms the lower amount of opioids used in the elderly digestive terminal cancer patients and also within younger males.

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Introduction

The proportion of people aged 65 years and older in Europe is steadily increasing. In 2009, this age group represented almost 15% of the whole population. By 2050, estimates indicate that more than one quarter will be aged 65 years and older. The greatest percentage increase will be among people aged over 85 years [1]. This group is more likely to die from other diseases than cancer, also some studies have indicated age-related differences in symptom prevalence, e.g. pain decreased with age [2]. Besides, undertreatment and misdiagnosis frequently occur owing to the assumptions made by health care providers that pain can be the normal consequence of aging. Divergent observation exists according to the amount of analgetics used in the elderly. Higher pain prevalence in women is consistently observed as well by not well understood [3]. The aim of this work was to estimate the influence of the age and gender on the opioids daily consumption in the terminal digestive cancer patients.

Methods

A retrospective observational study assessing opioid consumption in terminally ill digestive tract cancer patients was performed. Patients died between 2005 and 2009 in St. Lazarus Hospice and in Department of Pain Treatment and Palliative Care, University Hospital in Krakow, Poland were included. All files of patients that were hospitalized in that time were searched.

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These who were admitted for at least 3 days before death and received strong opioids were included. Patients were divided according to their age into three groups: below 60 (< 60), between 60 and 70 (60–70) and over 70 (> 70) years old. The primary outcome was total dose of opioids used over the course of 24 hours converted to an equivalent dose of parenteral morphine in milligrams (MEDD — Morphine Equivalent Daily Dose), following the standard equianalgesic conversion tables [4]. MEDD values on admission and on the last full day before death were measured. Mean values between groups were compared. Mean MEDD for the last 3 days and 5 days of stay for each group were calculated and compared. MEDD on admission was compared with the last day of hospitalization and differences between men and women were analyzed. The secondary outcomes were the number of patients receiving coanalgesicss and the mean number of coanalgesics used.

Statistics

To compare differences between groups analysis of variance (ANOVA) was used with the Shaffe *post hoc* test. To compare within group differences paired Student *t*-test was used. To compare number of patients using coanalgesicss Spearman correlation was applied. All statistical calculations were performed using STATISTICA software. Statistical significance was set at the $P < 0,05$ level.

Results

During 5-years period of assessing 2189 patients died of cancer, among them 771 of primary digestive tract. 344 patients (44,6%) received strong opioids and were included in further analysis. In the oldest group there were significantly more females and in the medium group more males ($P < 0,05$). The characteristics of assessed group are illustrated in Table 1.

The amount of opioids remained stable through the last 5 days. In the youngest group it tend to be higher than on admission. The mean daily MEDD values in every time interval were significantly higher in the youngest group than in both older groups ($P < 0,05$). In the youngest group the difference between the daily dose in the last and the first day of hospitalization was found to be the largest (Fig. 1).

The number of co-analgetics used was the highest in the youngest group (mean 3,13) in comparison with intermediate group (2,60) and the oldest (2,35). The difference between the youngest and the oldest group occurred statistically significant ($P < 0,05$) (Tab. 2).

In the oldest group smaller number of patients (43% of all the subjects) received co-analgetics (Spearman correlation = -0,21; $P < 0,05$).

Women < 60 years old had a significantly higher MEDD than men every time interval, except of the admission time ($P < 0.05$) (Fig. 2).

There was no significant difference between men and women in older groups. The mean MEDD values in the group > 74 years were slightly higher among the male patients (NS).

Discussion

Studies indicate that > 90% of the elderly living in the community experienced pain within the past month, with 41% reporting discomforting, distressing, horrible, or excruciating pain [5]. Musculoskeletal pain seems to be the most predominant pain, and inactivity is the most effective strategy used to lessen pain. While many of the patients report that activity make their pain better, the consequence of inactivity can result in additional problems for the elderly. Surveys indicate that pain is experienced by more than two thirds of those with advanced disease, in cancer it is reported in 35–96% of patients. In our population 44,6% of patients received strong opioids which corresponds to other observations that 25–40% of older cancer patients experience daily pain and on admission to hospice care more than 50% had severe pain [6]. Some studies outline the same level of pain in older groups, other point that it decreases with age [7]. In practice undertreatment and misdiagnosis can frequently occur owing to the assumptions made by health care providers that pain is a normal consequence of aging [8]. That is probably one of the reasons that older patients in daily pain are less likely to receive any analgesic agent and also three times less frequent received strong opioids [9].

