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Prescribing of pain medication in palliative care. A survey in general practice[y].

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SUMMARY

Purpose To examine what pain and adjuvant medication is prescribed in palliative care patients at home in The Netherlands.

Methods In a nationwide, representative, prospective study in general practice in The Netherlands, prescribed medication was registered in 95 general practices with a listed population of 374 070 patients. The GPs identified those who received palliative care in a retrospective survey of the 2169 patients who died within the 1-year study period. We analysed the analgesics, laxatives and anti-emetics that were prescribed during the last 3 months of life for these patients.

Results The response rate of the survey was 74%. 425 patients received palliative care and 73% of them were prescribed pain medication: 55% a non-opioid analgesic (paracetamol, NSAIDs), 21% a weak opioid (tramadol, codeine), and 51% a strong opioid. Relatively more younger than older patients were prescribed strong opioids, and more cancer than non-cancer patients were prescribed an analgesic. During the last 3 months of life, the proportion of patients prescribed a non-opioid or a weak opioid increased gradually. The proportion of

patients prescribed a strong opioid increased considerably nearing the patient's death. About one third of the non-cancer patients were prescribed strong opioids, mostly commencing in the last 2 weeks before death. In 48% of all patients with an opioid prescription, the GP did not prescribe a laxative.

INTRODUCTION

Most people with an incurable disease prefer to remain at home surrounded by their relatives during the last part of their lives.[1–3] In The Netherlands, health care is characterised by its strong emphasis on primary care, where the general practitioner (GP) is the central professional in the management of the patient's treatment.[4] Almost 60% of patients with non-acute illnesses die at home,[5] and there is a general consensus that palliative care should be provided in the patient's home.[6] Pain is one of the symptoms that physicians most frequently encounter in palliative care patients.[7,8] An important aid for pain management is theWorld Health Organisation (WHO) analgesic ladder.[9] Drug treatment is the mainstay of pain management and is composed of three steps of pharmacological therapy. The sequential use of drugs starts with the non-opioid analgesics in step 1, as well as adjuvant drugs.[9] Opioids for mild to moderate pain—weak opioids—are prescribed in step 2 and strong opioids for moderate to severe pain in step 3. In most patients it is possible to manage pain effectively[10]; however, substantial improvement in the control of pain is still possible as pain management by clinicians and in the community is suboptimal.[11–13] Although recommendations state that opioids should be combined with laxatives to prevent constipation, and might be combined with anti-emetics to prevent nausea, many doctors still prescribe opioids without a simultaneous laxative.[14–16] Financial issues are acknowledged to be important at the end-of-life[17]; however, with respect to medication this is not an issue as the costs of pain medication for long-term use is reimbursed in The Netherlands by the health care system.

Data about the treatment of pain and the prescribing of pain medication are often derived from specialised settings,[18,19] and these are not always transposable to the community as the prevalence and treatment of pain differ between settings.[10] Other studies restrict their study population to cancer patients.[20,21] To the best of our knowledge, there is no study in primary care that has measured the prescribing of pain medication in a general population that includes cancer and non-cancer patients receiving palliative care at home from their GPs.

This study investigates the following research question: what pain and adjuvant medication is prescribed in patients receiving palliative care at home in general practice in The Netherlands, and how does the proportion of patients prescribed non-opioid analgesics, weak-opioids and strong opioids change during the last 3 months of life?

METHODS

Patient selection

The data used in this study were obtained from the second Dutch National Survey of General Practice (DNSGP-2), in which a sample of 104 Dutch general practices with 195 GPs registered the content of all patient/GP contacts in a 1-year period.[22] The participating GPs were representative of all Dutch GPs (n=7217).[22] The GPs coded the symptoms or diseases according to the International Classification of Primary Care.[23] The 1-year period of each practice ended between April 2001 and January 2002. Data from nine practices were excluded: four practices delivered incomplete data and five practices were excluded because the data did not meet the quality criteria. The listed population of the remaining 95 practices was 374 070 patients. In these practices 2169 patients died during the study period (0.6%).

At the end of the study period, the GPs received a retrospective post-mortem questionnaire for each patient who died during the survey year. They reported the patient's underlying disease, and labelled each patient who received palliative care. The GP's own subjective label was chosen because this allows all the factors which in the perception of the labeller are related to palliative care to be taken into account. The labelling of the patient served as the first inclusion criterion. As all patients died during the study period, to ensure that we had an observation period of at least 3 months for each patient, the second inclusion criterion was that the patient died at least 3 months after the start of the prospective study.

