Continuing methadone for pain in palliative care

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BACKGROUND: Methadone is one of the most important medications used for the treatment of refractory pain in the palliative care setting, and is usually initially prescribed by one of a limited number of physicians who have acquired authorization for its use. A lack of authorized physicians able to take over prescribing when the patient is stable is a barrier to accessing methadone for analgesia.
OBJECTIVE: To determine the barriers to family physicians becoming authorized to prescribe methadone for pain in palliative care.
METHODS: A survey exploring the perceived barriers to continuing methadone for pain in palliative care following initial prescription by a specialist was mailed to a randomly selected group of 870 family physicians in British Columbia.
RESULTS: The response rate was 30.9%. Of the 204 responding physicians, 76.1% described themselves as positioned to provide ongoing palliative care to their patients. Within this group, 38 (18.6%) were already authorized to prescribe methadone for pain. The remaining 166 (81.4%) had significant knowledge deficits regarding methadone use in palliative care, but were largely aware of their deficits, and more than one-half were willing to learn more and to obtain an authorization if requested.
CONCLUSIONS: Responding family physicians had mostly received little education regarding methadone for pain, but were aware of their need for education and were willing to learn. Physicians who had already become authorized were generally satisfied with the process of authorization, and believed the process of education through authorization was appropriate and not onerous.

Key Words: *Education; General practice; Methadone; Pain management; Palliative care*

Le maintien de la méthadone pour soulager la douleur en soins palliatifs

HISTORIQUE : La méthadone est l'un des médicaments les plus importants pour traiter la douleur réfractaire en soins palliatifs, et en général, il est d'abord prescrit par un médecin qui fait partie du petit nombre à être autorisé à l'utiliser. Le peu de médecins autorisés à rédiger des prescriptions lorsque l'état du patient s'est stabilisé constitue un obstacle pour l'accès à la méthadone en guise d'analgésie.
OBJECTIF : Déterminer les obstacles pour que les médecins de famille soient autorisés à prescrire de la méthadone pour soulager la douleur en soins palliatifs.
MÉTHODOLOGIE : Les chercheurs ont posté à un groupe sélectionné de 870 médecins de famille de la Colombie-Britanniqueun sondage explorant les obstacles perçus au maintien d'un traitement à la méthadone pour soulager la douleur en soins palliatifs après une prescription initiale par un spécialiste.
RÉSULTATS : Le taux de réponse s'est élevé à 30,9 %. Sur les 204 médecins répondants, 76,1 % se sont décrits comme en position pour prodiguer des soins palliatifs à leurs patients. Au sein de ce groupe, 38 (18,6 %) étaient déjà autorisés à prescrire de la méthadone pour soulager la douleur. Les 166 autres (81,4 %) possédaient peu de connaissances sur l'utilisation de la méthadone en soins palliatifs, mais en étaient largement conscients, et plus de la moitié d'entre eux étaient prêts à en apprendre davantage et à obtenir une autorisation, au besoin.
CONCLUSIONS : La plupart des médecins de famille répondants possédaient peu d'information sur l'utilisation de la méthadone pour soulager la douleur, mais étaient conscients de leur besoin de formation et étaient prêts à apprendre. Les médecins déjà autorisés étaient généralement satisfaits du processus d'autorisation et trouvaient que le processus de formation prévu dans le cadre de l'autorisation était à la fois pertinent et peu coûteux.

Palliative care physicians or pain specialists often initiate and supervise trials of methadone for analgesia. If the trial is successful, there may be either no need for further close monitoring by a specialist or the patient may move to an environment where the specialist is not routinely available. The family physician is then the most appropriate person to provide appropriately spaced prescriptions as part of regular patient care, identify any medical issues that may interact with methadone and refer the patient back to the specialist if necessary.

Methadone is a synthetic opioid that is indicated for opioid dependence and as a second-line opioid analgesic. There has been a dramatic increase in methadone use for pain over the past 10 years (1). Shared worldwide experience has led to methadone becoming an essential agent in the treatment of severe chronic pain, particularly in cancer. Although there are no large randomized controlled trials demonstrating that methadone is superior to morphine or other opioids, this is ethically a very challenging environment to research, and smaller controlled trials and studies using other methodologies have clearly shown that a switch to methadone from other opioids is usually helpful, sometimes dramatically so, when other opioids are not tolerated or not effective (2,3).

