Use of Morphine and Other Opioids in the Nordic Countries

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According to the statistics of the International Narcotics Control Board of United Nations (INCB), there are large differences in the yearly consumption of morphine among the Nordic countries. In order to assess the quality of management of cancer pain in each country, nationwide questionnaire studies were carried out in Finland, Norway, Denmark and Sweden in 1989–1992. This is a review based on the results of those four surveys.

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In Finland, Norway and Denmark, the same questionnaire was used and mailed to a 5–10% random sample of all physicians, when specialities not expected in the treatment of cancer patients were excluded. Among 21 open and multiple-choice questions, three simulated patient cases were presented and the physicians were asked how they would treat the pain. In Sweden, a separate study was carried out. Questionnaires containing 56–60 questions were sent to the chairmen of 228 hospital departments representing six main specialities in the treatment of cancer pain. The physicians most acquainted with cancer pain were asked to respond.

The response rate was 40–100%. According to the studies, Finnish doctors still avoided prescribing strong opioids, which leads to severe undertreatment of cancer pain. In Norway, the proportion of physicians suggesting opioid treatment was larger, but too low doses were often suggested. In Sweden, the majority of departments were reported to be familiar with the recommended principles of opioid use, and the problems identified were in not using laxatives with opioids and poor skills in the management of neuropathic pain. In Denmark, adequate use of opioids was recognized. However, the high total consumption of morphine in the country is probably due to a large population of patients using morphine for non-malignant chronic pain in contrast to other countries where the use has been more restricted to cancer pain. The authors of the Danish study found the results 'encouraging' but identified some problems in the management of neuropathic pain and side effects of opioids.

GLOBAL CONSUMPTION OF OPIOIDS

In all European countries, the legal framework regarding trade, prescription, recording and dispensing of opioid drugs arises because their governments have become signatories to the Single Convention of Narcotic Drugs in 1961. The Single Convention requires control of the production, distribution and illicit consumption of these drugs. The Single Convention established the International Narcotics Control Board (INCB) whose function is to record statistics for the amount of opioids consumed for licit purposes, quantities of opioids used for manufacture of other opioids, the international movement of opioids as well as areas of land under poppy cultivation.

According to the statistics of the INCB, global consumption of morphine for medication has increased 7-fold during the past 20 years (1). The increase is due to the increased use of morphine for pain, especially for chronic cancer pain in 10 western industrialized countries (1). The greatest users are the Anglo Saxon and North European countries, with the exception of Finland, but a more gradual increase in the consumption of morphine is going on in many other countries, too. Table 1 shows the development in daily consumption of morphine in some countries, indicated as defined daily doses per million inhabitants (1). A defined daily dose for the INCB is 30 mg parenterally and 100 mg orally. The greatest usage of morphine worldwide is in its conversion to codeine, dihydrocodeine, ethylmorphine and pholcodine. Table 2 shows the consumption of different opioids in the Scandinavian countries (2).

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Table 1

Average daily consumption of defined daily doses of morphine per million inhabitants during 1986–1990, 1988–1992, 1989–1993, 1990–1994 and 1991–1995

Country	1986–1990	1988–1992	1989–1993	1990–1994	1991–1995
Denmark	3 048	4 066	4 684	5 332	5 929
New Zealand	1 826	2 040	2 003	2 103	1 586
United Kingdom	1 483	1 779	2 224	2 623	2 824
Iceland	1 471	1 493	1 715	1 988	2 172
Canada	1 670	2 038	2 242	2 382	2 597
Norway	1 335	1 644	1 853	1 990	2 009
Ireland	1 062	1 504	1 626	1 794	1 972
Australia	1 033	1 342	1 963	2 378	2 765
Sweden	1 080	1 940	2 348	2 570	3 202
USA	801	1 120	1 339	1 531	1 721
Switzerland	605	740	876	1 079	1 202
South Africa	276	266	217	224	263
Portugal	329	341	341	232	227
The Netherlands	371	589	667	771	858
Austria	290	543	661	792	984
Finland	263	317	408	406	454
Israel	261	457	631	646	637
Belgium	222	356	432	534	622
Germany	212	350	276	524	626
France	196	371	453	646	1 077
Spain	168	283	321	388	505
Hungary	111	114	112	193	264
Japan	82	139	177	221	276
Bulgaria	73	58	56	60	65
Greece	39	55	58	66	86