[TABLE 1]

Prescriptions

All prescriptions were derived from the database of the DNSGP-2 and contained digitally recorded information about the prescribed drugs, including the Anatomical Therapeutic Chemical classification code (ATC-code).[24] We included all analgesics, with the exception of anti-depressants and neuroleptics, and classified them in three classes: non-opioid analgesics, weak opioids and strong opioids (see Table 1). Of the adjuvant drugs prescribed to control adverse effects,[9] we included laxatives and anti-emetics.

[TABLE 2]

Measurements

Steps in theWHOana*lgesic ladder*: for each patient we analysed whether, and if so how many weeks before death, each of the three classes of analgesics had been prescribed during the 3 months observation period.

First prescription: each prescription was recorded as a first issue or a repeat prescription. A first prescription was defined as such when it was the first prescription in the observation period, and when it had not prescribed in the preceding 6 months. When a drug was first prescribed, the number of weeks between the date of prescription and the patient's death was calculated.

Combination with laxatives and anti-emetics: for each patient who was prescribed an opioid, we specified whether any laxative or anti-emetic had been prescribed.

Analysis

Descriptive analyses were carried out for patient characteristics and for the most frequently prescribed drugs in the three steps of the WHO analgesic ladder.

Differences in prescribing between sub-populations were calculated for medication initiated before the observation period, and over the last 3 months of life, for the characteristics gender, age and underlying disease, i.e. cancer versus non-cancer patients, using χsquare test (α=0.05). For both cancer and non-cancer patients, we analysed changes in prescribing during the last 3 months of life by calculating the cumulative proportion of patients prescribed a drug in each of the three classes, starting at 3 months before the patient's death. The week in which the drug was first prescribed counted as the starting point. Furthermore, we analysed increases in the prescribed class of analgesics during the last 3 months and whether laxatives or antiemetics were prescribed as concomitant drugs in patients prescribed weak or strong opioids.

RESULTS

Out of the 2169 questionnaires sent to GPs, 1760 were returned (81%), and 1596 were filled in completely (74% valid response rate). In total, 736 (46%) of patients received palliative care and 425 patients had an observation period of at least 3 months before death.

Characteristics of the patients studied are presented in Table 2.

[TABLE 2]

Of all patients who received palliative care, 73% were prescribed at least one drug for pain during the observation period (Table 3). Of these patients, 31% received this prescription before the observation period. For most of these patients, the prescriptions were for non-opioid analgesics, with paracetamol prescribed for 14% of the patients. Weak and strong opioids were prescribed for 5.6 and 6.4% of the patients at 3 months before the patient's death. During the observation period, 55% of the patients received a non-opioid prescription, 21% a weak opioid prescription and 51% a prescription for a strong opioid. More cancer patients than non-cancer patients received a prescription for a strong opioid at 3 months before death and over the full observation period.

Table 4 shows that during the full observation period, there were no differences by gender in the proportion of patients who were prescribed pain medication.

Relatively more younger patients were prescribed a strong opioid than were older patients.

[TABLE 3]

Prescribing different classes of analgesics during the last 3 months of life

Figures 1 and 2 show the proportion of cancer and noncancer patients who were prescribed no drug, and at least one drug from any of the three analgesic classes in the 3 months preceding death. At 3 months before death, the proportion of cancer patients who had no prescription was 65% compared to 73% for non-cancer patients. This proportion decreased gradually towards death for both cancer and non-cancer patients, with a steeper decrease in the last week, resulting in 19% of the cancer patients and 36% of the non-cancer patients having received no prescription over the observation period. During the last 3 months of life the proportion of patients who were prescribed a non-opioid analgesic or a weak opioid analgesic increased gradually. The proportion of patients prescribed a strong opioid showed a considerable increase starting at 3 weeks before death for cancer patients, and 1 week later for non-cancer patients.

Increase in analgesic classes and prescribing co-medication to treat adverse effects Table 5 shows that in the 3-month time frame, 16% of all patients were prescribed a strong opioid without firstly being prescribed a weak opioid. This occurred more frequently in cancer than in non-cancer patients (p=0.016). Out of the 29 patients prescribed only a weak opioid and the 215 patients prescribed a strong opioid, respectively 59 and 46% were not prescribed a laxative during the last 3 months of life. For all patients prescribed a weak and/or a strong opioid the proportion of not prescribing any laxative was 48%.

In the patients who were prescribed an opioid more than 2 weeks before death, 46% was prescribed a laxative, compared to 60% of the patients who were prescribed an opioid in the last 2 weeks of life. Not prescribing a laxative was more frequent in non-cancer patients than in cancer patients (p=0.006). In total, 29% (n=70) of patients prescribed an opioid received a prescription against nausea.