Table 1. Included group characteristics

	Under 60	60–74	Above 74
Number of patients (%)	71 (20,7)	125 (36,3)	148 (43,0)
Mean age ± SD (years)	52,8 ± 6,4	67,9 ± 4,2	80,3 ± 4,2
Males (%)	42 (59,1)	84 (62,4)*	72 (48,6)*
Mean hospitalization (days)	16,3 (± 21,0)	15,5 (± 21,1)	19,9 (± 25,9)

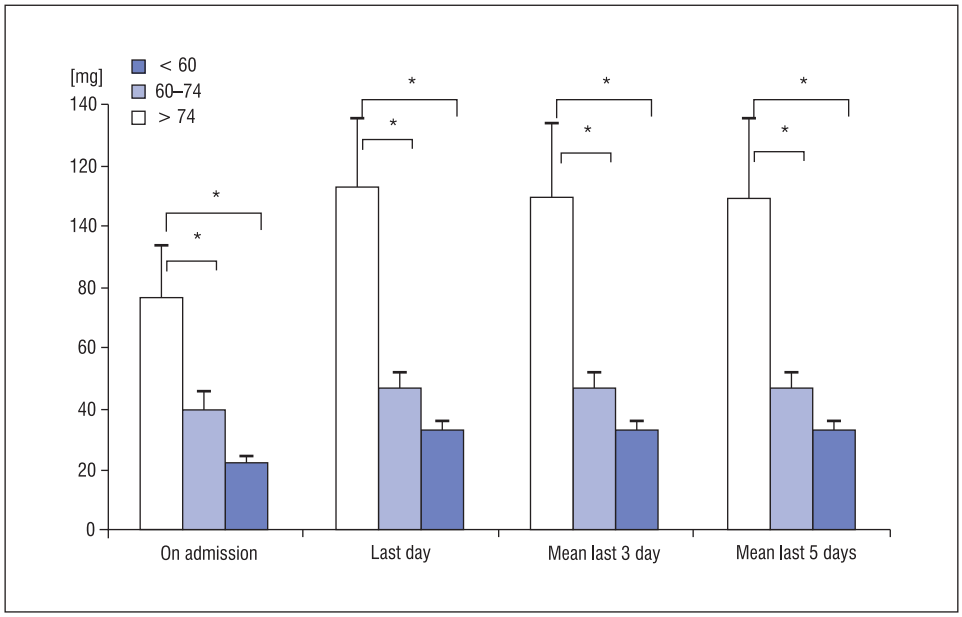

Figure 1. MEDD (mean and standard error) values within the groups

Table 2. Coanalgesics used in three groups of patients

	Under 60	60–74	Above 74
Number of patients received coanalgesics	61 (86%)	109 (87%)	124 (84%)
Mean number of coanalgesics used (± SD)	3,13 (1,99)*	2,60 (1,88)	2,35 (2,08)*