LAWS AND REGULATIONS CONCERNING USE OF OPIOIDS

In all European countries, with the exception of Belgium, The Netherlands, and the United Kingdom, special prescription forms or official prescription books are needed when strong opioid agonists are prescribed for outpatients. In Germany, Austria and the southern European countries, governments and legislators are very restrictive about the use of opioids, whereas the Scandinavian countries are seen as having a relatively liberal legal framework. For example, there are no rules concerning the maximal amounts (milligrams of drug) prescribed or the duration of validity of the prescription (3).

STUDIES ON OPIOID USE IN EUROPE

There are two types of studies which address the issue of opioid use in the treatment of pain: questionnaire studies measuring the clinical practice, knowledge and attitudes of a sample of physicians in a hospital setting, region or country, and studies measuring actual prescribing. Almost all studies concern cancer pain; there is only one regional prescription study on the treatment of non-malignant pain with opioid analgesics (4).

A nationwide questionnaire study on current practice in the treatment of cancer pain was carried out in Finland in 1985, 1990 and 1995 (5–7). The same study has been repeated in Norway, Denmark, France and Colombia, which facilitates comparison of prescription practices between these countries (Table 3) (8–10). Somewhat different studies using different samples of physicians have also been carried out in Sweden, Belgium, Switzerland, The Netherlands and the United Kingdom (11–15). The statistics from these studies are less comparable but give a picture of the prescribing status of those countries.

The repetitive study in Finland reflects the development of current practice in one country, but the results of the Nordic studies may also explain the differences in opioid consumption between these countries, indicated by the INCB statistics. The aim of this review is to compare the main results of the four Scandinavian studies, and to describe some differences in current practices in pain treatment in these countries.

FOUR SCANDINAVIAN PRESCRIBING STUDIES IN 1989–1992

In Finland, Norway and Denmark, questionnaires containing 18 (Denmark) or 21 (Norway and Finland) open and multiple-choice questions were sent to 5% and 10% random samples of physicians treating cancer pain. The names and addresses of the physicians were obtained from the registers of the National Boards of Health. In Sweden,

Table 2

Average daily consumption of defined daily doses per million inhabitants during the years 1986 to 1990 (INCB)

	Morphine	Codeine	Dextropropoxyphene	Pethidine	Total
Denmark	3 048	11 259	4 967	266	26 946
Finland	263	2 074	–	33	3 524
Iceland	1 471	5 118	34	55	051
Norway	1 335	11 673	926	66	17 248
Sweden	1 080	6 048	2 154	76	11 159

Defined Daily Doses: Morphine 30 mg parenterally, 100 mg orally; Codeine 100 mg; dextropropoxyphene 300 mg; pethidine 400 mg.

a separate study was performed, sending questionnaires to the chairmen and head nurses of six major specialities in 228 hospital departments that treat cancer pain. The chairmen were requested to hand out the questionnaire to the physician most knowledgeable in the management of cancer pain. The sample sizes and response rates of these studies are presented in Table 3.

Among questions concerning the current practice in treating cancer pain, three simulated patient cases were presented (Table 4). These cases were formulated in cooperation with the Department of Public Health of the University of Helsinki in 1985, and piloted among a group of 30 specialists and residents at the Clinic of Radiotherapy and Oncology of the Helsinki University Central Hospital, where the prescription practice was familiar to the investigator. Although no formal validity tests have been carried out, the treatment suggestions for the simulated patient cases have proved to correspond to the differences in clinical practice between particular groups of physicians, and between the countries examined (6–10). The results of the previous studies also correspond to the INCB statistics of morphine consumption (see Table 1).