[TABLE 4]

DISCUSSION

Summary of main findings In the last 3 months before death, 73% of patients receiving palliative care from their GP were prescribed pain medication: 55% a non-opioid analgesic, 21% a weak opioid, and 51% a strong opioid. Over the full period, relatively more younger than older patients were prescribed a strong opioid. During the last 3 months of life, the proportion of patients prescribed a non-opioid or a weak opioid increased gradually.

The proportion of patients prescribed a strong opioid increased considerably nearing the patient's death.

About one-third of the non-cancer patients were prescribed strong opioids, most of them starting in the last 2 weeks before death. In 48% of all patients with an opioid prescription, the GP did not prescribe a laxative.

Strengths and the limitations of this study

Limitations of this study were that no information was obtained about the severity of the pain, or whether the drugs prescribed were used by the patient.

[FIGURE 1]

[FIGURE 2]

Furthermore, we were unable to measure whether, in the prescriber's or the patient's opinion, pain control had been achieved. Also, we had no details about dose adjustments, hence these were not included in the analysis. We did not include drugs started 3 months before the patient's death.

This study was embedded in the second Dutch National Survey of General Practice, which has generated solid data due to its quality and size,[22] and has allowed us to analyse the prescribing of pain medication longitudinally over the last 3 months before a patient's death. The total response rate of 74% for the additional questionnaire was high compared to mean response rates of 61% reported in population-based studies carried out in general practice.[25] As most studies in palliative care are limited to cancer patients,[26] a further strength of this study is that we included both cancer and non-cancer patients.

[TABLE 5]

Comparison with existing literature

A total of 27% of all patients in general practice receiving palliative care, and 19% of cancer patients, were not prescribed analgesics. Although pain is common in cancer patients, studies report a wide variation in its prevalence (33–88%).[27] However, the proportion of patients receiving a prescription for analgesics in our study is comparable to numbers found in other studies.[10,27] Weak opioids, step 2 of the WHO analgesic ladder, are prescribed to 27% of the cancer population, which is substantially lower than in Italy (52%)[10] and Germany (60%).[28] This may be due to the fact that in both studies doctors were instructed to follow the WHO analgesic ladder. Also differences in knowledge and attitude towards strong opioids (e.g.'opiophobia') might explain differences in prescribing across Europe.[29] Our study shows that GPs often pass over weak opioids, and suggests that for the optimal management of pain, patients might benefit from the omission of step 2 of the WHO analgesic ladder, as is common practice and advised in recent Dutch guidelines[30] and also suggested by other authors.[31,32] Reasons for the omission of weak opioids may be that they frequently induce side effects such as nausea and constipation.[33,34] Nearing end of life, another reason for prescribing a strong opioid without firstly prescribing a weak one may be that it is more important to achieve pain control quickly than to explore whether it could first be controlled with a weaker opioid.

It is striking that the increase in opioid prescribing occurs in non-cancer as well as in cancer patients, as pain is less common in non-cancer diseases. Possibly non-cancer patients share with cancer patients an increasing need for strong opioids to manage pain and/ or dyspnea.[35,36] The prescribing of opioids in noncancer patients may reflect a typical pattern, with an increase in pain starting 2 weeks before death. It might also be that GPs are reluctant to prescribe strong opioids for non-cancer patients[37–39] until death is close.

A point of concern is the lack of prescribing of comedication with opioids. Antiemetics are prescribed in only 27% of cases. In 48%, no laxative has been prescribed. This proportion is comparable to in the findings of other studies.[20,40] On the other hand, this number is low as compared to existing guidelines, that advise to combine strong opioids with laxatives.[9,41,42] This study shows that GPs do not act according to these guidelines. Co-prescribing of laxatives and antiemetics needs more attention in education and attention of—and cooperation with—other health care professionals, such as pharmacists.[16] Also, regular evaluation of the medication regimen might enhance the use of laxatives.[43]

Finally, we found that 34% of patients receive fentanyl via a transdermal patch. This could be an indication that GPs prescribe the fentanyl patch more often than advised in the WHO recommendations, which recommend—if possible—oral administration of strong opioids.[9] It appears that the practical advantages of the use of the transdermal patches for many patients and their GPs outweigh those of oral dosing, a trend seen in other countries as well.[44]

Implications for future research or clinical practice

In total, 27% of patients receiving end-of-life care in general practice are not prescribed analgesics. Future, studies need to investigate why: because there is no need for pharmacological pain management, or because GPs do not manage pain adequately. Pain management for non-cancer patients also needs attention, especially in the period nearing death. To optimise pain management, we need to know why current practice with regard to the WHO analgesic ladder and the prescription of laxatives differs from the guidelines. The possibility that greater awareness and education in general practice over recent years has led to new insights into the optimising of pain management in palliative care which are not reflected in the guidelines cannot be excluded. Also, we need to know how we can optimally manage pain in non-cancer patients nearing the end of life.