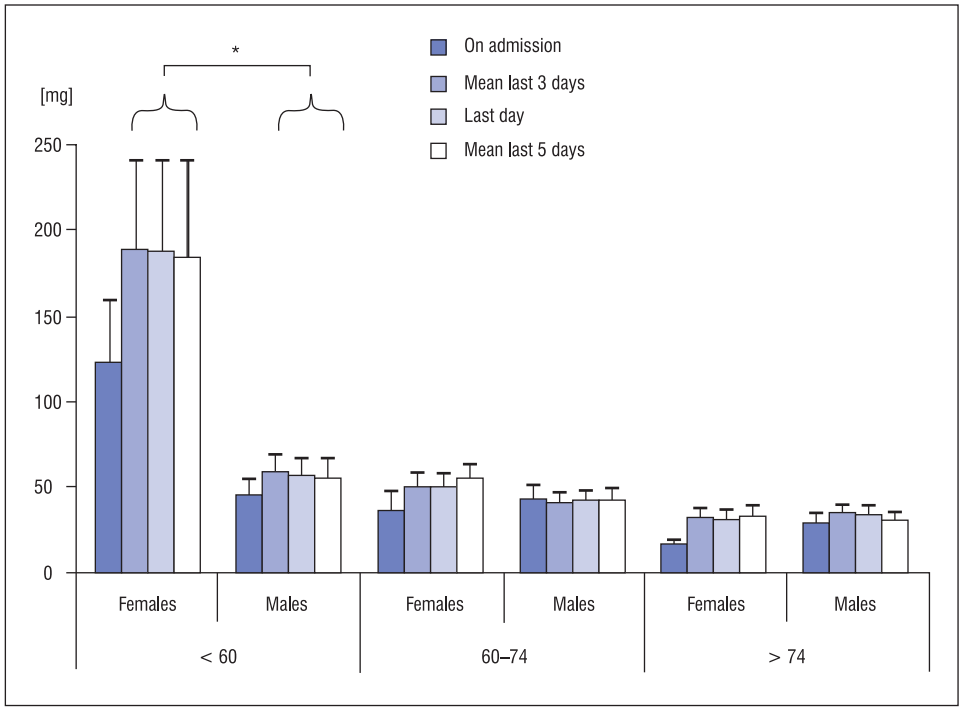

Figure 2. MEDD (mean and standard error) sex difference

The mean MEDD of 22,1 was observed in our older cancer patients. Other studies showed much higher amounts of opioids given: 105,5 (± 116,2 SD), with an increase that ranged between 82–137 mg, associated with the presence of neuropathic pain [10]. In our analysis younger patients who were on opioids demanded higher doses of opioids and coanalgetics. Only one small observation showed that older patient can receive more opioids than those under 60 [11]. Our results are analogous with the other studies: in spite of that overall symptom profiles between the older and younger groups are similar, in the last days of life, patients aged 80 years and older receive significantly less parenteral morphine equivalents [12]. Concerns exists if older cancer patients experience less effective pain management. In a recent study the experience and the management of pain (including non-opioids, even OTC medications) in older cancer patients was no different from that in younger subjects. Older patients are less likely to receive adequate analgesia than younger, even though, in relation of pain intensity, studies have found no difference between them. The problem existing with determine the effectiveness of cancer pain management depends on selecting an appropriate outcome measure [13]. These findings may be related to several factors. Specialist palliative and geriatric pharmacotherapy is based on a slow titration with detailed adverse symptoms monitoring, so the assessed elder group could be treated more cautiously. Older patients may be more sensitive to the analgetic effects of opioids with higher peek effect and lower duration of action secondary to decreased elimination. Besides, having higher risk of poor opioid absorption may also have increased drug toxicity due to impaired analgesic metabolism [14]. Lower metabolic reserve often leads to more pain distress in older patients during the titration phase. In the stable phase, after titration, opioid adverse effects do not differ between the age groups suggesting that older patients are not more susceptible than younger adults [15]. Some authors mention older patients stoicism and belief that only intolerable suffering is a justified reason for complains [16].

The very old appear to have a lower requirements for medication. They are at higher risk of gastric and renal toxicities, e.g. silent and fatal bleeds. General recommendations remain regarding the cautious use of non-steroid anti-inflammatory drugs in this population. Much safer appears to reach earlier for the second and third step of WHO analgetic ladder, provided that the titration with cause using short acting medication first, titrated to comfort and then converting to a long acting medications. A better understanding of the needs of this population at the end of life will enable adequate service planning and improved care.

In our study younger women needed more opioids than the men in this group of age. This difference decreased with the age and the oldest group was homogeneous. Higher pain prevalence (from 1,5 times in headache to 4 times in fibromyalgia) in women is consistently observed but not well explained and understood. This observation can be associated with sex differences in basic pain mechanisms (nociceptive pathways, opioid system, physiology, perceptual sensitivity) and also gender differences in psychological factors (like cognitive or emotional appraisal of pain, by pain behaviours or even different social roles). Females are judged using „virtual human" technology by the health care students as having more pain than males [17]. Women are more likely to report receiving health care for musculoskeletal pain and higher rates of long-term opioid use is observed in them. Further research is needed to address whether gender-specific pain treatment may sometimes be warranted [3].