The physicians were asked how they would treat the pain of each patient. If opioid analgesics were suggested, the doses of all opioids suggested were converted into milligrams of parenteral morphine for comparison, using tables of equianalgesic potencies. In Finland and Norway, the adequacy of the daily doses, dose intervals and the overall relevance of the suggested treatment was assessed by the investigator using the guidelines recommended by the expert group of the World Health Organization (WHO), and textbooks in pharmacology, pain and palliative care as references. In Denmark, somewhat different criteria for acceptable and unacceptable treatment practices were used. In Sweden, the questionnaire did not contain simulated patient cases.

Table 3

The four national surveys on treatment of cancer pain in the Scandinavian countries, referred to in this review

Country Year	Finland 1990	Norway 1989	Sweden 1989	Denmark 1992
N	489	800	456	1409
Response rate	40%	69%	79–100%	77%
No. of questions	21	21	50–60	18

The WHO Analgesic ladder principle was used in 86–100% of departments in Sweden, where it was explicitly asked in the questionnaire. In Norway and Finland, no such question was posed, but the presence of the WHO Analgesic ladder was noted in the answers to the open question: 'How do you treat the pain of your typical cancer pain patient?' Here, 25% of Norwegian physicians and 22% of Finnish physicians mentioned the WHO principle spontaneously as the first alternative (Table 5). Strong opioids were used by 86% of physicians in Norway, by 92% in Denmark, by 31% in Finland, and by 95% in Sweden. Adjuvant drugs were used by 56% of Norwegian physicians, neuroleptics being their favorite coanalgesics. In Denmark, 23% of the doctors reported antidepressants or anticonvulsants as a part of their usual therapy. In Sweden, diazepam was used by 50%, laxatives by 38–83% and antidepressants by only 2–4% of the doctors. In Finland, only 6% mentioned spontaneously a combination of analgesics and coanalgesics as the drug of choice for their typical cancer patient.

THE SIMULATED PATIENT CASES

The patient examples and the criteria used to categorize the treatment suggestions as 'adequate' or 'inadequate', used in Finland and Norway, are presented in Table 6. For the patient with bone metastases of breast cancer, 30% of the doctors in Norway, and 42% in Finland suggested non-steroid, anti-inflammatory analgesics (NSAIDs) as a part of the pain therapy. In Denmark, 58% of the physicians included peripherally acting analgesics (NSAIDs or paracetamol) in their suggestions. In Sweden, NSAIDs were used by 50–100% of the departments for bone pain. Strong-acting opioid agonists were suggested by 80% (Norway), 95% (Denmark) and 13% (Finland), either alone or in combination. The suggested mean daily doses are indicated in Table 6.

Table 4

Simulated patient cases. Three cases will be presented to you where the clinical problem is cancer pain. Please give your suggestion for the best pain treatment: What would you do as a physician? All patients are assumed to weigh 70 kg, and no allergies or other contraindications are present