KEY POINTS

Many patients were prescribed a strong opioid without a weak opioid being prescribed first.

_ About half of patients were prescribed an opioid without a laxative being prescribed.

_ About one third of the non-cancer patients were prescribed strong opioids, mostly commencing only in the last 2 weeks before death.

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TABLES AND FIGURES

Table 1. Prescribed pain medication and their corresponding ATC-codes classified in non-opioid analgesics, weak and strong opioids

Class of drug	ATC-code	Drug name
Non-opioid analgesics	N02BE01	Paracetamol*
	N02AA59	Paracetamol (+codeine)*
	N02BE51	Paracetamol (+other) (excl.psycholeptics)*
	M01AE01	Diclofenac
	M01 (other)	Other NSAIDs
	N02BA	Salicylic acid + derivates
Weak opioids	N02AA59	Codeine (+paracetamol)*
	N02BE51	Codeine (+paracetamol)*
	N02AX02	Tramadol
	N02AC04	Dextropropoxyphene
Strong opioids	N02AA01	Morphine
	N02BA03	Fentanyl (transdermal patch)
	N02	Other
Laxatives	A06	
Antiemitics	A03FA	
	A04	

*Paracetamol and/or codeine were prescribed alone, or in combinations. Therefore, different ATC-codes could identify these drugs.

Table 2. Characteristics of patients who received palliative care in general practice ($N = 425$).

	% ($N = 425$)
Sex	
Male	47
Female	53
Age (years)	
<70	28
70–79	24
80–89	32
≥90	16
Mean age (SD)	76.9 (14.0)
Underlying disease*	
Cancer	55
Non-cancer	45
Heart failure	11
COPD	3.1
Other disease	26
Multiple non-cancer diseases	4.5

*Number of missing values for underlying diseases was 3.

Table 3. Proportion of cancer and non-cancer patients who received palliative care in general practice and prescribed pain medication during the last 3 months of life ($N=422$)

(A) Pain medication initiated before the observation period*

Prescribed drug	Cancer† ($n=234$)	Non-cancer ($n=188$)	P (χ-square)	Total ($n=422$)
No prescription (%)	65	73	0.113	69
At least one prescription (%)	35	27		31
Non-opioid analgesics (%)	28	24	0.315	26
Paracetamol (%)	15	13	0.675	14
Diclofenac (%)	12	5.3	0.017	9.2
Other NSAIDs (%)	7.3	7.4	1.000	7.3
Weak opioids (%)	6.8	4.3	0.295	5.6
Codeine (%)	2.6	2.7	1.000	2.6
Tramadol + other‡ (%)	4.3	2.1	0.280	3.3
Strong opioids (%)	8.5	3.7	0.047	6.4
Morphine (%)	5.6	2.1	0.085	4.0
Fentanyl (%)	4.7	2.1	0.192	3.5
Other (%)	0.4	0.0	1.000	0.2

(B) Pain medication prescribed during the full observation period

Prescribed drug	Cancer† ($n=234$)	Non-cancer ($n=188$)	P (χ-square)	Total ($n=422$)
No prescription (%)	19	36	0.000	27
At least one prescription (%)	81	64		73
Non-opioid analgesics (%)	62	46	0.001	55
Paracetamol (%)	39	34	0.312	37
Diclofenac (%)	29	13	0.000	22
Other NSAIDs (%)	17	11	0.095	14
Weak opioids (%)	27	14	0.001	21
Codeine (%)	12	9.6	0.530	11
Tramadol + other‡ (%)	19	7.4	0.001	14
Strong opioids (%)	62	37	0.000	51
Morphine (%)	39	24	0.001	32
Fentanyl (%)	45	20	0.000	34
Other (%)	5.1	1.6	0.064	3.5

*A drug was initiated before the observation period, as it was identified as repeat prescribing.
†Number of missing values for underlying diseases was 3.
‡One patient was prescribed dextropropoxyphene.