Methadone is primarily a μ opioid receptor agonist but also has the unique properties of δ opioid receptor agonism, N-methyl-D-aspartate antagonism and serotonin and norepinephrine reuptake inhibition (4), all of which contribute to its potency as an analgesic. Advantages of methadone include its high oral bioavailability, long duration of action, multimodal analgesic effect, lack of active metabolites, safety in renal failure and relative lack of associated constipation (1). Methadone has been widely found to be particularly useful for neuropathic pain. It is very inexpensive and may be administered orally, rectally, subcutaneously and intravenously. Injectable methadone can be imported from the United Kingdom with Health Canada approval, but supplies are available in most tertiary palliative care units and can be transferred between pharmacies when required urgently. Injectable methadone can also be compounded locally for immediate use. In British Columbia, methadone tablets are covered through Pharmacare by the Palliative Drug Benefit Program, but only the liquid product is fully covered for those ineligible for this program.

Despite the advantages of methadone, similar to many drugs, it also has potentially serious risks (5,6). Methadone has a long and variable half life, there is risk of accumulation and respiratory depression if it is titrated up too rapidly, and it interacts with grapefruit and certain drugs via multiple cytochrome P450 pathways. At high doses it has been reported to prolong the QT interval, although this is usually observed only in conjunction with other QT-prolonging

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drugs (eg, certain antidepressants and antipsychotics) or with other QT-prolonging conditions such as hereditary syndromes or hypomagnesemia. Methadone has a variable equianalgesic ratio to other opioids, and converting to methadone from another opioid can be time consuming in the first few days to weeks. Most problems with methadone occur either within the first four weeks of therapy or after inadvertent coadministration with an interacting drug, particularly ciprofloxacin.

In Canada, these risks are managed by a federal restriction from prescribing methadone. Exemptions from this restriction for analgesic purposes are obtained separately from the exemption for addiction, and the administration of these exemptions is delegated to provincial regulatory agencies, including the College of Physicians and Surgeons of British Columbia (CPSBC). In British Columbia, authorization to prescribe methadone for opioid dependency requires an 8 h course followed by a preceptorship period and interview, plus registration of patients receiving methadone. In contrast, an exemption to allow prescribing for analgesic purposes is obtained by reading the CPSBC's "Recommendations for the use of Methadone for Pain" and some selected articles, followed by a brief telephone interview to confirm that key safety issues specific to methadone are well understood (7). Registration of individual patents has not been required for approximately 10 years, although many older physicians remember this being a requirement.

There have been no published reports regarding why physicians may be hesitant to obtain a methadone exemption for analgesia. Informal communication among British Columbia palliative care physicians suggested that lack of knowledge of the benefits and concerns regarding the safety of methadone would be reported barriers to prescribing, and workload issues may be important, especially if the physician was becoming the sole prescriber in a smaller community. We also hypothesized that many physicians may not be aware of the substantial improvements that have been made over the past 10 years to the process of becoming authorized to prescribe methadone for analgesia rather than for opioid dependence.

METHODS

A one-page survey (Appendix 1) was sent via Canada Post in June/July 2010 to a random selection of 870 family physicians in Greater Vancouver, Victoria and Prince George, British Columbia – all geographical locations with good access to palliative care consultation. An alphabetical list of family physicians and general practitioners was obtained from the CPSBC. The survey was sent to every third physician listed in Victoria or Prince George and every fourth physician listed in Vancouver.

Physicians were considered to be eligible if they reported being in a position to manage patients who may benefit from palliative care referral with some continuity of care, regardless of whether the physician had any current patients receiving palliative care. Physicians who did not report any continuity of care or who did not manage patients with a palliative diagnosis (eg, cancer, chronic obstructive pulmonary disease, congestive heart failure, chronic renal failure) were excluded. Physicians who already held an exemption to prescribe methadone for analgesia were identified at the beginning of the survey. Responses were anonymously returned from July to October 2010 in postage-paid envelopes. No remuneration or other incentive was offered. Ethics approval to distribute the surveys was obtained from the Behavioral Research Ethics Board at the University of British Columbia (UBC; Vancouver, British Columbia). The CPSBC was supportive of the present project, but the surveys were not identified as being associated with the college. Funding to cover postage and supplies was provided from the UBC Residents' Research Fund.