	Criteria for correct pain treatment
Case 1. Breast cancer A female patient was given surgery for breast cancer two years ago. She has increasing pains in her back, thoracic region and hip. Multiple bone metastases can be seen in the isotope scanning. The anti-tumour treatment alleviates the pain but does not eliminate it. How would you treat her pain? In the case of analgesics, give also the name, dosage and route of medication.	A sufficient, continuing amount of anti-inflammatory agent (NSAID) is expected for pain treatment. Prostaglandin inhibitors are effective in treating moderate to severe pain due to bone metastases, many of which induce the production of prostaglandins. Prostaglandins also cause osteolysis and sensitize local nociceptors. The adequate dose is equivalent to 1 g of acetosalicylic acid 3–4 times daily. If anti-inflammatory analgesics are suggested in lower doses, efficient analgesia has to be ensured by a 2nd-step opioid, either codeine, dextropropoxyphene or, alternatively, buprenorphine.
Case 2. Melanoma The patient suffers from a widespread melanoma. He has been hospitalized for the terminal phase of the disease. He has difficulty in moving, eating and sleeping because of excruciating pain. How would you treat this patient?	The pain is not adequately managed without potent 3rd-step opioids. The minimal dose required corresponds to 10 mg intramuscular morphine given 6 times daily. A variation of 20% is allowed, when estimating the adequacy of the suggested daily doses. Thus, the lower limit of an adequate daily dose of intramuscular morphine is 45 mg. Various anti-inflammatory drugs, steroids and adjuvant psychotropics can be added to the therapeutic regimen, but they do not compensate for the absence of a potent narcotic analgesic. Neurolytic blocks or other regional analgesic methods alone are not regarded as sufficient because of the widespread nature of the pain.
	Criteria for the correct treatment.
Case 3. Rectal carcinoma Six months ago the patient was surgically treated for carcinoma of the rectum. Now he is suffering from tearing pain in the low back and left buttock, radiating to his left leg. Even high-dose narcotic therapy is not effective. You suspect a recurrent tumor infiltrating into the lumbar plexus. What would you do?	In this case, systemic analgesic therapy has already proved to be ineffective. Thus, the method of choice will be a regional pain treatment. The following options are accepted by the author: further diagnostic procedures to determine the cause of the pain, spinal opioids, neurolytic blocks, neurosurgical pain treatment, and consultation with an oncologist or anesthesiologist. Radiotherapy alone is not regarded as correct, because the pain relief is not obtained until after 3 weeks. Therefore, other methods (e.g. spinal opioids) are necessary for immediate pain relief.

For a terminal patient with intractable pain caused by widespread melanoma, a strong opioid agonist was considered to be the prerequisite for a correct treatment (Table 4). The proportions of doctors suggesting strong opioids were 93% in Norway, 96% in Denmark and 80% in Finland. In Norway, 46% suggested a daily dose below 50 mg, 21% suggested 50–99 mg, and 33% a dose above 100 mg. In Denmark, the proportions were 17%, 31%, and 52%, and in Finland, 71%, 22% and 7%, respectively. The suggested mean daily doses and the proportion of doctors proposing an adequate pain treatment are indicated in Table 6.

More than 90% of the respondents reported having difficulties in the treatment of cancer pain. The most frequent problem in Finland (50%) and Norway (52%) was the inefficacy of the treatment: the patients continued to have pain despite the pain therapy. In Denmark, the primary difficulty mentioned was the side effects (36%), and the second problem was insufficient pain relief (29%). In Norway and Finland, the majority of physicians found their medical education in cancer pain treatment inadequate, whereas in Denmark, only 25% were dissatisfied with their education. The most important factor determining the choice of pain therapy in all three countries was the physician's own clinical experience, followed by postgraduate education. Basic medical education was ranked low in all countries. In Sweden, the educational needs were also queried. The answers to these questions can be found in Table 7.

DISCUSSION

Methodological problems connected with the use of questionnaires in the evaluation of prescribing practices are discussed in the original articles (5–11). Studies monitoring actual prescription of opioids in the treatment of cancer pain are available from the United Kingdom, The Netherlands, Denmark and Finland (4, 14, 16, 17). The reluctance to prescribe opioids emerges in the Finnish

Table 5

Physicians' reports of their use of different modalities of pain treatment for their typical cancer patient, as presented in the four surveys from (6, 8, 9, 11)

	Finland (1990) %	Norway (1989) %	Sweden (1989) %	Denmark (1992) %
WHO analgesic ladder	22	25	86–100	–
NSAID	20	30	50–100	28
Weak opioids	40	49	–	–
Strong opioids	31	86	95	92
Adjuvant medication	6	56	23–57	23

Table 6

Proportion of physicians suggesting adequate pain treatment for simulated patient cases and suggested daily doses converted into milligrams of parenteral morphine

	Finland	Norway	Denmark	Sweden
Metastatic bone pain/adequate suggestions (%)	56	35	49	–
Melanoma 'total pain'/adequate suggestions (%)	62	59	–	–
Mean daily dose (mg) of morphine/bone pain	31 (7–90)	20 (0–130)	220 (0–600)	–
Mean daily dose (mg) of morphine/melanoma	60 (2–1 000)	35 (0–170)	321 (0–500)	–

study comparing treatment of cancer pain in 1987, 1990 and 1994 in one hospital. In this hospital, only 28% of cancer patients received strong opioids during their last week of life, when the prevalence of pain in this period of the disease is 80% (17). The mean daily dose of parenteral morphine was 24 mg, 58 mg and 43 mg in 1987, 1991, and 1994, respectively.