Table 4. Proportion of palliative care patients in general practice by gender and age category prescribed at least one analgesic in different classes of pain medication ($n=425$)

(A) Pain medication initiated before the observation period*

		No prescription	At least one prescription	Non-opioid analgesic	Weak opioid	Strong opioid
Age category ($N=425$)	<70 years (%)	72	28	22	6.8	9.3
	70–79 years (%)	69	31	26	5.0	5.9
	80–89 years (%)	65	35	29	7.4	5.9
	≥90 years (%)	71	29	27	1.4	2.9
	P (χ-square)†		*0.557*	*0.290*	*0.329*	*0.090*
Gender ($N=425$)	Male (%)	74	26	24	7.0	6.0
	Female (%)	65	35	28	4.5	6.7
	P (χ-square)		*0.059*	*0.378*	*0.297*	*0.843*

(B) Pain medication prescribed during the full observation period

		No prescription	At least one prescription	Non-opioid analgesic	Weak opioid	Strong opioid
Age category ($N=425$)	<70 years (%)	21	79	54	31	63
	70–79 years (%)	28	72	61	21	46
	80–89 years (%)	28	72	52	19	46
	≥90 years (%)	34	66	53	10	46
	P (χ-square)†		*0.060*	*0.581*	*0.001*	*0.014*
Gender ($N=425$)	Male (%)	30	70	53	22	52
	Female (%)	25	75	57	21	50
	P (χ-square)		*0.231*	*0.495*	*0.812*	*0.698*

*A drug was initiated before the observation period, as it was identified as repeat prescribing.
†χ-Square for trend. Linear-by-linear association.

Figure 1. Proportion of cancer patients in the weeks preceding death who were prescribed no analgesic and at least one analgesic of the following classes: nonopioid analgesics, weak opioids or the strong opioids ladder (N=234)

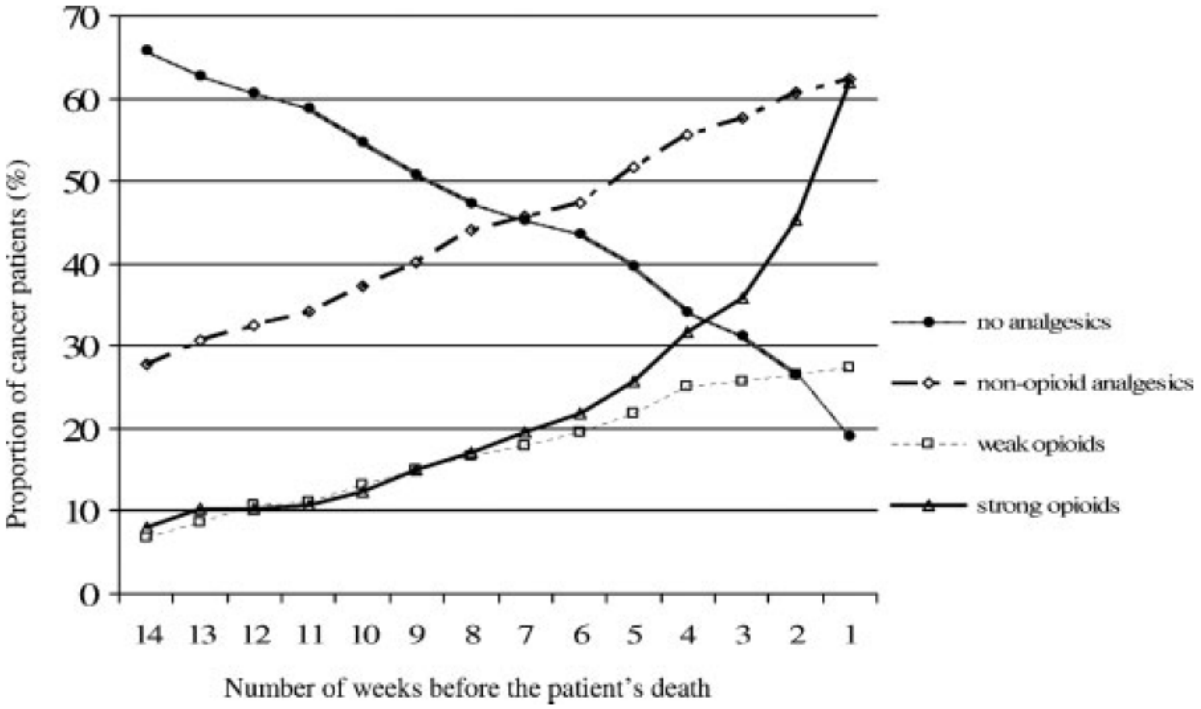

Figure 2. Proportion of non-cancer patients in the weeks preceding death who were prescribed no analgesic and at least one analgesic of the following classes: non-opioid analgesics, weak opioids or strong opioids (N=¼188)