RESULTS

Of the 870 surveys mailed, 268 were returned, yielding an overall response rate of 30.9%. A total of 204 (76.1%) responders met the inclusion criteria (Appendix 1), 166 (81.4%) of whom did not already have authorization and 38 (18.6%) of whom reported already being authorized to prescribe methadone for analgesia. The previously authorized physicians' comments regarding the authorization process were overwhelmingly positive, with only two of the 18 written comments conveying negative opinions that they believed an authorization should not be required. One example is:

> The exemption is a tragic piece of historical silliness and it creates great difficulties for patients and those few of us with an exemption. Methadone is no more dangerous or difficult than many other drugs we prescribe. Get rid of the exemption please.

The remaining 16 comments about the authorization process were positive and in agreement with there being a need for some mechanism to ensure prescribers were properly informed on the use of methadone in palliative care. Examples include:

> Very good organized process. The careful education (not onerous, given by a college registrar) was most helpful.

> It was no problem.

> It was easy. Took over prescribing started by palliative care doctor … Use can be tricky – some training/experience necessary.

The 166 responses to the remainder of the survey from physicians who were not already authorized to prescribe are summarized as follows. These respondents represented the target demographic of physicians who were in a position to provide palliative care, but did not currently have authorization to prescribe methadone for analgesia.

Demographics

Nearly 76% of respondents identified Greater Vancouver as their location, with 17.5% identifying Victoria and 5% identifying Prince George. Consistent with the demographics of British Columbia family physicians, slightly more than one-half of the respondents (56%) were older than 50 years of age, and 17.5% were 40 years of age or younger. Although 39.8% identified themselves as male and 30.7% as female, 29.5% did not identify sex on the survey. The high nonresponse rate to this question prevented comments on sex in relation to the study results.

Knowledge and attitudes

Despite the inclusion of methadone for analgesia in many continuing medical educaton events, only 20.5% of the 166 respondents recalled having had any training or education on methadone for analgesia. The Victoria physicians reported the least (14%), and 22% and 25% of respondents in Vancouver and Prince George recalling having had education regarding methadone for analgesia, respectively. Analysis of the ages of responders showed that the requirement for education has been better met for recent graduates, with the reporting of having received education regarding methadone for analgesia dropping off over the years since graduation from 38% for those younger than 40 years of age to 24% for 40 to 50 years of age, 18% for 51 to 60 years of age and only 6% for those older than 60 years of age.

As the respondents were well aware, their knowledge regarding methadone was poor, and there was no trend to any of the three cities' respondents being better informed than another. Nearly one-half (45%) of respondents admitted they were not sure why methadone was useful for pain, and 41% believed that methadone was dosed only once daily (as for prevention of withdrawal), whereas for analgesia it usually needs to be dosed at least every 8 h. Only 42% knew that methadone can be used for pain that is not responsive to other opioids, when this is, in fact, its main role. Even fewer (31%) were aware of the particular benefits of methadone for neuropathic pain. Only 16% of respondents knew that methadone is cleared almost entirely by the liver and is, thus, safe for use in patients with renal failure. Very few (8.4%) were aware that methadone can overcome tolerance when patients have been on high doses of other opioids. Only 21.7% of respondents were

able to report that obtaining an exemption to prescribe methadone for analgesia was not similar to the process for addiction prescribing, and 59% of respondents were not sure, indicating widespread lack of awareness of the process of authorization.

Barriers

The factors respondents reported as influencing their willingness (or reluctance) to apply for a methadone prescribing exemption were grouped into themes, and are listed in Table 1. Lack of knowledge and the need to obtain an exemption were reported to be equal barriers by three-quarters of respondents. Concerns regarding College scrutiny and the perception of addiction risk were less frequent, being reported by less than one-half of participants. Safety issues with the drug itself were infrequently reported to be barriers. This suggests that if physicians were equipped with knowledge and realized that the process to obtain an exemption was straightforward, they may be willing to apply when requested to do so. The response 'too much hassle' could have been interpreted as applying to the care of patients on methadone for analgesia rather than the process of obtaining an authorization, but this factor was reported to be a barrier by 60% of respondents.