In Finland, special prescription forms are obtainable by single physicians or communal institutions at the Bank of Finland, after a registration procedure at the Public Health Assurance Institution. The case sheets are confidential and numbered. Special prescription rules are established in order to avoid false prescriptions. Physicians are personally responsible for their sheets in the event of theft, and in institutions they are secured in double-locked cupboards. Physicians must also keep a diary of their prescriptions. The National Center of Medicolegal Affairs checks the prescriptions and may demand an explanation from frequent prescribers. Despite all these constraints, the proportion of Finnish physicians having prescription forms at their disposal increased from 61% to 79% between 1990 and 1995.

In Finland, most restrictions date from 1980, when 12 physicians were sued for prescribing methadone tablets for drug addicts. The yellow press denounced the abusive prescribing in an atmosphere generally hostile to physicians, and the Medical Board of Health chose to withdraw methadone from the market, in order to 'discipline the physicians' by criminalizing opioid prescription in public commentaries and constricting the prescription rules. As a consequence, many physicians ceased to prescribe strong opioids for outpatients. In the second half of the 1980s, when undertreatment of cancer pain became a matter of concern to pain specialists, Finland had to start from zero.

As already indicated, Denmark is the leading country in opioid consumption for medical purposes, the consumption of morphine per million inhabitants being about 2- to 3-fold compared to other Scandinavian countries, and 10-fold compared to Finland (Table 1). Although the mean daily dose suggested by the physicians for severe cancer pain in the questionnaire study by Sjogren et al. (9) was several times higher than that in other Scandinavian countries, the main factor contributing to the difference between Denmark and the other countries in total consumption is the larger population using morphine for chronic non-cancer related pain. According to a study by Sorensen et al, (4), nearly a half of all morphine prescribed goes to patients suffering from chronic non-malignant pain, only 17% being prescribed to cancer patients. Chronic pain of musculoskeletal origin, mainly back pain, gastrointestinal pain and headache were the most frequent non-malignant pain syndromes treated with opioids.

DRUG ABUSE AND MEDICAL PRESCRIBING

The number of illicit drug users and the number of drug addict deaths have been increasing rapidly (by 170% in 1986–1990) in almost all European countries. The figures in individual countries vary from 6% to 328%. Do the figures bear any relation to the ease of obtaining opioid prescriptions? They do not: in countries with liberal regulations (the UK, The Netherlands, Belgium, Denmark) the rate of drug deaths is no higher than in those with restricted regulations (Germany, Italy and Spain). In Den-

Table 7

Proportion of physicians expressing educational needs in the treatment of cancer pain and these needs defined by the Swedish physicians

Problems identified	Finland %	Norway %	Denmark %	Sweden %
Difficulties in the treatment of cancer pain	93	97	97	–
Insufficient education in pain treatment	61	72	25	39–59
1. Pain evaluation				
2. Newer drug delivery techniques				
3. Tolerance development				
4. Psychosocial aspects of pain				
5. WHO analgesic ladder principle				

mark, morphine consumption increased by 106% in 1986–1990, and the number of drug-related deaths by 6%. The corresponding numbers for Greece are 0% (morphine consumption) and 136% (drug deaths). In Sweden between 1975 and 1980 there was a 17-fold increase in the medical use of morphine without any obvious increase in illicit drug use or diversion of drug to established addicts (Zenz & Willweber-Strumpf 1993).

The present Scandinavian studies demonstrate a connection between the national opioid consumption and knowledge, attitudes and treatment practices of prescribing physicians. More data are needed to determine more precisely the relationship between national opioid consumption and patient outcome (pain level and patient satisfaction) in cancer pain management.

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