There are some limitations in this study. First, the patients had been recruited through palliative care wards and this involvement may have resulted in some bias. Second, in a retrospective method, we have not analyzed pain levels assuming that all patients were equally sufficiently treated. However also in other studies retrospective observation of pain by different medical staff using different methods can be a source of bias. Finally MEDD equivalents may be the confounding factor, especially when oral and subcutaneous methods of drug delivery was administered.

In conclusion, this study confirmed the lower amount of opioids used in the elderly digestive cancer patients also within younger males.

References

1. Hall S., Petkova H., Tsouros A.D., Costantini M., Higginson I.J. (red.). World Health Organization, Regional Office for Europe. Palliative care for older people: Better practices. WHO, Denmark 2011: 6–8.
2. Teunissen S., Wesker W., Kruitwagen C., de Haes H., Voest E.E., de Graeff A. Symptom prevalence in patients with incurable cancer: A systematic review. J. Pain Symptom Manage 2007; 34: 94–104.
3. LeResche L. Defining gender disparities in pain management. Clin. Orthop. Relat. Res. 2011; 469 (7): 1871–1877.
4. http://www.palliative.org/PC/ClinicalInfo/AssessmentTools/INSTRUCTIONS%20FOR%20MORPHINE%20EQUIVALENT%20DAILY%20DOSE11092011.pdf.
5. Brown S.T., Kirkpatrick M.K., Swanson M.S., McKenzie I.L. Pain experience of the elderly. Pain Management Nursing 2011; 12 (4): 190–196.
6. Rozzi A., Scirocchi R., Fava A., Bordin F., D'Addario M.E. i wsp. Pain assessment in terminally-ill cancer patients on admission in hospice and its modification after the first three days of care. A monocentric experience. Clin. Ter. 2011; 162 (5): 413–417.

7. Teunissen S., Wesker W., Kruitwagen C., de Haes H., Voest E.E., de Graef A.A. Symptom prevalence in patients with incurable cancer: a systematic review. J. Pain Symptom Manage 2007; 34: 94–104.
8. Weiner D.K. Office management of chronic pain in the elderly. American Journal of Medicne 2007; 120 (4): 306–315.
9. Bernabei R., Gambassi G., Lapane K., Landi F., Gatsonis C. Management of Pain in the elderly patients with cancer. JAMA 1998; 279 (23): 1877–1882.
10. Vigano A., Bruera E., Suarez-Almazor M.E. Age, pain intensity, and opioid dose in patients with advanced cancer. Cancer 1998; 83: 1244–1250.
11. Loick G., Radbruch L., Sabatowski R., Siessegger M., Grond S., Lehmann K.A. Morphine dose and side effects: a comparison of older and younger patients with tumor pain. Dtsch. Med. Wochenschr. 2000; 125 (41): 1216–1221.
12. Rashidi N.M., Zordan R.D., Flynn E., Philip J.A. The care of the very old in the last three days of life. J. Palliat. Med. 2011; 14 (12): 1339–1344.
13. Bennet M.I., Closs S.J., Chatwin J. Cancer pain management at home (I): do older patients experience less effective management than younger patients? Support Care Cancer 2009; 17: 787–792.
14. Pergolizzi J., Boger R.H., Budd K., Dahan A., Erdine S. i wsp. Opioids and the Management of Chronic Severe Pain in the Elderly: Consensus Statement of an International Expert Panel with Focus on the Six Clinically Most Often Used World Health Organization step III Opioids. Pain Practice 2008; 8 (4): 287–313.
15. Mercadante S., Ferrera P., Villari P., Casuccio A. Opioid escalation in patients with cancer pain: the effect of age. J. Pain Symptom Manage 2006; 32: 413–419.
16. Closs S.J., Chatwin J., Bennet M.I. Cancer pain management at home (II): Does age influence attitudes towards pain analgesia? Support Care Cancer 2009; 17: 781–786.
17. Snutts L.A., Hirsh A.T., George S.Z., Robinson M.E. Investigating patient characteristics on pain assessment using virtual human technology. Eur. J. Pain 2010; 14: 1040–1045.