Despite these barriers and misconceptions, 87 of the 166 eligible physicians (52.4%) stated that they would be somewhat or very likely to apply for an exemption to continue methadone prescription for one of their patients if requested, after initiation by a palliative care physician.

TABLE 1
Factors influencing the decision whether to apply for methadone prescribing exemption

Barrier	n (%)
Need for exemption	126 (75.9)
Lack of knowledge	125 (75.3)
'Too much hassle'	100 (60.2)
College scrutiny	65 (39.2)
Addiction risk	57 (34.3)
Side effects	54 (32.5)
Drug interactions	46 (27.7)
Electrocardiogram changes	23 (13.9)

The selection of multiple barriers was allowed

DISCUSSION

Methadone is one of the most important tools for the treatment of pain that is nonresponsive or refractory to opioids in palliative care. As of spring 2012, there are only 685 medical practitioners in British Columbia authorized to prescribe methadone for analgesia (6.4% of registered British Columbia physicians), a significant proportion of whom are pain or palliative care specialists. There are a limited number of palliative care specialists available, and with the aging of the 'baby boomers' now living with cancer and other chronically painful illnesses, it is important that methadone analgesia be equitably accessible. The paucity of family doctors able to assume responsibility for methadone prescribing for stable patients is a barrier to the use of methadone by palliative care and pain and symptom management teams. This is becoming a critical issue to allowing anticipated natural deaths to occur at home, in hospice and in residential care under the care of family physicians, rather than in acute care hospitals. It is necessary to explore the barriers to quality palliative care to overcome them. Specific attitudes surrounding the prescription of methadone for cancer pain management have not been previously documented. The present study aimed to explore the barriers to physicians obtaining an authorization to prescribe methadone for pain, thereby informing future educational initiatives.

It should be noted that the present survey included only physicians in British Columbia. The knowledge and attitudes of physicians in other provinces may not be the same as those in British Columbia. It should also be noted that the conclusions drawn from responders to the survey (30.9%) may not be representative of all British Columbia physicians, and may be biased toward those who are more enthusiastic about prescribing methadone for pain. Prescription of opioids for noncancer pain has historically caused more concerns for physicians than for cancer-related pain (8,9); however, less is known regarding the barriers to prescribing opioids for cancer pain, and there are no data specifically related to methadone.

In 2004, a British Columbia physician survey (10) showed that the inconvenience of a triplicate pad (but not fear of regulatory scrutiny) was a barrier to prescribing opioids. Another study (11) showed that some physicians are unwilling to prescribe opioids because of fear of side effects, tolerance, respiratory depression and the 'image' of morphine as being associated with dying and addiction. In 1993, a survey of oncologists in the United States (12) reported the biggest barrier to pain management to be poor pain assessment. In 2009, a review of barriers to cancer pain management (13) emphasized patient pain assessment and knowledge regarding cancer pain management as the most common barriers in countries with easy access to appropriate opioid preparations. Other barriers to opioid use in cancer patients may be more surprising; a survey of French general practitioners and oncologists released in 2003 (14) found that prescriptions of opioids for cancer pain were less frequent for female patients, especially by male physicians.

It was reassuring that respondents to the present survey who already had authorization to prescribe methadone for analgesia reported that the process of obtaining authorizations was easy and that, in general, they were supportive of the requirement for authorization because there are pharmacological concerns specific to methadone that prescribers must be aware of to avoid inadvertent overdose.

The primary limitation of surveys is the bias inherent in the group of respondents possibly not being representative of the entire group. Of those contacted, only one-third of physicians responded to the present survey; however, this response rate was better than similar surveys (eg, 10% for Nwokeji et al [9] and 17.8% for family doctors in the 2010 Canadian National Physicians Survey [15]), and was better than we had expected. Reasons for expecting a low response rate that are not related to the topic of the survey include the documented findings that Canadian physician mail-out surveys have a lower than international average response rate, and that survey response rates have been falling over the past 20 years, in parallel with physicians' administrative workloads increasing (16). We were not able to contact participants in advance, there was no financial incentive to respond and, because of confidentiality concerns, we were not able to contact nonresponders to encourage them to participate – all strategies that have been shown to enhance survey response rates (17). Related to the survey topic, a general fear of regulatory scrutiny noted in a previous British Columbia family physician survey regarding opioids (10) and the collective impression of British Columbia palliative care physicians that family physicians are often reluctant to agree to assume responsibility for methadone prescribing from specialists also led us to expect many physicians to decline to respond.

The purpose of the present survey was to inform future educational initiatives, and we expected the response rate would be biased to include physicians who would be more likely than their nonresponding colleagues to participate in pain management and palliative care. The high proportion of responders who already had authorizations compared with the total proportion of authorized British Columbia physicians (18.6% versus 6.4%) suggests that this was the case, and their anonymous feedback on the process and value of authorization was very valuable. Opinions of the physicians currently without authorization, but who recognize they are in a position to potentially need one, are the most important to explore. These physicians would be most likely to be receptive to efforts to increase the number of physicians willing to assume ongoing responsibility for the routine care of these patients from palliative care and pain management specialists and, thus, should be the primary target of educational initiatives.

We were gratified that more than one-half (52.4%) of the eligible physicians without previous authorizations stated that they would be somewhat or very likely to apply for an exemption to continue methadone prescription for one of their patients if requested, after initiation by a palliative care physician. Although their knowledge of the benefits, properties, process of authorization and pharmacology of methadone was generally very poor, the physicians were aware of the need to learn more to be able to prescribe safely, which suggests that they would be receptive to educational initiatives.

SUMMARY

The results of the present survey suggest that, if provided with suitable education and support, there is significant opportunity to increase the number of physicians who could safely assume responsibility for continuing their patients' methadone treatment, thereby improving access to this very useful medication. The current process for obtaining an authorization from the CPSBC appears to be considered (by physicians who have it) to be effective in ensuring that safety concerns are addressed without being overly difficult or burdensome. Physicians who have not considered becoming authorized have limited knowledge of the process but are generally willing to apply if needed. There is, however, still much work to be performed to inform family physicians of this important treatment option in palliative care. An informational article on this subject was published in the *British Columbia Medical Journal* in the summer of 2012 (18).

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STUDY ROLES: Dr Hawley is the Medical Leader of the Pain and Symptom Management/Palliative Care Team of the Vancouver Centre of the British Columbia Cancer Agency and was Residency Program Director for the UBC Division of Palliative Care at the time the present study was performed. Dr Liebscher was a Year of Added Competence R3 resident in Palliative Care at UBC until July 2010, and now works as a family and palliative care physician in Victoria, British Columbia. Dr Hawley and Dr Leibscher jointly conceived and carried out the survey. Dr Wilford is a UBC Dermatology resident and graduated from the UBC Northern Medical Program. Dr Wilford performed the data analysis. All authors contributed to the production of the manuscript.

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APPENDIX 1: SURVEY QUESTIONS AND OPTIONS AVAILABLE TO RESPONDERS

1. Do you meet the inclusion criteria? If yes please continue. If no, please return.
   Inclusion criteria: Please complete this survey if you are a family physician or general practitioner who currently has (or has the potential to have) an ongoing therapeutic relationship with a patient who would benefit from palliative care consultation.
   Exclusion criteria: No continuity of care with patients. No patients now nor in the foreseeable future that would receive a palliative diagnosis. No access to palliative care services.
2. Do you hold an exemption from Health Canada to prescribe methadone for analgesia? If yes, thank you. You do not need to fill out the questionnaire but we would appreciate any thoughts you have on the process of obtaining the exemption (write below). If not, why not?
3. If approached by a palliative care physician to continue to prescribe methadone after its initiation, would you be willing to apply for the exemption if the consultant will provide continued support? Extremely unlikely/Somewhat unlikely/Not sure/Somewhat likely/Very likely. If unlikely, why?
4. Have you had any training or education on using methadone for analgesia? Yes/No
5. Methadone is useful for pain because it (circle those that you think apply): Reverses tolerance/Is dosed once daily/Benefits neuropathic pain/Is safe in renal failure/Not sure.
6. Methadone is used in palliative care for pain which is not responsive to other opioids. True/False/Don't know.
7. Obtaining an exemption to prescribe methadone for analgesia is a similar process to that for prescribing methadone for opioid addiction (eg, course required). True/False/Don't know.
8. The following factors influence my decision to prescribe methadone (circle): Drug interactions, ECG changes, addiction risk, college scrutiny, side effects, need for exemption, lack of knowledge, too much hassle. Yes/No/Don't know for each factor.

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